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, 2021

☐ 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 ☐

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, 2021, was approximately $9,105,256,378.

As of February 7, 2022, 95,242,683 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, 2021 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

At Neurocrine Biosciences, our purpose is simple: to relieve suffering for people with great needs, but few options. For three decades, we have applied our unique insight into neuroscience to advance medicines for neurology, neuroendocrinology and neuropsychiatry-related disorders and diseases. Our efforts have resulted in 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 investigational therapies with the potential to address unmet clinical needs of patients worldwide living with neurological, endocrine and psychiatric disorders. *(*in collaboration with AbbVie Inc., or AbbVie)*

Impact of COVID-19

The COVID-19 pandemic has dramatically changed the ways in which we live and interact with one another. While we adapt to this new shared reality, our purpose remains unchanged: to relieve suffering for people with great needs, but few options.

Although the initial impact of the pandemic has subsided, we are uncertain as to how more transmissible variants may impact our business. 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 clinical studies.

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 arrangement 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, a remote work model may nevertheless need to be reinstated at some point in the future. We continue to evaluate the impact of global spikes or surges in COVID-19 infection and hospitalization rates, as well as the impact of emerging COVID-19 variants on the efficacy of vaccines.

Most hospitals, community mental health facilities, physicians' offices, pharmacies and other healthcare facilities have relaxed their policies that limited access of patients and our employees to such facilities and limited the ability of patients, pharmacies and prescribers to interact with each other. However, we anticipate these policies may change from time to time as communities or regions grapple with outbreaks. The ultimate impact of the COVID-19 pandemic, including any lasting effects on our revenue and the way we conduct our business, is highly uncertain and subject to continued change. We recognize that this pandemic will continue to present unique challenges for us throughout 2022.

Product Pipeline

Commercially Available Medicines

* Mitsubishi Tanabe Pharma has commercialization rights in East Asia. ‡ Under License from BIAL.

† AbbVie has global commercialization rights.

INGREZZA® (valbenazine). We launched INGREZZA in the United States in May 2017 as the first FDA-approved drug for the treatment of tardive dyskinesia. INGREZZA net product sales totaled $1.1 billion for 2021, $993.1 million for 2020 and $752.9 million for 2019 and represent the significant majority 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.

We out-licensed the rights to valbenazine in Japan and other select Asian markets to Mitsubishi Tanabe Pharmaceutical Company, or MTPC, in 2015, in which markets valbenazine is a royalty-bearing product for us. In 2021, MTPC received approvals for marketing authorization for valbenazine for the treatment of tardive dyskinesia in Indonesia, Singapore, South Korea and Thailand. In addition, MTPC has submitted filings for marketing authorization, which are currently under review, in Japan and Malaysia.

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.

ONGENTYS is a once-daily, peripheral, selective and reversible catechol-O-methyltransferase, or COMT, inhibitor. COMT inhibitors are utilized to prolong the duration of effect of levodopa, the primary treatment option for Parkinson's disease patients, during periods of the day where the effects of levodopa wear off and motor symptoms worsen, also known as "off" time.

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.

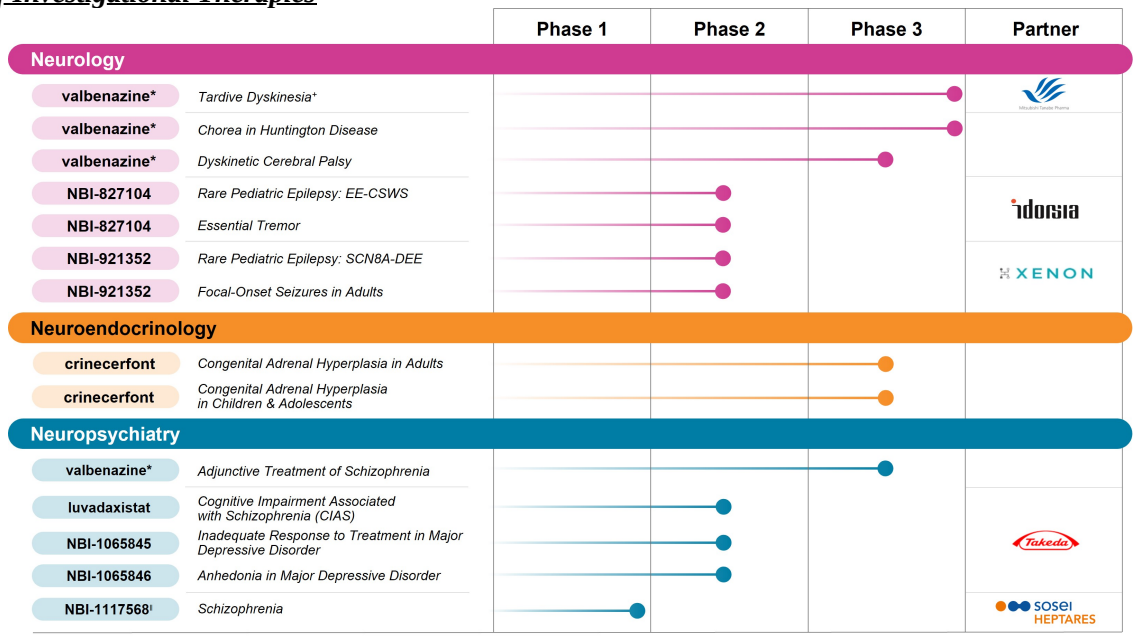
ORILISSA® (elagolix tablets). AbbVie launched ORILISSA in the United States in August 2018 as an FDA-approved oral medication for the management of moderate to severe endometriosis pain in women. We out-licensed the global rights to elagolix to AbbVie in 2010. Elagolix is a royalty-bearing product for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

Our Pipeline of Investigational Therapies



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.

+ In 2021, MTPC received approvals for marketing authorization for valbenazine for the treatment of tardive dyskinesia in Indonesia, Singapore, South Korea and Thailand. In addition, MTPC has submitted filings for marketing authorization, which are currently under review, in Japan and Malaysia.

‖ In-licensed from Sosei Heptares.

Neurology

Chorea in Huntington Disease (valbenazine – VMAT2 Inhibitor). We have announced positive top-line data from the KINECT-HD study, a Phase III randomized, double-blind, placebo-controlled clinical study evaluating the efficacy, safety, and tolerability of valbenazine in 120 adult patients with chorea in Huntington disease. The study met the primary endpoint of reduction in severity of chorea, the cardinal motor feature in Huntington disease, as measured by the change in the Unified Huntington's Disease Rating Scale, or UHDRS®, total maximal chorea, or TMC, score from baseline to the average score at weeks 10 and 12. Treatment with valbenazine resulted in a placebo-adjusted mean reduction in the TMC score of 3.2 units ($p < 0.0001$), indicating a highly statistically significant improvement in chorea. The TMC score is part of the motor assessment of the UHDRS and measures chorea in seven different body parts, including the face, oral-buccal-lingual region, trunk, and each limb independently. The TMC score is the sum of the individual scores and ranges from 0 to 28. The secondary endpoints of Clinical Global Impression of Change (CGI-C) Response Status and Patient Global Impression of Change (PGI-C) Response Status were also statistically significant in favor of treatment with valbenazine. We plan to submit a supplemental new drug application for valbenazine for the treatment of Huntington chorea with the FDA in the second half of 2022.

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. In neurology, disease states such as tardive dyskinesia, Huntington chorea and tardive dystonia are characterized in part by a hyperdopaminergic state in the brain and modulation of neuronal dopamine levels may provide symptomatic benefits for patients with these conditions, among others. 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.

Dyskinetic Cerebral Palsy (valbenazine – VMAT2 Inhibitor). 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 144 pediatric and adult patients (aged 6 and older). We anticipate having top-line data for this clinical study in 2023.

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. In neurology, disease states such as tardive dyskinesia, Huntington chorea and tardive dystonia are characterized in part by a hyperdopaminergic state in the brain and modulation of neuronal dopamine levels may provide symptomatic benefits for patients with these conditions, among others. 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.

Essential Tremor (NBI-827104 – T-Type Calcium Channel Blocker). We have initiated a Phase II randomized, double-blind, placebo-controlled, crossover clinical study to evaluate the efficacy, safety, tolerability and pharmacokinetics of NBI-827104 in 28 adult patients with essential tremor. We anticipate having top-line data from this clinical study during the middle of 2022.

