UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

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

For the fiscal year ended December 31, 2022

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

For the transition period from _____to_____

Commission file number **0-22705**

NEUROCRINE BIOSCIENCES, INC.

(Exact name of registrant as specified in its charter)

Delaware	**33-0525145**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
12780 El Camino Real, San Diego, California	**92130**
(Address of principal executive offices)	(Zip Code)

(858) 617-7600

(Registrant's telephone number, including area code)

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

Common Stock, $0.001 par value	**NBIX**	**Nasdaq Global Select Market**
(Title of each class)	(Trading Symbol)	(Name of each exchange on which registered)

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

None

(Title of class)

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

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

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

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☑ No ☐

Indicate by check mark 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.

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

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

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. Yes ☑ No ☐

If securities are registered pursuant to Section 12(b) of the Act, indicate by check mark whether the financial statements of the registrant included in the filing reflect the correction of an error to previously issued financial statements. ☐

Indicate by check mark whether any of those error corrections are restatements that required a recovery analysis of incentive-based compensation received by any of the registrant's executive officers during the relevant recovery period pursuant to § 240.10D-1(b). ☐

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

The aggregate market value of registrant's common stock held by non-affiliates of the registrant, computed by reference to the closing price as of the last business day of the registrant's most recently completed second fiscal quarter, June 30, 2022, was $8,097,146,859.

As of January 31, 2023, 96,587,911 shares of the registrant's common stock were outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant's definitive proxy statement relating to the registrant's annual meeting of stockholders to be filed pursuant to Regulation 14A within 120 days following the end of the registrant's fiscal year ended December 31, 2022 are incorporated by reference into Part III of this Form 10-K.

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PART I

Forward-Looking Statements

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

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

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

Item 1. Business

Overview

Neurocrine Biosciences is a neuroscience-focused, biopharmaceutical company with a simple purpose: to relieve suffering for people with great needs, but few options. We are dedicated to discovering and developing life-changing treatments for patients with under-addressed neurological, neuroendocrine and neuropsychiatric disorders. The Company's diverse portfolio includes United States Food and Drug Administration, or FDA, approved treatments for tardive dyskinesia, Parkinson's disease, endometriosis* and uterine fibroids* and a diversified portfolio of advanced clinical-stage programs in multiple therapeutic areas. For three decades, we have applied our unique insight into neuroscience and the interconnections between brain and body systems to treat complex conditions and we will continue to relentlessly pursue medicines to ease the burden of debilitating diseases and disorders. (*in collaboration with AbbVie Inc., or AbbVie)

Product Pipeline

Commercially Available Medicines

INGREZZA® (valbenazine). We launched INGREZZA in the United States in May 2017 as the first FDA-approved product for the treatment of tardive dyskinesia. INGREZZA net product sales totaled $1.4 billion for 2022, $1.1 billion for 2021 and $993.1 million for 2020 and represent nearly all of our total net product sales.

INGREZZA provides a once-daily dosing treatment option for tardive dyskinesia and has three dosing options (40 mg, 60 mg and 80 mg capsules), with a recommended dose of 40 mg taken for the first seven days of treatment and an option to take 40 mg, 60 mg or 80 mg thereafter, depending on the patient's dosing needs.

DYSVAL® (valbenazine). Mitsubishi Tanabe Pharma Corporation, or MTPC, launched DYSVAL in Japan in June 2022 for the treatment of tardive dyskinesia. In 2021, MTPC received approvals for marketing authorization for valbenazine for the treatment of tardive dyskinesia in Indonesia, Singapore, South Korea and Thailand and has submitted a filing for marketing authorization, which is currently under review, in Malaysia. We out-licensed the rights to valbenazine in Japan and other select Asian markets to MTPC in 2015, in which markets valbenazine is a royalty-bearing product for us.

Tardive dyskinesia is a movement disorder that is characterized by uncontrollable, abnormal and repetitive movements of the face, torso and/or other body parts, which may be disruptive and negatively impact patients. The condition is associated with prolonged use of treatments that block dopamine receptors in the brain, such as antipsychotics commonly prescribed to treat mental illnesses such as schizophrenia, bipolar disorder, depression and certain anti-nausea medications. In patients with tardive dyskinesia, these treatments are thought to result in irregular dopamine signaling in a region of the brain that controls movement. The symptoms of tardive dyskinesia can be severe and are often persistent and irreversible. Tardive dyskinesia affects an estimated 600,000 people in the United States.

ONGENTYS® (opicapone). We launched ONGENTYS in the United States in September 2020 as an FDA-approved add-on treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing motor fluctuations. We acquired the United States and Canada rights to ONGENTYS in February 2017.

Parkinson’s disease is a chronic, progressive and debilitating neurodegenerative disorder that is caused by low dopamine levels produced in the brain. Dopamine helps transmit signals between the areas of the brain that control all purposeful movements, including talking, walking and writing. As Parkinson’s disease progresses, dopamine production steadily decreases, resulting in increased problems with motor symptoms including slowed movement, tremor, rigidity, impaired posture and balance and difficulty with speech and writing. Parkinson’s disease affects an estimated 1 million people in the United States and more than 10 million people worldwide.

ORILISSA® (elagolix tablets). AbbVie launched ORILISSA in the United States in August 2018 as an FDA-approved oral medication for the management of moderate to severe endometriosis pain in women. We out-licensed the global rights to elagolix to AbbVie in 2010. Elagolix is a royalty-bearing product for us.

Endometriosis affects nearly 200 million women worldwide, including more than 10 million women in the United States.

ORIAHNN® (elagolix, estradiol, and norethindrone acetate capsules and elagolix capsules). AbbVie launched ORIAHNN in the United States in June 2020 as the first FDA-approved non-surgical, oral medication option for the management of heavy menstrual bleeding associated with uterine fibroids in pre-menopausal women. We out-licensed the global rights to elagolix to AbbVie in 2010. Elagolix is a royalty-bearing product for us.

Uterine fibroids are benign hormonally responsive tumors that form in the wall of the uterus with a prevalence rate of at least 25% and are a leading indication for hysterectomy, resulting in the performance of more than 200,000 hysterectomies per year in the United States alone.

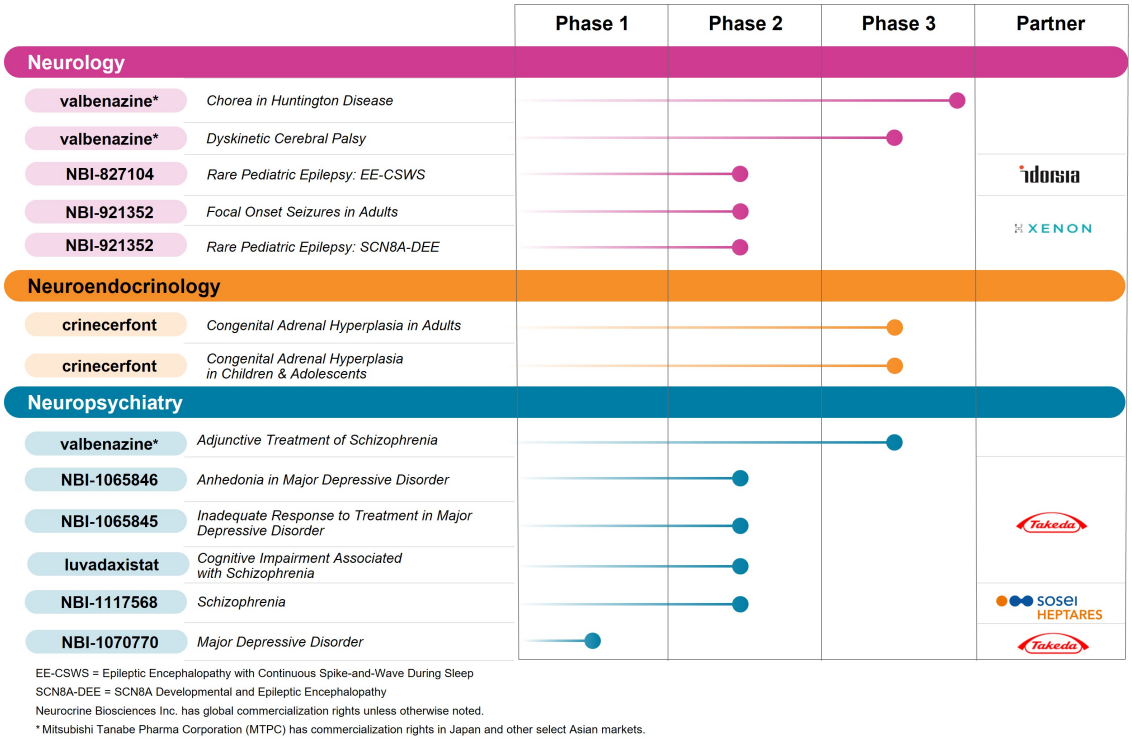
ALKINDI® / ALKINDI SPRINKLE® (hydrocortisone). Alkindi was launched in its core markets (the United Kingdom, Germany, Austria and Italy) in 2018 as replacement therapy of adrenal insufficiency in infants, children and adolescents (aged 18 years and younger) and subsequently outside of its core markets through a network of distribution partners, including in the United States, where Alkindi is marketed as Alkindi Sprinkle by our partner, Eton Pharmaceuticals, Inc., or Eton Pharmaceuticals. Alkindi Sprinkle has been granted orphan drug designation for the treatment of pediatric adrenal insufficiency in the United States, where it is a royalty-bearing product for us.

Adrenal insufficiency is a rare condition caused by inadequate production of steroid hormones in the cortex of the adrenal glands. Adrenal insufficiency can result in severe fatigue and, if left untreated, adrenal crisis that may be life threatening.

EFMODY®* *(hydrocortisone modified-release hard capsules). Efmody was launched in the United Kingdom, Germany and Austria in 2021 for the treatment of classic congenital adrenal hyperplasia, or CAH, in adolescents and adults (aged 12 years and older) and subsequently in the Netherlands through a distribution partner.

CAH is a rare condition usually caused by deficiency of the enzyme 21-hydroxylase, which is required to produce the adrenal steroid hormone, cortisol. The block in the cortisol production pathway causes the over-production of male steroid hormones (androgens), which are precursors to cortisol. CAH is congenital (inherited at birth), affects both sexes and can lead to increased mortality, infertility and severe development defects, including ambiguous genitalia, premature sexual development and short stature. CAH affects an estimated 30,000 people in the United States and 50,000 people in Europe.

Our Pipeline of Investigational Therapies



EE-CSWS = Epileptic Encephalopathy with Continuous Spike-and-Wave During Sleep
SCN8A-DEE = SCN8A Developmental and Epileptic Encephalopathy
Neurocrine Biosciences Inc. has global commercialization rights unless otherwise noted.
* Mitsubishi Tanabe Pharma Corporation (MTPC) has commercialization rights in Japan and other select Asian markets.

Neurology

Chorea in Huntington Disease (valbenazine – VMAT2 Inhibitor[(1)]). In April 2022, we presented data from the KINECT-HD study, a Phase III randomized, double-blind, placebo-controlled clinical study that evaluated the efficacy, safety and tolerability of valbenazine in 120 adult patients with chorea associated with Huntington disease. In the study, valbenazine met the primary endpoint of significant ($p < 0.0001$) improvement in chorea severity versus placebo, as measured by the Unified Huntington's Disease Rating Scale Total Maximal Chorea Score, with improvements beginning in Week 2. Clinically meaningful results, demonstrated by greater response rates, were seen by clinicians (CGI-C) and patients (PGI-C) for valbenazine versus placebo. In addition, the safety profile was consistent with the known safety profile of valbenazine. In December 2022, the FDA accepted our supplemental new drug application, or sNDA, for valbenazine for the treatment of chorea associated with Huntington disease. The agency set a Prescription Drug User Fee Act target action date of August 20, 2023.

Huntington disease is a hereditary progressive neurodegenerative disorder, in which destruction of neuronal cells within the brain results in motor, cognitive, and psychiatric symptoms. Symptoms generally appear between the ages of 30 to 50 and worsen over a 10 to 25-year period. Many patients with Huntington disease experience chorea, a troublesome involuntary movement disorder, in which patients develop sudden, irregular, unpredictable and non-stereotyped movements. Chorea can affect various body parts, and may interfere with speech, swallowing, posture, and gait. Approximately 90% of the estimated 30,000 people affected by Huntington disease in the United Sates will develop chorea over the course of the disease. Valbenazine has been granted orphan drug designation for the treatment of chorea associated with Huntington disease in the United States.

Dyskinetic Cerebral Palsy (valbenazine – VMAT2 Inhibitor[1]). We have initiated a Phase III randomized, double-blind, placebo-controlled clinical study to evaluate the efficacy, safety and tolerability of valbenazine for the treatment of dyskinetic cerebral palsy in 80 pediatric and adult patients (aged 6 to 70 years). We anticipate having top-line data for this clinical study in 2024.

Dyskinetic cerebral palsy is a non-progressive, permanent disorder marked by involuntary movement and is a result of damage to the fetal or infant brain's basal ganglia. The basal ganglia are responsible for submitting messages to the body to help coordinate and control movements. When damaged, voluntary movements are compromised, resulting in involuntary and abnormal movements. It affects development and movement and has long term effects on patients' quality of life. The long-term outlook for patients with dyskinetic cerebral palsy will depend upon the severity of the brain damage and how well the treatment works. Dyskinetic cerebral palsy affects up to 15% of the estimated 500,000 to 1 million people affected by cerebral palsy in the United States.

Epilepsy.

Epilepsy is one of the most common neurological disorders and is characterized by abnormal electrical activity in the brain that leads to unpredictable seizures that can vary in frequency, from less than one seizure per year to several seizures per day. A description of our investigational treatments for potential use in epilepsy follows.

SCN8A-DEE (NBI-921352 – Nav1.6 Sodium Channel Inhibitor[2]). We have initiated the KAYAK™ study, a Phase II randomized, double-blind, placebo-controlled clinical study to evaluate the efficacy, safety and pharmacokinetics of NBI-921352 as adjunctive therapy in 52 adolescent patients (aged 12 to 21 years) with SCN8A-DEE. In January 2022, the study protocol was amended to include pediatric patients (aged 2 to 11 years) with SCN8A-DEE.

SCN8A-DEE is a rare, extremely severe, single-gene epilepsy caused by mutations in the SCN8A gene that activates Nav1.6, the most highly expressed sodium channel in the excitatory pathways of the central nervous system. Children born with SCN8A-DEE typically start experiencing seizures between birth and 18 months of age, and most have multiple seizures per day. Other symptoms include learning difficulties, muscle spasms, low or high muscle tone, poor coordination, developmental delay and features similar to autism. As SCN8a mutations were discovered only recently, prevalence estimates will be determined in the future as awareness of and access to genetic surveillance increases. NBI-921352 has been granted orphan drug and rare pediatric disease designations for the treatment of SCN8A-DEE in the United States.

Focal Onset Seizures (NBI-921352 – Nav1.6 Sodium Channel Inhibitor[2]). We have initiated a Phase II randomized, double-blind, placebo-controlled clinical study to evaluate the efficacy, safety and pharmacokinetics of NBI-921352 as adjunctive therapy in 100 adult patients with focal onset seizures. We anticipate having top-line data for this clinical study in the second half of 2023.

Focal epilepsy is a neurological condition in which the predominant symptom is recurring seizures that affect one hemisphere of the brain. Focal epilepsies are also known as partial-onset seizures and include idiopathic location-related epilepsies, frontal lobe epilepsy, temporal lobe epilepsy, parietal lobe epilepsy and occipital lobe epilepsy. It is estimated that focal onset seizures affect 1.8 million adults in the United States, approximately 35% of whom are refractory to existing treatments.

Neuroendocrinology

Classic Congenital Adrenal Hyperplasia, or CAH.

CAH is a rare condition usually caused by deficiency of the enzyme 21-hydroxylase, which is required to produce the adrenal steroid hormone, cortisol. The block in the cortisol production pathway causes the over-production of male steroid hormones (androgens), which are precursors to cortisol. CAH is congenital (inherited at birth), affects both sexes and can lead to increased mortality, infertility and severe development defects, including ambiguous genitalia, premature sexual development and short stature. CAH affects an estimated 30,000 people in the United States and 50,000 people in Europe.

CAH in Adults (crinecerfont – CRF1 Antagonist[3]). We have completed enrollment of the CAHtalyst study, a global, registrational Phase III randomized, double-blind, placebo-controlled clinical study to evaluate the efficacy and safety of crinecerfont in 165 adult patients with CAH, followed by an open-label treatment period. We anticipate having top-line data for this clinical study in the second half of 2023.

CAH in Pediatrics (crinecerfont – CRF1 Antagonist[3]). We have completed enrollment of a global, registrational Phase III randomized, double-blind, placebo-controlled clinical study to evaluate the efficacy and safety of crinecerfont in 81 pediatric patients (aged 2 to 17 years) with CAH. Crinecerfont has been granted orphan drug designation for the treatment of CAH in the United States and the European Union. We anticipate having top-line data for this clinical study in the second half of 2023.

Adrenal Insufficiency (DNL-0200 – hydrocortisone modified-release hard capsules[4]). We have initiated the CHAMPAIN study, a Phase II randomized, double-blind, double-dummy, two-way crossover clinical study to evaluate the efficacy, safety and tolerability of twice-daily DNL-0200 compared with once-daily Plenadren® (modified-release hydrocortisone) in 67 adult patients with primary adrenal insufficiency.

Adrenal insufficiency is a rare condition caused by inadequate production of steroid hormones in the cortex of the adrenal glands. Adrenal insufficiency can result in severe fatigue and, if left untreated, adrenal crisis that may be life threatening.

Neuropsychiatry

Schizophrenia.

Schizophrenia is a spectrum of serious neuropsychiatric brain diseases in which people interpret reality abnormally. Schizophrenia may result in some combination of hallucinations, delusions and extremely disordered thinking and behavior that impairs daily life. People with schizophrenia typically require lifelong treatment. Early treatment may help improve long-term prognosis and get symptoms under control before serious complications develop. Schizophrenia affects an estimated 3.5 million people in the United States. A description of our investigational treatments for potential use in schizophrenia follows.

Adjunctive Treatment of Schizophrenia (valbenazine – VMAT2 Inhibitor[1]).

In November 2021, we initiated a Phase III randomized, double-blind, placebo-controlled clinical study to evaluate the efficacy, safety and tolerability of valbenazine when administered orally once daily as adjunctive treatment in 400 adolescent and adult patients (aged 13 years and older) with schizophrenia who have had an inadequate response to antipsychotics. We anticipate having top-line data for this clinical study in 2024.

In December 2022, we initiated a second Phase III randomized, double-blind, placebo-controlled clinical study to evaluate the efficacy, safety and tolerability of valbenazine when administered orally once daily as adjunctive treatment in 400 adolescent and adult patients (aged 13 years and older) with schizophrenia who have had an inadequate response to antipsychotics.

Approximately 30% of the estimated 3.5 million people affected by schizophrenia in the United States fail to respond to current antipsychotic therapy.

Schizophrenia (NBI-1117568 – Muscarinic M4 Agonist[5]). We have initiated a Phase II multi-center, randomized, double-blind, placebo-controlled, multi-arm, multi-stage clinical study to evaluate the efficacy, safety and tolerability of NBI-1117568 in 213 adult patients with schizophrenia who are experiencing an acute exacerbation or relapse of symptoms.

All currently approved antipsychotic medications are believed to work through direct action on monoaminergic receptors, with approximately 40% of patients reporting negative side effects and approximately 30% not benefiting adequately from these medications.

Cognitive Impairment Associated with Schizophrenia, or CIAS (luvadaxistat – DAAO Inhibitor[6]). We have initiated a Phase II randomized, double-blind, parallel, placebo-controlled clinical study to evaluate the efficacy, safety, tolerability and pharmacokinetics of luvadaxistat when administered orally once daily as adjunctive treatment in 308 adult patients with CIAS.

CIAS, which may include deficits in attention, working memory and executive function, has a negative impact on patients' quality of life and ability to function. Although cognitive symptoms in schizophrenia are well characterized, no formal diagnostic criteria exist. Furthermore, no pharmacological agents are approved to treat the condition, and no marketed therapy tested to date has established clear, meaningful efficacy, which underscores the difficulty of drug development in this arena and accentuates the unmet need for proven treatment options.

Approximately 80% of the estimated 3.5 million people affected by schizophrenia in the United States experience clinically relevant cognitive impairment.

Major Depressive Disorder.

Major depressive disorder is one of the leading causes of disability and is characterized by a persistently depressed mood or loss of interest in daily activities that is present most of the day in addition to other symptoms that can impact normal daily functioning, relationships and overall quality of life. Treatments range from selective serotonin reuptake inhibitors, serotonin norepinephrine reuptake inhibitors, atypical antipsychotics, tricyclic antidepressants and psychotherapies, among others. Major depressive disorder affects more than 16 million people in the United States. A description of our investigational treatments for potential use in major depressive disorder follows.

Inadequate Response to Treatment in Major Depressive Disorder (NBI-1065845 – AMPA Potentiator[7]). We have initiated a Phase II randomized, double-blind, placebo-controlled clinical study to evaluate the efficacy and safety of NBI-1065845 as adjunctive treatment in 212 adult patients with inadequate response to treatment in major depressive disorder. We anticipate having top-line data for this clinical study in 2024.

While there are a number of marketed treatments for major depressive disorder, approximately 30% of the more than 16 million people affected by the disorder in the United States do not adequately respond to treatment.

Anhedonia in Major Depressive Disorder (NBI-1065846 – GPR139 Agonist[8]). We have initiated a Phase II randomized, double-blind, placebo-controlled, two-period cross-over, Proof of Activity clinical study to evaluate the effects of NBI-1065846 as adjunctive treatment in 88 adult patients with major depressive disorder experiencing anhedonia. We anticipate having top-line data for this clinical study in the second half of 2023.

Anhedonia is characterized by the inability to experience pleasure and has been associated with changes in neurotransmitter levels involved in the brain's reward system. Anhedonia is a core symptom of major depressive disorder and also frequently presents in people with bipolar depression, schizophrenia, substance-abuse disorders, Parkinson's disease, diabetes and coronary artery disease.

(1) 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.

(2) NBI-921352 is a potent, highly selective Nav1.6 sodium channel inhibitor being developed to treat pediatric patients with SCN8A-DEE and other potential indications, including adult focal epilepsy. We acquired the global rights to NBI-921352 in December 2019.

(3) Crinecerfont is a potent, selective, orally active, corticotropin-releasing factor1, or CRF1, receptor antagonist as demonstrated in a range of in vitro and in vivo assays. CRF1 is a hypothalamic hormone released directly into the hypophyseal portal vasculature which acts on the CRF1 receptor, a G protein-coupled receptor, or GPCR, in the anterior pituitary to stimulate the release of the adrenocorticotropin hormone, or 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 CRF1 release as well as at the level of the pituitary to inhibit the release of ACTH. This tight control loop is known as the hypothalamic-pituitary-adrenal axis. Blockade of CRF1 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 CAH. Lower ACTH levels would also reduce the amount of exogenous corticosteroid necessary for CAH patients to thrive avoiding the side-effects currently associated with excessive steroid therapy.

(4) DNL-0200 is a modified-release preparation of hydrocortisone that mimics the physiological circadian rhythm of cortisol and has been specifically designed for patients with diseases of cortisol deficiency, such as adrenal insufficiency and CAH.

(5) NBI-1117568 is a potential first-in-class muscarinic M4 receptor agonist with the potential to be developed for the treatment of schizophrenia. As a selective M4 orthosteric agonist, NBI-1117568 offers the potential for an improved safety profile without the need for combination therapy to ameliorate off-target effects or for cooperativity with acetylcholine. Muscarinic receptors are central to brain function and validated as drug targets in psychosis and cognitive disorders. We acquired the global rights to NBI-1117568 in December 2021.

(6) Luvadaxistat is a potential first-in-class D-Amino Acid Oxidase, or DAAO, inhibitor with the potential to be developed for the treatment of cognitive impairment associated with schizophrenia. We acquired the global rights to luvadaxistat in June 2020.

(7) NBI-1065845 is a potential first-in-class Alpha-Amino-3-Hydroxy-5-Methyl-4-Isoxazole Propionic Acid, or AMPA, potentiator with the potential to be developed for the treatment of inadequate response to treatment in major depressive disorder. We acquired the global rights to NBI-1065845 in June 2020. NBI-1065845 is currently designated as a 50:50 profit-share product with Takeda Pharmaceutical Company Limited, which retains a one-time opt-out right to convert the designation to a royalty-bearing product.

(8) NBI-1065846 is a potential first-in-class G Protein-Coupled Receptor 139, or GPR139, agonist with the potential to be developed for the treatment of anhedonia in major depressive disorder. We acquired the global rights NBI-1065846 in June 2020. NBI-1065846 is currently designated as a 50:50 profit-share product with Takeda Pharmaceutical Company Limited, which retains a one-time opt-out right to convert the designation to a royalty-bearing product.

Business Strategy

Our core business strategy is to continue applying our unique insight into neuroscience to advance medicines for the treatment of under-addressed neurological, neuroendocrine and neuropsychiatric disorders to relieve suffering for people with great needs, but few options.

We focus our internal research and development efforts on innovative therapies with improved probabilities of technical and commercial success by taking a portfolio approach to managing our pipeline that balances the size of market opportunities with clear and defined clinical and regulatory paths to approval. In addition, from time to time we supplement our internal efforts by acquiring businesses or in-licensing certain rights to commercial products or clinical programs to enhance and capitalize on our commercial and development capabilities.

In 2022, we were able to help more people affected by tardive dyskinesia than ever before, reflecting sustained growth for INGREZZA as we continued to invest in our branded direct-to-consumer INGREZZA advertising campaign launched in May 2021 and completed the reorganization and expansion of our sales force in April 2022, transitioning from a single team structure to three distinct teams dedicated to psychiatry, neurology and long-term care, respectively.

Going forward, key elements of our commercial strategy include maximizing the opportunity in INGREZZA through consistent and effective commercial execution, continued development of valbenazine as the best-in-class treatment for new patient populations, including for the potential treatment of chorea associated with Huntington disease, dyskinetic cerebral palsy and schizophrenia, and to lead the evolving understanding of VMAT2 biology and its role in disease.

Collaboration and License Agreements

Refer to Note 2 to the consolidated financial statements for more information on our significant collaboration and license agreements.

Intellectual Property

We actively seek to protect our products, product candidates, and related inventions and improvements that we consider important to our business. We own a portfolio of United States and ex-United States patents and patent applications, and have also licensed rights to a number of United States and ex-United States patents and patent applications. Our owned and licensed patents and patent applications cover or relate to our products and product candidates, including certain formulations, uses to treat particular conditions, methods of administration, drug delivery technologies and delivery profiles, and methods of manufacturing.

Below is a description of the United States and ex-United States patents to INGREZZA and the following product candidates:

- INGREZZA, our highly selective VMAT2 inhibitor approved in the United States (and other countries) for the treatment of tardive dyskinesia, is covered by 20 issued, FDA Orange Book-listed United States patents which are set to expire between 2027 and 2040. Patent term extension corresponding to regulatory approval delay of 552 days has been received for United States Patent No. 8,039,627, which now expires in 2031 and covers valbenazine, the active pharmaceutical ingredient contained in INGREZZA. In Japan and in certain other East Asian markets, we are actively pursuing most of the patents corresponding to those listed in the FDA's Orange Book entry for INGREZZA.
- Valbenazine, our highly selective VMAT2 inhibitor under clinical development for the treatment of chorea associated with Huntington disease, is covered by at least 12 of the issued United States patents currently listed in the FDA's Orange Book entry for INGREZZA. Issued patents and pending patent applications that also cover the treatment of chorea associated with Huntington disease are set to expire between 2027 and 2043.
- Valbenazine, additionally under clinical development for dyskinetic cerebral palsy (DCP) and for adjunctive treatment of schizophrenia (ATS), is covered by issued patents and pending patent applications set to expire between 2027 and 2042, including several issued, Orange Book-listed United States patents.
- Crinecerfont, a CRF1 receptor antagonist under clinical development for the treatment of congenital adrenal hyperplasia (CAH) in adults and children, is covered by United States Patent Nos. 10,905,690 and 11,311,544, among other patents and pending patent applications, set to expire between 2035 and 2041 (not including any potential patent term extensions).

We also own, or have licensed rights to, patents covering our other products and earlier stage product candidates. In addition to the potential patent term extensions referenced above, the products and product candidates in our pipeline may be subject to additional terms of exclusivity that we may obtain by future patent issuances.

Separately, the United States, European Union, and Japan each 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, which is measured from the date of marketing approval by the FDA or corresponding foreign regulatory authority. This period of exclusivity is generally five years in the United States, six years in Japan and 10 years in the European Union, except that for biologics, the period of exclusivity in the United States is 12 years under the Biologics Price Competition and Innovation Act. In addition, if granted orphan drug designation, certain of our product candidates, including, for example, crinecerfont, may also be eligible for marketing exclusivity in the United States for seven years and in the European Union for 10 years.

Refer to Part I Item 1A. Risk Factors for a discussion of the challenges we may face in obtaining or maintaining patent and/or trade secret protection and Item 3. Legal Proceedings for a description of our legal proceedings related to intellectual property matters.

Manufacturing and Supply

We currently rely on, and intend to continue to rely on, third-party manufacturers for the production of INGREZZA and our product candidates. Raw materials, active pharmaceutical ingredients, or API, and other supplies required for the production of INGREZZA and our product candidates are sourced from various third-party manufacturers and suppliers in quantities adequate to meet our needs. Continuing adequate supply of such raw materials and API is assured through our long-term commercial supply and manufacturing agreements with multiple manufacturers and our continued focus on the expansion and diversification of our third-party manufacturing relationships. In addition, we rely on BIAL – Portela & Ca, S.A. for the commercial supply of ONGENTYS.

We believe our outsourced manufacturing strategy enables us to direct our financial resources to the maximization of our opportunities with INGREZZA and ONGENTYS, investment in our internal R&D programs and expansion of our clinical pipeline through business development opportunities.

Our third-party manufacturers, suppliers and service providers may be subject to routine current Good Manufacturing Practice, or cGMP, inspections by the FDA or comparable agencies in other jurisdictions. We depend on our third-party partners and our quality system oversight of them for continued compliance with cGMP requirements and applicable foreign standards.

Marketing, Sales and Distribution

Our specialty sales force consists of approximately 350 experienced sales professionals located in the United States and is divided into three dedicated sales teams focused on psychiatry, neurology and long-term care.