NBI-827104 is a potent, selective, orally active and brain penetrating T-type calcium channel blocker. We acquired the global rights to NBI-827104 in May 2020. Essential tremor is one of the most common neurological disorders in adults. The disorder is characterized by involuntary, rhythmic, oscillatory movements that most often affect the upper limbs. As the disease progresses, tremor severity often increases and spreads to other parts of the body. Essential tremor has a significant impact on the activities of daily living often resulting in functional disability as the disease progresses and is associated with a high comorbidity rate of social phobia, depression and anxiety. Essential tremor affects an estimated 10 million people 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 per year to several per day A description of our investigational treatments for potential use in epilepsy follow.

Epileptic Encephalopathy with Continuous Spike and Wave During Sleep, or EE-CSWS (NBI-827104 – T-Type Calcium Channel Blocker). We have initiated the STEAMBOAT™ study, a Phase II multi-center, randomized, double-blind, placebo-controlled, parallel-group clinical study to evaluate the efficacy, safety, tolerability and pharmacokinetics of NBI-827104 in 24 pediatric patients (aged 4 to 12 years) with EE-CSWS, a rare pediatric form of epilepsy. We anticipate having top-line data from this clinical study during the second half of 2022.

NBI-827104 is a potent, selective, orally active and brain penetrating T-type calcium channel blocker. Due to the differentiated mechanism of action of this molecule, when compared to non-selective calcium channel inhibitors, treatment with NBI-827104 could lead to an enhanced benefit risk profile for patients with this rare pediatric form of epilepsy. We acquired the global rights to NBI-827104 in May 2020. EE-CSWS is a rare pediatric form of epilepsy. The typical onset of EE-CSWS occurs in children (aged 2 to 4 years) with a variety of seizure types, including atypical absence seizures, generalized tonic-clonic seizures and focal seizures, that occur primarily during sleep. Seizures associated with EE-CSWS, which often resolve around puberty, interfere with processes critical to learning and memory. Children with EE-CSWS often present with neurocognitive regression that can remain even after the seizures associated with EE-CSWS have resolved. It is estimated that EE-CSWS affects less than 2% of the estimated 470,000 children with active epilepsy in the United States.

SCN8A-DEE (NBI-921352 – Nav1.6 Sodium Channel Inhibitor). 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. The FDA has granted us orphan drug and rare pediatric disease designations for NBI-921352 in SCN8A-DEE.

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. 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.

Focal Onset Seizures (NBI-921352 – Nav1.6 Sodium Channel Inhibitor). 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 2023.

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. 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

Congenital Adrenal Hyperplasia, or CAH.

Classic CAH in Adults (crinecerfont – CRF1 Antagonist). We have initiated 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 classic CAH, followed by an open-label treatment period. We anticipate having top-line data for this clinical study in 2023.

Classic CAH in Pediatrics (crinecerfont – CRF1 Antagonist). We have initiated 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 classic CAH. We anticipate having top-line data for this clinical study in 2023.

We have been granted orphan drug designation for crinecerfont in the treatment of classic CAH in the United States and the European Union. 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 classic CAH. Lower ACTH levels would also reduce the amount of exogenous corticosteroid necessary for classic CAH patients to thrive avoiding the side-effects currently associated with excessive steroid therapy. Corticosteroids are the current standard of care for classic CAH and are used chronically to both correct the endogenous cortisol deficiency and to reduce the excessive ACTH levels and androgen excess. However, the dose and duration of steroid use required to suppress ACTH is well above the normal physiological level of cortisol; resulting in metabolic syndrome, bone loss, growth impairment and Cushing's syndrome as common and serious side effects. Classic CAH refers to a group of autosomal recessive genetic conditions that result in an enzyme deficiency that alters the production of adrenal hormones. If left untreated, classic CAH can result in salt wasting, dehydration and eventually death. Even with cortisol replacement, persistent elevation of ACTH from the pituitary gland results in excessive androgen levels, leading to virilization of females including precocious puberty, menstrual irregularity, short stature, hirsutism, acne and fertility problems. Classic CAH affects an estimated 30,000 people in the United States and 50,000 people in the European Union.

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 follow.

Adjunctive Treatment of Schizophrenia (valbenazine – VMAT2 Inhibitor). We have 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 2023.

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. In psychiatry, disease states such as schizophrenia are characterized in part by a hyperdopaminergic state in the brain and modulation of neuronal dopamine levels may provide symptomatic benefits for patients with this condition, among others. 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). We plan to submit an investigational new drug application and initiate a placebo-controlled Phase II clinical study of NBI-1117568 as a potential treatment for schizophrenia in 2022. 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. 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). 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.

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. 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 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 follow.

Inadequate Response to Treatment in Major Depressive Disorder (NBI-1065845 – AMPA Potentiator). 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 2023.

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, also known as treatment-resistant depression. 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. Major depressive disorder is one of the leading causes of disability. 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 – GPR Agonist). 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 2023.

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. 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.

Business Strategy

Commercializing Our Product Portfolio. We launched INGREZZA in the United States in May 2017 as the first FDA-approved drug for the treatment of tardive dyskinesia. In September 2020, we launched ONGENTYS in the United States as an FDA-approved add-on treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing motor fluctuations. Our experience in marketing and selling pharmaceutical products began with INGREZZA's approval in 2017, when we hired our salesforce and established our distribution and reimbursement capabilities, all of which are necessary to successfully commercialize our marketed products and products candidates. Our specialty salesforce in the United States consists of approximately 250 experienced sales professionals focused on educating healthcare professionals, including psychiatrists and neurologists, who treat patients with tardive dyskinesia and Parkinson's disease. In the third quarter of 2021, we announced an expansion of our specialty salesforce, which is expected to be completed in the second quarter of 2022, to approximately 350 experienced sales professionals that will establish three dedicated sales teams focused on psychiatry, neurology and providers in long-term care, respectively. Our commercial team is comprised of experienced professionals in marketing, access and reimbursement, managed markets, market research, commercial operations and salesforce planning and management. In addition, our commercial infrastructure includes capabilities in manufacturing, medical affairs, quality control and compliance. We intend to retain commercial rights to certain products, including INGREZZA, that we can effectively and efficiently develop, secure regulatory approval and commercialize, which includes products with a concentrated prescriber base and well-defined patient population that can be accessed with an efficient patient and prescriber outreach program.

Advancing Life-Changing Discoveries in Neurology, Neuroendocrinology and Neuropsychiatry. We believe that by continuing to advance and expand our product pipeline, we can mitigate some of the risks associated with drug development. We currently have multiple programs in various stages of research and development, including symptomatic disease modifying treatments. We take a portfolio approach to managing our pipeline that balances the size of market opportunities with clear and defined clinical and regulatory paths to approval. By doing so, we focus our internal development resources on innovative therapies with improved probabilities of technical and commercial success.

Discovering Novel Medicines to Address Unmet Patient Needs. We seek to identify and validate new medicines on novel targets for internal development or collaboration. We believe the creativity and productivity of our discovery research group will continue to be a critical component for our ongoing success.

Acquiring Rights to Commercial Products and Drug Development Candidates. We aim to continue to selectively acquire rights to commercial products and programs in all stages of clinical development to capitalize on our commercial and drug development capabilities.

Collaboration and License Agreements

In addition to our independent efforts to develop and market products, we may enter into collaboration and license agreements from time to time to enhance our drug development and commercial capabilities. 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 and 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 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, used to treat particular conditions and methods of administration, drug delivery technologies and delivery profiles and methods of manufacturing.