For INGREZZA, our customers in the United States consist of a limited network of specialty pharmacy providers that deliver INGREZZA to patients by mail, wholesale distributors that distribute INGREZZA primarily to certain specialty pharmacies, and specialty distributors that distribute INGREZZA primarily to closed-door pharmacies and government facilities. For ONGENTYS, our customers in the United States consist primarily of wholesale distributors. We rely on third-party service providers to perform a variety of functions related to the packaging, storage and distribution of INGREZZA and ONGENTYS.

Government Regulation

Our business activities 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, tracking, 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. 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 addition, federal and state healthcare laws restrict business practices in the pharmaceutical industry. These laws include, without limitation, federal and state fraud and abuse laws, false claims laws, data privacy and security laws, as well as transparency laws regarding payments or other items of value provided to healthcare providers. We have a comprehensive compliance program designed to ensure our business practices remain compliant.

The federal Anti-Kickback Statute makes it illegal for any person or entity to knowingly and willfully, directly or indirectly, solicit, receive, offer, or pay any remuneration that is intended to induce the referral of business, including the purchase, order, lease of any good, facility, item or service for which payment may be made under a federal healthcare program, such as Medicare or Medicaid.

Federal civil and criminal false claims laws 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 to avoid or decrease an obligation to pay money to the federal government.

The Health Insurance Portability and Accountability Act of 1996, or 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 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.

We may be subject to HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act of 2009, or HITECH, and their privacy and security regulations, which impose certain obligations, including the adoption of administrative, physical and technical safeguards to protect individually identifiable health information on covered entities subject to HIPAA (i.e., health plans, healthcare clearinghouses and certain healthcare providers) and their business associates that perform certain services for or on their behalf involving the use or disclosure of individually identifiable health information as well as their covered subcontractors. If we or the third parties on which we rely fail, or are perceived to have failed, to address or comply with applicable HIPAA obligations, we could face significant consequences, including but not limited to: government enforcement actions (e.g., investigations, fines, penalties, audits, inspections, and similar); litigation (including class-action claims); additional reporting requirements and/or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials.

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, information related to payments or other transfers of value made to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, as well as information regarding ownership and investment interests held by physicians and their immediate family members.

Also, many states have similar healthcare statutes or regulations that may be broader in scope and may apply regardless of payor. Additionally, to the extent that our product is sold in a foreign country, we may be subject to similar foreign laws.

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, imprisonment, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, and additional reporting requirements and regulatory oversight, any of which could adversely affect our ability to operate our business and our results of operations.

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

Phase I	Clinical trials are conducted with a small number of subjects to determine the early safety profile, maximum tolerated dose and pharmacokinetic properties of the product in human volunteers or in patients with the target disease.
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	Larger, 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. Institutional Review Boards, Institutional Ethics Committees and Data Safety Monitoring Boards also closely monitor the conduct of our trials and may also place holds on our clinical trials or recommend that we voluntarily do so. 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 for approval to commence commercial sales. In most cases, the submission of an NDA is subject to a substantial application user fee. Under the Prescription Drug User Fee Act, or PDUFA, 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. The FDA generally has a six-month review goal of priority NDAs.

In addition, under the Pediatric Research Equity Act of 2003 as amended and reauthorized, certain applications or supplements to an application 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 to ensure that the benefits of the drug outweigh its risks. The risk evaluation and mitigation strategy could include medication guides, physician communication plans, assessment plans and/or additional 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 application 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 for its intended use and whether the facility in which it is manufactured, processed, packaged or held meets standards designed to assure the product's continued safety, quality and purity.

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

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

After evaluating the NDA and all related information, including the advisory committee recommendation, if any, and inspection reports regarding the manufacturing facilities and clinical trial sites, the FDA may issue an approval letter, or, in some cases, a complete response letter. A complete response letter generally contains a statement of specific conditions that must be met in order to secure final approval of the application and may require additional clinical or preclinical testing in order for FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If and when those conditions have been met to the FDA's satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications.

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

We will also have to complete an approval process similar to that in the United States in order to commercialize our product candidates in each foreign country. 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, except for a certain limited number of drugs sold to certain Medicare beneficiaries beginning in 2023. The resulting prices may not be sufficient to generate an acceptable return to us or our corporate collaborators.

In the European Union, there are currently two potential tracks for seeking marketing approval for a product not authorized in any European Union member state: a decentralized procedure and a centralized procedure. In the decentralized procedure, identical applications for marketing authorization are submitted simultaneously to the national regulatory agencies. Regulatory review is led by one member state (the reference-member state), and its assessment—based on safety, quality and efficacy—is reviewed and approved (assuming there are no concerns that the product poses a serious risk to public health) by the other member states from which the applicant is seeking approval (the concerned-member states). The decentralized procedure leads to a series of single national approvals in all relevant countries. In the centralized procedure, which is required of all products derived from biotechnology, a company submits a single marketing authorization application to the European Medicines Agency, or EMA, which conducts an evaluation of the dossier, drawing upon its scientific resources across Europe. If the drug product is proven to fulfill the requirements for quality, safety and efficacy, the EMA's Committee for Medicinal Products for Human Use, or CHMP, adopts a positive opinion, which is transmitted to the European Commission for final decision on grant of the marketing authorization. While the EC generally follows the CHMP's opinion, it is not bound to do so. Subsequent commercialization is enabled by country-by-country reimbursement approval.

Orphan Drug Designation. Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is a disease or condition that affects fewer than 200,000 individuals in the United States, or if it affects more than 200,000, there is no reasonable expectation that sales of the drug in the United States will be sufficient to offset the costs of developing and making the drug available in the United States Orphan drug designation must be requested before submitting an NDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

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

Legislation similar to the Orphan Drug Act has been enacted in other countries outside of the United States, including the European Union. The orphan legislation in the European Union is available for therapies addressing conditions that affect five or fewer out of 10,000 persons, are life-threatening or chronically debilitating conditions and for which no satisfactory treatment is authorized. The market exclusivity period is for 10 years, although that period can be reduced to six years if, at the end of the fifth year, available evidence establishes that the product does not justify maintenance of market exclusivity.

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

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

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

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements and standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in mandatory revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess new safety risks; or imposition of distribution or other restrictions. 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 indication(s) and in accordance with the provisions of the approved label. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. 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. Physicians may prescribe legally available products for uses that are not described in the product's labeling and that differ from those tested by us and approved by the FDA. The FDA does not regulate behavior of physicians in their choice of treatments. The FDA does, however, restrict manufacturer's communications on the subject of off-label use of their products.

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 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. No uniform policy for coverage and reimbursement exists in the United States, and coverage and reimbursement can differ significantly from payor to payor. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement rates, but also have their own methods and approval process apart from Medicare determinations. 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 drug products to each payor separately, with no assurance that coverage and adequate reimbursement will be obtained in the first instance or applied consistently.

Third-party payors are increasingly challenging the price, examining the medical necessity and reviewing the cost-effectiveness of drug products and medical services, in addition to questioning their safety, efficacy and clinical appropriateness. Such payors may limit coverage to specific drug products on an approved list, also known as a formulary, which might not include all of the FDA-approved drugs for a particular indication. We may need to conduct expensive pharmaco-economic studies in order to demonstrate the medical necessity and cost-effectiveness of our products, in addition to the costs required to obtain the FDA approvals. Nonetheless, our products or product candidates, including INGREZZA, may not be considered medically necessary or cost-effective.

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

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

Enacted Healthcare Reform Measures

The United States and some foreign jurisdictions 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. In the United States, the pharmaceutical industry and the cost of prescription drugs has been a continuous focus of these efforts and has been significantly affected by major legislative initiatives.

Most recently, in August 2022, President Biden signed into law the Inflation Reduction Act of 2022, or the IRA, which, among other things, (1) directs the Secretary of the U.S. Department of Health and Human Services, or HHS, to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare, (2) redesigns the Medicare Part D prescription drug benefit to lower patient out-of-pocket costs and increase manufacturer liability and (3) requires drug manufacturers to pay rebates on drugs whose prices increase greater than the rate of inflation. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in the ACA marketplaces through plan year 2025 and eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost to $2,000 through a newly established manufacturer discount program. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented; however, it is likely to have a significant impact on the pharmaceutical industry and prescription drug pricing.

While the IRA targets high-expenditure drugs that have been on the market for several years without generic or biosimilar competition, we have qualified for the small biotech manufacturer exemption that is set to expire in 2029. However, the qualification for this exemption is subject to various requirements and there is no assurance that we will continue to qualify for this exemption in the future. Further, the loss of this exemption or the potential loss of this exemption, including as a result of a potential acquisition or strategic transaction, could have an adverse impact on our business.

The most significant prior revisions to federal law governing the pharmaceutical industry and prescription drug pricing was enacted through the March 2010 the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, collectively the ACA. This law was intended to broaden access to health insurance by reducing the number of uninsured persons, reducing or constraining the growth of healthcare spending, enhancing remedies against fraud and abuse, adding transparency requirements for the healthcare and health insurance industries, imposing taxes and fees on the health industry and imposing additional health policy reforms.

We expect that these health reform measures, may result in more rigorous coverage criteria and lower reimbursement for prescription drugs, as well as result in additional downward pressure on any price that we receive for any approved product. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private third-party payors.

Other significant legislative changes impacting the pharmaceutical industry and prescription drug pricing have been adopted since the ACA was enacted. These changes include, among others, aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and, due to subsequent legislative amendments, including the Investment and Jobs Act, will remain in effect through 2031, except for a temporary suspension from May 1, 2020 through March 31, 2022. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequestration.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to examine and/or 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.

Proposed Healthcare Reform Measures

The United States and some foreign jurisdictions are considering 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 may be significantly affected by major legislative initiatives.

We are currently unable to predict what other 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.

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 products and product candidates from academic institutions, government agencies, research institutions and biotechnology and pharmaceutical companies. Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approval and marketing than we do.

Competition may also arise from, among other things, new drug development technologies, new or improved treatment options for preventing or reducing the incidence of disease in diseases our products treat and new small molecule or other classes of therapeutic agents. Such developments by competitors could reduce or eliminate the use of our products or may limit the utility and application of ongoing clinical trials for our product candidates.

Tardive Dyskinesia. INGREZZA competes with AUSTEDO® (deutetrabenazine), which was approved by the FDA for the treatment of tardive dyskinesia in adults in August 2017 and is marketed by Teva Pharmaceutical Industries, and several clinical development-stage programs targeting tardive dyskinesia and related movement disorders. Additionally, there are a number of commercially available medicines used to treat tardive dyskinesia off-label, such as XENAZINE® (tetrabenazine) and generic equivalents, and various antipsychotic medications (e.g., clozapine), anticholinergics, benzodiazepines (off-label), and botulinum toxin.

Parkinson's Disease. ONGENTYS competes with two other FDA-approved COMT inhibitors and their generic equivalents. Additionally, there are a number of alternative adjunctive treatment options (FDA-approved and in clinical development) for Parkinson's patients which compete with ONGENTYS, including various L-dopa preparations, dopamine agonists, MAO-B inhibitors and others. In terms of potential future competition, there are several programs in late-stage clinical development.

Endometriosis and Uterine Fibroids. ORILISSA and ORIAHNN each compete with several FDA-approved products for the treatment of endometriosis, uterine fibroids, infertility and central precocious puberty. Additionally, there is also competition from surgical intervention, including hysterectomies and ablations. Separate from these options, there are many programs in clinical development which serve as potential future competition. Lastly, there are numerous medicines used to treat the symptoms of disease (vs. endometriosis or uterine fibroids directly) which may also serve as competition: oral contraceptives, NSAIDs and other pain medications, including opioids.

Classic Congenital Adrenal Hyperplasia, or CAH. For CAH, 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. In the United States alone, there are more than two dozen companies manufacturing steroid-based products. In addition, there are several programs in clinical development targeting CAH and several companies developing medicinal treatments for CAH.

Epilepsy. Our investigational treatments for potential use in epilepsy may in the future compete with numerous approved anti-seizure medications and development-stage programs being pursued by several other companies. Commonly used anti-seizure medications include phenytoin, levetiracetam, brivaracetam, cenobamate, carbamazepine, clobazam, lamotrigine, valproate, oxcarbazepine, topiramate, lacosamide, perampanel and cannabidiol, among others. There are currently no FDA-approved treatments specifically indicated for the early infantile epileptic encephalopathy SCN8A-DEE; however, a number of different anti-seizure medications are currently used in these patient populations.

Neuropsychiatry. Our investigational treatments for potential use in schizophrenia and depression may in the future compete with several development-stage programs being pursued by other companies. Currently, there are no FDA-approved treatments specifically indicated for CIAS; however, there are a number of different anti-psychotic medications currently used in these patient populations.

Other. Our investigational treatments for potential use in neurology, neuroendocrinology and neuropsychiatry may in the future compete with numerous approved products and development-stage programs being pursued by several other companies.

Human Capital

Our Employees. We have grown to a team of more than 1,200 employees as of December 31, 2022, primarily employed in the United States. Our highly qualified and experienced team, which includes scientists, physicians and professionals across sales, marketing, manufacturing, regulatory, finance and other essential functions are critical to our success. We also leverage temporary workers to provide flexibility for our business needs. During 2022, we added more than 250 new employees to our team, reflecting the completion of our sales force expansion to approximately 350 experienced sales professionals.

We expect to add additional employees in 2023 with a focus on expanding our research and development organization. We continually evaluate our business needs and opportunities and balance in-house expertise and capacity with external expertise and capacity. Currently, we rely on third-party contract manufacturers.

Our Culture. The success of our human capital management investments is evidenced by our low employee turnover, a number which is regularly reviewed by our Board of Directors as part of their oversight of our human capital strategy. In recognition of our efforts, in 2022, we were ranked in #8 in Fortune Best Small & Medium Workplaces in Biopharma™.

Employee Engagement, Talent Development & Benefits. We believe that our future success largely depends upon our continued ability to attract and retain highly skilled employees. We provide our employees with competitive salaries and bonuses, opportunities for equity ownership, development programs that enable continued learning and growth and a robust employment package that promotes well-being across all aspects of their lives, including health care, retirement planning and paid time off. As part of our promotion and retention efforts, we also invest in ongoing leadership development programs as well as offer tuition reimbursement. In addition, we regularly conduct employee surveys to gauge employee engagement and identify areas of focus.

Diversity & Inclusion. Much of our success is rooted in the diversity of our teams and our commitment to inclusion. We value diversity at all levels and continue to focus on extending our diversity and inclusion initiatives across our entire workforce. We believe that our business benefits from the different perspectives a diverse workforce brings, and we pride ourselves on having a strong, inclusive and positive culture based on our shared mission and values.

Corporate Information

We were originally incorporated in California in January 1992 and reincorporated in Delaware in May 1996. Our principal executive offices are located at 12780 El Camino Real, San Diego, California 92130. Our telephone number is (858) 617-7600.

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, or SEC, website at *www.sec.gov*. Additionally, copies of our Annual Report will be made available, free of charge, upon written request. Information found on, or accessible through, our website is not a part of, and is not incorporated into, this Annual Report on Form 10-K.

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.

Summary Risk Factors

We face risks and uncertainties related to our business, many of which are beyond our control. In particular, risks associated with our business include:

- We may not be able to continue to successfully commercialize INGREZZA, ONGENTYS, or any of our other products, or any of our product candidates if they are approved in the future.
- If physicians and patients do not continue to accept INGREZZA or do not accept ONGENTYS, or do not accept any of our other products, or our sales and marketing efforts are not effective, we may not generate sufficient revenue.
- Governmental and third-party payors may impose additional sales and pharmaceutical pricing controls on our products or further limit coverage and/or reimbursement for our products that could negatively impact our product revenues and impact or delay sustained profitability.
- Our business could be adversely affected by the effects of health pandemics or epidemics, including the COVID-19 pandemic, which could also cause significant disruption in the operations of third-party manufacturers, contract research organizations, or CROs, or other third parties upon whom we rely.
- We face intense competition, and if we are unable to compete effectively, the demand for our products may be reduced.
- 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.
- Our clinical trials may be delayed for safety or other reasons, or fail to demonstrate the safety and efficacy of our product candidates, which could prevent or significantly delay their regulatory approval.
- Several of our planned clinical trial sites have been impacted and could be delayed or suspended as a result of the conflict between Russia and Ukraine.
- We depend on our current collaborators for the development and commercialization of several of our products and product candidates and may need to enter into future collaborations to develop and commercialize certain of our product candidates.
- Use of our approved products or those of our collaborators could be associated with side effects or adverse events.

- 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.
- If we are unable to retain and recruit qualified scientists and other employees 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, ONGENTYS, or any of our other products, or any product candidate approved by the FDA in the future.
- We currently have no manufacturing capabilities. If third-party manufacturers of INGREZZA, ONGENTYS, or any of our other products, 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 currently depend on a limited number of third-party suppliers. The loss of these suppliers, or delays or problems in the supply of INGREZZA, ONGENTYS, or any of our other products, could materially and adversely affect our ability to successfully commercialize INGREZZA, ONGENTYS, or any of our other products.
- 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.
- 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.
- Health care reform measures and other recent legislative initiatives could adversely affect our business.
- 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.
- We have a history of losses and expect to increase our expenses for the foreseeable future, and we may not be able to sustain profitability.
- Our customers are concentrated and therefore the loss of a significant customer may harm our business.
- 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.

Risks Related to Our Company

We may not be able to continue to successfully commercialize INGREZZA, ONGENTYS, or any of our other products, or any of our product candidates if they are approved in the future.

Our ability to produce INGREZZA revenues consistent with expectations ultimately depends on our ability to continue to successfully commercialize INGREZZA and secure adequate third-party reimbursement. Our experience in marketing and selling pharmaceutical products began with INGREZZA's approval in 2017, when we hired our sales force and established our distribution and reimbursement capabilities, all of which are necessary to successfully commercialize our current and future products. We have continued to invest in our commercial infrastructure and distribution capabilities in the past four years, including the expansion of our specialty sales force, which we announced in the third quarter of 2021 and completed in April 2022. While our team members and consultants have experience marketing and selling pharmaceutical products, we may face difficulties related to managing the rapid growth of our personnel and infrastructure, and there can be no guarantee that we will be able to maintain the personnel, systems, arrangements and capabilities necessary to continue to successfully commercialize INGREZZA, or to successfully commercialize ONGENTYS or any of our other products, or any product candidate approved by the FDA in the future.

In addition, our business has been and may continue to be adversely affected by the effects of health pandemics or epidemics, including the ongoing COVID-19 pandemic. In parts of the country where the pandemic is having a greater impact, some hospitals, community mental health facilities, and other healthcare facilities continue to have policies that limit access of our sales representatives, medical affairs personnel and patients to such facilities. These policies are likely to change from time to time as communities or regions grapple with outbreaks. These facilities also may be facing staffing shortages that impact their ability to see patients and conduct necessary screenings. In addition, many health care practitioners have adopted telehealth for patient interactions, which may impact the ability of the health care practitioner to screen for and diagnose tardive dyskinesia. Further, during the COVID-19 pandemic, the use of physician telehealth services increased significantly, fueled by an expansion of coverage and reimbursement from government and other payors. The limitations that telehealth places on the ability to conduct a thorough visual and physical examination may impact the ability of providers to screen for movement disorders, leading to potentially fewer patients to be diagnosed and referred for treatment. The ultimate impact of the COVID-19 pandemic, including any lasting effects on the way we conduct our business, is highly uncertain and subject to continued change. If we fail to maintain successful marketing, sales and reimbursement capabilities, our product revenues may suffer.

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

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

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

- the timing of receipt of marketing approvals for additional indications;
- the safety and efficacy of the products;
- the pricing of our products;
- the availability of healthcare payor coverage and adequate reimbursement for the products;
- public perception regarding any products we may develop;
- the success of existing competitor products addressing our target markets or the emergence of equivalent or superior products; and
- the cost-effectiveness of the products.

If the medical community, patients and payors do not continue to accept our products as being safe, effective, superior and/or cost-effective, we may not generate sufficient revenue.

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

Our ability to continue to commercialize INGREZZA successfully or to successfully commercialize ONGENTYS or any of our other products, 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 and the price of prescription drugs through various means may impact our revenues. These payors' efforts could decrease the price that we receive for any products we may develop and sell in the future.

Assuming we obtain coverage for a given product by a third-party payor, the resulting reimbursement payment rates may not be adequate or may require co-payments that patients find unacceptably high. Patients who are prescribed medications for the treatment of their conditions, and their prescribing physicians, generally rely on third-party payors to reimburse all or part of the costs associated with their prescription drugs. Patients are unlikely to use our products unless coverage is provided and reimbursement is adequate to cover all or a significant portion of the out-of-pocket 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. Coverage decisions by payors for our competitors' products may also impact coverage for our products.

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, media outlets, and others 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 or indications, 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. 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.

If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may be unable to successfully commercialize INGREZZA, ONGENTYS, or any of our other products, or any other product candidate for which we obtain marketing approval in the future. 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. Further, a majority of our current revenue is derived from federal healthcare program payors, including Medicare and Medicaid. Thus, changes in government reimbursement policies, reductions in payments and/or our suspension or exclusion from participation in federal healthcare programs could have a material adverse effect on our business.

Further, during the COVID-19 pandemic, the use of physician telehealth services has rapidly increased, fueled by an unprecedented expansion of coverage and reimbursement across insurers. The limitations that telehealth places on the ability to conduct a thorough physical examination may impact the ability of providers to screen for movement disorders, leading to fewer patients being diagnosed and/or treated.

Our business could be adversely affected by the effects of health pandemics or epidemics, including the COVID-19 pandemic, which could also cause significant disruption in the operations of third-party manufacturers CROs, or other third parties upon whom we rely.

Our business could be adversely affected by the effects of health pandemics or epidemics, which could also cause significant disruption in the operations of third-party manufacturers, CROs and other third parties upon whom we rely. As a result of the ongoing COVID-19 pandemic, we may experience disruptions that could severely impact our supply chain, ongoing and future clinical trials and commercialization of INGREZZA, ONGENTYS, or any of our other products. For example, the COVID-19 pandemic has resulted in travel restrictions and the shutdown or delay of business activities in various regions. In response to the COVID-19 pandemic, we implemented a remote work model for all employees except certain key essential members involved in business-critical activities. Most of our field-based employees have resumed in-person interactions in accordance with location-specific guidance. Our office-based employees have returned to the office under flexible work guidelines to help balance business needs, employee health, well-being and safety and the evolving work environment. However, as the effects of the pandemic continue to rapidly evolve with the emergence of new COVID-19 variants and spikes or surges in infection and hospitalization rates, a remote work model may nevertheless need to be reinstated at some point in the future. The effects of a remote and flexible work model may negatively impact productivity, disrupt our business and delay our clinical programs and timelines, the magnitude of which will depend, in part, on the length and severity of the restrictions and other limitations on our ability to conduct our business in the ordinary course. Remote work may also create increased risks to our information technology systems and data, as more of our employees utilize network connections, computers and devices outside our premises or network, including working at home, while in transit and in public locations. In addition, we may face several challenges or disruptions upon a return back to the workplace, including re-integration challenges by our employees and distractions to management related to such transition. These and similar, and perhaps more severe, disruptions in our operations due to the COVID-19 pandemic could negatively impact our business, operating results and financial condition. We continue to evaluate the impact of the COVID-19 pandemic on our business and will update our plans and policies as needed going forward.

Quarantines, stay at home orders, travel restrictions and other state and local restrictions, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases, could impact personnel at third-party manufacturing facilities in the United States and other countries, or the availability or cost of materials, which would disrupt our supply chain.

In addition, clinical site initiation and patient enrollment may be delayed due to concerns for patient safety and prioritization of healthcare resources toward the COVID-19 pandemic. Some patients may not be able to comply with clinical trial protocols if quarantines impede patient travel or interrupt healthcare services. Similarly, our ability to recruit and retain patients, principal investigators and site staff may be hindered, which would adversely impact our clinical trial operations. Increases in COVID-19 cases or hospitalizations in the future could cause us or any of our clinical sites to again limit or suspend our patient enrollment and screening activities.

The COVID-19 pandemic, which has caused a broad impact globally, may materially affect us economically. While the potential economic impact brought by, and the duration of, the COVID-19 pandemic may be difficult to assess or predict, the pandemic has caused disruption in the global financial markets. This disruption, if sustained or recurrent, could make it more difficult for us to access capital, which could in the future negatively affect our liquidity. In addition, a recession or market correction resulting from the COVID-19 pandemic could materially affect our business and the value of our common stock.

The effects of the COVID-19 pandemic continue to evolve. The ultimate impact of the COVID-19 pandemic or a similar health pandemic or epidemic is highly uncertain and subject to continued change. We do not yet know the full extent of potential delays or impacts on our business, our clinical trials, healthcare systems or the global economy as a whole. These effects could have a material impact on our operations, or the operations of third parties on whom we rely.

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 (including the development of generic equivalents) 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, tardive dyskinesia, uterine fibroids, essential tremor, classic congenital adrenal hyperplasia, pain, Parkinson's disease and other neurology, neuroendocrinology and neuropsychiatry-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 (including the development of generic equivalents), the market for our products may be reduced or eliminated.

- INGREZZA competes with AUSTEDO® (deutetrabenazine), which was approved by the FDA for the treatment of tardive dyskinesia in adults in August 2017 and is marketed by Teva Pharmaceutical Industries, and several clinical development-stage programs targeting tardive dyskinesia and related movement disorders. Additionally, there are a number of commercially available medicines used to treat tardive dyskinesia off-label, such as XENAZINE® (tetrabenazine) and generic equivalents, and various antipsychotic medications (e.g., clozapine), anticholinergics, benzodiazepines (off-label), and botulinum toxin.
- ONGENTYS competes with two other FDA-approved COMT inhibitors and their generic equivalents. Additionally, there are a number of alternative adjunctive treatment options (FDA-approved and in clinical development) for Parkinson's patients which compete with ONGENTYS, including various L-dopa preparations, dopamine agonists, MAO-B inhibitors and others. In terms of potential future competition, there are several programs in late-stage clinical development.
- ORILISSA and ORIAHNN each compete with several FDA-approved products for the treatment of endometriosis, uterine fibroids, infertility and central precocious puberty. Additionally, there is also competition from surgical intervention, including hysterectomies and ablations. Separate from these options, there are many programs in clinical development which serve as potential future competition. Lastly, there are numerous medicines used to treat the symptoms of disease (vs. endometriosis or uterine fibroids directly) which may also serve as competition: oral contraceptives, NSAIDs and other pain medications, including opioids.
- For CAH, 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. In the United States alone, there are more than two dozen companies manufacturing steroid-based products. In addition, there are several programs in clinical development targeting CAH and several companies developing medicinal treatments for CAH.
- Our investigational treatments for potential use in epilepsy may in the future compete with numerous approved anti-seizure medications and development-stage programs being pursued by several other companies. Commonly used anti-seizure medications include phenytoin, levetiracetam, brivaracetam, cenobamate, carbamazepine, clobazam, lamotrigine, valproate, oxcarbazepine, topiramate, lacosamide, perampanel and cannabidiol, among others. There are currently no FDA-approved treatments specifically indicated for the early infantile epileptic encephalopathy SCN8A-DEE; however, a number of different anti-seizure medications are currently used in these patient populations.

- Our investigational treatments for potential use in schizophrenia and depression may in the future compete with several development-stage programs being pursued by other companies. Currently, there are no FDA-approved treatments specifically indicated for cognitive impairment associated with schizophrenia, or CIAS; however, there are a number of different anti-psychotic medications currently used in these patient populations.
- Our investigational treatments for potential use in neurology, neuroendocrinology and neuropsychiatry may in the future compete with numerous approved products and development-stage programs being pursued by several other companies.

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

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

Moreover, increased competition in certain disorders or therapies may make it more difficult for us to recruit or enroll patients in our clinical trials for similar disorders or therapies.

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.

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 clinical trials may be delayed for safety or other reasons or 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 and the outcomes are uncertain.

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

- the FDA or similar foreign regulatory authority may not allow an IND or foreign equivalent filings required to initiate human clinical studies for our drug candidates or the FDA may require additional preclinical studies as a condition of the initiation of Phase I clinical studies, or additional clinical studies for progression from Phase I to Phase II, or Phase II to Phase III, or for NDA approval;
- the product candidate may not prove to be effective or as effective as other competing product candidates;
- we may discover that a product candidate may cause harmful side effects or results of required toxicology or other studies may not be acceptable to the FDA;
- clinical trial results may not replicate the results of previous 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;
- clinical site initiation or patient recruitment and enrollment may be slower or more difficult than expected;
- the FDA may not accept the data from any trial or trial site outside of the United States;
- patients may drop out of the trials;
- unforeseen disruptions or delays may occur, caused by man-made or natural disasters or public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic and the conflict between Russia and Ukraine; and
- regulatory requirements may change.

These risks and uncertainties impact all of our clinical programs and any of the clinical, regulatory or operational events described above could change our planned clinical and regulatory activities. In addition, due to the impact of the COVID-19 pandemic, clinical site initiation and new patient enrollment has been negatively impacted. 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 conduct, completion and 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.

Several of our planned clinical trial sites have been impacted and could be delayed or suspended as a result of the conflict between Russia and Ukraine.

In February 2022, Russia commenced a military invasion of Ukraine. We have planned clinical trial sites in both Russia and Ukraine, but no patients yet enrolled. Ongoing geopolitical turmoil and continuing military action in the region, together with widening sanctions imposed on Russia, have caused us to suspend all planned clinical trial activities in Russia and Ukraine. Alternative clinical trial sites that would fully and timely compensate for our planned clinical trial activities in Ukraine and Russia may not be available and we may need to find other countries in which to conduct such activities. Our planned clinical development timelines for valbenazine and luvadaxistat could be significantly delayed, which would increase our development costs and delay the development and/or regulatory approval process of such product candidates and jeopardize our ability to commence product sales and generate revenues.

We depend on our current collaborators for the development and commercialization of several of our products and product candidates and may need to enter into future collaborations to develop and commercialize certain of our product candidates.