We own or have licensed rights to the following United States patents relating to INGREZZA and our other products and product candidates in our pipeline (in addition to non-United States patents and certain patents covering our early-stage product candidates):

- INGREZZA, our highly selective VMAT2 inhibitor for the treatment of tardive dyskinesia, is covered by 19 issued United States patents that are listed in the FDA's Orange Book and are set to expire between 2027 and 2040. There is also a potential patent term extension of up to an additional 2 years for United States Patent No. 8,039,627, which is currently set to expire in 2029 and is the earliest patent covering valbenazine, the active pharmaceutical ingredient contained in INGREZZA. In Japan and 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.
- ONGENTYS, a highly selective COMT inhibitor for Parkinson's disease, is covered by 9 issued United States patents that are listed in the FDA's Orange Book and set to expire between 2026 to 2035 (not including a potential patent term extension of up to an additional 4 years for one of these patents).
- ORILISSA, our small molecule GnRH antagonist for the treatment of endometriosis pain, is covered by 5 issued United States patents that are listed in the FDA's Orange Book (the number of patents being dependent on dosage amount) and are set to expire between 2024 to 2036 (not including patent term extension of up to 5 years for patents listed in the Orange Book expiring in 2024).
- ORIAHNN, containing our small molecule GnRH antagonist for the treatment of menstrual bleeding associated with uterine fibroids, is covered by 4issued United States patents that are listed in the FDA's Orange Book and are set to expire between 2024 to 2034 (not including a potential patent term extension of up to an additional 5 years for one of the patents).
- Valbenazine, our highly selective VMAT2 inhibitor under further clinical development for the treatment of chorea in Huntington's disease, is covered by at least 12 of the issued United States patents that are listed in the FDA's Orange Book entry for INGREZZA and are set to expire between 2027 and 2038 . There is also a potential patent term extension of up to an additional 2 years for United States Patent No. 8,039,627, which is currently set to expire in 2029.
- Crinecerfont, a CRF1 antagonist for the treatment of congenital adrenal hyperplasia (CAH), is covered by United States Patent No. 10,905,690, which expires in 2035 (not including a potential patent term extension of up to an additional 5 years).
- Luvadaxistat, a DAAO inhibitor for the treatment of cognitive impairment associated with Schizophrenia (CIAS), is covered by United States Patent No. 9,290,456, among others, which expires in 2032 (not including a potential patent term extension of up to an additional 5 years).
- NBI-827104, an inhibitor of T-type calcium channels for the treatment of CSWS epilepsy, is covered by United States Patent No. US 9,932,314, among others, which expires in 2035 (not including a potential patent term extension of up to an additional 5 years).
- NBI-921352, an inhibitor of the Nav1.6 voltage-gated sodium channel for the treatment of SCN8A-DEE epilepsy, is covered by United States Patent No. US 10,246,453, among others, which expires in 2037 (not including a potential patent term extension of up to an additional 5 years).
- NBI-1065845, a positive allosteric modulator of AMPA for the treatment of inadequate response to treatment in major depressive disorder is covered by United States Patent No. 8,778,934, among others, which expires in 2031 (not including a potential patent term extension of up to an additional 5 years).

- NBI-1065846, a GPR139 agonist for the treatment of anhedonia in major depressive disorder, is covered by United States Patent No. 9,556,130, among others, which expires in 2035 (not including a potential patent term extension of up to an additional 5 years).
- NBI-1117568, a selective M4 agonist for the treatment of schizophrenia, is covered by United States Patent No. 10,961,225, among others, which expire in 2035 (not including a potential patent term extension of up to an additional 5 years).

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 5 years in the United States, 6 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 crinecerfont, may also be eligible for marketing exclusivity in the United States for 7 years and European Union for 10 years.

Refer to 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 experience in marketing and selling pharmaceutical products began with INGREZZA's approval in 2017, when we hired our salesforce and established our distribution and reimbursement capabilities, all of which are necessary to successfully commercialize our marketed products and products candidates. Our expanded specialty salesforce in the United States will consist of approximately 350 experienced sales professionals divided into three dedicated sales teams focused on psychiatry, neurology and long-term care. We anticipate completing our salesforce expansion during the second quarter of 2022.

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.

In addition, 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.

The federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare and 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 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 of 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 7 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 6 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 under a risk evaluation and mitigation strategy program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending NDAs or supplements to approved NDAs, or suspension or revocation of product approvals;
- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates marketing, labeling, advertising and promotion of products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label. 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 markets in other countries, sales of any products for which we receive regulatory approval will depend, in part, on the extent to which third-party payors provide coverage and establish adequate reimbursement levels for such drug products.

In the United States, third-party payors include federal and state healthcare programs, government authorities, private managed care providers, private health insurers and other organizations. 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 applied consistently or obtained in the first instance.

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

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

The marketability of any product or product candidates for which we or our collaborators receive regulatory approval for commercial sale may suffer if third-party payors fail to provide coverage and adequate reimbursement. In addition, emphasis on managed care in the 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.

Healthcare Reform

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

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

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

There have been legal and political challenges to certain aspects of the ACA. Since January 2017, the Trump administration signed several executive orders and other directives designed to delay, circumvent, or loosen certain requirements mandated by the ACA. Concurrently, Congress considered legislation that would repeal or repeal and replace all or part of the ACA. For example, legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act, includes a provision that repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form. Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how such challenges and the healthcare reform measures of the Biden administration will impact the ACA.

Other legislative changes have been proposed and 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 due to the COVID-19 pandemic, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% in the final fiscal year of this sequestration.

Also, there has been heightened governmental scrutiny recently over pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several 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, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to drug pricing that sought to implement several of the administration's proposals. As a result, the FDA concurrently released a final rule and guidance in September 2020, providing pathways for states to build and submit importation plans for drugs from Canada. This rule is undergoing legal challenge.

Further, on November 20, 2020, the U.S. Department of Health and Human Services, or HHS, finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers. This rule has been stayed by the Biden Administration until 2023 while pending litigation is heard in the courts.

On November 20, 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries, effective January 1, 2021. As a result of litigation challenging the Most Favored Nation model, on December 27, 2021, CMS published a final rule that rescinds the Most Favored Nation model interim final rule.

Additionally, 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 as well as potential administrative actions HHS can take to advance these principles. No legislation or administrative actions have been finalized to implement these principles. It is unclear whether these or similar policy initiatives will be implemented in the future.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

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.

Congenital Adrenal Hyperplasia. 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 encephalopathies SCN8A-DEE and EE-CSWS; 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 900 employees as of December 31, 2021, all of whom were 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 2021, we added over 200 new employees to our team.

We expect to continue to add additional employees in 2022 with a focus on expanding our commercial salesforce, research, and development organizations. 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 2021, we received the following rewards:

- #4 in Fortune Best Workplaces in Health Care & Biopharma™
- #7 in Fortune Best Small & Medium Workplaces™
- #13 in Fortune Best Workplaces for Women™
- #25 in Fortune Best Workplaces for Millennials™

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 an employee survey 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 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 our sales and marketing efforts are not 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 that could limit our product revenues and 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 studies 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.
- 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 product candidate approved by the FDA.
- We currently have no manufacturing capabilities. If third-party manufacturers of INGREZZA, ONGENTYS 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 or ONGENTYS, could materially and adversely affect our ability to successfully commercialize INGREZZA or ONGENTYS.
- 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 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 salesforce 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 4 years, including the expansion of our specialty salesforce, which we announced in the third quarter of 2021 and anticipate completing in the second quarter of 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 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. 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 our sales and marketing efforts are not effective, we may not generate sufficient revenue.

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

The market acceptance of INGREZZA or ONGENTYS 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, 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 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 not successfully commercialize INGREZZA, ONGENTYS or any other product candidate for which we obtain marketing approval. Our inability to promptly obtain coverage and profitable reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition. 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 potentially fewer patients to be 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 and ONGENTYS. 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, a remote work model may nevertheless need to be reinstated at some point in the future. We continue to evaluate the impact of global spikes or surges in COVID-19 infection and hospitalization rates, as well as the impact of emerging COVID-19 variants on the efficacy of vaccines. 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. 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.

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 rapidly 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 encephalopathies SCN8A-DEE and EE-CSWS; 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 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
- 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.

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 development and commercialization of valbenazine for movement disorders in Japan and 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 salesforce, 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, 2021, we had more than 900 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 planned increase in the size of our salesforce. 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 other product candidates that receive regulatory approval will depend, in part, on our ability to manage any future growth effectively. In particular, as we commercialize INGREZZA and ONGENTYS, we will need to support the training and ongoing activities of our salesforce 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 product candidate approved by the FDA.

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 product candidate approved by the FDA. Furthermore, recruiting and retaining qualified scientific personnel to perform research and development work in the future, along with personnel with experience marketing and selling pharmaceutical products, is critical to our success. We may be unable to attract and retain personnel on acceptable terms given 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 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 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 or ONGENTYS, could materially and adversely affect our ability to successfully commercialize INGREZZA or ONGENTYS.

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. 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 current 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.