We depend on our current collaborators for the development and commercialization of several of our products and product candidates and may need to enter into future collaborations to develop and commercialize certain of our product candidates. For example, we depend on AbbVie for the manufacture and commercialization of ORILISSA and ORIAHNN and for the continued development of elagolix. We collaborate with MTPC for the commercialization of DYSVAL in Japan and for the continued development and commercialization of valbenazine for movement disorders in other select Asian markets. We also rely on BIAL for the commercial supply of ONGENTYS. In addition, we collaborate with Xenon Pharmaceuticals, Inc. for the development of NBI-921352, Idorsia Pharmaceuticals Ltd. for the development of NBI-827104, Takeda Pharmaceutical Company Limited for the development of luvadaxistat, NBI-1065845 and NBI-1065846 and Heptares Therapeutics Limited for the development of NBI-1117568.

Our current and future collaborations and licenses could subject us to a number of risks, including:

- strategic collaborators may sell, transfer or divest assets or programs related to our partnered product or product candidates;
- we may be required to undertake the expenditure of substantial operational, financial and management resources;
- we may be required to assume substantial actual or contingent liabilities;
- we may not be able to control the amount and timing of resources that our strategic collaborators devote to the development or commercialization of our products or product candidates;
- we may not be able to influence our strategic collaborator's decisions regarding the development and collaboration of our partnered product and product candidates, and as a result, our collaboration partners may not pursue or prioritize the development and commercialization of those partnered products and product candidates in a manner that is in our best interest;
- strategic collaborators may select indications or design clinical trials in a way that may be less successful than if we were doing so;
- strategic collaborators may not conduct collaborative activities in a timely manner, provide insufficient funding, terminate a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new version of a product candidate for clinical testing;
- strategic collaborators may not pursue further development and commercialization of products resulting from the strategic collaboration arrangement or may elect to discontinue research and development programs;
- disagreements or disputes may arise between us and our strategic collaborators that result in delays or in costly litigation or arbitration that diverts management's attention and consumes resources;
- strategic collaborators may experience financial difficulties;
- strategic collaborators may not properly maintain, enforce or defend our intellectual property rights or may use our proprietary information in a manner that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- strategic collaborators could terminate the arrangement or allow it to expire, which would delay the development and commercialization and may increase the cost of developing and commercializing our products or product candidates; and
- strategic collaborators could develop, either alone or with others, products or product candidates that may compete with ours.

If any of these issues arise, it may delay and/or negatively impact the development and commercialization of drug candidates and, ultimately, our generation of product revenues.

We may not be able to successfully commercialize ONGENTYS.

In April 2020, we received FDA approval for ONGENTYS as an adjunctive therapy to levodopa/DOPA decarboxylase inhibitors in adult Parkinson's disease patients, and in September 2020, we launched the commercial sale of ONGENTYS with our existing commercial infrastructure. The successful commercialization of ONGENTYS is subject to many risks, and there are numerous examples of unsuccessful product launches and failures, including by pharmaceutical companies with more experience and resources than us. If we are unable to effectively train our employees and equip them with effective materials, including medical and sales literature to help them inform and educate health care practitioners about the benefits of ONGENTYS and its proper administration, our commercialization of ONGENTYS may not be successful. Even if we are successful in effectively training and equipping our sales force, there are many factors that could cause the commercialization of ONGENTYS to be unsuccessful, including a number of factors that are outside our control. Health care practitioners may not prescribe ONGENTYS and patients may be unwilling to use ONGENTYS if insurance coverage is not provided or reimbursement is inadequate. In addition, our ability to train our employees and effectively communicate with potential prescribers could be adversely affected by the effects of health pandemics or epidemics, including the ongoing COVID-19 pandemic.

Use of our approved products or those of our collaborators could be associated with side effects or adverse events.

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

We 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, 2022, we had more than 1,200 full-time employees. Although we have substantially increased the size of our organization, we may need to add additional qualified personnel and resources, especially with the recent increase in the size of our 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 our organization, including the need to identify, recruit, maintain and integrate additional employees, and may take time away from running other aspects of our business, including development and commercialization of our product candidates.

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

- manage our development efforts effectively;
- integrate additional management, administrative and manufacturing personnel;
- further develop our marketing and sales organization;

- compensate our employees on adequate terms in an increasingly competitive, inflationary market;
- attract and retain personnel; 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.

If we are unable to retain and recruit qualified scientists and other employees 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, ONGENTYS, or any of our other products, or any product candidate approved by the FDA in the future.

We are highly dependent on the principal members of our management, commercial and scientific staff. The loss of any of these people could impede the achievement of our objectives, including the successful commercialization of INGREZZA, ONGENTYS, or any of our other products, or any product candidate approved by the FDA in the future. 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 effects of the COVID-19 pandemic, as well as the competition among biotechnology, pharmaceutical and health care companies, universities and non-profit research institutions for experienced scientists and individuals with experience marketing and selling pharmaceutical products. We may face particular retention challenges in light of the recent rapid growth in our personnel and infrastructure and the perceived impact of those changes upon our corporate culture. In addition, we rely on a significant number of consultants to assist us in formulating our research and development strategy and our commercialization strategy. Our consultants may have commitments to, or advisory or consulting agreements with, other entities that may limit their availability to us.

We currently have no manufacturing capabilities. If third-party manufacturers of INGREZZA, ONGENTYS, or any of our other products, 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. Establishing internal commercial manufacturing capabilities would require significant time and resources, and we may not be able to timely or successfully establish such capabilities. 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 and ONGENTYS. If we are unable to obtain or retain third-party manufacturers, we will not be able to develop or commercialize our products, including INGREZZA and ONGENTYS. 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, including BIAL and its suppliers, 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 or 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 cGMP and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.

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

We currently depend on a limited number of third-party suppliers. The loss of these suppliers, or delays or problems in the supply of INGREZZA, ONGENTYS, or any of our other products, could materially and adversely affect our ability to successfully commercialize INGREZZA, ONGENTYS, or any of our other products.

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, or API, the finished drug product and packaging in sufficient quantities while meeting detailed product specifications on a repeated basis. Manufacturers of pharmaceutical products may encounter difficulties in production, such as 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, compliance with strictly enforced United States, state and non-United States regulations, and disruptions or delays caused by man-made or natural disasters, pandemics or epidemics, or other business interruptions, including, for example, the COVID-19 pandemic and the conflict between Russia and Ukraine. We depend on a limited number of suppliers for the production and packaging of INGREZZA and its API. 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, under the terms of our agreement with BIAL, although we are responsible for the management of all ONGENTYS commercialization activities, we rely on BIAL and its suppliers to supply all drug product for the commercialization of ONGENTYS. BIAL relies on third-party contract manufacturers to produce ONGENTYS. These contract manufacturers may encounter difficulties in achieving volume production, quality control, or quality assurance. As a result, these contract manufacturers may not be able to adequately produce ONGENTYS in commercial quantities when required, which may impact our ability to deliver ONGENTYS on a timely basis.

In addition, if our suppliers fail or refuse to supply us with INGREZZA or its API 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 API or product manufacturing processes. If there are delays in qualifying new suppliers or facilities or if a new supplier is unable to meet FDA or a similar international regulatory body's requirements for approval, there could be a shortage of INGREZZA, which could materially and adversely affect our ability to successfully commercialize INGREZZA. If BIAL is unable or refuses to supply us with ONGENTYS drug product for any reason, or does not meet FDA or international regulators' requirements for approval, we have limited opportunity to qualify a new supplier. This could materially and adversely affect our ability to successfully commercialize ONGENTYS.

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 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 regulatory applications and our introduction of new treatments. The CROs we contract with for execution of our clinical trials play a significant role in the conduct of the trials and the subsequent collection and analysis of data. Failure of the CROs to meet their obligations could adversely affect clinical development of our products. Moreover, these independent investigators and CROs may also have relationships with other commercial entities, some of which may compete with us. If independent investigators and CROs assist our competitors at our expense, it could harm our competitive position.

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

We do not and will not have access to all information regarding elagolix, including potentially material information about commercialization plans, medical information strategies, clinical trial design and execution, safety reports from clinical trials, safety reports, regulatory affairs, process development, manufacturing and other areas known by AbbVie. In addition, we have confidentiality obligations under our agreement with AbbVie. Thus, our ability to keep our shareholders informed about the status of elagolix will be limited by the degree to which AbbVie keeps us informed and allows us to disclose such information to the public. If AbbVie fails to keep us informed about commercialization efforts related to elagolix, or the status of the clinical development or regulatory approval pathway of other product candidates licensed to it, we may make operational and/or investment decisions that we would not have made had we been fully informed, which may materially and adversely affect our business and operations.

We are subject to ongoing obligations and continued regulatory review for INGREZZA. Additionally, our other product candidates, if approved, could be subject to labeling and other post-marketing requirements and restrictions.

Regulatory approvals for any of our product candidates may 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. For example, with respect to the FDA's approval of INGREZZA for tardive dyskinesia in April 2017, we are subject to certain post-marketing requirements and commitments. 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 Good Clinical Practices for any clinical trials that we conduct post-approval. Failure to comply with these ongoing regulatory requirements, or 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, may result in, among other things:

- restrictions on the marketing or manufacturing of the product, changes in the product's label, withdrawal of the product from the market, or voluntary or mandatory product recalls;
- fines, warning or untitled 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;
- adverse inspection findings or other activities that temporarily delay manufacture and distribution of our products;

- 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 occurrence of any of these events may adversely affect our business, prospects and ability to achieve or sustain profitability on a sustained basis.

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

Certain of the diseases that INGREZZA, ONGENTYS and our other 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, ONGENTYS and our other 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 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 commercialize ONGENTYS, if we fail to use commercially reasonable efforts to comply with specified obligations under the license agreement, or if we otherwise breach the license agreement. In addition, several of our collaboration and license agreements allow our licensors to terminate such agreements if we challenge the validity or enforceability of certain intellectual property rights or if we commit a material breach in whole or in part of the agreement and do not cure such breach within the agreed upon cure period. In addition, if we were to violate any of the terms of our licenses, we could become subject to damages. Likewise, if we were to lose our rights under a license to use proprietary research tools, it could adversely affect our existing collaborations or adversely affect our ability to form new collaborations. We also face the risk that our licensors could, for a number of reasons, lose patent protection or lose their rights to the technologies we have licensed, thereby impairing or extinguishing our rights under our licenses with them.

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

As of December 31, 2022, the conditional conversion feature of the 2024 Notes had been triggered, allowing holders of 2024 Notes to convert their 2024 Notes at any time during the period beginning on January 1, 2023 and ending at the close of business on March 31, 2023. The future conditional convertibility of the 2024 Notes will be monitored at each quarterly reporting date and analyzed dependent upon market prices of our common stock during the prescribed measurement periods, and as a result, it is possible that holders of 2024 Notes will continue to 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 2024 Notes, we would be required to settle the principal amount of our conversion obligation in cash, which could adversely affect our liquidity.

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.

In May 2017, we sold $517.5 million aggregate principal amount of the 2024 Notes. In the fourth quarter of 2020, we entered into separate, privately negotiated transactions with certain holders of the 2024 Notes to repurchase $136.2 million aggregate principal amount of the 2024 Notes for an aggregate repurchase price of $186.9 million in cash. In the second quarter of 2022, we entered into separate, privately negotiated transactions with certain holders of the 2024 Notes to repurchase $210.8 million aggregate principal amount of the 2024 Notes for an aggregate repurchase price of $279.0 million in cash. As of December 31, 2022, $170.4 million aggregate principal amount of the 2024 Notes remained outstanding. 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.

We have a history of losses and expect to increase our expenses for the foreseeable future, and we may not be able to sustain profitability.

Since our inception, we have incurred significant net losses and negative cash flow from operations. As of December 31, 2022, we had an accumulated deficit of $406.8 million as a result of historical operating losses.

We received FDA approval for INGREZZA for tardive dyskinesia in April 2017 and for ONGENTYS for Parkinson’s disease in April 2020. Our partner AbbVie received FDA approval for ORILISSA for endometriosis in July 2018 and for ORIAHNN for uterine fibroids in May 2020. Additionally, our partner MTPC received Japanese Ministry of Health, Labour and Welfare approval for DYSVAL for the treatment of tardive dyskinesia in March 2022. However, we have not yet obtained regulatory approvals for any other product candidates. Even if we continue to succeed in commercializing INGREZZA, or if we successfully commercialize ONGENTYS or are successful in developing and commercializing any of our other product candidates, we may not be able to sustain profitability. We also expect to continue to incur significant operating and capital expenditures as we:

- commercialize INGREZZA for tardive dyskinesia;
- commercialize ONGENTYS for Parkinson’s disease;
- seek regulatory approvals for our product candidates or for additional indications for our current products;
- 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 and capital expenditures. Thus, our future operating results and profitability may fluctuate from period to period due to the factors described above, and we will need to generate significant revenues to achieve and maintain profitability and positive cash flow on a sustained basis. We may not be able to generate these revenues, and we may never achieve profitability on a sustained basis in the future. Our failure to maintain or increase profitability on a sustained basis could negatively impact the market price of our common stock.

We 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.

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 seasonality and timing of customer purchases and commercial sales of INGREZZA, impact of the commercial launch of ONGENTYS and ORIAHNN, royalties from out-licensed products, the impact of Medicare Part D coverage, our achievement of product development objectives and milestones, clinical trial enrollment and expenses, research and development expenses and the timing and nature of contract manufacturing, contract research payments, fluctuations in our effective tax rate, and disruptions caused by man-made or natural disasters or public health pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic and the conflict between Russia and Ukraine. Because a majority of our costs are predetermined on an annual basis, due in part to our significant research and development costs, small declines in revenue could disproportionately affect financial results in a quarter. Thus, our future operating results and profitability may fluctuate from period to period, and even if we become profitable on a quarterly or annual basis, we may not be able to sustain or increase our profitability. Moreover, as our company and our market capitalization have grown, our financial performance has become increasingly subject to quarterly and annual comparisons with the expectations of securities analysts or investors. The failure of our financial results to meet these expectations, either in a single quarterly or annual period over a sustained period time, could cause our stock price to decline.

Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business, cash flows, financial condition or results of operations.

Effective January 1, 2022, the Tax Cuts and Jobs Act of 2017 eliminated the option to deduct research and development expenses for tax purposes in the year incurred and requires taxpayers to capitalize and subsequently amortize such expenses over five years for research activities conducted in the United States and over 15 years for research activities conducted outside the United States. Unless the United States Department of the Treasury issues regulations that narrow the application of this provision to a smaller subset of our research and development expenses or the provision is deferred, modified, or repealed by Congress, we expect a material decrease in our cash flows from operations and an offsetting similarly sized increase in our net deferred tax assets over these amortization periods. The actual impact of this provision will depend on multiple factors, including the amount of research and development expenses we will incur and whether we conduct our research and development activities inside or outside the United States.

In addition, new income, sales, use, excise or other tax laws, statutes, rules, regulations or ordinances could be enacted at any time, which could adversely affect our business and financial condition. Further, existing tax laws, statutes, rules, regulations or ordinances could be interpreted, changed, modified or applied adversely to us. For example, Tax Cut and Jobs Act of 2017, the Coronavirus Aid, Relief, and Economic Security Act and the Inflation Reduction Act enacted many significant changes to the United States tax laws. Future guidance from the Internal Revenue Service and other tax authorities with respect to such legislation may affect us, and certain aspects of such legislation could be repealed or modified in future legislation. Furthermore, it is uncertain if and to what extent various states will conform to federal tax laws. Future tax reform legislation could have a material impact on the value of our deferred tax assets, could result in significant one-time charges, and could increase our future United States tax expense.

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

Our net operating loss, or NOL, carryforwards generated in tax years beginning on or prior to December 31, 2017, are only permitted to be carried forward for 20 years under applicable United States tax law. Under current law, our federal NOLs generated in tax years beginning after December 31, 2017, may be carried forward indefinitely, but the deductibility of such federal NOLs in tax years beginning after December 31, 2020, is limited to 80% of taxable income. It is uncertain if and to what extent various states will conform to federal tax laws. In addition, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50% change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. Based on completed Section 382 analysis done, we do not believe we have experienced any previous ownership changes, but the determination is complex and there can be no assurance we are correct. Furthermore, we may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control.

As a result, our pre-2018 NOL carryforwards may expire prior to being used and our NOL carryforwards generated in tax years beginning after December 31, 2017, will be subject to a percentage limitation and, if we undergo an ownership change (or if we previously underwent such an ownership change), our ability to use all of our pre-change NOLs and other pre-change tax attributes (such as research tax credits) to offset our post-change income or taxes may be limited. Similar provisions of state tax law may also apply to limit our use of accumulated state tax attributes. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. As a result, we may be unable to use all or a material portion of our NOLs and other tax attributes, which could adversely affect our future cash flows.

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

Our effective tax rate is derived from a combination of applicable tax rates in the various places that we operate. In preparing our financial statements, we estimate the amount of tax that will become payable in each such place. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including the impact of stock-based compensation, changes in the mix of our profitability from jurisdiction to jurisdiction, 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.

In addition, on December 31, 2020, we determined, based on our facts and circumstances, that it was more likely than not that a substantial portion of our deferred tax assets would be realized and, as a result, substantially all of our valuation allowance against our deferred tax assets was released. Therefore, beginning in 2021, we commenced recording income tax expense at an estimated tax rate that will likely approximate statutory tax rates, which could result in a significant reduction in our net income and net income per share.

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. The COVID-19 pandemic, for example, has negatively affected the stock market and investor sentiment and has resulted in significant volatility. Furthermore, especially as we and our market capitalization have grown, the price of our common stock has been increasingly affected by quarterly and annual comparisons with the valuations and recommendations of the analysts who cover our business. If our results do not meet these analysts' forecasts, the expectations of our investors or the financial guidance we provide to investors in any period, which is based on assumptions that may be incorrect or that may change from quarter to quarter, the market price of our common stock could decline. Over the course of the last 12 months, the price of our common stock has ranged from approximately $72 per share to approximately $129 per share.

The market price of our common stock may fluctuate in response to many factors, including:

- sales of INGREZZA and our other products;
- the status and cost of our post-marketing commitments for INGREZZA;
- the results of our clinical trials;
- reports of safety issues related to INGREZZA, ONGENTYS, ORILISSA, ORIAHNN, DYSVAL, or any of our other products;
- 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 and foreign regulatory agencies;
- future sales of our common stock by us or our stockholders;
- comments by securities analysts;
- additions or departures of key personnel;
- fluctuations in our operating results;
- potential litigation matters and developments in existing litigation matters, such as the ANDA litigation matters;
- government regulation;
- government and third-party payor coverage and reimbursement;
- failure of any of our product candidates, if approved, to achieve commercial success;
- disruptions caused by man-made or natural disasters, pandemics or epidemics or other business interruptions, including, for example, the COVID-19 pandemic and the conflict between Russia and Ukraine; and
- public concern as to the safety of our drugs.

In addition, we are a member of the S&P MidCap 400 index. If we cease to be represented in the S&P MidCap 400 index, or other indexes or indexed products, as a result of our market capitalization falling below the threshold for inclusion in the index, certain institutional shareholders may, due to their internal policies and investment guidelines, be required to sell their shareholdings. Such sales may result in further negative pressure on our stock price and, when combined with reduced trading volume and liquidity, could adversely affect the value of your investment and your ability to sell your shares.

Our customers are concentrated and therefore the loss of a significant customer may harm our business.

We have entered into agreements for the distribution of INGREZZA with a limited number of specialty pharmacy providers and distributors, and all of our product sales of INGREZZA are to these customers. Four of these customers represented approximately 89% of our total product revenue for the twelve months ended December 31, 2022 and approximately 95% of our accounts receivable balance as of December 31, 2022. If any of these significant customers becomes subject to bankruptcy, is unable to pay us for our products or is acquired by a company that wants to terminate the relationship with us, or if we otherwise lose any of these significant customers, our revenue, results of operations and cash flows would be adversely affected. Even if we replace the loss of a significant customer, we cannot predict with certainty that such transition would not result in a decline in our revenue, results of operations and cash flows.

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 continue our research and development programs, to conduct preclinical studies and clinical trials, for operating expenses, to pursue regulatory approvals for our product candidates, for the costs involved in filing and prosecuting patent applications and enforcing or defending patent claims, if any, and the cost of product in-licensing and any possible acquisitions. In addition, we may require additional funding to establish manufacturing and marketing capabilities in the future. We believe that our existing capital resources and anticipated revenues will be sufficient to satisfy our current and projected funding requirements for at least the next 12 months. However, these resources might be insufficient to conduct research and development programs, the cost of product in-taking and possible acquisitions, fully commercialize products and operate the company to the full extent currently planned. If we cannot obtain adequate funds, we may be required to significantly curtail 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, ONGENTYS, ORILISSA, ORIAHNN, DYSVAL, and/or any of our other products;
- debt services obligations on the 2024 Notes;
- continued scientific progress in our R&D and clinical development programs;
- the magnitude and complexity of our research and development programs;
- progress with preclinical testing and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the cost involved in filing and pursuing patent applications, enforcing patent claims, or engaging in interference proceedings or other patent litigation;
- competing technological and market developments;
- developments related to any future litigation;
- the cost of commercialization activities and arrangements, including advertising campaigns;
- the cost of manufacturing our product candidates;
- the impact of the COVID-19 pandemic on our business; and
- the cost of any strategic alliances, collaborations, product in-licensing, or 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. 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. In the fourth quarter of 2020, we entered into separate, privately negotiated transactions with certain holders of the 2024 Notes to repurchase $136.2 million aggregate principal amount of the 2024 Notes for an aggregate repurchase price of $186.9 million in cash. In the second quarter of 2022, we entered into separate, privately negotiated transactions with certain holders of the 2024 Notes to repurchase $210.8 million aggregate principal amount of the 2024 Notes for an aggregate repurchase price of $279.0 million in cash. As of December 31, 2022, $170.4 million aggregate principal amount of the 2024 Notes remained outstanding. Additional equity or debt financing might not be available on reasonable terms, if at all. In addition, disruptions due to the COVID-19 pandemic could make it more difficult for us to access capital. 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 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 selling, 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.

Increasing use of social media could give rise to liability and result in harm to our business.

Our employees are increasingly utilizing social media tools and our website as a means of communication. Despite our efforts to monitor social media communications, there is risk that the unauthorized use of social media by our employees to communicate about our products or business, or any inadvertent disclosure of material, nonpublic information through these means, may result in violations of applicable laws and regulations, which may give rise to liability and result in harm to our business. In addition, there is also risk of inappropriate disclosure of sensitive information, which could result in significant legal and financial exposure and reputational damages that could potentially have a material adverse impact on our business, financial condition and results of operations. Furthermore, negative posts or comments about us or our products on social media could seriously damage our reputation, brand image and goodwill.

Risks Related to Our Industry

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

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

- obtain patent protection for our products;
- preserve our trade secrets;
- prevent third parties from infringing upon our proprietary rights; and
- operate without infringing upon the proprietary rights of others, both in the United States and internationally.

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

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

In addition, although we own a number of patents, the issuance of a patent is not conclusive as to its validity or enforceability, and third parties may challenge the validity or enforceability of our patents. We cannot assure you how much protection, if any, will be given to our patents if we attempt to enforce them and they are challenged in court or in other proceedings. It is possible that a competitor may successfully challenge our patents or that challenges will result in limitations of their coverage. Moreover, competitors may infringe our patents or successfully avoid them through design innovation. In addition, potential competitors have in the past and may in the future file an ANDA with the FDA seeking approval to market a generic version of our products, or our competitors' products, before the expiration of the patents covering our products or our competitors' products, as applicable. To prevent infringement or unauthorized use, we have in the past and may in the future need to file infringement claims, which are expensive and time-consuming. For example, we are currently engaged in various intellectual property litigation matters against potential competitors related to INGREZZA. Refer to Item 1. Legal Proceedings for a more detailed description of these matters. In addition, in an infringement proceeding a court may decide that a patent of ours or a patent of a competitor 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. Derivation 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) or a patent of a competitor. Litigation or derivation proceedings may fail and, even if successful, may result in substantial costs and be a distraction to management. Litigation or derivation proceedings, including proceedings of a competitor, may also result in a competitor entering the marketplace faster than expected. 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.

Enacted 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 and to lower drug prices. In the United States, comprehensive health care reform legislation has been enacted by the Federal government to implement government control over the pricing of prescription pharmaceuticals. Moreover, in some foreign jurisdictions, pricing of prescription pharmaceuticals is also subject to government control. Additionally, other federal and state legislation impose obligations on manufacturers of pharmaceutical products, among others, related to disclosure of new drug products introduced to the market and increases in drug prices above a specified threshold.

For example, in August 2022, President Biden signed into law the Inflation Reduction Act of 2022, or the IRA, which, among other things, (1) directs the Secretary of the U.S. Department of Health and Human Services, or HHS, to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare, (2) redesigns the Medicare Part D prescription drug benefit to lower patient out-of-pocket costs and increase manufacturer liability and (3) requires drug manufacturers to pay rebates on drugs whose prices increase greater than the rate of inflation. The IRA also extends enhanced subsidies for individuals purchasing health insurance coverage in the ACA marketplaces through plan year 2025 and eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket cost to $2,000 through a newly established manufacturer discount program. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented; however, it is likely to have a significant impact on the pharmaceutical industry and prescription drug pricing.

While the IRA targets high-expenditure drugs that have been on the market for several years without generic or biosimilar competition, we have qualified for the small biotech manufacturer exemption that is set to expire in 2029. However, the qualification for this exemption is subject to various requirements and there is no assurance that we will continue to qualify for this exemption in the future. Further, the loss of this exemption or the potential loss of this exemption, including as a result of a potential acquisition or strategic transaction, could have an adverse impact on our business.

Prior to the IRA's enactment, the most significant recent federal legislation impacting the pharmaceutical industry occurred in March 2010. The Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA, was signed into law, which was intended to broaden access to health insurance and reduce the number of uninsured individuals, 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.

Other legislative changes have been adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and, due to subsequent legislative amendments to the statute, including the Infrastructure Investment and Jobs Act, will remain in effect until 2031, except for a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 4% in the final fiscal year of this sequestration. 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.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. The implementation of these cost containment measures may prevent us from being able to generate revenue, attain sustained profitability or commercialize our drugs, particularly since the majority of our current revenue is derived from federal healthcare programs, including Medicare and Medicaid.

Proposed health care reform measures and other prospective legislative initiatives could adversely affect our business.

The United States and some foreign jurisdictions are considering 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. The business and financial condition of pharmaceutical and biotechnology companies may be affected by the efforts of governmental and third-party payors to contain or reduce the costs of health care and to lower drug prices. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives. 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 pricing and reimbursement of prescription pharmaceuticals.

The heightened governmental scrutiny over pharmaceutical pricing practices has resulted in several Congressional hearings 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. For example, in July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform and sets out a variety of potential legislative policies that Congress could pursue to advance these principles. Further, the Biden administration released an additional executive order on October 14, 2022, directing HHS to submit a report within 90 days on how the Center for Medicare and Medicaid Innovation can be further leveraged to test new models for lowering drug costs for Medicare and Medicaid beneficiaries. It is unclear whether this executive order or similar policy initiatives will be implemented in the future.

We are currently unable to predict what other 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.

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

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

Such laws include:

- the federal Anti-Kickback Statute which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward, or in return for, either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the federal civil False Claims Act, and Civil Monetary Penalties Laws, which impose criminal and civil penalties against individuals or entities for, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the Health Insurance Portability and Accountability Act, or 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 (HITECH) implementing regulations, which also imposes obligations, including mandatory contractual terms, on covered entities, including certain healthcare providers, health plans and healthcare clearinghouses, as well as their business associates and their covered subcontractors, 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 (defined to include doctors, dentists, optometrists, podiatrists and chiropractors), other healthcare professionals (such as physician assistants and nurse practitioners) and teaching hospitals, and applicable manufacturers and applicable group purchasing organizations to report annually to CMS ownership and investment interests held by physicians and their immediate family members; and

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

Efforts to ensure that our business arrangements will comply with applicable healthcare laws may involve substantial costs. While our interactions with healthcare professionals, including our speaker programs and other arrangements have been structured to comply with these laws and related guidance, 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. For example, we maintain a patient assistance program to help eligible patients afford our products. These types of programs have become the subject of governmental scrutiny, and numerous organizations, including pharmaceutical manufacturers, have been subject to litigation, enforcement actions and settlements related to their patient assistance programs. 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, significant 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.

We could face liability if a regulatory authority determines that we are promoting INGREZZA, ONGENTYS 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. However, companies may share truthful and not misleading information that is otherwise consistent with a product's FDA approved labeling. 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 and ONGENTYS, 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.

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 brought by a private plaintiff on behalf of the government, 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.

If our information technology systems or data is or were compromised, we could experience adverse impacts resulting from such compromise, including, but not limited to, interruptions to our operations such as our clinical trials, claims that we breached our data protection obligations, harm to our reputation, and a loss of customers or sales.

We are increasingly dependent on information technology systems and infrastructure, including mobile technologies, to operate our business. In the ordinary course of our business, we collect, use, safeguard, share and transfer, or collectively, process, confidential and sensitive electronic information on our networks and in our data centers. This information includes, among other things, de-identified or pseudonymous sensitive personal data (including health data), our intellectual property and proprietary information, the confidential information of our collaborators and licensees, and the personal data of our employees. It is important to our operations and business strategy that this electronic information remains secure and is perceived to be secure. The size and complexity of our information technology systems, and those of third-party vendors with whom we contract, and the volume of data we retain, make such systems potentially vulnerable to breakdown, malicious intrusion, security breaches, ransomware attacks, social engineering attacks, supply-chain attacks, and other cyber-attacks. Cyber-attacks, malicious internet-based activity, online and offline fraud, and other similar activities threaten the confidentiality, integrity, and availability of our sensitive information and information technology systems, and those of the third parties upon which we rely. Such threats continue to rise, are increasingly difficult to detect, and come from a variety of sources, including traditional computer "hackers," threat actors, "hacktivists," organized criminal threat actors, personnel (such as through theft or misuse), sophisticated nation states, and nation-state-supported actors. Some actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we and the third parties upon which we rely may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, as well as our ability to conduct clinical trials. Ransomware attacks are also becoming increasingly prevalent and severe, and can lead to significant interruptions in our operations, loss of sensitive data and income, reputational harm, and diversion of funds. To alleviate the financial, operational and reputational impact of a ransomware attack, it may be preferable to make extortion payments, but we may be unwilling or unable to do so (including, for example, if applicable laws or regulations prohibit such payments). Similarly, supply chain attacks have increased in frequency and severity, and we cannot guarantee that third parties in our supply chain have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems and infrastructure or the information technology systems and infrastructure of third parties that support our operations. Furthermore, if the COVID-19 pandemic requires us to reinstate a remote workforce model, our information technology systems and data will be at increased risk as more of our employees work from home, utilizing network connections outside our premises.