In the event the conditional conversion feature of the 2.25% convertible senior notes due May 15, 2024, or the 2024 Notes, is triggered, holders of 2024 Notes will be entitled to convert their 2024 Notes at any time during specified periods at their option. If one or more of the holders of the 2024 Notes elects to convert their notes, unless we satisfy

our conversion obligation by delivering only shares of our common stock with respect to any conversion premium, we would be required to settle all or a portion of our conversion obligation through the payment of cash, which could adversely affect our liquidity. The conditional convertibility of the 2024 Notes will be monitored at each quarterly reporting date and analyzed dependent upon market prices of our common stock during the prescribed measurement periods. In the event that we have the election to redeem the 2024 Notes or the holders of the 2024 Notes have the election to convert the 2024 Notes at any time during the prescribed measurement period, the 2024 Notes would then be considered a current obligation and classified as such. We are not aware of any events or market conditions that would allow us to redeem the 2024 Notes or the holders of the 2024 Notes to convert the 2024 Notes for the quarterly period ended December 31, 2021, or as of the date of this report.

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 November 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. As of December 31, 2021, $381.2 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, 2021, we had an accumulated deficit of $0.6 billion 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. 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, in-licensing or acquisition opportunities, and capital expenditures. While we were profitable for the year ended December 31, 2021, 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. A high portion of our costs are predetermined on an annual basis, due in part to our significant research and development costs. Thus, small declines in revenue could disproportionately affect financial results in a quarter. While we were profitable for the year ended December 31, 2021, 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.

New income, sales, use 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, the Biden administration and Congress have proposed various United States federal tax law changes which, if enacted, could have a material impact on our business, cash flows, financial condition, or results of operations. In addition, 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 US 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. 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 of such places. Nevertheless, our effective tax rate may be different than experienced in the past due to numerous factors, including changes in the mix of our profitability from state to state, the results of examinations and audits of our tax filings, our inability to secure or sustain acceptable agreements with tax authorities, changes in accounting for income taxes and changes in tax laws. Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations and may result in tax obligations in excess of amounts accrued in our financial statements.

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 twelve months, the price of our common stock has ranged from approximately $72 per share to approximately $120 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, or ORIAHNN;
- 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
- 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. Two of these customers represented approximately 82% of our total product revenue for 2021 and a significant majority of our accounts receivable balance as of December 31, 2021. 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, together with investment income and future payments due under our strategic alliances, will be sufficient to satisfy our current and projected funding requirements for at least the next twelve months. However, these resources might be insufficient to conduct research and development programs, the cost of product in-taking and possible

acquisitions, fully commercialize products and operate the company to the full extent currently planned. If we cannot obtain adequate funds, we may be required to curtail significantly our commercial plans or one or more of our research and development programs or obtain funds through additional arrangements with corporate collaborators or others that may require us to relinquish rights to some of our technologies or product candidates.

Our future capital requirements will depend on many factors, including:

- the commercial success of INGREZZA, ONGENTYS, ORILISSA and/or ORIAHNN;
- 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 November 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. As of December 31, 2021, $381.2 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 3. 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. Interference proceedings declared by the United States Patent and Trademark Office may be necessary to determine the priority of inventions with respect to our patent applications (or those of our licensors) or a patent of a competitor. Litigation or interference proceedings may fail and, even if successful, may result in substantial costs and be a distraction to management. Litigation or interference 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.

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 and we expect that there will continue to be a number of federal and state proposals to implement government control over the pricing of prescription pharmaceuticals. In addition, increasing emphasis on reducing the cost of health care in the United States will continue to put pressure on the pricing and reimbursement of prescription pharmaceuticals. Moreover, in some foreign jurisdictions, pricing of prescription pharmaceuticals is already subject to government control. Additionally, other federal and state legislation impose obligations on manufacturers of pharmaceutical products, among others, related to product tracking and tracing. Among the requirements of this legislation, manufacturers are required to provide certain information regarding the drug product provided to individuals and entities to which product ownership is transferred, label drug product with a product identifier, and keep certain records regarding distribution of the drug product. Further, under this legislation, manufacturers will have drug product investigation, quarantine, disposition, notification and purchaser license verification responsibilities related to counterfeit, diverted, stolen and intentionally adulterated products, as well as products that are the subject of fraudulent transactions or which are otherwise unfit for distribution such that they would be reasonably likely to result in serious health consequences or death.

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

- an annual, nondeductible fee on any entity that manufactures, or imports, specified branded prescription drugs and biologic agents, apportioned among these entities according to their market share in certain government healthcare programs;
- an increase in the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program to 23.1% and 13.0% of the average manufacturer price for branded and generic drugs, respectively;
- a new methodology by which rebates owed by manufacturers under the Medicaid Drug Rebate Program are calculated for drugs that are inhaled, infused, instilled, implanted or injected;
- extension of a manufacturer's Medicaid rebate liability to covered drugs dispensed to individuals who are enrolled in Medicaid managed care organizations;
- expansion of eligibility criteria for Medicaid programs by, among other things, allowing states to offer Medicaid coverage to certain individuals with income at or below 133% of the federal poverty level, thereby potentially increasing a manufacturer's Medicaid rebate liability;
- a new Medicare Part D coverage gap discount program, in which manufacturers must now agree to offer 70% point-of-sale discounts off negotiated prices of applicable brand drugs to eligible beneficiaries during their coverage gap period, as a condition for a manufacturer's outpatient drugs to be covered under Medicare Part D;
- expansion of the entities eligible for discounts under the Public Health Service pharmaceutical pricing program; and
- a new Patient-Centered Outcomes Research Institute to oversee, identify priorities in, and conduct comparative clinical effectiveness research, along with funding for such research.

There have been executive legal and political challenges to certain aspects of the ACA. For example, on June 17, 2021 the United States Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. Thus, the ACA will remain in effect in its current form.

Further, prior to the United States Supreme Court ruling, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace, which began February 15, 2021 and remained open through August 15, 2021. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. It is possible that the ACA will be subject to judicial or Congressional challenges in the future. It is unclear how any such challenges and the healthcare reform measures of the Biden administration will impact the ACA.

Other legislative changes have been proposed and adopted since the ACA was enacted. These changes include aggregate reductions to Medicare payments to providers of up to 2% per fiscal year pursuant to the Budget Control Act of 2011, which began in 2013 and, due to subsequent legislative amendments to the statute, including the Infrastructure Investment and Jobs Act, will remain in effect through 2031, except for a temporary suspension from May 1, 2020 through March 31, 2022 due to the COVID-19 pandemic, unless additional Congressional action is taken. Under current legislation, the actual reduction in Medicare payments will vary from 1% in 2022 to up to 3% 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 3 to 5 years.

Additional changes that may affect our business include the expansion of new programs such as Medicare payment for performance initiatives for physicians under the Medicare Access and CHIP Reauthorization Act of 2015, which ended the use of the statutory formula, also referred to as the Sustainable Growth Rate, for clinician payment and established a quality payment incentive program, also referred to as the Quality Payment Program. This program provides clinicians with two ways to participate, including through the Advanced Alternative Payment Models, or APMs, and the Merit-based Incentive Payment System, or MIPS. In November 2019, the Centers for Medicare & Medicaid Services, or CMS, issued a final rule finalizing the changes to the Quality Payment Program. At this time, it remains unclear how the introduction of the Quality Payment Program will impact overall physician reimbursement.

Also, there has been heightened governmental scrutiny recently over pharmaceutical pricing practices in light of the rising cost of prescription drugs and biologics. Such scrutiny has resulted in several recent Congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. At the federal level, the Trump administration used several means to propose or implement drug pricing reform, including through federal budget proposals, executive orders and policy initiatives. For example, on July 24, 2020 and September 13, 2020, the Trump administration announced several executive orders related to prescription drug pricing that attempted to implement several of the administration's proposals. As a result, the FDA concurrently released a final rule and guidance in September 2020 providing pathways for states to build and submit importation plans for drugs from Canada. Further, on November 20, 2020, the United States Department of Health and Human Services, or HHS, finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023. On November 20, 2020, CMS issued an interim final rule implementing President Trump's Most Favored Nation executive order, which would tie Medicare Part B payments for certain physician-administered drugs to the lowest price paid in other economically advanced countries. As a result of litigation challenging the Most Favored Nation model, on December 27, 2021, CMS published a final rule that rescinds the Most Favored Nation interim final rule. 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. No legislation or administrative actions have been finalized to implement these principles. In addition, Congress is considering drug pricing as part of other

reform measures. It is unclear whether these or similar policy initiatives will be implemented in the future. At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing.