Additionally, natural disasters, public health pandemics or epidemics (including, for example, the COVID-19 pandemic), terrorism, war and geopolitical conflicts (including, for example, the conflict between Russia and Ukraine) and telecommunication and electrical failures may result in damage to or the interruption or impairment of key business processes, or the loss or corruption of confidential information, including intellectual property, proprietary business information and personal data. Information security risks have significantly increased in recent years in part due to the proliferation of new technologies and the increased sophistication and activities of organized crime, hackers, terrorists and other external parties, including foreign private parties and state actors.

As cyber threats continue to evolve, we may be required to expend significant additional resources to continue to modify or enhance our protective measures or to investigate and remediate any information security vulnerabilities. Our efforts to identify and remediate such vulnerabilities may not be successful and we may experience delays in developing and deploying remedial measures designed to address any such identified vulnerabilities. Further, we may be unable to detect such vulnerabilities in the future because such threats and techniques change frequently, are often sophisticated in nature and may not be detected until after a security breach has occurred.

We may rely on third-party service providers and technologies to operate critical business systems to process sensitive information in a variety of contexts, including, without limitation, cloud-based infrastructure, data center facilities, encryption and authentication technology, employee email and other functions. We may also rely on third-party service providers to provide other products, services, parts, or otherwise to operate our business, including clinical trial sites and investigators, contractors, manufacturers, suppliers and consultants. Our ability to monitor these third parties' information security practices is limited, and these third parties may not have adequate information security measures in place. If our third-party service providers or CROs experience a security incident or other interruption, we could experience adverse consequences. While we may be entitled to damages if our third-party service providers fail to satisfy their privacy or security-related obligations to us, any award may be insufficient to cover our damages, or we may be unable to recover such award.

Although to our knowledge we, or the third parties upon who we rely, have not experienced any material incident or disruption to date, we and our vendors have been the target of cybersecurity incidents of this nature and expect them to continue. While we have implemented security measures to protect our data security and information technology systems, such measures may not prevent such events.

If we (or a third party upon whom we rely) experience a security breach or are perceived to have experienced a security breach, we may experience adverse consequences. Such consequences may include: government enforcement actions (for example, investigations, fines, penalties, audits and inspections); additional reporting requirements and/or oversight; restrictions on processing sensitive information (including personal data); litigation (including class claims); indemnification obligations; negative publicity; reputational harm (including but not limited to damage to our patient, partner, or employee relationships); monetary fund diversions; interruptions in our operations (including availability of data); financial loss; and other similar harms. Similarly, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. In addition, theft of our intellectual property or proprietary business information could require substantial expenditures to remedy. Applicable data privacy and security obligations may also require us to notify relevant stakeholders of security breaches or incidents. Such disclosures are costly, and the disclosure or the failure to comply with such requirements could lead to adverse consequences.

Our contracts, with for example third parties or CROs, may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We also cannot be sure that our insurance coverage will be adequate or sufficient to protect us from or to mitigate liabilities arising out of our privacy and security practices, that such coverage will continue to be available on commercially reasonable terms or at all, or that such coverage will pay future claims.

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.

In addition to any patent protection, we rely on forms of regulatory exclusivity to protect our products such as orphan drug designation. 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 for seven years and the European Union for 10 years 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 European Union, orphan exclusivity may be reduced to 6 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.

If we do not have adequate patent protection for our products, then the relative importance of obtaining regulatory exclusivity is even greater. We may not be successful obtaining orphan drug designations for any indications and, even if we succeed, such product candidates with such orphan drug designations may fail to achieve FDA approval. Even if a product candidate with orphan drug designation may receive marketing approval from the FDA, it 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 business operations may subject us to disputes, claims and lawsuits, which may be costly and time-consuming and could materially and adversely impact our financial position and results of operations.

From time to time, we may become involved in disputes, claims and lawsuits relating to our business operations. In particular, we may face claims related to the safety of our products, intellectual property matters, employment matters, tax matters, commercial disputes, competition, sales and marketing practices, environmental matters, personal injury, insurance coverage and acquisition or divestiture-related matters. Any dispute, claim or lawsuit may divert management's attention away from our business, we may incur significant expenses in addressing or defending any dispute, claim or lawsuit, and we may be required to pay damage awards or settlements or become subject to equitable remedies that could adversely affect our operations and financial results. For example, we are currently engaged in various intellectual property litigation matters against potential competitors related to INGREZZA. Refer to Item 1. Legal Proceedings for a more detailed description of these matters.

Litigation related to these disputes may be costly and time-consuming and could materially and adversely impact our financial position and results of operations if resolved against us. In addition, the uncertainty associated with litigation could lead to increased volatility in our stock price.

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

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

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

The use of any of our potential products in clinical trials, and the sale of any approved products, including INGREZZA and ONGENTYS, 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 product liability insurance coverage for our clinical trials in the amount of $45.0 million per occurrence and $45.0 million in the aggregate. In addition, we have product liability insurance related to the sale of INGREZZA and ONGENTYS in the amount of $45.0 million per occurrence and $45.0 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 from any current or future clinical trials or approved products. A successful product liability claim, or series of claims, brought against us would decrease our cash reserves and could cause our stock price to fall. Furthermore, regardless of the eventual outcome of a product liability claim, any product liability claim against us may decrease demand for our approved products, including INGREZZA and ONGENTYS, damage our reputation, result in regulatory investigations that could require costly recalls or product modifications, cause clinical trial participants to withdrawal, result in costs to defend the related litigation, decrease our revenue, and divert management's attention from managing our business.

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

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

We are subject to stringent and changing obligations related to data privacy and information security. Our actual or perceived failure to comply with such obligations could have a material adverse effect on our reputation, business, financial condition or results of operations.

In the ordinary course of our business, we collect, receive, store, process, generate, use, transfer, disclose, make accessible, protect, secure, dispose of, transmit, and share (collectively, processing) confidential and sensitive information, including personal data, proprietary and confidential business data, trade secrets, intellectual property, data we collect about clinical trial participants in connection with clinical trials, and sensitive third-party data, on our networks and in our data centers. We are subject to numerous federal, state, local and foreign laws, orders, codes, regulations and regulatory guidance regarding privacy, data protection, information security and the processing of personal information (including clinical trial data), the number and scope of which are expanding, changing, subject to differing applications and interpretations, and may be inconsistent among jurisdictions. Our data processing activities may also subject us to other data privacy and security obligations, such as industry standards, external and internal privacy and security policies, contracts and other obligations that govern the processing of data by us and by third parties on our behalf.

Laws regarding privacy, data protection, information security and the processing of personal data are becoming increasingly common in the United States at both the federal and state level. For example, the California Consumer Privacy Act, or CCPA, which went into effect in 2020, imposes obligations on businesses to which it applies. These obligations include, without limitation, providing specific disclosures in privacy notices, affording California residents certain rights related to their personal data, and requiring businesses subject to the CCPA to implement certain measures to effectuate California residents' personal data rights. The CCPA allows for statutory fines for noncompliance (up to $7,500 per violation). In addition, the California Privacy Rights Act of 2020, or the CPRA, which became effective January 1, 2023, expands the CCPA by establishing a new California Privacy Protection Agency to implement and enforce the CCPA (as amended), which could increase the risk of an enforcement action. Other states have also enacted data privacy laws. For example, Virginia passed its Consumer Data Protection Act, Colorado passed the Colorado Privacy Act, and Utah passed the Utah Consumer Privacy Act, all of which become effective in 2023. Similar laws are being considered in several other states, as well as at the federal and local levels. These developments may further complicate compliance efforts, and may increase legal risk and compliance costs for us and the third parties upon whom we rely.

Additionally, the federal Health Insurance Portability and Accountability Act of 1996 (“HIPAA”), as amended by the Health Information Technology for Economic and Clinical Health Act (“HITECH”), imposes specific requirements relating to the privacy, security, and transmission of individually identifiable health information.

Laws in Europe regarding privacy, data protection, information security and the processing of personal data have also been significantly reformed and continue to undergo reform. For example, the European Union’s General Data Protection Regulation, or the EU GDPR, and the United Kingdom’s GDPR, or the UK GDPR, impose strict requirements for processing the personal data of individuals located, respectively, within the European Economic Area, or EEA, and the United Kingdom, or the UK. The EU GDPR and the UK GDPR enhance data protection obligations for processors and controllers of personal data, including, for example, obligations relating to: processing health and other sensitive data; obtaining consent of individuals; providing notice to individuals regarding data processing activities; responding to data subject requests; taking certain measures when engaging third-party processors; notifying data subjects and regulators of data breaches; and implementing safeguards to protect the security and confidentiality of personal data. The EU GDPR and the UK GDPR impose substantial fines for breaches of data protection requirements. For example, under the EU GDPR, such fines can be up to four percent of global revenue or 20 million euros, whichever is greater, and also allow for private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests. The EU GDPR, the UK GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as EU regulations governing clinical trial data and other healthcare data, could require us to change our business practices or lead to government enforcement actions, private litigation or significant penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

We may be subject to additional foreign data laws. For example, in Canada, the Personal Information Protection and Electronic Documents Act (“PIPEDA”) and various related provincial laws, as well as Canada’s Anti-Spam Legislation (“CASL”), may apply to our operations. As another example, the General Data Protection Law (Lei Geral de Proteção de Dados Pessoais, or “LGPD”) (Law No. 13,709/2018) may apply to our operations. The LGPD broadly regulates processing personal data of individuals in Brazil and imposes compliance obligations and penalties comparable to those of the EU GDPR. We also target customers in Asia and may be subject to new and emerging data privacy regimes in Asia, including Japan’s Act on the Protection of Personal Information and Singapore’s Personal Data Protection Act.

In the ordinary course of business, we may transfer personal data from Europe and other jurisdictions to the United States or other countries. Certain jurisdictions have enacted data localization laws and cross-border personal data transfers laws. For example, absent appropriate safeguards or other circumstances, the EU GDPR may restrict the transfer of personal data to countries outside of the EEA, such as the United States, which the European Commission does not consider to provide an adequate level of personal data protection. Although there are currently various mechanisms that may be used to transfer personal data from the EEA and UK to the United States in compliance with law, such as the EEA and UK’s standard contractual clauses, these mechanisms are subject to legal challenges, and there is no assurance that we can satisfy or rely on these measures to lawfully transfer personal data to the United States. If we cannot implement a valid compliance mechanism for cross-border personal data transfers, we may face increased exposure to regulatory actions, substantial fines and injunctions against processing or transferring personal data from Europe or elsewhere. The inability to import personal data to the United States may significantly and negatively impact our business operations, including by limiting our ability to conduct clinical trial activities in Europe and elsewhere; limiting our ability to collaborate with parties subject to European and other data protection laws or requiring us to increase our personal data processing capabilities in Europe and/or elsewhere at significant expense. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross-border data transfer laws.

Our obligations related to data privacy and security are quickly changing in an increasingly stringent fashion. These obligations may be subject to differing applications and interpretations, which may be inconsistent among jurisdictions or in conflict. Preparing for and complying with these obligations requires us to devote significant resources (including, without limitation, financial and time-related resources). These obligations may necessitate changes to our information technologies, systems and practices and those of any third parties that process personal data on our behalf. In addition, these obligations may even require us to change to our business model.

Although we endeavor to comply with all applicable data privacy and security obligations, we may at times fail (or be perceived to have failed) to do so. Moreover, despite our efforts, our personnel or third-parties upon whom we rely may fail to comply such obligations that impacts our compliance posture. If we fail, or are perceived to have failed, to address or comply with data privacy and security obligations, we could face significant consequences. These consequences may include, but are not limited to, government enforcement actions, litigation, additional reporting requirements and/or oversight, bans on processing personal data, imprisonment of company officials, and orders to destroy or not use personal data. Any of these events could have a material adverse effect on our reputation, business, financial condition or results of operations.

Item 1B. *Unresolved Staff Comments*

None.

Item 2. *Properties*

Our corporate headquarters are located in San Diego, California. We believe that our property and equipment are generally well maintained, in good operating condition and suitable for the conduct of our business.

Details of our leased facilities, which include our corporate headquarters and consist of office space and research and development laboratories, follow.

Address	Type	Square Feet
12780 El Camino Real, San Diego, California	Office Space, Research and Development Laboratories	141,000
12790 El Camino Real, San Diego, California	Office Space	88,000
10420 Wateridge Circle, San Diego, California	Research and Development Laboratories	46,000
12777 High Bluff Drive, San Diego, California	Office Space	45,000
12770 El Camino Real, San Diego, California	Office Space	26,000

On February 8, 2022, we entered into a lease agreement for a four-building campus facility consisting of up to approximately 535,000 gross square feet, to be constructed in San Diego, California, pursuant to which we also secured a six-year option for the construction of a fifth building consisting of up to approximately 121,000 gross square feet and an option to purchase the entire campus facility, which will consist of office space and research and development laboratories, in the future. Upon completion of construction, we expect to utilize the campus facility as our new corporate headquarters and expect to begin subleasing our existing leased facilities.

Item 3. *Legal Proceedings*

During 2021 and 2022, we received notices from (i) Teva Pharmaceuticals Development, Inc., (ii) Lupin Limited, (iii) Crystal Pharmaceutical (Suzhou) Co. Ltd., (iv) Sandoz Inc. and (v) Zydus Pharmaceuticals (USA) Inc. that each company had filed an abbreviated new drug application, or ANDA, with the FDA seeking approval of a generic version of INGREZZA. These companies represented that their respective ANDAs each contained a Paragraph IV Patent Certification alleging that certain of our patents covering INGREZZA are invalid and/or will not be infringed by the manufacture, use or sale of the medicine for which the ANDA was submitted.

We filed suit in the United States District Court for the District of Delaware during 2021 and 2022, against (i) Teva Pharmaceuticals, Inc., Teva Pharmaceuticals Development, Inc., Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries Ltd. (entity dismissed), (ii) Lupin Limited, Lupin Pharmaceuticals, Inc., Lupin Inc. and Lupin Atlantis Holdings S.A., (iii) Crystal Pharmaceutical (Suzhou) Co., Ltd., Crystal Pharmatech Co., Ltd., (iv) Sandoz Inc., Sandoz International GmbH (entity dismissed) and Sandoz AG (entity dismissed) and (v) Zydus Pharmaceuticals (USA) Inc., Zydus Worldwide DMCC, Zydus Lifesciences Limited (formerly known as Cadila Healthcare Limited d/b/a Zydus Cadila) and Zydus Healthcare (USA) LLC (entity dismissed). Sandoz Inc. has been joined in the cases against Crystal Pharmaceutical (Suzhou) Co., Ltd. and Crystal Pharmatech Co., Ltd. These cases have been consolidated in the United States District Court for the District of Delaware and the trial is currently scheduled for January 2, 2024.

We also filed suit in the United States District Court for the District of New Jersey during 2021 and 2022 against Zydus Pharmaceuticals (USA) Inc., Zydus Worldwide DMCC, Zydus Lifesciences Limited (formerly known as Cadila Healthcare Limited d/b/a Zydus Cadila) and Zydus Healthcare (USA) LLC and these cases were dismissed in favor of continued prosecution of the Delaware proceedings against the same entities.

From time to time, we may also become subject to other legal proceedings or claims arising in the ordinary course of our business. We currently believe that none of the claims or actions pending against us is likely to have, individually or in the aggregate, a material adverse effect on our business, financial condition or results of operations. Given the unpredictability inherent in litigation, however, we cannot predict the outcome of these matters.

Item 4. *Mine Safety Disclosures*

None.

PART II

Item 5. *Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities*

Our common stock is traded on the Nasdaq Global Select Market under the symbol "NBIX".

As of January 31, 2023, there were approximately 44 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.

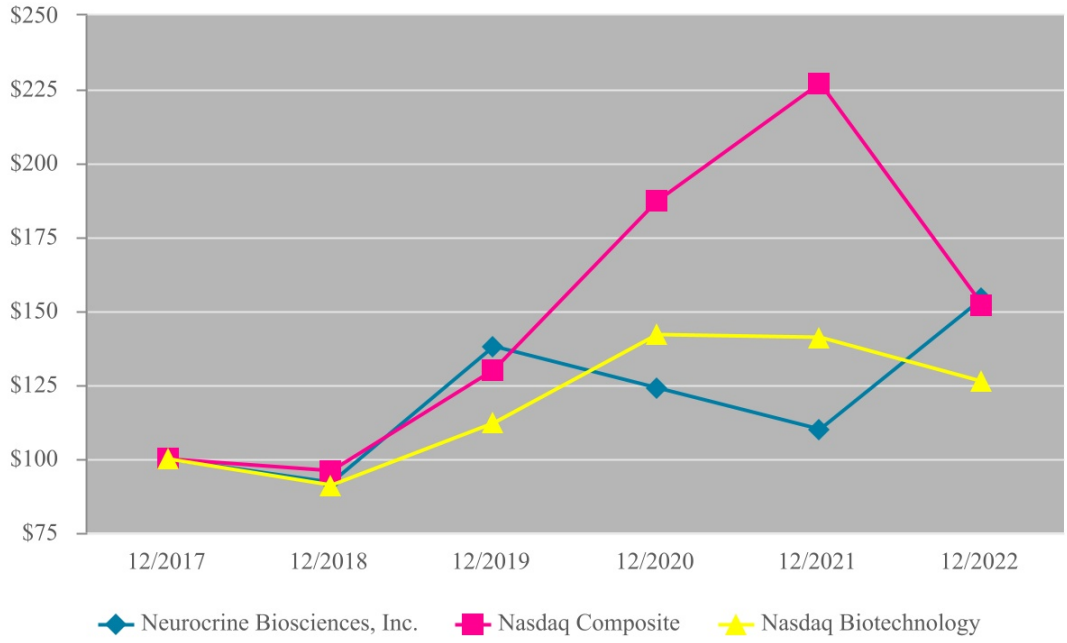
Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

Recent Sales of Unregistered Securities and Issuer Purchases of Equity Securities

There were no unregistered sales of our equity securities and we did not repurchase any of our equity securities during 2022.

Stock Performance Graph and Cumulative Total Return*

The following graph presents the cumulative total stockholder return assuming the investment of $100 on December 31, 2017 (and the reinvestment of dividends thereafter) in each of (i) Neurocrine Biosciences, Inc.'s common stock, (ii) the Nasdaq Composite Index and (iii) the Nasdaq Biotechnology Index. The comparisons in the graph below are based upon historical data and are not indicative of, or intended to forecast, future performance of our common stock or Indexes.



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

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations

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

Overview

Neurocrine Biosciences is a neuroscience-focused, biopharmaceutical company with a simple purpose: to relieve suffering for people with great needs, but few options. We are dedicated to discovering and developing life-changing treatments for patients with under-addressed neurological, neuroendocrine and neuropsychiatric disorders. The Company's diverse portfolio includes United States Food and Drug Administration, or FDA, approved treatments for tardive dyskinesia, Parkinson's disease, endometriosis* and uterine fibroids* and a diversified portfolio of advanced clinical-stage programs in multiple therapeutic areas. For three decades, we have applied our unique insight into neuroscience and the interconnections between brain and body systems to treat complex conditions and we will continue to relentlessly pursue medicines to ease the burden of debilitating diseases and disorders. (*in collaboration with AbbVie Inc., or AbbVie)

We launched INGREZZA® (valbenazine) in the United States in May 2017 as the first FDA-approved drug for the treatment of tardive dyskinesia and launched ONGENTYS® (opicapone) in the United States in September 2020 as an FDA-approved add-on treatment for levodopa/carbidopa in patients with Parkinson's disease experiencing motor fluctuations. INGREZZA net product sales represent nearly all of our total net product sales.

Our partner Mitsubishi Tanabe Pharma Corporation, or MTPC, launched DYSVAL® (valbenazine) in Japan in June 2022 for the treatment of tardive dyskinesia. We receive royalties at tiered percentage rates on MTPC net sales of DYSVAL.

Our partner AbbVie launched ORILISSA® (elagolix tablets) in the United States in August 2018 for the treatment of moderate to severe pain associated with endometriosis and launched ORIAHNN® (elagolix, estradiol and norethindrone acetate capsules and elagolix capsules) in the United States in June 2020 for the treatment of heavy menstrual bleeding related to uterine fibroids in premenopausal women. We receive royalties at tiered percentage rates on AbbVie net sales of elagolix.

Business Highlights

- INGREZZA net product sales for 2022 increased $345.9 million, or 32.0%, to $1.4 billion, driven by increased new patient starts and increased total prescriptions on higher customer demand and increased commercial activities, including continued investment in our branded direct-to-consumer INGREZZA advertising campaign launched in May 2021 and deployment of our expanded sales force in April 2022.
- Total debt outstanding decreased by $210.8 million to $170.4 million following our repurchase of approximately 55% of total debt outstanding in the second quarter of 2022. The total aggregate repurchase price of $279.0 million was paid in cash and resulted in the recognition of a $70.0 million loss on extinguishment.
- On November 1, 2022, we acquired Diurnal in an all-cash transaction, for an aggregate value of $55.2 million to accelerate the establishment of our clinical development and commercial capabilities in the United Kingdom to the benefit of patient communities and other stakeholders.

- On January 8, 2023, we entered into a new strategic collaboration with Voyager Therapeutics, Inc., or Voyager, under which we agreed to pay Voyager $175 million upfront, including a $39 million equity investment, to acquire the worldwide rights to Voyager's GBA1 gene therapy program for Parkinson's disease and other GBA1-mediated diseases and three gene therapy programs directed to rare central nervous system targets, each enabled by Voyager's next-generation TRACER™ capsids. The effectiveness of the collaboration agreement and the closing of the sale and issuance of Voyager common stock are expected to be completed before the end of the first quarter of 2023 and are subject to certain conditions including the expiration or termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and other customary closing conditions.

Pipeline Highlights

- In December 2022, the FDA accepted our supplemental new drug application, or sNDA, for valbenazine for the treatment of chorea associated with Huntington disease. The agency set a Prescription Drug User Fee Act target action date of August 20, 2023.
- In 2022, we initiated a second Phase III clinical study of valbenazine as adjunctive treatment in patients with schizophrenia who have had an inadequate response to antipsychotics and a Phase II clinical study of NBI-1117568 in patients with schizophrenia who are experiencing an acute exacerbation or relapse of symptoms.
- In December 2022, we announced our Phase II study of NBI-827104 in EE-CSWS did not meet specified endpoints. We continue to analyze the complete dataset from this study to determine next steps in the further development of NBI-827104.
- In August 2022, we announced the Phase IIa study of NBI-827104 in essential tremor did not meet specified endpoints. Based on the totality of data from the Phase IIa study, at this time, we do not plan to proceed further with the clinical development of NBI-827104 in essential tremor.
- We recently completed enrollment in our adult and pediatric registrational studies of crinecerfont to treat congenital adrenal hyperplasia with top-line data expected for each study in the second half of 2023.

Impacts of Macro-Economic Factors on Our Business

COVID-19 Global Pandemic.

We continue to monitor the impact of the COVID-19 pandemic on our business, including our clinical trials, third-party manufacturers, suppliers and service providers. We remain committed to (1) prioritizing the safety, health and well-being of patients and their caregivers, healthcare providers, and our employees; (2) ensuring patients with tardive dyskinesia are well supported and have continued uninterrupted access to INGREZZA, for which we have not experienced and currently do not expect any supply disruption; and (3) advancing our clinical studies.

The extent to which COVID-19 may impact our financial condition and results of operations remains uncertain and is dependent on numerous evolving factors, including the measures being taken by authorities to mitigate against the spread of COVID-19, the emergence of new variants and the availability and successful administration of effective vaccines. For more information on the risks and uncertainties associated with the evolving effects of COVID-19 on our business, our ability to generate sales of and revenues from our approved products and our clinical development and regulatory efforts, refer to Part I Item 1A. Risk Factors.

Russia/Ukraine Conflict.

In February 2022, Russia commenced a military invasion of Ukraine. The ongoing geopolitical turmoil and continuing military action in the region, together with widening sanctions imposed on Russia, have caused us to suspend all planned clinical trial activities for valbenazine and luvadaxistat in Russia and Ukraine.

The duration and impact of the conflict between Russia and Ukraine is highly unpredictable and the extent to which the conflict may impact certain of our clinical development and regulatory efforts remains uncertain. For more information on the risks and uncertainties associated with the evolving effects of the conflict between Russia and Ukraine on our business and certain of our clinical development and regulatory efforts, refer to Part I Item 1A. Risk Factors.

Inflation Reduction Act.

In August 2022, President Biden signed into law the Inflation Reduction Act of 2022, or the IRA, which, among other things, (1) directs the Secretary of the U.S. Department of Health and Human Services, or HHS, to negotiate the price of certain high-expenditure, single-source drugs and biologics covered under Medicare, (2) redesigns the Medicare Part D prescription drug benefit to lower patient out-of-pocket costs and increase manufacturer liability and (3) requires drug manufacturers to pay rebates on drugs whose prices increase greater than the rate of inflation. These provisions will take effect progressively starting in 2023, although they may be subject to legal challenges. It is currently unclear how the IRA will be implemented; however, it is likely to have a significant impact on the pharmaceutical industry and prescription drug pricing. While the IRA targets high-expenditure drugs that have been on the market for several years without generic or biosimilar competition, we have qualified for the small biotech manufacturer exemption that is set to expire in 2029. However, the qualification for this exemption is subject to various requirements and there is no assurance that we will continue to qualify for this exemption in the future. Further, the loss of this exemption or the potential loss of this exemption, including as a result of a potential acquisition or strategic transaction, could have an adverse impact on our business. For more information on the risks and uncertainties associated with the evolving effects of the IRA on our business, refer to Part I Item 1A. Risk Factors.

Results of Operations

Revenues

Net Product Sales by Sales Product.

	Year Ended December 31,		
(in millions)	**2022**	**2021**	**2020**
INGREZZA	$ 1,427.8	$ 1,081.9	$ 993.1
ONGENTYS and other	13.1	8.2	1.0
Total net product sales	$ 1,440.9	$ 1,090.1	$ 994.1

The increases in total net product sales from 2020 to 2021 and from 2021 to 2022 primarily reflected increased INGREZZA net product sales driven by increased new patient starts and increased total prescriptions on higher customer demand and increased commercial activities.

Collaboration Revenues by Category.

	Year Ended December 31,		
(in millions)	**2022**	**2021**	**2020**
Royalties	$ 22.3	$ 22.3	$ 19.2
Milestones	20.0	15.0	30.0
Collaboration and other	5.5	6.1	2.6
Total collaboration revenue	$ 47.8	$ 43.4	$ 51.8

For 2022, total collaboration revenue primarily reflected the achievement of a $20.0 million milestone in connection with MTPC's first commercial sale of DYSVAL in Japan in June 2022 and royalties earned on AbbVie net sales of elagolix.

For 2021, total collaboration revenue primarily reflected the achievement of a $15.0 million milestone in connection with MTPC's marketing authorization application submission for valbenazine for the treatment of tardive dyskinesia in Japan and royalties earned on AbbVie net sales of elagolix.

For 2020, total collaboration revenue primarily reflected the achievement of a $30.0 million milestone in connection with AbbVie’s receipt of FDA approval of ORIAHNN for uterine fibroids and royalties earned on AbbVie net sales of elagolix.

Operating Expenses

Cost of Revenues.

(in millions)	Year Ended December 31, 2022	2021	2020
Cost of revenues	$ 23.2	$ 14.3	$ 10.1

The increases in cost of revenues from 2020 to 2021 and from 2021 to 2022 primarily reflected increased INGREZZA net product sales driven by increased new patient starts and increased total prescriptions on higher customer demand and increased commercial activities.

Research and Development by Category.

We support our drug discovery and development efforts through the commitment of significant resources to discovery, research and development programs, and business development opportunities. Costs are reflected in the applicable development stage based upon the program status when incurred. Therefore, the same program could be reflected in different development stages in the same reporting period. For several of our programs, the research and development activities are part of our collaborative arrangements.

(in millions)	Year Ended December 31, 2022	2021	2020
Late stage	$ 68.7	$ 55.7	$ 55.1
Early stage	81.1	43.9	30.2
Research and discovery	63.7	50.5	43.3
Milestones	42.7	5.4	20.0
Payroll and benefits	163.8	129.1	95.4
Facilities and other	43.8	43.5	31.0
Research and development	$ 463.8	$ 328.1	$ 275.0

Late Stage. Consists of costs incurred for product candidates in Phase II registrational studies and all subsequent activities.

For 2022 compared to 2021, the increase in late stage expenses primarily reflected continued investment in our Phase III programs for crinecerfont in CAH and valbenazine in schizophrenia.

For 2021 compared to 2020, the increase in late stage expenses primarily reflected continued investment in Phase III programs for crinecerfont in CAH and valbenazine in Huntington disease and initiation of a Phase III program for valbenazine in schizophrenia, partially offset by lower spend due to our termination of the NBIb-1817 program in Parkinson’s disease, which became effective in August 2021.

Early Stage. Consists of costs incurred for product candidates after the approval of an investigational new drug application by the applicable regulatory agency through Phase II non-registrational studies.

For 2022 compared to 2021, the increase in early stage expenses primarily reflected continued investment in our Phase II programs for NBI-921352 in epilepsy, luvadaxistat in schizophrenia, and NBI-1065845 and NBI-1065846 in major depressive disorder, and initiation of a Phase II program for NBI-1117568 in schizophrenia.

For 2021 compared to 2020, the increase in early stage expenses primarily reflected continued enrollment in our Phase II programs for NBI-827104 in EE-CSWS and essential tremor and initiation of Phase II programs for NBI-921352 in focal onset seizures and SCN8A-DEE.

Research and Discovery. Consists of expenses incurred prior to the approval of an investigational new drug application by the applicable regulatory agency.

For 2022 compared to 2021, the increase in research and discovery expenses reflected continued investment in our preclinical development programs, including psychiatry, epilepsy and gene therapy programs.

For 2021 compared to 2020, the increase in research and discovery expenses primarily reflected a full year of investment in certain of our in-licensed preclinical psychiatry and epilepsy programs, partially offset by lower spend on our preclinical gene therapy programs.

Milestones. Consist of development and regulatory milestone expenses incurred in connection with our collaborative arrangements.

In 2022, we recognized milestone expenses of $30.0 million in connection with the FDA's acceptance of our investigational new drug application for NBI-1117568 in schizophrenia, $7.3 million in connection with the FDA's acceptance of our amended KAYAK™ study protocol, and $5.0 million in connection with the approval of our clinical trial application for NBI-1070770 in major depressive disorder.

In 2021, we recognized milestone expense of $5.4 million in connection with the European Union’s approval of our clinical trial application for NBI-921352 in epilepsy.

In 2020, we recognized milestone expense of $20.0 million in connection with the FDA’s approval of ONGENTYS for Parkinson’s disease.

Payroll and Benefits. Consists of costs incurred for salaries and wages, payroll taxes, benefits and stock-based compensation associated with employees involved in research and development activities. Stock-based compensation may fluctuate from period to period based on factors that are not within our control, such as our stock price on the dates stock-based grants are issued.

For 2022 compared to 2021, the change in payroll and benefits expenses primarily reflected higher headcount, including an increase of $9.3 million in non-cash stock-based compensation expense driven by an August 2021 equity grant of approximately 0.5 million restricted stock units to our full-time employees other than our executive officers, which are vesting over a two-year period, and performance-based restricted stock units to our executive officers for which attainment of the performance-based criteria was achieved in 2022.

For 2021 compared to 2020, the change in payroll and benefits expenses primarily reflected higher headcount, including an increase of $14.7 million in non-cash stock-based compensation expense partially driven by a $6.4 million charge related to the modification of certain stock-based awards.

Facilities and Other. Consists of indirect costs incurred for the benefit of multiple programs, including depreciation, information technology, and other facility-based expenses, such as rent expense.

Acquired In-Process Research and Development, or IPR&D.

	Year Ended December 31,		
(in millions)	**2022**	**2021**	**2020**
Acquired in-process research and development	$ —	$ 105.3	$ 164.5

In 2021, we recognized $100.3 million of IPR&D expense in connection with our payment of the upfront fee pursuant to our collaboration with Heptares Therapeutics Limited.

In 2020, we recognized $46.0 million and $118.5 million, respectively, of IPR&D expenses in connection with our payments of the upfront fees pursuant to our collaborations with Idorsia Pharmaceuticals Ltd. and Takeda Pharmaceutical Limited.

Selling, General and Administrative, or SG&A.

(in millions)	Year Ended December 31, 2022	2021	2020
Selling, general and administrative	$ 752.7	$ 583.3	$ 433.3

For 2022 compared to 2021, the increase in SG&A expenses was primarily driven by continued investment in our commercial initiatives, including our branded direct-to-consumer INGREZZA advertising campaign launched in May 2021 and deployment of our expanded sales force in April 2022, reflecting increased payroll and benefits expenses on higher headcount, including an increase of $29.6 million in non-cash stock-based compensation expense partially driven by an August 2021 equity grant of approximately 0.5 million restricted stock units to our full-time employees other than our executive officers, which are vesting over a two-year period, and performance-based restricted stock units to our executive officers for which attainment of the performance-based criteria was achieved in 2022.

For 2021 compared to 2020, the increase in SG&A expenses primarily reflected increased investment in support of our commercial initiatives, including the launch of our branded direct-to-consumer INGREZZA advertising campaign in May 2021, and increased payroll and benefits expenses on higher headcount, including an increase of $19.5 million in non-cash stock-based compensation expense.

Other Expense, Net.

(in millions)	Year Ended December 31, 2022	2021	2020
Interest expense	$ (7.1)	$ (25.8)	$ (32.8)
Unrealized gain (loss) on equity securities	30.8	20.9	(17.7)
Loss on extinguishment of convertible senior notes	(70.0)	—	(18.4)
Investment income and other, net	11.2	3.8	12.6
Total other expense, net	$ (35.1)	$ (1.1)	$ (56.3)

For 2022 compared to 2021, the change in other expense, net, primarily reflected a debt extinguishment charge of $70.0 million in connection with the repurchase of our convertible senior notes in the second quarter of 2022, periodic fluctuations in the fair values of our equity security investments, decreased interest expense on lower total debt outstanding and the adoption of ASU 2020-06 on January 1, 2022, and higher yields on our debt security investments.

For 2021 compared to 2020, the change in other expense, net, primarily reflected periodic fluctuations in the fair values of our equity security investments, lower yields on our debt security investments, and a non-recurring debt extinguishment charge of $18.4 million in connection with the repurchase of our convertible senior notes in the fourth quarter of 2020.

Provision for (Benefit from) Income Taxes.

(in millions)	Year Ended December 31, 2022	2021	2020
Provision for (benefit from) income taxes	$ 59.4	$ 11.8	$ (300.6)

For 2022, the effective tax rate varied from the federal and state statutory rates primarily due to credits generated for research activities and certain nondeductible expenses, including the premium paid on the repurchase of our convertible senior notes in the second quarter of 2022. In addition, all federal net operating loss carry forwards have been fully utilized and we began making federal estimated tax payments in 2022.

For 2021, the effective tax rate varied from the federal and state statutory rates primarily due to excess tax benefits associated with stock-based compensation and credits generated for research activities. In the first quarter of 2021, we began recording a provision for income taxes using an effective tax rate that approximated federal and state statutory rates. Due to our ability to offset any pre-tax income against federal net operating losses, no federal cash tax was paid in 2021.

For 2020, the benefit from income taxes reflected a $296.3 million benefit associated with the release of substantially all of our valuation allowance against our deferred tax assets on December 31, 2020. The effective tax rate for 2020 varied from the statutory rate primarily due to changes in our valuation allowance, net of other permanent book/tax differences, tax credits generated and impacts of changes in tax laws.

Net Income.

	Year Ended December 31,		
(in millions)	**2022**	**2021**	**2020**
Net income	$ 154.5	$ 89.6	$ 407.3

For 2022 compared to 2021, the change in net income primarily reflected increased INGREZZA net product sales, lower upfront payments for asset acquisitions, continued investment in our commercial initiatives and expanded clinical portfolio, and a debt extinguishment charge of $70.0 million in connection with the repurchase of our convertible senior notes in the second quarter of 2022.

For 2021 compared to 2020, the change in net income primarily reflected increased INGREZZA net product sales driven by increased total prescriptions, decreased milestone expenses in connection with certain of our collaborative arrangements, lower upfront payments for asset acquisitions, a non-recurring debt extinguishment charge of $18.4 million in connection with the repurchase of our convertible senior notes in the fourth quarter of 2020, increased investment in our commercial initiatives and expanded clinical portfolio, and a non-recurring benefit of $296.3 million in 2020 resulting from the release of substantially all of our valuation allowance against our deferred tax assets on December 31, 2020.

Liquidity and Capital Resources

Sources of Liquidity

We believe that our existing capital resources, funds generated by anticipated INGREZZA net product sales and investment income will be sufficient to satisfy our current and projected funding requirements for at least the next 12 months. However, we cannot guarantee that our existing capital resources and anticipated revenues will be sufficient to conduct and complete all of our research and development programs or commercialization activities as planned. We may seek to access the public or private equity markets whenever conditions are favorable or pursue opportunities to obtain additional debt financing in the future. We may also seek additional funding through strategic alliances or other financing mechanisms. However, we cannot provide assurance that adequate funding will be available on terms acceptable to us, if at all. In addition, the disruption of global financial markets caused by the COVID-19 pandemic, if sustained or recurrent, could make it more difficult for us to access capital, which could in the future negatively affect our liquidity.

Information Regarding Our Financial Condition.

	December 31,	
(in millions)	**2022**	**2021**
Total cash, cash equivalents and marketable securities	$ 1,288.7	$ 1,272.0
Working Capital:		
Total current assets	$ 1,453.5	$ 972.8
Less total current liabilities	537.7	245.8
Total working capital	$ 915.8	$ 727.0

Information Regarding Our Cash Flows.

(in millions)	Year Ended December 31, 2022	2021	2020
Cash flows from operating activities	$ 339.4	$ 256.5	$ 228.5
Cash flows from investing activities	(177.1)	(130.2)	4.1
Cash flows from financing activities	(234.3)	27.4	(157.8)
Effect of exchange rate changes on cash and cash equivalents	(1.3)	—	—
Change in cash, cash equivalents and restricted cash	$ (73.3)	$ 153.7	$ 74.8

Cash Flows from Operating Activities.

For 2022 compared to 2021, the change in cash flows from operating activities primarily reflected increased INGREZZA net product sales, lower upfront payments for asset acquisitions, and continued investment in our commercial initiatives and expanded clinical portfolio. In addition, we experienced an increase in accounts receivable driven by increased INGREZZA net product sales on extended customer payment terms attributed to the expansion of our distribution network at the end of 2021 and an increase in accrued liabilities driven by increased revenue-related reserves for discounts and allowances on higher INGREZZA net product sales and the timing of payments.

For 2021 compared to 2020, the change in cash flows from operating activities primarily reflected increased INGREZZA net product sales, lower upfront payments for asset acquisitions, lower milestone payments in connection with certain of our collaborative arrangements, and increased investment in our commercial initiatives and expanded clinical portfolio.

Cash Flows from Investing Activities.

For 2022 compared to 2021, the change in cash flows from investing activities primarily reflected our acquisition of Diurnal in November 2022 for $42.7 million in cash, which is net of cash acquired, timing differences in the purchases, sales, and maturities of our marketable security investments, and a $7.7 million equity investment in Xenon associated with the FDA's acceptance of our amended KAYAK™ study protocol.

For 2021 compared to 2020, the change in cash flows from investing activities primarily reflected timing differences in the purchases, sales, and maturities of our marketable security investments and a $4.6 million equity investment in Xenon associated with the European Union's approval of our clinical trial application for NBI-921352 in focal onset seizures.

Cash Flows from Financing Activities.

For 2022 compared to 2021, the change in cash flows from financing activities primarily reflected the repurchase of $210.8 million aggregate principal amount of our convertible senior notes for an aggregate repurchase price of $279.0 million in cash in the second quarter of 2022 and increased proceeds from issuances of our common stock under benefit plans.

For 2021 compared to 2020, the change in cash flows from financing activities primarily reflected the non-recurring repurchase of $136.2 million aggregate principal amount of our convertible senior notes for an aggregate repurchase price of $186.9 million in cash in the fourth quarter of 2020.

Material Cash Requirements

In the pharmaceutical industry, it can take a significant amount of time and capital resources to successfully complete all stages of research and development and commercialize a product candidate, which ultimate length of time and spend required cannot be accurately estimated as it varies substantially according to the type, complexity, novelty and intended use of a product candidate.

The funding necessary to execute our business strategies is subject to numerous uncertainties and we may be required to make substantial expenditures if unforeseen difficulties arise in certain areas of our business. In particular, our future capital requirements will depend on many factors, including:

- the commercial success of INGREZZA, ONGENTYS, ORILISSA, ORIAHNN and/or DYSVAL;
- continued scientific progress in our research and clinical development programs;
- the magnitude and complexity of our research and development programs;
- progress with preclinical testing and clinical trials;
- the time and costs involved in obtaining regulatory approvals;
- the cost of commercialization activities and arrangements, including our advertising campaigns;
- the cost of manufacturing of our product candidates;
- 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;
- developments related to any future litigation; and
- the impact of the COVID-19 pandemic on our business.

In addition to the foregoing factors, we have significant future capital requirements, including:

External Business Developments. In addition to our independent efforts to develop and market products, we may enter into collaboration and license agreements or acquire businesses from time-to-time to enhance our drug development and commercial capabilities. With respect to our existing collaboration and license agreements, we may be required to make potential future payments of up to $10.8 billion upon the achievement of certain event-based milestones. Refer to Note 2 to the consolidated financial statements for more information on our significant collaboration and license agreements.

On November 1, 2022, we acquired Diurnal in an all-cash transaction, for an aggregate value of $55.2 million to accelerate the establishment of our clinical development and commercial capabilities in the United Kingdom to the benefit of patient communities and other stakeholders. Refer to Note 3 to the consolidated financial statements for more information on our acquisition of Diurnal.

On January 8, 2023, we entered into a new strategic collaboration with Voyager, under which we agreed to pay Voyager $175 million upfront, including a $39 million equity investment, to acquire the worldwide rights to Voyager's GBA1 gene therapy program for Parkinson's disease and other GBA1-mediated diseases and three gene therapy programs directed to rare central nervous system targets, each enabled by Voyager's next-generation TRACER™ capsids. The effectiveness of the collaboration agreement and the closing of the sale and issuance of Voyager common stock are expected to be completed prior to the end of the first quarter of 2023 and are subject to certain conditions including the expiration or termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and other customary closing conditions.

Convertible Senior Notes. On May 2, 2017, we completed a private placement of $517.5 million in aggregate principal amount of 2.25% fixed-rated convertible senior notes due May 15, 2024, or the 2024 Notes. In the fourth quarter of 2020 and second quarter of 2022, we entered into separate, privately negotiated transactions with certain holders of the 2024 Notes to repurchase $136.2 million and $210.8 million, respectively, aggregate principal amount of the 2024 Notes for an aggregate repurchase price of $186.9 million and $279.0 million, respectively, in cash. As of December 31, 2022, $170.4 million aggregate principal amount of the 2024 Notes remained outstanding.

At our election, we may redeem all or any portion of the 2024 Notes under certain circumstances. Further, as the conditional conversion feature of the 2024 Notes was triggered as of December 31, 2022, holders of the 2024 Notes may convert the 2024 Notes at any time during the period beginning on January 1, 2023, and ending at the close of business on March 31, 2023. With respect to the 2024 Notes, unless earlier converted, redeemed, or repurchased, we would be required to pay interest of $3.8 million in 2023 and $1.9 million in 2024 and pay the aggregate principal amount outstanding of $170.4 million upon maturity of the 2024 Notes.

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

Refer to Note 6 to the consolidated financial statements for more information on the 2024 Notes.

Leases. Our operating leases that have commenced have terms that expire beginning 2024 through 2031 and consist of office space and research and development laboratories, including our corporate headquarters.

On February 8, 2022, we entered into a lease agreement for a four-building campus facility to be constructed in San Diego, California, pursuant to which we also secured a six-year option for the construction of a fifth building and an option to purchase the entire campus facility, which will consist of office space and research and development laboratories, in the future. Upon completion of construction, we expect to utilize the campus facility as our new corporate headquarters and expect to begin subleasing our existing leased facilities.

Refer to Note 12 to the consolidated financial statements for more information on our leases, including a presentation of our approximate future minimum lease payments under non-cancelable operating leases.

Critical Accounting Policies and Estimates

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

The items in our financial statements requiring significant estimates and judgments are as follows:

Net Product Sales. Revenues from product sales are recorded net of reserves established for applicable discounts and allowances that are offered within contracts with our customers, payors and other third parties. The transaction price, which includes variable consideration reflecting the impact of discounts and allowances, may be subject to constraint and is included in the net sales price only to the extent that it is probable that a significant reversal of the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts may ultimately differ from our estimates. If actual results vary, we adjust these estimates, which could have an effect on earnings in the period of adjustment.

Government Rebates. We are obligated to pay rebates for mandated discounts under the Medicaid Drug Rebate Program. The liability for such rebates consists of invoices received for claims from prior quarters that remain unpaid, or for which an invoice has not been received, and estimated rebates for the current applicable reporting period, which are primarily based on actual historical rebates, estimated payor mix, state and federal regulations and related contractual terms. Estimated rebates are recorded as a reduction of revenue in the period the related sale is recognized. To date, actual government rebates have not differed materially from our estimates.

Income Taxes. Our income tax provision is computed under the asset and liability method. Significant estimates are required in determining our income tax provision. Some of these estimates are based on interpretations of existing tax laws or regulations. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Under this method, deferred tax assets and liabilities are determined on the basis of the difference between the tax basis of assets and liabilities and their respective financial reporting amounts (temporary differences) at enacted tax rates in effect for the years in which the differences are expected to reverse. A valuation allowance is established for deferred tax assets for which it is more likely than not that some portion or all of the deferred tax assets, including net operating losses and tax credits, will not be realized. We periodically re-assess the need for a valuation allowance against our deferred tax assets based on various factors including our historical earnings experience by taxing jurisdiction, and forecasts of future operating results and utilization of net operating losses and tax credits prior to their expiration. Significant judgment is required in making this assessment and, to the extent that a reversal of any portion of our valuation allowance against our deferred tax assets is deemed appropriate, a tax benefit will be recognized against our income tax provision in the period of such reversal. On December 31, 2020, based on our evaluation of various factors, such as our achievement of a cumulative three-year income position as of December 31, 2020, as well as our consideration of forecasts of future operating results and utilization of net operating losses and tax credits prior to their expiration, we released substantially all of our valuation allowance against our deferred tax assets and recorded a corresponding income tax benefit. We continue to maintain a valuation allowance against our California state deferred tax assets.

Additional Information

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

Item 7A. *Quantitative and Qualitative Disclosures About Market Risk*

Interest Rate Risk

We are exposed to interest rate risk on our short-term investments. The primary objective of our investment activities is to preserve principal while at the same time maximizing yields without significantly increasing risk. To achieve this objective, we invest in highly liquid and high-quality government and other debt securities. To minimize our exposure due to adverse shifts in interest rates, we invest in short-term securities and ensure that the maximum average maturity of our investments does not exceed 12 months. If a 1% change in interest rates were to have occurred on December 31, 2022, this change would not have had a material effect on the fair value of our investment portfolio as of that date. Due to the short holding period of our investments, we have concluded that we do not have a material financial market risk exposure.

Item 8. *Financial Statements and Supplementary Data*

NEUROCRINE BIOSCIENCES, INC.

INDEX TO THE CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Neurocrine Biosciences, Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of Neurocrine Biosciences, Inc. (the "Company") as of December 31, 2022 and 2021, the related consolidated statements of income and comprehensive income, stockholders' equity, and cash flows for each of the three years in the period ended December 31, 2022, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2022 and 2021, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2022, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the Company's internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 9, 2023 expressed an unqualified opinion thereon.

Adoption of ASU No. 2020-06

As discussed in Note 1 to the consolidated financial statements, the Company changed its method of accounting for convertible debt instruments as a result of the adoption of Accounting Standards Update (ASU) No. 2020-06, Debt – Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging – Contracts in Entity's Own Equity (Subtopic 815-40), effective January 1, 2022.

Basis for Opinion

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

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

Critical Audit Matter

The critical audit matter communicated below is a matter arising from the current period audit of the financial statements that was communicated or required to be communicated to the audit committee and that: (1) relates to accounts or disclosures that are material to the financial statements and (2) involved our especially challenging, subjective, or complex judgments. The communication of the critical audit matter does not alter in any way our opinion on the consolidated financial statements, taken as a whole, and we are not, by communicating the critical audit matter below providing a separate opinion on the critical audit matter or on the account or disclosure to which it relates.

Reserves for government rebates related to product sales

Description of the Matter

The Company sells drugs to specialty pharmacies and specialty distributors in the US (collectively, "customers"). As described in Note 1 to the consolidated financial statements, the Company recognizes revenues for sales of INGREZZA to its customers after deducting management's estimates of reserves, including drug coverage gap rebates, it will provide under government rebate programs ("government rebates"). Estimated government rebates are presented within accounts payable and accrued liabilities on the consolidated balance sheet.

Auditing the estimates of government rebates was complex and judgmental due to the level of uncertainty involved in management's assumptions used in the measurement process. In particular, management was required to estimate, for product that remains in the distribution channel at December 31, 2022, the portion of product that is expected to be subject to a government rebate and the applicable contractual government rebate percentage by payor type underlying the revenue and the applicable rebate amount applicable for the payor type.

How We Addressed the Matter in Our Audit

We tested the Company's internal controls over management's process for estimating the portion of product that is expected to be subject to a government rebate for product that remains in the distribution channel at December 31, 2022. This included controls over management's review of significant assumptions and other inputs into the estimation of government rebates including the accuracy of data used in the calculation.

To test management's estimate of government rebate reserves our audit procedures included, among others, evaluating the methodologies used, testing the significant assumptions discussed above and testing the completeness and accuracy of the underlying data used by the Company in its analyses. Specifically, we compared the significant assumptions to third-party reports used by the Company to estimate product remaining in the distribution channel at December 31, 2022. In addition, we compared the underlying government rebate percentages used in the Company's analyses to those published by the applicable government entity. We assessed the historical accuracy of management's rebate estimates, tested payments of rebates and performed a sensitivity analysis of significant assumptions to evaluate the changes in the rebate allowance that would result from changes in the assumptions.

/s/ Ernst & Young LLP

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

San Diego, California

February 9, 2023

NEUROCRINE BIOSCIENCES, INC.

CONSOLIDATED BALANCE SHEETS

(in millions, except per share data)	December 31, 2022	December 31, 2021
Assets		
Current assets:		
Cash and cash equivalents	$ 262.9	$ 340.8
Debt securities available-for-sale	726.4	370.5
Accounts receivable	350.0	185.5
Inventories	35.1	30.5
Other current assets	79.1	45.5
Total current assets	1,453.5	972.8
Deferred tax assets	305.9	315.1
Debt securities available-for-sale	299.4	560.7
Right-of-use assets	87.0	97.2
Equity securities	102.1	63.7
Property and equipment, net	58.6	58.6
Intangible assets, net	37.2	—
Other assets	25.0	4.4
Total assets	$ 2,368.7	$ 2,072.5
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable and accrued liabilities	$ 347.6	$ 225.8
Convertible senior notes	169.4	—
Other current liabilities	20.7	20.0
Total current liabilities	537.7	245.8
Convertible senior notes	—	335.1
Noncurrent operating lease liabilities	93.5	105.3
Other long-term liabilities	29.7	12.3
Total liabilities	660.9	698.5
Stockholders' equity:		
Preferred stock, $0.001 par value; 5.0 million shares authorized; no shares issued and outstanding	—	—
Common stock, $0.001 par value; 220.0 million shares authorized; 96.5 million and 94.9 million shares issued and outstanding, respectively	0.1	0.1
Additional paid-in capital	2,122.4	2,011.4
Accumulated other comprehensive loss	(7.9)	(1.7)
Accumulated deficit	(406.8)	(635.8)
Total stockholders' equity	1,707.8	1,374.0
Total liabilities and stockholders' equity	$ 2,368.7	$ 2,072.5

See accompanying notes to consolidated financial statements.

NEUROCRINE BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS INCOME

AND COMPREHENSIVE INCOME

(in millions, except per share data)	Year Ended December 31, 2022	2021	2020
Revenues:			
Product sales, net	$ 1,440.9	$ 1,090.1	$ 994.1
Collaboration revenue	47.8	43.4	51.8
Total revenues	1,488.7	1,133.5	1,045.9
Operating expenses:			
Cost of revenues	23.2	14.3	10.1
Research and development	463.8	328.1	275.0
Acquired in-process research and development	—	105.3	164.5
Selling, general and administrative	752.7	583.3	433.3
Total operating expenses	1,239.7	1,031.0	882.9
Operating income	249.0	102.5	163.0
Other (expense) income:			
Interest expense	(7.1)	(25.8)	(32.8)
Unrealized gain (loss) on equity securities	30.8	20.9	(17.7)
Loss on extinguishment of convertible senior notes	(70.0)	—	(18.4)
Investment income and other, net	11.2	3.8	12.6
Total other expense, net	(35.1)	(1.1)	(56.3)
Income before provision for (benefit from) income taxes	213.9	101.4	106.7
Provision for (benefit from) income taxes	59.4	11.8	(300.6)
Net income	154.5	89.6	407.3
Foreign currency translation adjustments	2.9	—	—
Unrealized (loss) gain on debt securities available-for-sale, net of tax	(9.1)	(3.5)	0.4
Comprehensive income	$ 148.3	$ 86.1	$ 407.7
Earnings per share, basic	$ 1.61	$ 0.95	$ 4.38
Earnings per share, diluted	$ 1.56	$ 0.92	$ 4.16
Weighted average common shares outstanding, basic	95.8	94.6	93.1
Weighted average common shares outstanding, diluted	98.9	97.9	97.8

See accompanying notes to consolidated financial statements.

NEUROCRINE BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY

(in millions)	Common Stock Shares	Common Stock $	Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders' Equity
Balances at December 31, 2019	92.3	$ 0.1	$ 1,768.1	$ 1.4	$ (1,132.7)	$ 636.9
Net income	—	—	—	—	407.3	407.3
Other comprehensive income, net of tax	—	—	—	0.4	—	0.4
Stock-based compensation expense	—	—	100.0	—	—	100.0
Equity component of repurchased convertible senior notes, net	—	—	(47.5)	—	—	(47.5)
Issuances of common stock under stock plans	1.2	—	29.1	—	—	29.1
Balances at December 31, 2020	93.5	$ 0.1	$ 1,849.7	$ 1.8	$ (725.4)	$ 1,126.2
Net income	—	—	—	—	89.6	89.6
Other comprehensive loss, net of tax	—	—	—	(3.5)	—	(3.5)
Stock-based compensation expense	—	—	134.2	—	—	134.2
Issuances of common stock under stock plans	1.4	—	27.5	—	—	27.5
Balances at December 31, 2021	94.9	$ 0.1	$ 2,011.4	$ (1.7)	$ (635.8)	$ 1,374.0
Net income	—	—	—	—	154.5	154.5
Other comprehensive loss, net of tax	—	—	—	(6.2)	—	(6.2)
Cumulative-effect adjustment due to adoption of ASU 2020-06	—	—	(106.8)	—	74.5	(32.3)
Stock-based compensation expense	—	—	173.1	—	—	173.1
Issuances of common stock under stock plans	1.6	—	44.7	—	—	44.7
Balances at December 31, 2022	96.5	$ 0.1	$ 2,122.4	$ (7.9)	$ (406.8)	$ 1,707.8

See accompanying notes to consolidated financial statements.

NEUROCRINE BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in millions)	Year Ended December 31, 2022	2021	2020
Cash flows from operating activities:			
Net income	$ 154.5	$ 89.6	$ 407.3
Adjustments to reconcile net income to net cash from operating activities:			
Stock-based compensation expense	173.1	134.2	100.0
Depreciation	15.1	10.9	8.6
Amortization of debt discount	—	16.2	20.0
Amortization of debt issuance costs	1.2	1.1	1.4
Amortization of intangible assets	0.5	—	—
Change in fair value of equity securities	(30.8)	(20.9)	17.7
Deferred income taxes	19.1	4.3	(310.7)
Loss on extinguishment of convertible senior notes	70.0	—	18.4
Other	4.1	4.4	3.7
Changes in operating assets and liabilities:			
Accounts receivable	(162.2)	(28.4)	(30.5)
Inventories	(2.6)	(2.5)	(10.7)
Accounts payable and accrued liabilities	114.6	56.8	26.9
Other assets and liabilities, net	(17.2)	(9.2)	(23.6)
Cash flows from operating activities	339.4	256.5	228.5
Cash flows from investing activities:			
Purchases of debt securities available-for-sale	(621.2)	(800.1)	(735.5)
Sales and maturities of debt securities available-for-sale	511.0	697.9	750.5
Acquisition of business, net of cash acquired	(42.7)	—	—
Purchases of equity securities	(7.7)	(4.6)	—
Capital expenditures	(16.5)	(23.4)	(10.9)
Cash flows from investing activities	(177.1)	(130.2)	4.1
Cash flows from financing activities:			
Issuances of common stock under benefit plans	44.7	27.5	29.1
Repurchases of convertible senior notes	(279.0)	(0.1)	(186.9)
Cash flows from financing activities	(234.3)	27.4	(157.8)
Effect of exchange rate changes on cash and cash equivalents	(1.3)	—	—
Change in cash and cash equivalents and restricted cash	(73.3)	153.7	74.8
Cash and cash equivalents and restricted cash at beginning of period	344.0	190.3	115.5
Cash and cash equivalents and restricted cash at end of period	$ 270.7	$ 344.0	$ 190.3
Supplemental Disclosure:			
Non-cash capital expenditures	$ 0.7	$ 1.9	$ 1.4
Right-of-use assets acquired through operating leases	$ —	$ 23.4	$ 12.8
Cash paid for interest	$ 6.6	$ 8.6	$ 11.6
Cash paid for income taxes	$ 14.4	$ 5.1	$ 15.3

See accompanying notes to consolidated financial statements.

1. Organization and Summary of Significant Accounting Policies

Organization and Business. Neurocrine Biosciences, Inc. and its subsidiaries, or Neurocrine Biosciences, the Company, we, our or us, is a neuroscience-focused biopharmaceutical company focused on discovering, developing and delivering innovative therapies to help ease the burden of debilitating disorders and diseases.

We operate in a single business segment, which includes all activities related to the research, development and commercialization of pharmaceuticals for the treatment of neurological, neuroendocrine and neuropsychiatric disorders.

Principles of Consolidation. The consolidated financial statements include the accounts of Neurocrine Biosciences as well as our wholly owned subsidiaries. All intercompany transactions and balances have been eliminated in consolidation.

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

Cash Equivalents. We consider all highly liquid investments that are readily convertible into cash without penalty and have an original maturity of three months or less at the time of purchase to be cash equivalents.

Accounts Receivable. Accounts receivable are recorded net of customer allowances for prompt payment discounts, chargebacks, and any allowance for credit losses. Our estimate for the allowance for credit losses, which has not been significant to date, is determined based on existing contractual payment terms, actual payment patterns of our customers, and individual customer circumstances.

Our exposure to credit losses may increase if our customers are adversely affected by changes in healthcare laws, coverage and reimbursement, economic pressures or uncertainty associated with local or global economic recessions, disruption associated with the current COVID-19 pandemic, or other customer-specific factors. It is possible that there could be a material adverse impact from potential adjustments of the carrying amount of trade receivables as customers' cash flows are impacted by their response to the COVID-19 pandemic.

Debt Securities. Debt securities consist of investments in certificates of deposit, corporate debt securities and securities of government-sponsored entities. We classify debt securities as available-for-sale. Debt securities available-for-sale are recorded at fair value, with unrealized gains and losses included in other comprehensive income or loss, net of tax. We exclude accrued interest from both the fair value and amortized cost basis of debt securities. A debt security is placed on nonaccrual status at the time any principal or interest payments become 90 days delinquent. Interest accrued but not received for a debt security placed on nonaccrual status is reversed against interest income.

Interest income includes amortization of purchase premium or discount. Premiums and discounts on debt securities are amortized using the effective interest rate method. Gains and losses on sales of debt securities are recorded on the trade date in investment income and other, net, and determined using the specific identification method.