We expect that the ACA, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and lower reimbursement, and in additional downward pressure on the price that we receive for any approved product. In particular, it is possible that additional governmental action is taken in response to the COVID-19 pandemic. Any reduction in reimbursement from Medicare or other government-funded programs may result in a similar reduction in payments from private payors. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain sustained profitability or commercialize our drugs, particularly since the majority of our current revenue is derived from federal healthcare programs, including Medicare and Medicaid.

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

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 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, such as our contributions to patient assistance programs, 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. 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 salesforce 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, transfer and otherwise process confidential and sensitive electronic information on our networks and in our data centers. This information includes, among other things, our intellectual property and proprietary information, the confidential information of our collaborators and licensees, and the personally identifiable information of our employees. It is important to our operations and business strategy that this electronic information remains secure and is perceived to be secure. The size and complexity of our information technology systems, and those of third-party vendors with whom we contract, and the volume of data we retain, make such systems potentially vulnerable to breakdown, malicious intrusion, security breaches, ransomware attacks, social engineering attacks, supply-chain attacks, and other cyber-attacks. Ransomware attacks are becoming increasingly prevalent and severe. 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 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 information. 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. A security breach or privacy violation that leads to disclosure or modification of or prevents access to personally identifiable information or other protected information could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to liability under laws and regulations that protect personal data, resulting in increased costs or loss of revenue. Similarly, the loss of clinical trial data from completed or ongoing or planned clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Additionally, theft of our intellectual property or proprietary business information could require substantial expenditures to remedy. If we are unable to prevent such security breaches or privacy violations or implement satisfactory remedial measures, our operations could be disrupted, and we may suffer loss of reputation, financial loss and other regulatory penalties because of lost or misappropriated information. In addition, these breaches and other inappropriate access can be difficult to detect, and any delay in identifying them may lead to increased harm of the type described above. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property. As cyber threats continue to evolve, we may be required to expend significant additional resources to continue to modify or enhance our protective measures or to investigate and remediate any information security vulnerabilities. Although to our knowledge we 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. Significant disruptions of our information technology systems or breaches of data security could have a material adverse effect on our business, financial condition and results of operations.

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 7 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 3. 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 process confidential and sensitive electronic information, including personal information, 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, the number and scope of which are expanding, changing, subject to differing applications and interpretations, and may be inconsistent among countries. 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 in Europe regarding privacy, data protection, information security and the processing of personal data have 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, which can be up to four percent of global revenue or 20 million euros, whichever is greater, and also confer a private right of action on data subjects for breaches of data protection requirements. 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.

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 generally restricts 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. 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.

Laws regarding privacy, data protection, information security and the processing of personal information are also 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, it is anticipated that the California Privacy Rights Act of 2020, or the CPRA, effective January 1, 2023, will expand the CCPA. For example, the CPRA establishes 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.

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 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 6-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*

In the second quarter of 2021, we received notices from (i) Teva Pharmaceuticals Development, Inc., (ii) Lupin Limited, (iii) Crystal Pharmaceutical (Suzhou) Co. Ltd., and (iv) Zydus Pharmaceuticals (USA) Inc. (each an “ANDA Filer”) that each company had filed an abbreviated new drug application, or ANDA, with the FDA seeking approval of a generic version of INGREZZA. The 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 each ANDA Filer’s 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 in July 2021 against (i) Teva Pharmaceuticals, Inc. and its affiliates Teva Pharmaceuticals Development, Inc., Teva Pharmaceuticals USA, Inc. and Teva Pharmaceutical Industries Ltd., (ii) Lupin Limited and its affiliates Lupin Pharmaceuticals, Inc., and Lupin Atlantis Holdings S.A., (iii) Crystal Pharmaceutical (Suzhou) Co., Ltd., and its affiliate Crystal Pharmatech Co., Ltd., and (iv) Zydus Pharmaceuticals (USA) Inc. and its affiliates Zydus Worldwide DMCC, Cadila Healthcare Limited d/b/a Zydus Cadila and Zydus Healthcare (USA) LLC. We also filed suit in the United States District Court for the District of New Jersey in July 2021 against Zydus Pharmaceuticals (USA) Inc. and its affiliates Zydus Worldwide DMCC, Cadila Healthcare Limited d/b/a Zydus Cadila and Zydus Healthcare (USA) LLC seeking to prevent any ANDA Filer from selling a generic version of INGREZZA.

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 February 7, 2022, there were approximately 47 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.

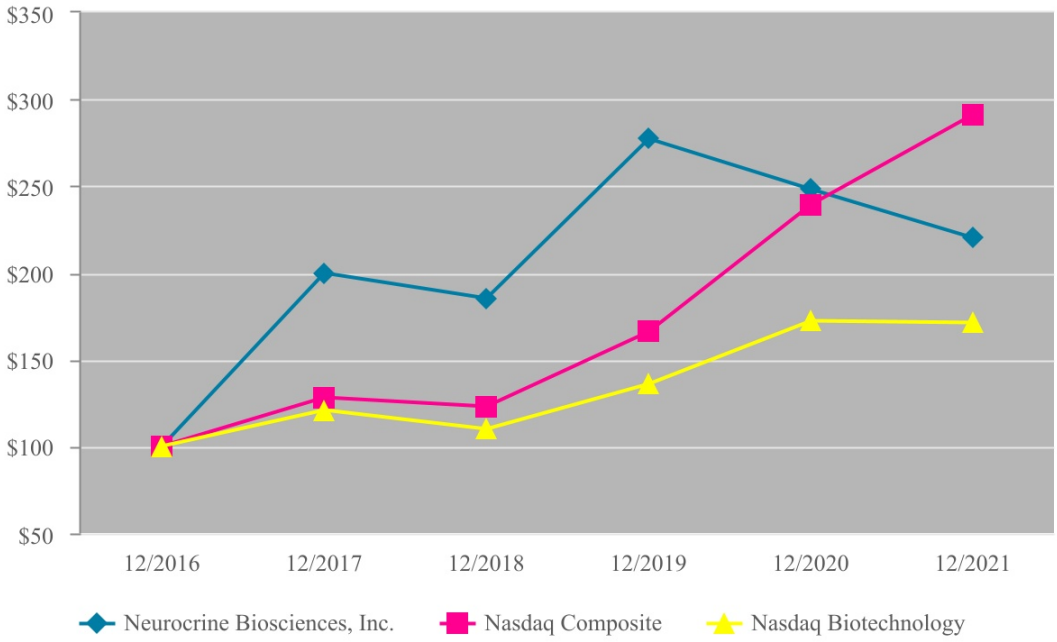
Information about our equity compensation plans is incorporated herein by reference to Item 12 of Part III of this Annual Report on Form 10-K.

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 2021.

Stock Performance Graph and Cumulative Total Return*

The graph below shows the cumulative total stockholder return assuming the investment of $100 on December 31, 2016 (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

At Neurocrine Biosciences, our purpose is simple: to relieve suffering for people with great needs, but few options. For three decades, we have applied our unique insight into neuroscience to advance medicines for neurological, endocrine and psychiatric disorders. Our efforts have resulted in 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 investigational therapies with the potential to address unmet clinical needs of patients worldwide living with neurological, endocrine and psychiatric 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 to levodopa/carbidopa in patients with Parkinson's disease experiencing motor fluctuations. INGREZZA net product sales represent the significant majority of our total net product sales.

Our partner AbbVie launched ORILISSA® (elagolix tablets) in the United States in August 2018 and launched ORIAHNN® (elagolix, estradiol and norethindrone acetate capsules and elagolix capsules) in the United States in June 2020. We receive royalties at tiered percentage rates on AbbVie net sales of elagolix.

Business Highlights

- INGREZZA net product sales for 2021 increased $88.8 million, or 8.9%, to $1.1 billion, primarily driven by increased total prescriptions reflecting higher customer demand and increased commercial activities.
- 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 6-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.

Pipeline Highlights

- In the fourth quarter of 2021, we announced positive top-line data from the Phase III KINECT-HD study evaluating the efficacy, safety and tolerability of valbenazine in 120 adult patients with chorea in Huntington disease, also known as Huntington chorea. The study met the primary endpoint of reduction in severity of chorea. We plan to submit a supplemental new drug application for valbenazine for the treatment of Huntington chorea with the FDA in second half of 2022.
- Completed strategic partnership with Heptares Therapeutics Limited, or Heptares, to expand clinical pipeline for psychiatry disorders. Upfront fee associated with the agreement totaled $100.0 million, which, including certain transaction-related costs, was expensed as in-process research and development in 2021.
- In 2021, Mitsubishi Tanabe Pharma Corporation, or MTPC, received approvals for marketing authorization for valbenazine for the treatment of tardive dyskinesia in Indonesia, Singapore, South Korea and Thailand. In addition, MTPC has submitted filings for marketing authorization, which are currently under review, in Japan and Malaysia.