Allowance for Credit Losses. For debt securities available-for-sale in an unrealized loss position, we first assess whether we intend to sell, or it is more likely than not that we will be required to sell, the security before recovery of its amortized cost basis. If either of the criteria regarding intent or requirement to sell is met, the security's amortized cost basis is written down to fair value through earnings. For debt securities available-for-sale that do not meet the aforementioned criteria, we evaluate whether the decline in fair value has resulted from credit losses or other factors. In making this assessment, we consider the extent to which fair value is less than amortized cost, any changes in interest rates, and any changes to the rating of the security by a rating agency, among other factors. If this assessment indicates that a credit loss exists, the present value of cash flows expected to be collected from the security is compared to the amortized cost basis of the security. If the present value of cash flows expected to be collected is less than the amortized cost basis, a credit loss exists and an allowance for credit losses is recorded, limited by the amount that the fair value is less than the amortized cost basis. Any impairment that has not been recorded through an allowance for credit losses is recognized in other comprehensive income or loss, as applicable.

Accrued interest receivables on debt securities available-for-sale were $4.7 million and $2.2 million, respectively, as of December 31, 2022 and 2021. We do not measure an allowance for credit losses for accrued interest receivables. For the purposes of identifying and measuring an impairment, accrued interest is excluded from both the fair value and amortized cost basis of the debt security. Uncollectible accrued interest receivables associated with an impaired debt security are reversed against interest income upon identification of the impairment. No accrued interest receivables were written off during 2022, 2021 or 2020.

Fair Value of Financial Instruments. We record cash equivalents, debt securities available-for-sale and equity security investments at fair value based on a fair value hierarchy that distinguishes between assumptions based on market data (observable inputs) and our own assumptions (unobservable inputs). The fair value hierarchy consists of the following three levels:

Level 1 – Quoted prices (unadjusted) in active markets for identical assets or liabilities.

Level 2 – Quoted prices for similar assets or liabilities in active markets, quoted prices for identical or similar assets or liabilities in markets that are not active or inputs that are observable, either directly or indirectly, for substantially the full term of the asset or liability.

Level 3 – Unobservable inputs that reflect our own assumptions about the assumptions that market participants would use in pricing the asset or liability when there is little, if any, market activity for the asset or liability at the measurement date.

Investments in debt securities available-for-sale are classified as Level 2 and carried at fair value. We estimate the fair value of debt securities available-for-sale by utilizing third-party pricing services. These pricing services utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. Such inputs include market pricing based on real-time trade data for similar instruments, issuer credit spreads, benchmark yields, broker/dealer quotes and other observable inputs. We validate valuations obtained from third-party pricing services by understanding the models used, obtaining market values from other pricing sources and analyzing data in certain instances.

We deem transfers between levels of the fair value hierarchy to have occurred at the end of the reporting period during which the event or change in circumstances that caused the transfer occurred.

Inventory. Inventory is valued at the lower of cost or net realizable value. We determine the cost of inventory using the standard-cost method, which approximates actual cost based on the first-in, first-out method. We assess the valuation of our inventory on a quarterly basis and adjust the value for excess and obsolete inventory to the extent management determines that the cost cannot be recovered based on estimates about future demand. Inventory costs resulting from these adjustments are recognized as cost of sales in the period in which they are incurred. When future commercialization is considered probable and the future economic benefit is expected to be realized, based on management’s judgment, we capitalize pre-launch inventory costs prior to regulatory approval.

Property and Equipment. Property and equipment are stated at cost and depreciated over the estimated useful lives of the assets using the straight-line method. Equipment is depreciated over an average estimated useful life of 3 to 7 years. Leasehold improvements are depreciated over the shorter of their estimated useful lives or the remaining lease term. Depreciation expense was $15.1 million for 2022, $10.9 million for 2021 and $8.6 million for 2020.

Business Combinations. Under the acquisition method of accounting, we allocate the fair value of the total consideration transferred to the tangible and identifiable intangible assets acquired and liabilities assumed based on their estimated fair values on the date of acquisition. These valuations require us to make estimates and assumptions, especially with respect to intangible assets. We record the excess consideration over the aggregate fair value of tangible and intangible assets, net of liabilities assumed, as goodwill. In addition, costs that we incur to complete the business combination, such as legal and other professional fees, are expensed as selling, general and administrative when incurred.

Goodwill, Intangible Assets and Other Long-Lived Assets. Assets acquired, including intangible assets and in-process research and development, or IPR&D, and liabilities assumed are measured at fair value as of the acquisition date. Goodwill, which has an indefinite useful life, represents the excess of cost over fair value of the net assets acquired. Intangible assets acquired in a business combination that are used for IPR&D activities are considered indefinite lived until the completion or abandonment of the associated research and development efforts. Upon reaching the end of the relevant research and development project (i.e., upon commercialization), the IPR&D asset is amortized over its estimated useful life. If the relevant research and development project is abandoned, the IPR&D asset is expensed in the period of abandonment.

Goodwill and IPR&D are not amortized; however, they are reviewed for impairment at least annually, as of October 1, and more frequently if an event occurs indicating the potential for impairment. Goodwill and IPR&D are considered to be impaired if the carrying value of the reporting unit or IPR&D asset exceeds its respective fair value.

We perform our goodwill impairment analysis at the reporting unit level, which aligns with our reporting structure and availability of discrete financial information. During the goodwill impairment review, we assess qualitative factors to determine whether it is more likely than not that the fair value of the reporting unit is less than the carrying amount, including goodwill. The qualitative factors include, but are not limited to, macroeconomic conditions, industry and market considerations, and our overall financial performance. If, after assessing the totality of these qualitative factors, we determine that it is not more likely than not that the fair value of the reporting unit is less than the carrying amount, then no additional assessment is deemed necessary. Otherwise, we proceed to compare the estimated fair value of the reporting unit with the carrying value, including goodwill. If the carrying amount of the reporting unit exceed the fair value, we record an impairment loss based on the difference. We may elect to bypass the qualitative assessment in a period and proceed to perform the quantitative goodwill impairment test.

Our identifiable intangible assets with a finite life are typically comprised of acquired product rights. The cost of identifiable intangible assets with finite lives is generally amortized on a straight-line basis over the assets' respective estimated useful lives.

We perform regular reviews to determine if any event has occurred that may indicate that intangible assets with finite useful lives and other long-lived assets are potentially impaired. If indicators of impairment exist, an impairment test is performed to assess the recoverability of the affected assets by determining whether the carrying amount of such assets exceeds the undiscounted expected future cash flows. If the affected assets are not recoverable, we estimate the fair value of the assets and record an impairment loss if the carrying value of the assets exceeds the fair value. Factors that may indicate potential impairment include a significant decline in our stock price and market capitalization compared to the net book value, significant changes in the ability of a particular asset to generate positive cash flows for our strategic business objectives, and the pattern of utilization of a particular asset.

Foreign currency. Assets and liabilities are translated into the reporting currency using the exchange rates in effect on the consolidated balance sheet dates. Equity accounts are translated at historical rates, except for the change in retained earnings during the period, which is the result of the income statement translation process. Revenue and expense accounts are translated using the weighted average exchange rate during the period. The cumulative translation adjustments associated with the net assets of foreign subsidiaries are recorded in accumulated other comprehensive income (loss) in the accompanying consolidated statements of stockholders' equity.

Revenue Recognition. We recognize revenue when the customer obtains control of promised goods or services in an amount that reflects the consideration which we expect to receive in exchange for such goods or services. Revenue is recognized using a five-step model: (i) identify contract(s) with a customer; (ii) identify the performance obligations in the contract; (iii) determine the transaction price; (iv) allocate the transaction price to the performance obligations in the contract; and (v) recognize revenues when (or as) we satisfy the performance obligation. We only apply the five-step model to contracts when it is probable that we will collect the consideration we are entitled to in exchange for the goods or services we transfer to the customer.

Net Product Sales. In the United States, we sell INGREZZA® (valbenazine) primarily to specialty pharmacy providers and distributors and ONGENTYS® (opicapone) primarily to wholesale distributors. We recognize net product sales when the customer obtains control of our product, which occurs at a point in time, typically upon delivery of our product to the customer.

Revenues from product sales are recorded net of reserves established for applicable discounts and allowances that are offered within contracts with our customers, payors, and other third parties. Such estimates are based on information received from external sources (such as written or oral information obtained from our customers with respect to their period-end inventory levels and sales to end-users during the reporting period), as supplemented by management's judgement. Our process for estimating reserves established for these variable consideration components does not differ materially from historical practices. The transaction price, which includes variable consideration reflecting the impact of discounts and allowances, may be subject to constraint and is included in the net sales price only to the extent that it is probable that a significant reversal of the amount of the cumulative revenue recognized will not occur in a future period. Actual amounts may ultimately differ from our estimates. If actual results vary, we adjust these estimates, which could have an effect on earnings in the period of adjustment.

Our significant categories of sales discounts and allowances are as follows:

Product Discounts. Product discounts are based on payment terms extended to our customers at the time of sale, which include incentives offered for prompt payment. We maintain a reserve for product discounts based on our historical experience, including the timing of customer payments. To date, actual product discounts have not differed materially from our estimates.

Government Rebates. We are obligated to pay rebates for mandated discounts under the Medicaid Drug Rebate Program. The liability for such rebates consists of invoices received for claims from prior quarters that remain unpaid, or for which an invoice has not been received, and estimated rebates for the current applicable reporting period. Such estimates are based on actual historical rebates by state, estimated payor mix, state and federal regulations, and relevant contractual terms, as supplemented by management's judgement. Our rebate accrual calculations require us to project the magnitude of our sales that will be subject to these rebates. There is a significant time-lag in our receiving rebate notices from each state (generally, several months or longer after a sale is recognized). Estimated rebates are recorded as a reduction of revenue in the period the related sale is recognized. To date, actual government rebates have not differed materially from our estimates.

Chargebacks. The difference between the list price, or the price at which we sell our products to our customers, and the contracted price, or the price at which our customers sell our products to qualified healthcare professionals, is charged back to us by our customers. In addition to actual chargebacks received, we maintain a reserve for chargebacks based on estimated contractual discounts on product inventory levels on-hand in our distribution channel. To date, actual chargebacks have not differed materially from our estimates.

Payor and Pharmacy Rebates. We are obligated to pay rebates as a percentage of sales under payor and pharmacy contracts. We estimate these rebates based on actual historical rebates, contractual rebate percentages, sales made through the payor channel, and purchases made by pharmacies. To date, actual payor and pharmacy rebates have not differed materially from our estimates.

Patient Financial Assistance. To help patients afford our products, we offer free trial vouchers to qualifying new patients and financial assistance to qualified patients with prescription drug copay requirements. We accrue for patient financial assistance based on estimated claims and the cost per claim we expect to receive in connection with inventory that remains in the distribution channel at period end. To date, actual patient financial assistance has not differed materially from our estimates.

Distributor and Other Fees. In connection with the sales of our products, we pay distributor and other fees, which are generally recorded as a reduction of revenue, to certain customers that provide us with inventory management, data, and/or distribution services. Costs associated with such services are expensed as selling, general and administrative to the extent we can demonstrate a separable benefit and fair value for such services. To date, actual distributor and other fees have not differed materially from our estimates.

Product Returns. We offer our customers product return rights primarily limited to errors in shipment, damaged product, and expiring product, provided it is within a specified period of the product expiration date, as set forth in the associated distribution agreement. Where actual returns history is not available, we estimate a returns allowance based on benchmarking data for similar products and industry experience. Such estimates are recorded as a reduction of revenue in the period the related sale is recognized. Once product is returned, it is destroyed. To date, actual product returns have not differed materially from our estimates.

Collaboration Revenues. We have entered into collaboration and license agreements under which we out-license certain rights to our product candidates to third parties. The terms of these arrangements typically include payment to us for one or more of the following: non-refundable, up-front license fees; development, regulatory, and/or commercial milestone payments; and royalties on net sales of the out-licensed products.

Licenses of Intellectual Property. If the license to our intellectual property is determined to be distinct from the other performance obligations identified in the arrangement, we recognize revenue from non-refundable, up-front fees allocated to the license when the license is transferred to the customer and the customer is able to use, and benefit from, the license. For licenses that are bundled with other promises, we assess the nature of the combined performance obligation to determine whether it is satisfied over time or at a point in time and, if over time, the appropriate method of measuring progress for purposes of recognizing revenue from non-refundable, up-front fees. We evaluate the measure of progress each reporting period and, if necessary, adjust the measure of performance and related revenue recognition.

Milestones. At the inception of each arrangement that includes development, regulatory, and/or commercial milestones, we evaluate whether achieving the milestones is considered probable and estimate the amount to be included in the transaction price using the most likely amount method. If it is probable that a significant revenue reversal would not occur, the value of the associated milestone is included in the transaction price. Amounts for milestones that are not within our control, such as when achievement of a specified event is dependent on the development activities of a third party or approvals from regulators, are not considered probable of being achieved until such specified event occurs. Revenue is recognized from the satisfaction of performance obligations in the amount billable to the customer.

Royalties. For arrangements that include sales-based royalties, and under which the license is deemed to be the predominant item to which the royalties relate, we recognize revenue at the later of (i) when the related sales occur, or (ii) when the performance obligation to which some or all of the royalty has been allocated has been satisfied (or partially satisfied). Each quarterly period, sales-based royalties are recorded based on estimated quarterly net sales of the associated collaboration products. Differences between actual results and estimated amounts are adjusted for in the period in which they become known, which typically follows the quarterly period in which the estimate was made. To date, actual royalties received have not differed materially from our estimates.

Concentration of Credit Risk. Financial instruments that potentially subject us to concentration of credit risk consist primarily of cash and cash equivalents and debt securities available-for-sale. We have established guidelines to limit our exposure to credit risk by diversifying our investment portfolio with low-risk investment-grade debt securities with maturities of up to three years and by placing our investments with high-credit-quality financial institutions to maintain liquidity. To date, we have not experienced any credit losses and do not believe we are exposed to any significant credit risk in connection with these financial instruments.

We have entered into agreements for the distribution of INGREZZA with a limited number of specialty pharmacy providers and distributors and all of our product sales of INGREZZA are to these customers. Four of these customers represented approximately 89% of our total product sales for 2022 and approximately 95% of our accounts receivable balance as of December 31, 2022.

Cost of Revenues. Cost of revenues includes third-party manufacturing, transportation, freight, and indirect overhead costs primarily for the manufacture and distribution of INGREZZA and ONGENTYS drug product sold, manufacturing costs in connection with our supply of valbenazine drug product under our collaboration with Mitsubishi Tanabe Pharma Corporation, royalty fees on net sales of elagolix, amortization of intangible assets, and adjustments for excess and obsolete inventory to the extent management determines that the cost cannot be recovered based on estimates about future demand.

Research and Development, or R&D. R&D expenses primarily consist of preclinical and clinical trial costs, payroll and benefits costs, including stock-based compensation associated with employees involved in R&D activities, certain facility-based costs, and costs associated with our collaborative arrangements, including event-based milestones. All such costs are expensed as R&D when incurred.

Asset Acquisitions. We account for acquisitions of assets (or groups of assets) that do not meet the definition of a business using the cost accumulation method, whereby the cost of the acquisition, including certain transaction costs, is allocated to the assets (or group of assets) acquired on the basis of their relative fair value(s) on the measurement date. No goodwill is recognized in an asset acquisition. Intangible assets acquired in an asset acquisition for use in R&D activities which have no alternative future use are expensed as IPR&D on the acquisition date. Future costs to develop these assets are expensed as R&D when incurred.

Advertising Expense. Advertising costs are expensed as selling, general and administrative when incurred. Advertising expense was $149.7 million for 2022, $139.8 million for 2021 and $64.8 million for 2020.

Stock-Based Compensation. We grant stock options to purchase our common stock to eligible employees and directors and also grant certain employees restricted stock units, or RSUs, and performance-based restricted stock units, or PRSUs. Additionally, we allow employees to participate in an employee stock purchase plan, or ESPP.

We estimate the fair value of stock options and shares to be issued under the ESPP using the Black-Scholes option-pricing model on the date of grant. RSUs are valued based on the closing price of our common stock on the date of grant. The fair value of equity instruments expected to vest is recognized and amortized on a straight-line basis over the requisite service period of the award, which is generally three to four years; however, certain provisions in our equity compensation plans provide for shorter vesting periods under certain circumstances. The fair value of shares to be issued under the ESPP is recognized and amortized on a straight-line basis over the purchase period, which is generally six months. PRSUs vest upon the achievement of certain predefined company-specific performance-based criteria. Expense related to PRSUs is generally recognized ratably over the expected performance period once the predefined performance-based criteria for vesting becomes probable.

Income Taxes. Our income tax provision is computed under the asset and liability method. Significant estimates are required in determining our income tax provision. Some of these estimates are based on interpretations of existing tax laws or regulations. We recognize deferred tax assets and liabilities for the expected future tax consequences of events that have been included in the financial statements or tax returns. Under this method, deferred tax assets and liabilities are determined on the basis of the difference between the tax basis of assets and liabilities and their respective financial reporting amounts (temporary differences) at enacted tax rates in effect for the years in which the differences are expected to reverse. A valuation allowance is established for deferred tax assets for which it is more likely than not that some portion or all of the deferred tax assets, including net operating losses and tax credits, will not be realized. We periodically re-assess the need for a valuation allowance against our deferred tax assets based on various factors including our historical earnings experience by taxing jurisdiction, and forecasts of future operating results and utilization of net operating losses and tax credits prior to their expiration. Significant judgment is required in making this assessment and, to the extent that a reversal of any portion of our valuation allowance against our deferred tax assets is deemed appropriate, a tax benefit will be recognized against our income tax provision in the period of such reversal.

We recognize tax benefits from uncertain tax positions only if it is more likely than not that the tax position will be sustained upon examination by the tax authorities based on the technical merits of the position. An adverse resolution of one or more of these uncertain tax positions in any period could have a material impact on the results of operations for that period.

Earnings Per Share. Basic earnings per share are computed using the weighted average number of common shares outstanding during the period. Diluted earnings per share are computed using the treasury stock method and reflect the weighted average number of common and potentially dilutive shares outstanding during the period, excluding those which effect would be anti-dilutive.

In December 2021, we entered into the First Supplemental Indenture to the 2017 Indenture, pursuant to which we irrevocably elected to settle the principal amount of the 2.25% fixed-rate convertible senior notes due May 15, 2024, or the 2024 Notes, in cash upon conversion and to settle any conversion premium in either cash or shares of our common stock. As a result, only the shares required to settle any conversion premium are considered dilutive under the if-converted method. Further, PRSUs for which the performance condition has not been achieved are excluded from the calculation of diluted earnings per share.

Recently Adopted Accounting Pronouncements.

ASU 2020-06. In August 2020, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update, or ASU, 2020-06, Debt – Debt with Conversion and Other Options (Subtopic 470-20) and Derivatives and Hedging – Contracts in Entity's Own Equity (Subtopic 815-40): Accounting for Convertible Instruments and Contracts in an Entity's Own Equity, which simplifies the accounting for certain financial instruments with characteristics of liabilities and equity, including convertible instruments and contracts in an entity's own equity. Among other changes, ASU 2020-06 removed the separation models for convertible instruments with cash or beneficial conversion features. Instead, entities now account for convertible debt instruments wholly as debt, unless certain other conditions are met. The adoption of ASU 2020-06 prospectively reduces reported interest expense and increases (decreases) reported net income (loss), and resulted in a reclassification of certain conversion feature balance sheet amounts from stockholders' equity to liabilities as it relates to the 2.25% fixed-rate convertible senior notes due May 15, 2024, or the 2024 Notes. We adopted ASU 2020-06 on January 1, 2022, using the modified retrospective transition method, which allowed for a cumulative-effect adjustment in the period of adoption and did not require restatement of prior period amounts. Under this transition method, the cumulative effect of the accounting change increased the carrying amount of the 2024 Notes by $42.2 million, reduced deferred tax liabilities by $9.9 million, reduced additional paid-in capital by $106.8 million and reduced the accumulated deficit by $74.5 million.

2. Collaboration and License Agreements

Under the terms of our existing collaboration and license agreements, we may be required to make potential future payments of up to $10.8 billion upon the achievement of certain event-based milestones. Such contingent payments are recorded when paid or payable.

Heptares Therapeutics Limited, or Heptares. We entered into a collaboration and license agreement with Heptares, which became effective in December 2021, to develop and commercialize certain compounds containing sub-type selective muscarinic M1, M4, or dual M1/M4 receptor agonists, which compounds we have the exclusive rights to develop, manufacture and commercialize worldwide, excluding in Japan, where Heptares retains the rights to develop, manufacture, and commercialize all compounds comprised of M1 receptor agonists, subject to certain exceptions. With respect to such rights retained by Heptares, we retain the rights to opt in to profit sharing arrangements, pursuant to which we and Heptares will equally share in the operating profits and losses for such compounds in Japan. Subject to specified conditions, we may elect to exercise such opt-in rights with respect to each such compound either before initiation of the first proof of concept Phase II clinical trial for such compound or following our receipt from Heptares of the top-line data from such clinical trial for such compound. We are responsible for all development, manufacturing, and commercialization costs of any collaboration product.

In connection with the agreement, we paid Heptares $100.0 million upfront, which, including certain transaction-related costs, was expensed as IPR&D in 2021. We accounted for the transaction as an asset acquisition as the set of acquired assets did not constitute a business.

In connection with the FDA's acceptance of our investigational new drug application for NBI-1117568 for the treatment of schizophrenia in June 2022, we paid Heptares a milestone of $30.0 million, which was expensed as R&D in 2022.

Under the terms of the agreement, Heptares may be entitled to receive potential future payments of up to $2.6 billion upon the achievement of certain event-based milestones and would be entitled to receive royalties on the future net sales of any collaboration product.

Unless earlier terminated, the agreement will continue on a licensed product-by-licensed product and country-by-country basis until the date on which the royalty term for such licensed product has expired in such country. On a licensed product-by-licensed product and country-by-country basis, royalty payments would commence on the first commercial sale of a licensed product and terminate on the later of (i) the expiration of the last patent covering such licensed product in such country, (ii) a number of years from the first commercial sale of such licensed product in such country and (iii) the expiration of regulatory exclusivity for such licensed product in such country.

We may terminate the agreement in its entirety or with respect to one or more targets upon 180 days' written notice to Heptares during the research collaboration term and upon 90 days' written notice to Heptares following the expiration of the research collaboration term. Following the expiration of the research collaboration term, Heptares may terminate the agreement on a target-by-target basis in the event that we do not conduct any material development activities outside of Japan with respect to a certain compound or licensed product within the applicable target class for a continuous period of not less than 365 days and do not commence any such activities within 120 days of receiving written notice. Either party may terminate the agreement, subject to specified conditions, (i) in the event of material breach by the other party, subject to a cure period, (ii) if the other party challenges the validity or enforceability of certain intellectual property rights, subject to a cure period, or (iii) if the other party becomes insolvent or takes certain actions related to insolvency.

Takeda Pharmaceutical Company Limited, or Takeda. In 2020, we entered into an exclusive license agreement with Takeda, pursuant to which we acquired the exclusive rights to develop and commercialize certain early-to-mid stage psychiatry compounds, including luvadaxistat, NBI-1065845, NBI-1065846 and four non-clinical stage compounds. Luvadaxistat and the 4 non-clinical stage compounds have each been designated as a royalty-bearing product. NBI-1065845 and NBI-1065846 are currently each designated as a profit-share product. We are responsible for all manufacturing, development, and commercialization costs of any royalty-bearing product.

With respect to NBI-1065845 and NBI-1065846, we and Takeda will equally share in the operating profits and losses. Takeda retains the rights to opt-out of the profit-sharing arrangements, pursuant to which Takeda would be entitled to receive potential future payments upon the achievement of certain event-based milestones with respect to such compounds and receive royalties on the future net sales of such compounds (in lieu of equally sharing in the operating profits and losses). Takeda may elect to exercise such opt-out right for such compound immediately following the completion of a second Phase II clinical trial for such compound, or, under certain circumstances related to the development and commercialization activities to be performed by us, before the initiation of a Phase III clinical trial for such compound.

In connection with the agreement, we paid Takeda $120.0 million upfront, which, including certain transaction-related costs, was expensed as IPR&D in 2020. We accounted for the transaction as an asset acquisition as the set of acquired assets did not constitute a business.

In connection with the approval of our clinical trial application for NBI-1070770 for the treatment of major depressive disorder in July 2022, we paid Takeda a milestone of $5.0 million, which was expensed as R&D in 2022.

Under the terms of the agreement, Takeda may be entitled to receive potential future payments of up to $1.9 billion upon the achievement of certain event-based milestones and would be entitled to receive royalties on the future net sales of any royalty-bearing product.

Unless earlier terminated, the agreement will continue on a licensed product-by-licensed product and country-by-country basis until the date on which, (i) for any royalty-bearing product, the royalty term has expired in such country; and (ii) for any profit-share product, for so long as we continue to develop, manufacture, or commercialize such licensed product. On a licensed product-by-licensed product and country-by-country basis, royalty payments would commence on the first commercial sale of a royalty-bearing product and terminate on the later of (i) the expiration of the last patent covering such royalty-bearing product in such country, (ii) a number of years from the first commercial sale of such royalty-bearing product in such country and (iii) the expiration of regulatory exclusivity for such royalty-bearing product in such country.

We may terminate the agreement in its entirety or in one or more (but not all) of the United States, Japan, the European Union and the United Kingdom, or, collectively, the major markets, upon six months' written notice to Takeda (i) with respect to all licensed products prior to the first commercial sale of the first licensed product for which first commercial sale occurs, or (ii) with respect to all licensed products in one or more given target classes, as defined in the agreement, prior to the first commercial sale of the first licensed product in such target class for which first commercial sale occurs. We may terminate the agreement in its entirety or in one or more (but not all) of the major markets upon 12 months' written notice to Takeda (i) with respect to all licensed products following the first commercial sale of the first licensed product for which first commercial sale occurs, or (ii) with respect to all licensed products in one or more given target classes following the first commercial sale of the first licensed product in such target class for which first commercial sale occurs. Takeda may terminate the agreement, subject to specified conditions, (i) if we challenge the validity or enforceability of certain Takeda intellectual property rights or (ii) on a target class-by-target class basis, in the event that we do not conduct any material development or commercialization activities with respect to any licensed product within such target class for a specified continuous period. Subject to a cure period, either party may terminate the agreement in the event of any material breach, solely with respect to the target class of a licensed product to which such material breach relates, or in its entirety in the event of any material breach that relates to all licensed products.

Idorsia Pharmaceuticals Ltd., or Idorsia. In 2020, we entered into a collaboration and license agreement with Idorsia, pursuant to which we acquired the global rights to NBI-827104, a potent, selective, orally active and brain penetrating T-type calcium channel blocker in clinical development for the treatment of a rare pediatric epilepsy and other potential indications, including essential tremor. We are responsible for all manufacturing, development, and commercialization costs of any collaboration product.

In connection with the agreement, we paid Idorsia $45.0 million upfront, which was expensed as IPR&D in 2020. We accounted for the transaction as an asset acquisition as the set of acquired assets did not constitute a business. Under the terms of the agreement, Idorsia may be entitled to receive potential future payments of up to $1.7 billion upon the achievement of certain event-based milestones and would be entitled to receive royalties on the future net sales of any collaboration product.

We may terminate the agreement, in its entirety or with respect to a particular compound or development candidate, upon 90 days' written notice to Idorsia. Further, in the event a party commits a material breach and fails to cure such material breach within 90 days after receiving written notice thereof, the non-breaching party may terminate the agreement in its entirety immediately upon written notice to the breaching party.

Xenon Pharmaceuticals Inc., or Xenon. In 2019, we entered into a collaboration and license agreement with Xenon to identify, research and develop sodium channel inhibitors, including NBI-921352 and three preclinical candidates, which compounds we have the exclusive rights to develop and commercialize. We are responsible for all development and manufacturing costs of any collaboration product, subject to certain exceptions.

In connection with the agreement, we paid Xenon $50.0 million upfront, including a purchase of approximately 1.4 million shares of Xenon common stock (at $14.196 per share). We accounted for the transaction as an asset acquisition as the set of acquired assets did not constitute a business. The purchased shares were recorded at a fair value of $14.1 million after considering Xenon's stock price on the measurement date and certain transfer restrictions applicable to the shares. The remaining $36.2 million of the purchase price, which includes certain transaction-related costs, was expensed as IPR&D in 2019.

In connection with the European Union's approval of our clinical trial application for NBI-921352 for the treatment of focal onset seizures in adults in September 2021, we paid Xenon a regulatory milestone of $10.0 million, including a purchase of approximately 0.3 million shares of Xenon common stock (at $19.9755 per share). The purchased shares were recorded at a fair value of $4.6 million after considering Xenon's stock price on the measurement date and certain transfer restrictions applicable to the shares. The remaining $5.4 million of the milestone payment was expensed as R&D in 2021.

In connection with the FDA's acceptance of our amended KAYAK™ study protocol in January 2022, we paid Xenon a regulatory milestone of $15.0 million, including a purchase of approximately 0.3 million shares of Xenon common stock (at $31.855 per share). The purchased shares were recorded at a fair value of $7.7 million after considering Xenon's stock price on the measurement date. The remaining $7.3 million of the milestone payment was expensed as R&D in 2022.

Under the terms of the agreement, Xenon may be entitled to receive potential future payments of up to $1.7 billion upon the achievement of certain event-based milestones and would be entitled to receive royalties on the future net sales of any collaboration product. Xenon retains the right to elect to co-develop one product in a major indication, pursuant to which Xenon would receive a mid-single digit percentage increase in royalties earned on the future net sales of such product in the United States and we and Xenon would equally share in the development costs of such product in the applicable indication, except where such development costs relate solely to the regulatory approval of such product outside the United States.

Unless earlier terminated, the agreement will continue on a licensed product-by-licensed product and country-by-country basis until the expiration of the royalty term for such product in such country. Upon the expiration of the royalty term for a particular licensed product and country, the license obtained by us with respect to such product and country will become fully paid, royalty free, perpetual and irrevocable. We may terminate the agreement upon 90 days' written notice to Xenon, provided that such unilateral termination will not be effective for certain products until we have used commercially reasonable efforts to complete certain specified clinical studies. Either party may terminate the agreement in the event of a material breach in whole or in part, subject to specified conditions.