Impact of COVID-19

The COVID-19 pandemic has dramatically changed the ways in which we live and interact with one another. While we adapt to this new shared reality, our purpose remains unchanged: to relieve suffering for people with great needs, but few options.

Although the initial impact of the pandemic has subsided, we are uncertain as to how more transmissible variants may impact our business. 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 clinical studies.

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 arrangement 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, a remote work model may nevertheless need to be reinstated at some point in the future. We continue to evaluate the impact of global spikes or surges in COVID-19 infection and hospitalization rates, as well as the impact of emerging COVID-19 variants on the efficacy of vaccines.

Most hospitals, community mental health facilities, physicians' offices, pharmacies and other healthcare facilities have relaxed their policies that limited access of patients and our employees to such facilities and limited the ability of patients, pharmacies and prescribers to interact with each other. However, we anticipate these policies may change from time to time as communities or regions grapple with outbreaks. The ultimate impact of the COVID-19 pandemic, including any lasting effects on our revenue and the way we conduct our business, is highly uncertain and subject to continued change. We recognize that this pandemic will continue to present unique challenges for us throughout 2022.

Results of Operations

Revenues

Net Product Sales by Sales Product.

	Year Ended December 31,		
(in millions)	**2021**	**2020**	**2019**
INGREZZA net product sales	$ 1,081.9	$ 993.1	$ 752.9
ONGENTYS net product sales	8.2	1.0	—
Total net product sales	$ 1,090.1	$ 994.1	$ 752.9

For 2021 compared to 2020, the increase in total net product sales primarily reflected increased INGREZZA net product sales mainly driven by increased total prescriptions reflecting higher customer demand and increased commercial activities.

For 2020 compared to 2019, the increase in total net product sales primarily reflected increased INGREZZA net product sales driven by increased total prescriptions.

Collaboration Revenues by Category.

	Year Ended December 31,		
(in millions)	**2021**	**2020**	**2019**
Elagolix royalties	$ 22.3	$ 19.2	$ 14.3
Milestone	15.0	30.0	20.0
Non-cash collaboration revenue and other	6.1	2.6	0.9
Total collaboration revenue	$ 43.4	$ 51.8	$ 35.2

For 2021, total collaboration revenue primarily reflected the achievement of a $15.0 million milestone associated 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 associated with the FDA's approval of AbbVie's ORIAHNN for uterine fibroids in 2020 and royalties earned on AbbVie net sales of elagolix.

For 2019, total collaboration revenue primarily reflected the achievement of a $20.0 million milestone associated with the FDA's acceptance of AbbVie's new drug application submission for elagolix for uterine fibroids and royalties earned on AbbVie net sales of elagolix.

Operating Expenses

Cost of Sales.

	Year Ended December 31,		
(in millions)	**2021**	**2020**	**2019**
Cost of sales	$ 14.3	$ 10.1	$ 7.4

The increase in cost of sales from 2020 to 2021 and 2019 to 2020 reflected increased INGREZZA net product sales driven by increased total prescriptions.

Research and Development, or R&D, Expenses by Category.

We support our drug discovery and development efforts through the commitment of significant resources to discovery, R&D 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 R&D activities are part of our collaborative arrangements.

	Year Ended December 31,		
(in millions)	**2021**	**2020**	**2019**
Late stage	$ 55.7	$ 55.1	$ 43.7
Early stage	43.9	30.2	25.3
Research and discovery	50.5	43.3	24.6
Milestone	5.4	20.0	10.0
Payroll and benefits	129.1	95.4	71.3
Facilities and other	43.5	31.0	25.1
Total R&D expense	$ 328.1	$ 275.0	$ 200.0

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

For 2021 compared to 2020, the increase in late stage R&D expense primarily reflected continued investment in Phase III programs for crinecerfont in congenital adrenal hyperplasia and valbenazine in Huntington disease and initiation of a Phase III program for valbenazine as adjunctive treatment of schizophrenia, offset by decreased investment associated with the termination of the NBIb-1817 program for Parkinson's disease, which became effective in August 2021.

For 2020 compared to 2019, the increase in late stage R&D expense primarily reflected increased investment in Phase III programs for crinecerfont in congenital adrenal hyperplasia and continued enrollment in the Phase III program for valbenazine Huntington disease.

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 2021 compared to 2020, the increase in early stage R&D expense primarily reflected continued enrollment in Phase II programs for NBI-827104 in epileptic encephalopathy with continuous spike and wave during sleep and essential tremor and initiation of Phase II programs for NBI-921352 in focal onset seizure and SCN8A developmental epileptic encephalopathy.

For 2020 compared to 2019, the increase in early stage R&D expense primarily reflected increased investment in three in-licensed psychiatry clinical development programs beginning in mid-2020 and two in-licensed epilepsy clinical development programs beginning at the end of 2019.

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

For 2021 compared to 2020, the increase in research and discovery R&D expense primarily reflected a full year of investment in psychiatry and epilepsy preclinical development programs in-licensed in 2020, offset by decreased investment in preclinical gene therapy programs.

For 2020 compared to 2019, the increase in research and discovery R&D expense primarily reflected increased investment in preclinical gene therapy programs and an epilepsy preclinical development program in-licensed in 2020.

Milestone. Consists of costs incurred for development and/or regulatory milestones in connection with our collaborative arrangements.

In 2021, we expensed a milestone of $5.4 million associated with the European Union’s approval for the NBI-921352 clinical trial application in September 2021.

In 2020, we expensed a milestone of $20.0 million associated the FDA’s approval for ONGENTYS for Parkinson’s disease.

In 2019, we expensed a milestone of $10.0 million associated with the FDA’s acceptance of the new drug application for opicapone as an adjunctive therapy to levodopa/DOPA decarboxylase inhibitors in adult Parkinson's disease patients.

Payroll and Benefits. Consists of costs incurred for salaries and wages, payroll taxes, benefits and share-based compensation associated with employees involved in R&D activities. Share-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 share-based grants are issued.

For 2021 compared to 2020, the increase in payroll and benefits R&D expense primarily reflected increased personnel expenses on higher headcount and a $14.7 million increase in non-cash share-based compensation expense, including a $6.4 million charge related to the modification of certain share-based awards.

For 2020 compared to 2019, the increase in payroll and benefits R&D expense primarily reflected increased personnel expenses on higher headcount.

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

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

	Year Ended December 31,		
(in millions)	**2021**	**2020**	**2019**
IPR&D expense	$ 105.3	$ 164.5	$ 154.3

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

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

In 2019, we expensed as IPR&D $118.1 million and $36.2 million, respectively, in connection with the payments of the upfront fees pursuant to our collaborations with Voyager Therapeutics, Inc., or Voyager, and Xenon Pharmaceuticals, Inc., or Xenon.

Selling, General and Administrative, or SG&A.

(in millions)	Year Ended December 31, 2021	2020	2019
SG&A expense	$ 583.3	$ 433.3	$ 354.1

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

For 2020 compared to 2019, the increase in SG&A expense primarily reflected increased personnel expenses on higher headcount and continued investment in INGREZZA marketing.

Other Expense, Net.

(in millions)	Year Ended December 31, 2021	2020	2019
Interest expense	$ (25.8)	$ (32.8)	$ (32.0)
Unrealized gain (loss) on equity securities	20.9	(17.7)	(13.0)
Loss on extinguishment of convertible senior notes	—	(18.4)	—
Investment income and other, net	3.8	12.6	19.2
Total other expense, net	$ (1.1)	$ (56.3)	$ (25.8)

For 2021 compared to 2020, the decrease in other expense, net, reflected a net unrealized gain of $20.9 million recognized to adjust our equity investments in Voyager and Xenon to fair value, a non-recurring debt extinguishment charge of $18.4 million in November 2020 associated with the partial repurchase of our convertible senior notes and decreased interest expense resulting from a lower convertible debt balance throughout 2021, partially offset by decreased interest income stemming from lower yields on our debt security investments.