Voyager Therapeutics, Inc., or Voyager. In 2019, we entered into a collaboration and license agreement with Voyager, pursuant to which we acquired certain rights to develop and commercialize the NBIb-1817 for Parkinson's disease program, Friedreich's ataxia program and two undisclosed programs. We are responsible for all development costs of any collaboration product, subject to certain co-development and co-commercialization rights retained by Voyager. In February 2021, we notified Voyager of our termination of the NBIb-1817 for Parkinson's disease program, which became effective August 2, 2021. The termination did not apply to any program other than the NBIb-1817 for Parkinson's disease program.

In connection with the agreement, we paid Voyager $165.0 million upfront, including a purchase of approximately 4.2 million shares of Voyager common stock (at $11.9625 per share). We accounted for the transaction as an asset acquisition as the set of acquired assets did not constitute a business. The purchased shares were recorded at a fair value of $54.7 million after considering Voyager's stock price on the measurement date and certain transfer restrictions applicable to the shares. The remaining $113.1 million of the purchase price, which includes certain transaction-related costs, was expensed as IPR&D in 2019. In addition, we paid Voyager $5.0 million upfront, which was expensed as IPR&D in 2019, to acquire the rights outside the United States to the Friedreich's ataxia program.

Under the terms of the agreement, Voyager may be entitled to receive potential future payments of up to $1.3 billion upon the achievement of certain event-based milestones and would be entitled to receive royalties on the future net sales of any collaboration product.

Unless terminated earlier, the agreement will continue in effect until the expiration of the last to expire royalty term with respect to any collaboration product or the last expiration or termination of any exercised co-development and co-commercialization rights by Voyager as provided for in the agreement. We may terminate the agreement upon 180 days' written notice to Voyager prior to the first commercial sale of any collaboration product or upon one year after the date of notice if such notice is provided after the first commercial sale of any collaboration product.

BIAL – Portela & Ca, S.A., or BIAL. We acquired the United States and Canada rights to ONGENTYS® (opicapone) from BIAL in 2017, and launched ONGENTYS in the United States in September 2020 as an FDA-approved add-on treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing motor fluctuations. We are responsible for all commercialization costs of ONGENTYS in the United States and Canada and rely on BIAL for the commercial supply of ONGENTYS.

Under the terms of the license agreement, BIAL may be entitled to receive potential future payments of up to $75.0 million upon the achievement of certain event-based milestones. In addition, with respect to ONGENTYS, in the event we fail to meet certain minimum sales requirements for a particular year in comparison to our annual sales forecast for such year, we would be obligated to pay BIAL an amount equal to the difference between the actual net sales and minimum sales requirements for such year. Further, upon our written request to BIAL 12 months prior to the estimated expiration of the term of a licensed product, we will negotiate the continuation of BIAL's supply of such licensed product after the term. After the term, and if BIAL is no longer supplying such licensed product, BIAL would be entitled to receive a low double-digit royalty on our future quarterly net sales of such licensed product.

Unless earlier terminated, the agreement will continue on a licensed product-by-licensed product and country-by-country basis until a generic product with respect to such licensed product 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.

We may terminate the agreement upon nine months' written notice to BIAL. BIAL may terminate the agreement in the event we fail to meet the minimum sales requirements for any two years, or under certain circumstances involving a change of control of Neurocrine Biosciences. Under certain circumstances where BIAL elects to terminate the agreement in connection with a change of control of Neurocrine Biosciences, BIAL would be obligated to pay us a termination fee. Either party may terminate the agreement 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.

Mitsubishi Tanabe Pharma Corporation, or MTPC. We out-licensed the rights to valbenazine in Japan and other select Asian markets to MTPC in 2015. In December 2020, we entered into a commercial supply agreement with MTPC, pursuant to which we agreed to supply MTPC with valbenazine drug product for commercial use in Japan and other select Asian markets. MTPC is responsible for all development, manufacturing, and commercialization costs of valbenazine in such markets.

In June 2022, MTPC launched DYSVAL® (valbenazine) in Japan for the treatment of tardive dyskinesia. In connection with MTPC's first commercial sale of DYSVAL in Japan, we received a milestone payment of $20.0 million in 2022. ASC 606 provides a royalty exception for a sales-based or usage-based royalty promised in exchange for a license of intellectual property. Under the royalty exception, the milestone would be recognized as revenue only when the later of (1) the subsequent sale or usage occurs or (2) the performance obligation to which some or all of the sales-based or usage-based royalty has been allocated has been satisfied (or partially satisfied). As the milestone related to a license of intellectual property and was contingent upon MTPC's first commercial sale of DYSVAL in Japan, the milestone was recognized as revenue in the second quarter of 2022. In addition, we receive royalties at tiered percentage rates on MTPC net sales of DYSVAL.

Under the terms of our license agreement with MTPC, we may be entitled to receive potential future payments of up to $30.0 million upon the achievement of certain sales-based milestones and are entitled to receive royalties at tiered percentage rates on future MTPC net sales of valbenazine for the longer of 10 years or the life of the related patent rights. MTPC may terminate the agreement upon 180 days' written notice to us. In such event, all out-licensed product rights would revert to us.

AbbVie Inc., or AbbVie. We out-licensed the global rights to elagolix to AbbVie in 2010. AbbVie is responsible for all development and commercialization costs of elagolix.

In August 2018, AbbVie launched ORILISSA® (elagolix tablets) in the United States for the treatment of moderate to severe pain associated with endometriosis. In June 2020, AbbVie launched ORIAHNN® (elagolix, estradiol and norethindrone acetate capsules and elagolix capsules) in the United States for the treatment of heavy menstrual bleeding related to uterine fibroids in premenopausal women. We receive royalties at tiered percentage rates on AbbVie net sales of elagolix and recognized elagolix royalty revenue of $21.2 million for 2022, $22.3 million for 2021 and $19.2 million for 2020.

Under the terms of our license agreement with AbbVie, we may be entitled to receive potential future payments of up to $366.0 million upon the achievement of certain event-based milestones and are entitled to receive royalties at tiered percentage rates on future AbbVie net sales of elagolix for the longer of 10 years or the life of the related patent rights. AbbVie may terminate the agreement upon 180 days' written notice to us. In such event, all out-licensed product rights would revert to us.

3. Diurnal Acquisition

On November 1, 2022, we completed our acquisition of Diurnal Group plc, or Diurnal, a United Kingdom-headquartered, specialty pharmaceutical company dedicated to developing hormone therapeutics to aid lifelong treatment for rare and chronic endocrine conditions, including congenital adrenal hyperplasia, adrenal insufficiency, hypogonadism and hypothyroidism. We believe our acquisition of Diurnal presents an opportunity to accelerate the establishment of our clinical development and commercial capabilities in the United Kingdom to the benefit of patient communities and other stakeholders.

The aggregate purchase price of this acquisition was $55.2 million in cash. The acquisition was accounted for in accordance with FASB ASC 805 as a Business Combinations and, accordingly, Diurnal's results of operations have been consolidated in Neurocrine Biosciences' financial statements since the date of acquisition. Pro forma results of operations for the years ended December 31, 2022 and 2021 would not be materially different as a result of this acquisition and therefore are not presented. In connection with the acquisition, we recognized transaction costs of $1.7 million, which were expensed as selling, general and administrative and primarily consisted of investment banker, advisory, legal and other professional fees.

The following table summarizes the consideration paid for Diurnal and the estimated fair values of the assets acquired and liabilities assumed at the date of acquisition.

(in millions)	Amount
Consideration	
Cash	$ 55.2
Total consideration transferred	$ 55.2
Recognized amounts of identifiable assets acquired and liabilities assumed	
Cash	$ 12.5
Intangible assets	32.6
Acquired in-process research and development	3.2
Other assets	12.4
Accounts payable and other accrued expenses	(10.7)
Total identifiable net assets acquired	$ 50.0
Goodwill	$ 5.2

4. Debt Securities

The following table presents the amortized cost, unrealized gain and loss recognized in accumulated other comprehensive income (loss) and fair value of debt securities available-for-sale, aggregated by major security type and contractual maturity.

		December 31, 2022				December 31, 2021			
(in millions)	**Contractual Maturity**	**Amortized Cost**	**Unrealized Gain**	**Unrealized Loss**	**Fair Value**	**Amortized Cost**	**Unrealized Gain**	**Unrealized Loss**	**Fair Value**
Commercial paper	0 to 1 years	$ 156.2	$ —	$ (0.2)	$ 156.0	$ 204.8	$ —	$ —	$ 204.8
Corporate debt securities	0 to 1 years	296.2	—	(3.2)	293.0	128.2	—	(0.1)	128.1
Securities of government-sponsored entities	0 to 1 years	283.4	—	(6.0)	277.4	37.6	—	—	37.6
		$ 735.8	$ —	$ (9.4)	$ 726.4	$ 370.6	$ —	$ (0.1)	$ 370.5
Corporate debt securities	1 to 3 years	$ 259.5	$ 0.2	$ (4.3)	$ 255.4	$ 358.9	$ —	$ (1.5)	$ 357.4
Securities of government-sponsored entities	1 to 3 years	45.0	—	(1.0)	44.0	204.3	—	(1.0)	203.3
		$ 304.5	$ 0.2	$ (5.3)	$ 299.4	$ 563.2	$ —	$ (2.5)	$ 560.7

As of December 31, 2022, our security portfolio consisted of 253 debt securities available-for-sale, including 199 such securities that were in an unrealized loss position but of high credit quality. Unrealized losses on these investments were primarily due to changes in interest rates. We do not intend to sell these investments and it is not more likely than not that we will be required to sell these investments before recovery of their amortized cost basis. No allowance for credit losses was recognized as of December 31, 2022 or 2021.

The following table presents debt securities available-for-sale that were in an unrealized loss position as of December 31, 2022, aggregated by major security type and length of time in a continuous loss position.

	Less Than 12 Months		12 Months or Longer		Total	
(in millions)	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss
Commercial paper	$ 32.1	$ (0.2)	$ —	$ —	$ 32.1	$ (0.2)
Corporate debt securities	$ 199.5	$ (1.9)	$ 299.1	$ (5.6)	$ 498.6	$ (7.5)
Securities of government-sponsored entities	$ 107.7	$ (2.5)	$ 198.4	$ (4.5)	$ 306.1	$ (7.0)

The following table presents debt securities available-for-sale that were in an unrealized loss position as of December 31, 2021, aggregated by major security type and length of time in a continuous loss position.

	Less Than 12 Months		12 Months or Longer		Total	
(in millions)	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss
Corporate debt securities	$ 428.6	$ (1.6)	$ —	$ —	$ 428.6	$ (1.6)
Securities of government-sponsored entities	$ 230.5	$ (1.0)	$ —	$ —	$ 230.5	$ (1.0)

5. Fair Value Measurements

The following table presents a summary of investments, which were measured at fair value on a recurring basis.

	December 31, 2022				December 31, 2021			
		Leveling				Leveling		
(in millions)	Fair Value	Level 1	Level 2	Level 3	Fair Value	Level 1	Level 2	Level 3
Cash and cash equivalents:								
Cash and money market funds	$ 262.9	$ 262.9	$ —	$ —	$ 340.8	$ 340.8	$ —	$ —
Restricted cash:								
Certificates of deposit	7.8	7.8	—	—	3.2	3.2	—	—
Debt securities available-for-sale:								
Commercial paper	156.0	—	156.0	—	204.8	—	204.8	—
Corporate debt securities	548.4	—	548.4	—	485.5	—	485.5	—
Securities of government-sponsored entities	321.4	—	321.4	—	240.9	—	240.9	—
Equity securities:								
Equity securities–biotechnology industry	102.1	102.1	—	—	63.7	52.7	—	11.0
	$ 1,398.6	$ 372.8	$ 1,025.8	$ —	$ 1,338.9	$ 396.7	$ 931.2	$ 11.0

The following table presents a reconciliation of equity security investments, which were measured at fair value on a recurring basis using significant unobservable inputs (Level 3):

	Year Ended December 31,		
(in millions)	2022	2021	2020
Balance at beginning of period	$ 11.0	$ 38.2	$ 55.9
Purchases	—	4.6	—
Unrealized gain (loss) included in earnings [1]	20.8	20.9	(17.7)
Transfers out of Level 3 [2]	(31.8)	(52.7)	—
Balance at end of period	$ —	$ 11.0	$ 38.2

(1) Unrealized gains and losses on equity security investments which were measured at fair value on a recurring basis using significant unobservable inputs (Level 3) and are included in other income (expense), net.

(2) Certain of our equity security investments were transferred from Level 3 to Level 1 during 2022 and 2021 as the associated holding period restriction expired.

6. Convertible Senior Notes

On May 2, 2017, we completed a private placement of $517.5 million in aggregate principal amount of 2.25% fixed-rate convertible senior notes due May 15, 2024, or the 2024 Notes, and entered into the 2017 Indenture with respect to the 2024 Notes. Interest on the 2024 Notes is due semi-annually on May 15 and November 15 of each year.

In accordance with authoritative guidance in effect at the time of issuance, we were required to separately account for the liability and equity components of the 2024 Notes. The initial carrying value of the liability component of $368.3 million was calculated using a 7.50% assumed borrowing rate, which reflected the market interest rate for a similar non-convertible instrument at the date of issuance. The equity component of $149.2 million, which was treated as a discount on the liability component and amortized over the seven-year term of the 2024 Notes using the effective interest rate method, was determined by deducting the fair value of the liability component from the par value of the 2024 Notes and recorded as an increase to additional paid-in capital on the issuance date. In addition, we allocated transaction costs of $14.7 million related to the issuance of the 2024 Notes to the liability and equity components based on their relative values on the issuance date. Transaction costs attributable to the liability component were being amortized over the seven-year term of the 2024 Notes using the effective interest rate method, while transaction costs attributable to the equity component were recorded as a reduction to additional paid-in capital on the issuance date.

In the fourth quarter of 2020, we entered into separate, privately negotiated transactions with certain holders of the 2024 Notes to repurchase $136.2 million aggregate principal amount of the 2024 Notes for an aggregate repurchase price of $186.9 million in cash. We accounted for the partial repurchase of the 2024 Notes as a debt extinguishment. As a result, we attributed $130.7 million of the aggregate repurchase price to the liability component based on the fair value of the liability component immediately before extinguishment. The fair value of the liability component was calculated at settlement using a discounted cash flow analysis with a discount rate of 3.37%, which was the market rate for similar notes that have no conversion rights. The difference of $56.3 million between the fair value of the aggregate consideration remitted to certain holders of the 2024 Notes and the fair value of the liability component was attributed to the reacquisition of the equity component and recorded as a reduction to additional paid-in capital. The carrying amount of the liability of $112.4 million at settlement was recognized as a reduction to the 2024 Notes and resulted in an $18.4 million loss on extinguishment, which we recognized in 2020.

On January 1, 2022, we adopted ASU 2020-06 using the modified retrospective transition method, which allowed for a cumulative-effect adjustment in the period of adoption and did not require restatement of prior period amounts. Under this transition method, the cumulative effect of the accounting change increased the carrying amount of the 2024 Notes by $42.2 million, reduced deferred tax liabilities by $9.9 million, reduced additional paid-in capital by $106.8 million, and reduced the accumulated deficit by $74.5 million.

In the second quarter of 2022, we entered into separate, privately negotiated transactions with certain holders of the 2024 Notes to repurchase $210.8 million aggregate principal amount of the 2024 Notes for an aggregate repurchase price of $279.0 million in cash. We accounted for the partial repurchase of the 2024 Notes as a debt extinguishment, which resulted in the recognition of a $70.0 million loss on extinguishment in 2022.

The following table presents a summary of the 2024 Notes as of December 31, 2022.

(in millions)	Principal Amount	Unamortized Debt		Net Carrying Amount	Fair Value	
		Discount	Issuance Costs		Amount	Leveling
2024 Notes	$ 170.4	$ —	$ (1.0)	$ 169.4	$ 268.0	Level 2

The following table presents a summary of the 2024 Notes as of December 31, 2021.

(in millions)	Principal Amount	Unamortized Debt		Net Carrying Amount	Fair Value	
		Discount	Issuance Costs		Amount	Leveling
2024 Notes	$ 381.2	$ (43.2)	$ (2.9)	$ 335.1	$ 464.7	Level 2

The following table presents a summary of the interest expense of the 2024 Notes.

(in millions)	Year Ended December 31, 2022	2021	2020
Coupon interest	$ 5.9	$ 8.5	$ 11.4
Amortization of debt discount and issuance costs	1.2	17.3	21.4
Total	$ 7.1	$ 25.8	$ 32.8

In December 2021, we entered into the First Supplemental Indenture to the 2017 Indenture, pursuant to which we irrevocably elected to settle the principal amount of the 2024 Notes in cash upon conversion and to settle any conversion premium, calculated based on the per share volume-weighted average price for each of the 30 consecutive trading days during the observation period (as more fully described in the 2017 Indenture), in either cash or shares of our common stock.

The initial conversion rate for the 2024 Notes, which is subject to adjustment in some events (as provided for in the 2017 Indenture), is 13.1711 shares of common stock per $1,000 principal amount and equivalent to an initial conversion price of approximately $75.92 per share, reflecting a conversion premium of approximately 42.5% above the closing price of $53.28 per share of our common stock on April 26, 2017.

We may redeem for cash all or part of the 2024 Notes if the last reported sale price (as defined in the 2017 Indenture) of our common stock has been at least 130% of the conversion price then in effect (equal to $98.70 as of December 31, 2022) for at least 20 trading days (whether or not consecutive) during any 30 consecutive trading-day period ending on, and including, the trading day immediately before the date which we provide notice of redemption.

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

(i) during any calendar quarter (and only during such calendar quarter), if the last reported sale price of our common stock for at least 20 trading days (whether or not consecutive) during a period of 30 consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than 130% of the conversion price (equal to $98.70 as of December 31, 2022) on each applicable trading day;

(ii) during the five business-day period immediately after any five consecutive trading-day period (the measurement period) in which the trading price (as defined in the 2017 Indenture) per $1,000 principal amount of the 2024 Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of our common stock and the conversion rate on each such trading day;

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

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

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

As the conditional conversion feature described under (i) above was triggered as of December 31, 2022, holders of the 2024 Notes may convert the 2024 Notes at any time during the period beginning on January 1, 2023, and ending at the close of business on March 31, 2023. Accordingly, the 2024 Notes have been classified as a current liability as of December 31, 2022. The future conditional convertibility of the 2024 Notes will be monitored at each quarterly reporting date and analyzed dependent upon market prices of our common stock during the prescribed measurement periods.

Upon conversion, holders will receive the principal amount of their 2024 Notes in cash and any excess conversion value, calculated based on the per share volume-weighted average price for each of the 30 consecutive trading days during the observation period (as more fully described in the 2017 Indenture), in either cash or shares of our common stock.

If we undergo a fundamental change (as defined in the 2017 Indenture), subject to certain conditions, holders of the 2024 Notes may require us to repurchase for cash all or part of their 2024 Notes at a repurchase price equal to 100% of the principal amount of the 2024 Notes to be repurchased, plus accrued and unpaid interest to, but excluding, the fundamental change repurchase date. In addition, if a make-whole fundamental change (as defined in the 2017 Indenture) occurs prior to January 15, 2024, we would, in certain circumstances, increase the conversion rate for a holder who elects to convert their notes in connection with the make-whole fundamental change.

The 2024 Notes are our general unsecured obligations that rank senior in right of payment to all of our indebtedness that is expressly subordinated in right of payment to the 2024 Notes, and equal in right of payment to our unsecured indebtedness. The 2024 Notes do not contain any financial or operating covenants or any restrictions on the payment of dividends, the issuance of other indebtedness or the issuance or repurchase of securities by us. The 2017 Indenture contains customary events of default with respect to the 2024 Notes, including that upon certain events of default, 100% of the principal and accrued and unpaid interest on the 2024 Notes will automatically become due and payable.

7. Goodwill and Intangible Assets

Goodwill

In connection with our acquisition of Diurnal in November 2022, we recognized goodwill of $5.2 million for the excess consideration transferred over the net assets acquired, reflecting the expected revenue and cost synergies of the combined company and assembled workforce.

The following table presents the changes in the carrying amount of goodwill.

(in millions)	Amount
Balance as of December 31, 2021	$ —
Goodwill recognized in connection with business combination	5.2
Foreign currency translation adjustments	0.2
Balance as of December 31, 2022	$ 5.4

Intangible Assets

The following table presents information relating to our recognized intangible assets as of December 31, 2022.

(dollars in millions)	Useful Life	Gross Carrying Amount	Accumulated Amortization	Net Carrying Amount
Developed product rights	10 years	$ 34.3	$ 0.5	$ 33.8
Acquired IPR&D	Indefinite	$ 3.4	$ —	3.4
Total intangible assets, net				$ 37.2

The following table presents the estimated annual amortization expense for our finite-lived intangible assets.

(in millions)	Amount
Year ending December 31, 2023	$ 3.5
Year ending December 31, 2024	$ 3.5
Year ending December 31, 2025	$ 3.5
Year ending December 31, 2026	$ 3.5
Year ending December 31, 2027	$ 3.5
Thereafter	$ 16.3

8. Other Balance Sheet Details

Inventories consisted of the following:

	December 31,	
(in millions)	2022	2021
Raw materials	$ 12.0	$ 11.2
Work in process	5.6	3.6
Finished goods	17.5	15.7
Total inventories	$ 35.1	$ 30.5

Property and equipment, net, consisted of the following:

(in millions)	December 31, 2022	December 31, 2021
Tenant improvements	$ 37.9	$ 34.9
Scientific equipment	58.8	51.6
Computer equipment	21.5	18.1
Furniture and fixtures	6.7	5.9
	124.9	110.5
Less accumulated depreciation	(66.3)	(51.9)
Total property and equipment, net	$ 58.6	$ 58.6

Accounts payable and accrued liabilities consisted of the following:

(in millions)	December 31, 2022	December 31, 2021
Accrued employee related costs	$ 72.8	$ 50.6
Revenue-related reserves for discounts and allowances	131.9	62.7
Accrued development costs	39.1	32.4
Current branded prescription drug fee	27.5	28.6
Accounts payable and other accrued liabilities	76.3	51.5
Total accounts payable and accrued liabilities	$ 347.6	$ 225.8

The following table presents a reconciliation of cash and cash equivalents and restricted cash reported within the consolidated balance sheets that sum to the total of the same such amounts shown in the consolidated statements of cash flows.

(in millions)	December 31, 2022	December 31, 2021
Cash and cash equivalents	$ 262.9	$ 340.8
Restricted cash	7.8	3.2
Total cash, cash equivalents and restricted cash	$ 270.7	$ 344.0

9. Earnings Per Share

Earnings per share were calculated as follows:

(in millions, except per share data)	Year Ended December 31, 2022	2021	2020
Net income - basic and diluted	$ 154.5	$ 89.6	$ 407.3
Weighted-average common shares outstanding:			
Basic	95.8	94.6	93.1
Effect of dilutive securities	3.1	3.3	4.7
Diluted	98.9	97.9	97.8
Earnings per share:			
Basic	$ 1.61	$ 0.95	$ 4.38
Diluted	$ 1.56	$ 0.92	$ 4.16

Shares which have been excluded from diluted per share amounts because their effect would have been anti-dilutive were 4.6 million for 2022, 4.1 million for 2021 and 2.5 million for 2020.

10. Stock-Based Compensation

2020 Equity Incentive Plan. In May 2022, our stockholders approved an amendment and restatement of the 2020 Equity Incentive Plan (as so amended and restated, the Amended 2020 Plan). The Amended 2020 Plan provides for the grant of stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, performance awards, and other awards. As of December 31, 2022, 7.9 million shares of common stock remain available for future grant under the Amended 2020 Plan.

Under the terms of the Amended 2020 Plan, the number of shares of common stock available for issuance will be: (i) reduced by (a) one share for each share issued pursuant to an appreciation award (as defined in the Amended 2020 Plan) granted under the Amended 2020 Plan and (b) 2.13 shares for each share issued pursuant to a full value award (as defined in the Amended 2020 Plan) granted under the Amended 2020 Plan on or after May 18, 2022; and (ii) increased by (a) one share for each share subject to an appreciation award that becomes available again for issuance under the terms of the Amended 2020 Plan and (b) 2.13 shares for each share subject to a full value award that becomes available again for issuance under the terms of the Amended 2020 Plan on or after May 18, 2022.

2011 Equity Incentive Plan. In May 2011, we adopted the 2011 Equity Incentive Plan, or the 2011 Plan. The 2011 Plan was a stockholder-approved plan pursuant to which outstanding awards have been made, but from which no further awards can or will be made.

2018 Employee Stock Purchase Plan. In May 2022, our stockholders approved an amendment and restatement of the 2018 Employee Stock Purchase Plan (as so amended and restated, the Amended 2018 ESPP). As of December 31, 2022, 0.6 million shares of common stock remain available for future issuance under the Amended 2018 ESPP.

Stock-Based Compensation Expense. The effect of stock-based compensation expense on our consolidated statements of income and comprehensive income by line-item follows:

	Year Ended December 31,		
(in millions)	**2022**	**2021**	**2020**
Selling, general and administrative expense	$ 115.4	$ 85.8	$ 66.3
Research and development expense	57.7	48.4	33.7
Total stock-based compensation expense	$ 173.1	$ 134.2	$ 100.0

Stock-based compensation expense by award-type follows:

	Year Ended December 31,		
(in millions)	**2022**	**2021**	**2020**
Stock options	$ 62.6	$ 60.5	$ 47.5
RSUs	86.4	62.5	44.2
PRSUs	20.1	7.6	5.3
ESPP	4.0	3.6	3.0
Total stock-based compensation expense	$ 173.1	$ 134.2	$ 100.0

As of December 31, 2022, unrecognized stock-based compensation expense by award-type and the weighted-average period over which such expense is expected to be recognized, as applicable, was as follows:

(dollars in millions)	**Unrecognized Expense**	**Weighted-Average Recognition Period**
Stock options	$ 106.1	2.5 years
RSUs	$ 151.4	2.3 years
PRSUs	$ 33.6	

Stock Options. Typically, stock options have a 10-year term and vest over a three to four-year period. The exercise price of stock options granted is equal to the closing price of our common stock on the date of grant. We estimate the fair value of stock options using the Black-Scholes option-pricing model on the date of grant. The Black-Scholes option-pricing model incorporates various and highly sensitive assumptions including expected volatility, term and interest rates. The weighted-average grant-date fair values of stock options granted were $32.05 for 2022, $45.02 for 2021 and $45.67 for 2020.

The fair value of each stock option granted was estimated on the date of grant using the Black-Scholes option-pricing valuation model with the following weighted-average assumptions:

	Year Ended December 31,		
	2022	2021	2020
Risk-free interest rate	1.8 %	0.6 %	1.4 %
Expected volatility of common stock	42.6 %	45.9 %	48.5 %
Dividend yield	0.0 %	0.0 %	0.0 %
Expected option term	5.0 years	5.2 years	5.3 years

The weighted-average valuation assumptions were determined as follows:

- The expected volatility of common stock is estimated based on the historical volatility of our common stock over the most recent period commensurate with the estimated expected term of our stock options.
- The expected option term is estimated based on historical experience as well as the status of the employee. For example, directors and officers have a longer expected option term than all other employees.
- The risk-free interest rate for periods within the contractual life of a stock option is based upon observed interest rates appropriate for the expected term of our employee stock options.
- We have not historically declared or paid dividends and do not intend to do so in the foreseeable future.

The following table presents summary of activity related to stock options.

(in millions, except weighted average data)	Number of Stock Options	Weighted Average Exercise Price	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at December 31, 2021	7.7	$ 76.38		
Granted	2.2	$ 81.27		
Exercised	(0.7)	$ 52.96		
Canceled	(0.2)	$ 96.28		
Outstanding at December 31, 2022	9.0	$ 79.10	6.5 years	$ 362.8
Exercisable at December 31, 2022	6.0	$ 72.27	5.4 years	$ 281.9

The total intrinsic value of stock options exercised was $39.7 million for 2022, $58.0 million for 2021 and $40.2 million for 2020. Cash received from stock option exercises was $37.0 million for 2022, $20.7 million for 2021 and $23.5 million for 2020.

Restricted Stock Units. RSUs typically vest over a four-year period and may be subject to a deferred delivery arrangement at the election of eligible employees. The fair value of RSUs is based on the closing sale price of our common stock on the date of issuance. The total fair value of RSUs that vested was $72.4 million for 2022, $64.3 million for 2021 and $49.7 million for 2020.

The following table presents a summary of activity related to RSUs.

(in millions, except weighted average data)	Number of RSUs	Weighted-Average Grant Date Fair Value	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Unvested at December 31, 2021	2.0	$ 99.96		
Granted	1.2	$ 83.01		
Released	(0.8)	$ 96.40		
Canceled	(0.1)	$ 94.05		
Unvested at December 31, 2022	2.3	$ 92.61	1.3 years	$ 276.6

Performance-Based Restricted Stock Units. PRSUs vest based on the achievement of certain predefined Company-specific performance criteria. Any unvested PRSUs will expire if it is determined the related performance criteria has not been met during the applicable three to four-year performance period. The fair value of PRSUs is estimated based on the closing sale price of our common stock on the date of grant. The fair value of PRSUs that vested during 2020 was $13.5 million. No PRSUs vested during 2021 or 2022.

The following table presents a summary of activity related to PRSUs.

(in millions, except weighted average data)	Number of PRSUs	Weighted-Average Grant Date Fair Value	Weighted-Average Remaining Contractual Term	Aggregate Intrinsic Value
Unvested at December 31, 2021	0.4	$ 109.31		
Granted	0.1	$ 80.04		
Released	—	$ —		
Canceled	—	$ —		
Unvested at December 31, 2022	0.5	$ 101.00	0.8 years	$ 60.5

Employee Stock Purchase Plan. Under the Amended 2018 ESPP, eligible employees may purchase shares of our common stock at a discount semi-annually based on a percentage of their annual compensation. The discounted purchase price is equal to the lower of 85% of (i) the market value per share of the common stock on the first day of the offering period or (ii) the market value per share of common stock on the purchase date.

11. Income Taxes

The following table presents income before the provision for income taxes from continuing domestic and foreign operations.

	Year Ended December 31,		
(in millions)	2022	2021	2020
Domestic	$ 218.0	$ 101.4	$ 106.7
Foreign	(4.1)	—	—
Income before provision for income taxes	$ 213.9	$ 101.4	$ 106.7

The following table presents the components of the provision for (benefit from) income taxes for continuing operations.

	Year Ended December 31,		
(in millions)	2022	2021	2020
Current:			
Federal	$ 17.1	$ —	$ —
State	20.3	6.3	10.1
Total current taxes	37.4	6.3	10.1
Deferred:			
Federal	27.5	5.9	(287.5)
State	(5.5)	(0.4)	(23.2)
Total deferred taxes	22.0	5.5	(310.7)
Provision for (benefit from) income taxes	$ 59.4	$ 11.8	$ (300.6)

The provision for (benefit from) income taxes on earnings subject to income taxes differs from the statutory federal rate due to the following:

	Year Ended December 31,		
(in millions)	**2022**	**2021**	**2020**
Federal income taxes at 21%	$ 44.9	$ 21.3	$ 22.4
State income tax, net of federal benefit	11.8	6.2	5.5
Branded prescription drug fee	6.5	4.8	4.9
Loss on extinguishment of convertible senior notes	12.0	—	—
Stock-based compensation expense	(2.5)	(11.3)	(6.7)
Officer compensation	9.2	7.0	3.7
Change in tax rate	(1.3)	0.2	3.3
Expired tax attributes	—	0.6	1.1
Research credits	(29.9)	(22.0)	(39.0)
Change in valuation allowance	7.4	5.0	(296.3)
Other	1.3	—	0.5
Provision for (benefit from) income taxes	$ 59.4	$ 11.8	$ (300.6)

The following table presents the significant components of our deferred tax assets.

	December 31,	
(in millions)	**2022**	**2021**
Deferred tax assets:		
Net operating losses	$ 27.4	$ 90.3
Research and development credits	108.9	129.7
Capitalized research and development	91.1	17.9
Stock-based compensation expense	45.9	38.9
Operating lease assets	26.8	29.3
Intangible assets	80.7	86.1
Other	24.9	21.6
Total deferred tax assets	405.7	413.8
Deferred tax liabilities:		
Convertible senior notes	—	(9.9)
Operating lease liabilities	(21.0)	(23.3)
Other	(11.8)	(10.7)
Total deferred tax liabilities	(32.8)	(43.9)
Net of deferred tax assets and liabilities	372.9	369.9
Valuation allowance	(67.0)	(54.8)
Net deferred tax assets	$ 305.9	$ 315.1

As of December 31, 2022, our deferred tax assets were primarily the result of net operating loss carry forwards, capitalized research costs, acquired intangible assets and tax credit carryforwards. As of December 31, 2022 and 2021, we recorded a valuation allowance of $67.0 million and $54.8 million, respectively, against our gross deferred tax asset balance.

As of each reporting date, management considers new evidence, both positive and negative, that could affect its assessment of the future realizability of our deferred tax assets. As of December 31, 2022, management determined there was sufficient positive evidence to conclude that it is more likely than not deferred tax assets of $305.9 million are realizable. The recorded valuation allowance of $67.0 million consisted primarily of state and foreign net operating loss carryforwards and state credit carryforwards for which management cannot conclude it is more likely than not to be realized.

As of December 31, 2022, we had state and foreign income tax net operating loss carryforwards of $324.6 million and $60.1 million, respectively. We had no federal income tax operating loss carryforwards as of December 31, 2022. California net operating losses will begin to expire in 2031 unless previously utilized and the net operating losses related to other states will begin to expire in 2026. Foreign net operating losses will carry forward indefinitely unless previously utilized.

As of December 31, 2022, we had federal and state R&D tax credit carryforwards of $98.2 million and $72.5 million, respectively. Federal R&D tax credits will begin to expire in 2037 unless previously utilized. California R&D tax credits carry forward indefinitely, while R&D tax credits related to other states will begin to expire in 2033 unless previously utilized.

Additionally, the future utilization of our net operating loss and R&D tax credit carryforwards to offset future taxable income may be subject to an annual limitation, pursuant to Internal Revenue Code Sections 382 and 383, as a result of ownership changes that could occur in the future. No ownership changes have occurred through December 31, 2022.

The impact of an uncertain income tax position on the income tax return must be recognized at the largest amount that is more-likely-than-not to be sustained upon audit by the relevant taxing authority. An uncertain income tax position will not be recognized if it has less than a 50% likelihood of being sustained.

We recognize interest and penalties related to income tax matters in income tax expense. As of December 31, 2022, we had accruals for interest and penalties related to income tax matters of $0.5 million and $0.4 million, respectively. Interest and penalties related to income tax matters were not material for 2021 or 2020.

We are subject to taxation in the United States and various state and foreign jurisdictions. Tax years for 2002 for federal, inception for California, 2015 to 2019 for other significant state jurisdictions, and 2019 and forward for foreign are subject to examination by tax authorities due to the carryforward of unutilized net operating losses and R&D tax credits.

The following table presents a summary of activity related to unrecognized tax benefits.

	Year Ended December 31,		
(in millions)	**2022**	**2021**	**2020**
Balance at January 1	$ 64.6	$ 60.8	$ 63.9
Increase (decrease) related to prior year tax positions	4.7	0.6	(5.7)
Increase related to current year tax positions	15.2	4.9	3.9
Settlements related to prior year tax positions	—	—	(0.2)
Expiration of the statute of limitations for the assessment of taxes	—	(1.7)	(1.1)
Balance at December 31	$ 84.5	$ 64.6	$ 60.8

As of December 31, 2022, we had $74.8 million of unrecognized tax benefits that, if recognized and realized, would affect the effective tax rate, subject to changes in the valuation allowance. We do not expect a significant change in our unrecognized tax benefits in the next 12 months.

12. Leases

Our operating leases that have commenced have terms that expire beginning 2024 through 2031 and consist of office space and research and development laboratories, including our corporate headquarters. Certain of these lease agreements contain clauses for renewal at our option. As we were not reasonably certain to exercise any of these renewal options at commencement of the associated leases, no such options were recognized as part of our operating lease right-of-use, or ROU, assets or operating lease liabilities.

On February 8, 2022, we entered into a lease agreement for a four-building campus facility to be constructed in San Diego, California, pursuant to which we also secured a six-year option for the construction of a fifth building and an option to purchase the entire campus facility, which will consist of office space and research and development laboratories, in the future. Upon completion of construction, we expect to utilize the campus facility as our new corporate headquarters. This lease has not commenced for accounting purposes. Under the terms of the lease, on a building-by-building basis, base rent will be subject to a 10-month rent abatement period following the respective lease commencement date, which dates will be determined in the future based upon achievement of substantial completion of construction with respect to each such building in the condition suitable for the installation of our furniture, fixtures, and equipment, and on which date we will record a lease liability, corresponding right-of-use asset, and begin lease expense recognition with respect to each such building. After the rent abatement period, monthly base rent will be $6 per square foot, subject to annual escalations of 3% during the initial 13.6-year lease term, which term we have the option to renew for two additional terms of five years each.

The following tables present supplemental operating lease information.

	Year Ended December 31,		
(in millions)	**2022**	**2021**	**2020**
Operating lease cost	$ 16.3	$ 15.3	$ 10.1
Cash paid for amounts included in the measurement of operating lease liabilities	$ 16.9	$ 12.6	$ 8.6

	December 31,	
(in millions, except weighted average data)	**2022**	**2021**
Weighted average remaining lease term	7.9 years	8.8 years
Weighted average discount rate	5.3 %	5.2 %
Restricted cash related to letters of credit issued in lieu of cash security deposits	$ 7.8	$ 3.2

Approximate future minimum lease payments under operating leases were as follows:

(in millions)	**Amount** [1]
Year ending December 31, 2023	$ 17.9
Year ending December 31, 2024	17.4
Year ending December 31, 2025	15.9
Year ending December 31, 2026	15.7
Year ending December 31, 2027	16.0
Thereafter	54.4
Total operating lease payments	137.3
Less accreted interest	26.4
Total operating lease liabilities	110.9
Less current operating lease liabilities included in other current liabilities	17.4
Noncurrent operating lease liabilities	$ 93.5

(1) Amounts presented in the table above exclude $17.2 million for 2024, $33.3 million for 2025, $41.9 million for 2026, and $479.7 million thereafter of approximate non-cancelable future minimum lease payments under operating leases that have not yet commenced.

13. Retirement Plan

We have a 401(k) defined contribution savings plan, or the 401(k) Plan. The 401(k) Plan is for the benefit of all qualifying employees and permits voluntary contributions by employees up to 60% of base salary limited by the IRS-imposed maximum. Employer contributions were $10.3 million for 2022, $8.1 million for 2021 and $6.7 million for 2020.

14. Legal Proceedings

During 2021 and 2022, we received notices from (i) Teva Pharmaceuticals Development, Inc., (ii) Lupin Limited, (iii) Crystal Pharmaceutical (Suzhou) Co. Ltd., (iv) Sandoz Inc. and (v) Zydus Pharmaceuticals (USA) Inc. that each company had filed an abbreviated new drug application, or ANDA, with the FDA seeking approval of a generic version of INGREZZA. These companies represented that their respective ANDAs each contained a Paragraph IV Patent Certification alleging that certain of our patents covering INGREZZA are invalid and/or will not be infringed by the manufacture, use or sale of the medicine for which the ANDA was submitted.

We filed suit in the United States District Court for the District of Delaware during 2021 and 2022, against (i) Teva Pharmaceuticals, Inc., Teva Pharmaceuticals Development, Inc., Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries Ltd. (entity dismissed), (ii) Lupin Limited, Lupin Pharmaceuticals, Inc., Lupin Inc. and Lupin Atlantis Holdings S.A., (iii) Crystal Pharmaceutical (Suzhou) Co., Ltd., Crystal Pharmatech Co., Ltd., (iv) Sandoz Inc., Sandoz International GmbH (entity dismissed) and Sandoz AG (entity dismissed) and (v) Zydus Pharmaceuticals (USA) Inc., Zydus Worldwide DMCC, Zydus Lifesciences Limited (formerly known as Cadila Healthcare Limited d/b/a Zydus Cadila) and Zydus Healthcare (USA) LLC (entity dismissed). Sandoz Inc. has been joined in the cases against Crystal Pharmaceutical (Suzhou) Co., Ltd. and Crystal Pharmatech Co., Ltd. These cases have been consolidated in the United States District Court for the District of Delaware and the trial is currently scheduled for January 2, 2024.

We also filed suit in the United States District Court for the District of New Jersey during 2021 and 2022 against Zydus Pharmaceuticals (USA) Inc., Zydus Worldwide DMCC, Zydus Lifesciences Limited (formerly known as Cadila Healthcare Limited d/b/a Zydus Cadila) and Zydus Healthcare (USA) LLC and these cases were dismissed in favor of continued prosecution of the Delaware proceedings against the same entities.

From time to time, we may also become subject to other legal proceedings or claims arising in the ordinary course of our business. We currently believe that none of the claims or actions pending against us is likely to have, individually or in the aggregate, a material adverse effect on our business, financial condition or results of operations. Given the unpredictability inherent in litigation, however, we cannot predict the outcome of these matters.

15. Subsequent Events

On January 8, 2023, we entered into a new strategic collaboration with Voyager, under which we agreed to pay Voyager $175 million upfront, including a $39 million equity investment, to acquire the worldwide rights to Voyager's GBA1 gene therapy program for Parkinson's disease and other GBA1-mediated diseases and three gene therapy programs directed to rare central nervous system targets, each enabled by Voyager's next-generation TRACER™ capsids. The effectiveness of the collaboration agreement and the closing of the sale and issuance of Voyager common stock are expected to be completed prior to the end of the first quarter of 2023 and are subject to certain conditions including the expiration or termination of the applicable waiting period under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended, and other customary closing conditions.

Item 9. *Changes and Disagreements with Accountants on Accounting and Financial Disclosure*

Not applicable.

Item 9A. *Controls and Procedures*

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

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

Management's Report on Internal Control Over Financial Reporting

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

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

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

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

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

Management has used the framework set forth in the report entitled Internal Control-Integrated Framework (2013 framework) published by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), known as COSO, to evaluate the effectiveness of our internal control over financial reporting. Based on this assessment, management has concluded that our internal control over financial reporting was effective as of December 31, 2022. Ernst & Young, LLP, our independent registered public accounting firm, has issued an attestation report on our internal control over financial reporting as of December 31, 2022, which is included herein.

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

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of Neurocrine Biosciences, Inc.

Opinion on Internal Control over Financial Reporting

We have audited Neurocrine Biosciences, Inc.'s internal control over financial reporting as of December 31, 2022, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), (the COSO criteria). In our opinion, Neurocrine Biosciences, Inc. (the Company) maintained, in all material respects, effective internal control over financial reporting as of December 31, 2022, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States) (PCAOB), the consolidated balance sheets of the Company as of December 31, 2022 and 2021, the related consolidated statements of income and comprehensive income, stockholders' equity, and cash flows, for each of the three years in the period ended December 31, 2022, and the related notes and our report dated February 9, 2023 expressed an unqualified opinion thereon.

Basis for Opinion

The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit. We are a public accounting firm registered with the PCAOB and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audit in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects.

Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

Definition and Limitations of Internal Control Over Financial Reporting

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

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

/s/ Ernst & Young LLP

San Diego, California

February 9, 2023

Item 9B. ***Other Information***

None.

Item 9C. ***Disclosure Regarding Foreign Jurisdictions that Prevent Inspections***

None.

PART III

Item 10. *Directors, Executive Officers and Corporate Governance*

Information required by this item will be contained in our Definitive Proxy Statement for our 2023 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2022. Such information is incorporated herein by reference.

We have adopted a code of ethics that applies to our Chief Executive Officer, Chief Financial Officer, and to all of our other officers, directors, employees and agents. The code of ethics is available at the Corporate Governance section of the Investors page on our website at www.neurocrine.com. We intend to disclose future amendments to, or waivers from, certain provisions of our code of ethics on the above website within four business days following the date of such amendment or waiver. Information found on, or accessible through, our website is not part of, and is not incorporated into, this Annual Report on Form 10-K.

Item 11. *Executive Compensation*

Information required by this item will be contained in our Definitive Proxy Statement for our 2023 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2022. Such information is incorporated herein by reference.

Item 12. *Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters*

Information required by this item will be contained in our Definitive Proxy Statement for our 2023 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2022. Such information is incorporated herein by reference.

Item 13. *Certain Relationships and Related Transactions, and Director Independence*

Information required by this item will be contained in our Definitive Proxy Statement for our 2023 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2022. Such information is incorporated herein by reference.

Item 14. *Principal Accounting Fees and Services*

Information required by this item will be contained in our Definitive Proxy Statement for our 2023 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2022. Such information is incorporated herein by reference.

PART IV

Item 15. *Exhibits, Financial Statement Schedules*

(a) Documents filed as part of this report.

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

Report of Independent Registered Public Accounting Firm

Consolidated Balance Sheets as of December 31, 2022 and 2021

Consolidated Statements of Income and Comprehensive Income for the years ended December 31, 2022, 2021 and 2020

Consolidated Statements of Stockholders' Equity for the years ended December 31, 2022, 2021 and 2020

Consolidated Statements of Cash Flows for the years ended December 31, 2022, 2021 and 2020

Notes to the Consolidated Financial Statements

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

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

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

Exhibit		
3.1	Description:	Certificate of Incorporation, as amended
	Reference:	Incorporated by reference to Exhibit 3.1 of the Company's Quarterly Report on Form 10-Q filed on November 5, 2018
3.2	Description:	Bylaws
	Reference:	Incorporated by reference to Exhibit 3.2 of the Company's Quarterly Report on Form 10-Q filed on May 5, 2021
4.1	Description:	Form of Common Stock Certificate
	Reference:	Incorporated by reference to the Company's Registration Statement on Form S-1 (Registration No. 333-03172)
4.2	Description:	Indenture, dated as of May 2, 2017, by and between the Company and U.S. Bank National Association, as Trustee
	Reference:	Incorporated by reference to Exhibit 4.1 of the Company's Current Report on Form 8-K filed on May 2, 2017
4.3	Description:	First Supplemental Indenture, dated as of December 22, 2021, by and between the Company and U.S. Bank National Association, as Trustee
	Reference:	Incorporated by reference to Exhibit 4.3 of the Company's Annual Report on Form 10-K filed on February 11, 2022
4.4	Description:	Form of Note representing the Company's 2.25% Convertible Notes due 2024
	Reference:	Incorporated by reference to Exhibit 99.1 of the Company's Current Report on Form 8-K filed on May 2, 2017
4.5	Description:	Description of Common Stock of the Company
	Reference:	Incorporated by reference to Exhibit 4.4 of the Company's Annual Report on Form 10-K filed on February 7, 2020
21.1	Description:	Subsidiaries of the Company
23.1	Description:	Consent of Independent Registered Public Accounting Firm
31.1	Description:	Certification of Chief Executive Officer pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934
31.2	Description:	Certification of Chief Financial Officer pursuant to Rules 13a-14 and 15d-14 promulgated under the Securities Exchange Act of 1934
32***	Description:	Certifications of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

101.INS	Description:	Inline XBRL Instance Document. – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.
101.SCH	Description:	Inline XBRL Taxonomy Extension Schema Document.
101.CAL	Description:	Inline XBRL Taxonomy Extension Calculation Linkbase Document.
101.DEF	Description:	Inline XBRL Taxonomy Extension Definition Linkbase Document.
101.LAB	Description:	Inline XBRL Taxonomy Extension Label Linkbase Document.
101.PRE	Description:	Inline XBRL Taxonomy Extension Presentation Linkbase Document.
104	Description:	Cover Page Interactive Data File (formatted as Inline XBRL with applicable taxonomy extension information contained in Exhibit 101)

Collaboration and License Agreements:

10.1**	Description:	Collaboration Agreement dated June 15, 2010, by and between Abbott International Luxembourg S.a.r.l. and the Company as amended on August 31, 2011
	Reference:	Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on May 5, 2021
10.2**	Description:	First Amendment to Collaboration and License Agreement Dated August 31, 2011 between the Company and Abbott International Luxemburg S.a.r.l.
	Reference:	Incorporated by reference to Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q filed on May 5, 2021
10.3**	Description:	Collaboration and License Agreement dated March 31, 2015 between Mitsubishi Tanabe Pharma Corporation and the Company
	Reference:	Incorporated by reference to Exhibit 10.3 of the Company's Quarterly Report on Form 10-Q filed on May 5, 2021
10.4*	Description:	Collaboration and License Agreement dated January 28, 2019 between Voyager Therapeutics, Inc. and the Company
	Reference:	Incorporated by reference to Exhibit 10.5 of the Company's Annual Report on Form 10-K filed on February 7, 2019
10.5	Description:	Stock Purchase Agreement dated January 28, 2019 between Voyager Therapeutics, Inc. and the Company
	Reference:	Incorporated by reference to Exhibit 10.6 of the Company's Annual Report on Form 10-K filed on February 7, 2019
10.6	Description:	Investor Agreement dated January 28, 2019 between Voyager Therapeutics, Inc. and the Company
	Reference:	Incorporated by reference to Exhibit 10.7 of the Company's Annual Report on Form 10-K filed on February 7, 2019
10.7	Description:	Amendment No. 1 to Collaboration and License Agreement dated June 14, 2019 between Voyager Therapeutics, Inc. and the Company
	Reference:	Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on July 29, 2019
10.8**	Description:	Exclusive License Agreement dated June 12, 2020 between Takeda Pharmaceutical Company Limited and the Company
	Reference:	Incorporated by reference to Exhibit 10.3 of the Company's Quarterly Report on Form 10-Q filed on August 3, 2020
10.9**	Description:	Collaboration and License Agreement dated November 22, 2021 between Heptares Therapeutics Limited and the Company
	Reference:	Incorporated by reference to Exhibit 10.10 of the Company's Annual Report on Form 10-K filed on February 11, 2022

Equity Plans and Related Agreements:

10.10+	Description:	Neurocrine Biosciences, Inc. 2011 Equity Incentive Plan, as amended
	Reference:	Incorporated by reference to Exhibit 99.1 of the Company's Current Report on Form 8-K filed on May 30, 2018

10.11+	Description:	Form of Stock Option Grant Notice and Option Agreement for use under the Neurocrine Biosciences, Inc. 2011 Equity Incentive Plan, and Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement for use under the Neurocrine Biosciences, Inc. 2011 Equity Incentive Plan
	Reference:	Incorporated by reference to Exhibit 99.1 of the Company's Current Report on Form 8-K filed on June 1, 2015
10.12+	Description:	Neurocrine Biosciences, Inc. Inducement Plan, as amended
	Reference:	Incorporated by reference to Exhibit 10.17 of the Company's Annual Report on Form 10-K filed on February 13, 2018
10.13+	Description:	Form of Stock Option Grant Notice and Option Agreement for use under the Neurocrine Biosciences, Inc. Inducement Plan, and Form of Restricted Stock Unit Grant Notice and Restricted Stock Unit Agreement for use under the Neurocrine Biosciences, Inc. Inducement Plan
	Reference:	Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on July 29, 2015
10.14+	Description:	Neurocrine Biosciences, Inc. 2018 Employee Stock Purchase Plan, as amended and restated
	Reference:	Incorporated by reference to Exhibit 10.3 of the Company's Quarterly Report on Form 10-Q filed on August 4, 2022
10.15+	Description:	Neurocrine Biosciences, Inc. 2020 Equity Incentive Plan, as amended and restated
	Reference:	Incorporated by reference to Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q filed on August 4, 2022
10.16+	Description:	Form of Stock Option Grant Notice and Option Agreement for use under the Neurocrine Biosciences, Inc. 2020 Equity Incentive Plan, and Form of Restricted Stock Unit Award Grant Notice and Restricted Stock Unit Award Agreement for use under the Neurocrine Biosciences, Inc. 2020 Equity Incentive Plan
	Reference:	Incorporated by reference to Exhibit 10.17 of the Company's Annual Report on Form 10-K filed on February 11, 2022

Agreements with Officers and Directors:

10.17+	Description:	Amended and Restated Employment Agreement effective August 1, 2007 between the Company and Kevin C. Gorman, Ph.D.
	Reference:	Incorporated by reference to Exhibit 10.3 of the Company's Quarterly Report on Form 10-Q filed on August 3, 2007
10.18+	Description:	Form of Amendment to Employment Agreement for executive officers, effective as of December 15, 2010
	Reference:	Incorporated by reference to Exhibit 10.32 of the Company's Annual Report on Form 10-K filed on February 11, 2008
10.19+	Description:	Employment Agreement dated May 26, 2015 between the Company and Eric Benevich
	Reference:	Incorporated by reference to Exhibit 10.3 of the Company's Annual Report on Form 10-K filed on February 14, 2017
10.20+	Description:	Employment Agreement effective November 29, 2017 between the Company and Matthew C. Abernethy
	Reference:	Incorporated by reference to Exhibit 10.26 of the Company's Annual Report on Form 10-K filed on February 13, 2018
10.21+	Description:	Form of Indemnity Agreement entered into between the Company and its officers and directors
	Reference:	Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on November 1, 2017
10.22+	Description:	Employment Agreement dated January 8, 2018 between the Company and Eiry W. Roberts, M.D.
	Reference:	Incorporated by reference to Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q filed on July 29, 2019
10.23+	Description:	Employment Agreement dated November 29, 2021 between the Company and Jude Onyia
	Reference:	Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on August 4, 2022

Agreements Related to Real Property:

10.24	Description:	Amended and Restated Lease dated November 1, 2011 between the Company and Kilroy Realty, L.P.
	Reference:	Incorporated by reference to Exhibit 99.2 of the Company's Current Report on Form 8-K filed on January 18, 2012
10.25	Description:	First Amendment to Amended and Restated Lease between the Company and Kilroy Realty, L.P., dated June 5, 2017
	Reference:	Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on August 3, 2017
10.26	Description:	Second Amendment to Amended and Restated Lease between the Company and Kilroy Realty, L.P., dated October 12, 2017
	Reference:	Incorporated by reference to Exhibit 10.3 of the Company's Quarterly Report on Form 10-Q filed on November 1, 2017
10.27	Description:	Third Amendment to Amended and Restated Lease between the Company and Kilroy Realty, L.P. dated August 7, 2019
	Reference:	Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on November 4, 2019
10.28	Description:	Commercial Lease dated February 8, 2022, by and between the Company and Gemdale Aperture Phase I, LLC
	Reference:	Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on May 4, 2022

\+ Management contract or compensatory plan or arrangement.

* Confidential treatment has been granted with respect to certain portions of the exhibit.

** Certain information in this exhibit has been omitted pursuant to Item 601 of Regulation S-K.

*** These certifications are being furnished solely to accompany this annual report pursuant to 18 U.S.C. Section 1350 and are not being filed for purposes of Section 18 of the Securities Exchange Act of 1934 and are not to be incorporated by reference into any filing of Neurocrine Biosciences, Inc., whether made before or after the date hereof, regardless of any general incorporation language in such filing.

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

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

SIGNATURES

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

NEUROCRINE BIOSCIENCES, INC.
(Registrant)

By: /s/ *Kevin C. Gorman*
Kevin C. Gorman
Chief Executive Officer

Date: February 9, 2023

By: /s/ *Matthew C. Abernethy*
Matthew C. Abernethy
Chief Financial Officer

Date: February 9, 2023

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Kevin C. Gorman and Matthew C. Abernethy, and each of them, as his or her true and lawful attorneys-in-fact and agents, with full power of substitution for him or her, and in his or her name in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power of authority to do and perform each and every act and thing requisite and necessary to be done therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, and any of them, his or her substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed by the following persons on behalf of the Registrant and in the capacities indicated as of February 9, 2023:

Signature	**Title**
/s/ *Kevin C. Gorman* Kevin C. Gorman, Ph.D.	Chief Executive Officer and Director *(Principal Executive Officer)*
/s/ *Matthew C. Abernethy* Matthew C. Abernethy	Chief Financial Officer *(Principal Financial and Accounting Officer)*
/s/ *William H. Rastetter* William H. Rastetter, Ph.D.	Chairman of the Board of Directors
/s/ *Gary A. Lyons* Gary A. Lyons	Director
/s/ *Johanna Mercier* Johanna Mercier	Director
/s/ *George J. Morrow* George J. Morrow	Director
/s/ *Leslie V. Norwalk* Leslie V. Norwalk	Director
/s/ *Richard F. Pops* Richard F. Pops	Director
/s/ *Shalini Sharp* Shalini Sharp	Director
/s/ *Stephen A. Sherwin* Stephen A. Sherwin, M.D.	Director

Exhibit 21.1

NEUROCRINE BIOSCIENCES INC. SUBSIDIARIES

Name of Subsidiary	**Jurisdiction**
Neurocrine Continental, Inc.	Delaware, USA
Neurocrine Europe, Ltd.	Ireland
Neurocrine Therapeutics, Ltd.	Ireland
Neurocrine UK Limited	England and Wales
Diurnal Group Limited	England and Wales
Diurnal Limited	England and Wales
Diurnal Europe B.V.	The Netherlands

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statements (Form S-8 Nos. 333-175889, 333-190178, 333-197916, and 333-212871) pertaining to the 2011 Equity Incentive Plan of Neurocrine Biosciences, Inc.,

(2) Registration Statements (Form S-8 Nos. 333-199837, and 333-216067) pertaining to the Inducement Plan of Neurocrine Biosciences, Inc.,

(3) Registration Statements (Form S-8 Nos. 333-205933 and 333-223020) pertaining to the 2011 Equity Incentive Plan and Inducement Plan of Neurocrine Biosciences, Inc.,

(4) Registration Statements (Form S-8 No. 333-226971) pertaining to the 2011 Equity Incentive Plan and 2018 Employee Stock Purchase Plan of Neurocrine Biosciences, Inc.,

(5) Registration Statements (Form S-8 No. 333-234501) pertaining to the 2011 Equity Incentive Plan of Neurocrine Biosciences, Inc.,

(6) Registration Statements (Form S-8 No. 333-240301) pertaining to the 2020 Equity Incentive Plan of Neurocrine Biosciences, Inc., and

(7) Registration Statements (Form S-8 No. 333-266530) pertaining to the 2020 Equity Incentive Plan and 2018 Employee Stock Purchase Plan of Neurocrine Biosciences, Inc.

of our reports dated February 9, 2023 with respect to the consolidated financial statements of Neurocrine Biosciences, Inc., and the effectiveness of internal control over financial reporting of Neurocrine Biosciences, Inc., included in this Annual Report (Form 10-K) of Neurocrine Biosciences, Inc. for the year ended December 31, 2022.

/s/ Ernst & Young LLP

San Diego, California
February 9, 2023

Exhibit 31.1

CERTIFICATION OF CHIEF EXECUTIVE OFFICER PURSUANT
TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Kevin C. Gorman, Chief Executive Officer of Neurocrine Biosciences, Inc., certify that:

1. I have reviewed this annual report on Form 10-K of Neurocrine Biosciences, Inc.;

2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this annual report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this annual report based on such evaluation; and

   d) Disclosed in this annual report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of the internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent function):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls over financial reporting.

Dated: February 9, 2023

/s/ *Kevin C. Gorman*
Kevin C. Gorman
Chief Executive Officer

Exhibit 31.2

CERTIFICATION OF CHIEF FINANCIAL OFFICER PURSUANT
TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Matthew C. Abernethy, Chief Financial Officer of Neurocrine Biosciences, Inc., certify that:

1. I have reviewed this annual report on Form 10-K of Neurocrine Biosciences, Inc.;

2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;

3. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this annual report based on such evaluation; and

   d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of the internal control over financial reporting, to the registrant's auditors and the audit committee of registrant's board of directors (or persons performing the equivalent function):

   a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal controls over financial reporting.

Dated: February 9, 2023

/s/ *Matthew C. Abernethy*
Matthew C. Abernethy
Chief Financial Officer

Exhibit 32

CERTIFICATIONS OF
CHIEF EXECUTIVE OFFICER AND CHIEF FINANCIAL OFFICER
PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Neurocrine Biosciences, Inc. (the "Company") for the year ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Kevin C. Gorman, Chief Executive Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d), of the Securities Exchange Act of 1934; and

(2) That information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

February 9, 2023

By: /s/ *Kevin C. Gorman*
Name: Kevin C. Gorman
Title: Chief Executive Officer

In connection with the Annual Report on Form 10-K of Neurocrine Biosciences, Inc. (the "Company") for the year ended December 31, 2022 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Matthew C. Abernethy, Chief Financial Officer of the Company, certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d), of the Securities Exchange Act of 1934; and

(2) That information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

February 9, 2023

By: /s/ *Matthew C. Abernethy*
Name: Matthew C. Abernethy
Title: Chief Financial Officer