For 2020 compared to 2019, the increase in other expense, net, primarily reflected a debt extinguishment charge of $18.4 million in November 2020 associated with the partial repurchase of our convertible senior notes.

Provision for (Benefit from) Income Taxes.

(in millions)	Year Ended December 31, 2021	2020	2019
Provision for (benefit from) income taxes	$ 11.8	$ (300.6)	$ 9.5

For 2021, the effective tax rate was lower than federal and state tax rates primarily due to excess tax benefits associated with share-based compensation and research tax credits. Beginning in the first quarter of 2021, we began recording a provision for income taxes using an effective tax rate approximating federal and state statutory tax rates. Due to the ability to offset any pre-tax income against previously benefited federal net operating losses, no federal cash tax was incurred 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 tax 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.

For 2019, the provision for income taxes reflected estimated and current state income taxes. The effective tax rate for 2019 varied from the statutory tax 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. As of December 31, 2019, we had a full valuation allowance against our net deferred tax assets as realization was uncertain.

Net Income and Diluted Earnings per Share.

(in millions, except per share data)	Year Ended December 31, 2021	2020	2019
Net income	$ 89.6	$ 407.3	$ 37.0
Diluted earnings per share	$ 0.92	$ 4.16	$ 0.39

For 2021 compared to 2020, the decrease in net income and diluted earnings per share primarily 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, increased investment to support our commercial initiatives, including the May 2021 launch of our INGREZZA direct-to-consumer advertising campaign, "TD Spotlight", and increased investment in our expanded clinical portfolio, partially offset by increased INGREZZA net product sales and decreased IPR&D expense reflecting lower upfront payments for asset acquisitions.

For 2020 compared to 2019, the increase in net income and diluted earnings per share primarily 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 and increased INGREZZA net product sales, partially offset by ongoing support for the commercial launch of INGREZZA for tardive dyskinesia and progression of our clinical pipeline.

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 twelve 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.

(in millions)	December 31, 2021	2020
Total cash, cash equivalents and marketable securities	$ 1,272.0	$ 1,028.1
Working Capital:		
Total current assets	$ 972.8	$ 1,016.2
Less total current liabilities	245.8	186.5
Total working capital	$ 727.0	$ 829.7

Information Regarding Our Cash Flows.

(in millions)	Year Ended December 31, 2021	2020	2019
Net cash provided by operating activities	$ 256.5	$ 228.5	$ 147.0
Net cash (used in) provided by investing activities	(130.2)	4.1	(211.1)
Net cash provided by (used in) financing activities	27.4	(157.8)	32.4
Change in cash, cash equivalents and restricted cash	$ 153.7	$ 74.8	$ (31.7)

Net Cash Provided by Operating Activities.

For 2021 compared to 2020, the increase in net cash provided by operating activities primarily reflected increased INGREZZA net product sales and lower upfront payments for asset acquisitions, partially offset by increased investment to support our commercial initiatives and advancing our expanded clinical portfolio.

For 2020 compared to 2019, the increase in net cash provided by operating activities primarily reflected increased INGREZZA net product sales, partially offset by incremental INGREZZA investment and progression of our clinical pipeline.

Net Cash (Used in) Provided by Investing Activities.

Periodic fluctuations in net cash (used in) provided by investing activities are generally driven by timing differences related to the purchases, sales and maturities of debt security investments and changes in our portfolio-mix.

For 2021, net cash used in investing activities reflected a $4.6 million equity investment in Xenon associated with the European Union's approval of our clinical trial application in September 2021 for NBI-921352 for the treatment of focal onset seizures in adults.

For 2019, net cash used in investing activities reflected equity investments of $54.7 million in Voyager and $14.2 million in Xenon associated with newly entered into collaboration and license agreements.

Net Cash Provided by (Used in) Financing Activities.

For 2021 and 2019, net cash provided by investing activities reflected proceeds from issuances of our common stock under benefit plans.

For 2020, net cash used in financing activities primarily reflected the partial repurchase of $136.2 million aggregate principal amount of our convertible senior notes for an aggregate repurchase price of $186.9 million in cash, partially offset by proceeds from issuances of our common stock under benefit plans.

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 and/or ORIAHNN;
- 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 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;
- the impact of the COVID-19 pandemic on our business; and

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 $10.9 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.

Convertible Senior Notes. In May 2017, we completed a private placement of $517.5 million in aggregate principal amount of 2.25% convertible senior notes due May 15, 2024, or the 2024 Notes. At our election, we may redeem all, or any portion, of the 2024 Notes under certain circumstances. The 2024 Notes do not contain any financial or operating covenants or any restrictions on the payment of dividends, the issuance of other indebtedness or the issuance or repurchase of securities by us. There are customary events of default with respect to the 2024 Notes, including that upon certain events of default, 100% of the principal and accrued and unpaid interest on the notes would become due and payable. In November 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. As of December 31, 2021, $381.2 million aggregate principal amount of the 2024 Notes remained outstanding. With respect to the 2024 Notes, unless earlier converted, redeemed or repurchased, we would be required to pay interest of $8.6 million in 2022, $8.6 million in 2023 and $4.3 million in 2024 and pay the aggregate principal amount outstanding of $381.2 million upon maturity of the notes in 2024.

Refer to Note 5 to the consolidated financial statements for more information on the 2024 Notes.

Leases. Our operating leases, which have terms that expire beginning 2024 through 2031, 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 6-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 10 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 and share-based compensation. Estimates are based on historical experience, information received from third parties and on various other assumptions that are believed to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. Historically, revisions to our estimates have not resulted in a material change to the financial statements. The items in our financial statements requiring significant estimates and judgments are as follows:

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.

Share-Based Compensation. For purposes of calculating share-based compensation, we estimate the fair value of share-based compensation awards using a Black-Scholes option-pricing model. The determination of the fair value of share-based compensation awards utilizing the Black-Scholes model is affected by our stock price and a number of assumptions, including but not limited to expected stock price volatility over the term of the awards and the expected term of stock options. Our stock options have characteristics significantly different from those of traded options, and changes in the assumptions can materially affect the fair value estimates. For example, an increase in the underlying stock price results in a significant increase in the Black-Scholes option-pricing. The fair value of performance-based restricted stock units, or PRSUs, is estimated based on the closing sale price of our common stock on the date of grant. Expense recognition for PRSUs commences when attainment of the associated performance-based criteria is determined to be probable.

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

Income Taxes. Our income tax benefit (provision) is computed under the asset and liability method. Significant estimates are required in determining our income tax benefit (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. Prior to 2020, we recorded a valuation allowance that fully offset our deferred tax assets. 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 twelve months. If a 1% change in interest rates were to have occurred on December 31, 2021, 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, 2021 and 2020, 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, 2021, 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, 2021 and 2020, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2021, 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, 2021, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (2013 framework), and our report dated February 11, 2022 expressed an unqualified opinion thereon.

Basis for Opinion

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

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

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 U.S. (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 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, 2021, the portion of product that is expected to be subject to a government rebate and the applicable contractual government rebate percentage by forecasting the revenue, the payor type underlying the revenue and the applicable rebate amount 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, 2021, including controls over management's forecast of revenue and 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, 2021. 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 impact of 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 11, 2022

NEUROCRINE BIOSCIENCES, INC.

CONSOLIDATED BALANCE SHEETS

(in millions, except per share data)	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 340.8	$ 187.1
Debt securities available-for-sale (amortized cost was $370.6 and $612.4 as of December 31, 2021 and 2020, respectively)	370.5	613.9
Accounts receivable	185.5	157.1
Inventory	30.5	28.0
Other current assets	45.5	30.1
Total current assets	972.8	1,016.2
Deferred tax assets	315.1	319.4
Debt securities available-for-sale (amortized cost was $563.2 and $226.7 as of December 31, 2021 and 2020, respectively)	560.7	227.1
Right-of-use assets	97.2	82.8
Equity securities	63.7	38.2
Property and equipment, net	58.6	44.6
Other long-term assets	4.4	6.4
Total assets	$ 2,072.5	$ 1,734.7
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable and accrued liabilities	$ 225.8	$ 168.7
Other current liabilities	20.0	17.8
Total current liabilities	245.8	186.5
Convertible senior notes	335.1	317.9
Noncurrent operating lease liabilities	105.3	94.4
Other long-term liabilities	12.3	9.7
Total liabilities	698.5	608.5
Stockholders' equity:		
Preferred stock, $0.001 par value; 5.0 shares authorized; no shares issued and outstanding as of December 31, 2021 and 2020	—	—
Common stock, $0.001 par value; 220.0 shares authorized; 94.9 and 93.5 shares issued and outstanding as of December 31, 2021 and 2020, respectively	0.1	0.1
Additional paid-in capital	2,011.4	1,849.7
Accumulated other comprehensive (loss) income	(1.7)	1.8
Accumulated deficit	(635.8)	(725.4)
Total stockholders' equity	1,374.0	1,126.2
Total liabilities and stockholders' equity	$ 2,072.5	$ 1,734.7

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, 2021	2020	2019
Revenues:			
Product sales, net	$ 1,090.1	$ 994.1	$ 752.9
Collaboration revenue	43.4	51.8	35.2
Total revenues	1,133.5	1,045.9	788.1
Operating expenses:			
Cost of sales	14.3	10.1	7.4
Research and development	328.1	275.0	200.0
Acquired in-process research and development	105.3	164.5	154.3
Selling, general and administrative	583.3	433.3	354.1
Total operating expenses	1,031.0	882.9	715.8
Operating income	102.5	163.0	72.3
Other (expense) income:			
Interest expense	(25.8)	(32.8)	(32.0)
Unrealized gain (loss) on equity securities	20.9	(17.7)	(13.0)
Loss on extinguishment of convertible senior notes	—	(18.4)	—
Investment income and other, net	3.8	12.6	19.2
Total other expense, net	(1.1)	(56.3)	(25.8)
Income before provision for (benefit from) income taxes	101.4	106.7	46.5
Provision for (benefit from) income taxes	11.8	(300.6)	9.5
Net income	89.6	407.3	37.0
Unrealized (loss) gain on debt securities available-for-sale	(3.5)	0.4	3.4
Comprehensive income	$ 86.1	$ 407.7	$ 40.4
Earnings per share, basic	$ 0.95	$ 4.38	$ 0.40
Earnings per share, diluted	$ 0.92	$ 4.16	$ 0.39
Weighted average common shares outstanding, basic	94.6	93.1	91.6
Weighted average common shares outstanding, diluted	97.9	97.8	95.7

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, 2018	90.8	$ 0.1	$ 1,660.4	$ (2.0)	$ (1,177.7)	$ 480.8
Net income	—	—	—	—	37.0	37.0
Unrealized gain on debt securities available-for-sale	—	—	—	3.4	—	3.4
Share-based compensation expense	—	—	75.3	—	—	75.3
Cumulative-effect adjustment to equity due to adoption of ASU 2016-02	—	—	—	—	8.0	8.0
Issuances of common stock under stock plans	1.5	—	32.4	—	—	32.4
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
Unrealized gain on debt securities available-for sale	—	—	—	0.4	—	0.4
Share-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
Unrealized loss on debt securities available-for-sale, net of tax	—	—	—	(3.5)	—	(3.5)
Share-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

See accompanying notes to consolidated financial statements.

NEUROCRINE BIOSCIENCES, INC.

CONSOLIDATED STATEMENTS OF CASH FLOWS

(in millions)	Year Ended December 31, 2021	2020	2019
Cash Flows from Operating Activities:			
Net income	$ 89.6	$ 407.3	$ 37.0
Reconciliation of net income to net cash provided by operating activities:			
Share-based compensation expense	134.2	100.0	75.3
Depreciation	10.9	8.6	7.4
Amortization of debt discount	16.2	20.0	18.9
Amortization of debt issuance costs	1.1	1.4	1.4
Change in fair value of equity securities	(20.9)	17.7	13.0
Deferred income taxes	4.3	(310.7)	—
Loss on extinguishment of convertible senior notes	—	18.4	—
Other	4.4	3.7	(1.2)
Changes in operating assets and liabilities:			
Accounts receivable	(28.4)	(30.5)	(69.2)
Inventories	(2.5)	(10.7)	(6.4)
Accounts payable and accrued liabilities	56.8	26.9	54.0
Other assets and liabilities, net	(9.2)	(23.6)	16.8
Net cash provided by operating activities	256.5	228.5	147.0
Cash Flows from Investing Activities:			
Purchases of debt securities available-for-sale	(800.1)	(735.5)	(797.2)
Sales and maturities of debt securities available-for-sale	697.9	750.5	669.7
Purchases of equity securities	(4.6)	—	(68.9)
Purchases of property and equipment	(23.4)	(10.9)	(14.7)
Net cash (used in) provided by investing activities	(130.2)	4.1	(211.1)
Cash Flows from Financing Activities:			
Issuances of common stock under benefit plans	27.5	29.1	32.4
Partial repurchase of convertible senior notes	(0.1)	(186.9)	—
Net cash provided by (used in) financing activities	27.4	(157.8)	32.4
Change in cash and cash equivalents and restricted cash	153.7	74.8	(31.7)
Cash and cash equivalents and restricted cash at beginning of period	190.3	115.5	147.2
Cash and cash equivalents and restricted cash at end of period	$ 344.0	$ 190.3	$ 115.5
Supplemental Disclosure:			
Non-cash capital expenditures	$ 1.9	$ 1.4	$ 1.0
Right-of-use assets acquired through operating leases	$ 23.4	$ 12.8	$ 77.1
Cash paid for interest	$ 8.6	$ 11.6	$ 11.6
Cash paid for income taxes	$ 5.1	$ 15.3	$ 0.5

See accompanying notes to consolidated financial statements.

1. Organization and Summary of Significant Accounting Policies

Business Activities. Neurocrine Biosciences, Inc., or Neurocrine Biosciences, the Company, we, our or us, was incorporated in California in 1992 and reincorporated in Delaware in 1996. Neurocrine Continental, Inc., is a Delaware corporation and a wholly owned subsidiary of Neurocrine Biosciences. We also have two wholly-owned Irish subsidiaries, Neurocrine Therapeutics, Ltd. and Neurocrine Europe, Ltd. both of which were formed in December 2014 and are inactive.

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.

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

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 doubtful accounts. We estimate the allowance for doubtful accounts based on existing contractual payment terms, actual payment patterns of our customers and individual customer circumstances. To date, an allowance for doubtful accounts has not been material.

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 totaled $2.2 million as of December 31, 2021 and $3.7 million as of December 31, 2020. 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 2021, 2020 or 2019.

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.

Investments in equity securities of certain companies that are subject to holding period restrictions longer than one year are classified as Level 3 and carried at fair value using an option pricing valuation model. The most significant assumptions within the option pricing valuation model are the stock price volatility, which is based on the historical volatility of similar companies and the discount for lack of marketability related to the term of the restrictions.

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 $10.9 million for 2021, $8.6 million for 2020 and $7.4 million for 2019.

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

Revenue Recognition. 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 those 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 financial assistance to qualified patients with prescription drug co-payments required by insurance as well as free trial vouchers to qualifying new patients. We accrue for patient financial assistance based on estimated claims and the cost per claim we expect to receive associated with inventory that remains in the distribution channel at period end. To date, actual copay assistance and free trial vouchers have 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 distribution services. To the extent we can demonstrate a separable benefit and fair value for these services, we classify the associated costs in selling, general and administrative expenses. These costs are typically known at the time of sale, resulting in minimal adjustments subsequent to the period of sale.

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. We record this estimate 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 licensing 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 of 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 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 developmental, regulatory 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 where achievement of the specified event is dependent on the development activities of a third party or approvals from regulators, are not considered probable of being achieved until the 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 and by placing investments with high credit quality financial institutions and maturities that maintain safety and liquidity. To date, we have not experienced any credit losses and do not believe we are exposed to any significant credit risk in relation to these financial instruments.

We are also subject to credit risk from our accounts receivable related to our product sales. Our two largest customers represented approximately 82% of our total product revenues for 2021 and approximately 86% for both 2020 and 2019, as well as the significant majority of our accounts receivable balances at December 31, 2021 and 2020. To date, we have not experienced any significant losses with respect to the collection of these accounts receivable.

Cost of Sales. Cost of sales includes third-party manufacturing, transportation, freight and indirect overhead costs associated with the manufacture and distribution of INGREZZA and ONGENTYS, royalty fees on net sales of ORILISSA and ORIAHNN, 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 Expenses. Research and development, or R&D, expenses consist primarily of salaries, payroll taxes, employee benefits and share-based compensation charges for those individuals involved in ongoing R&D efforts; as well as scientific consulting fees, preclinical and clinical trial costs, R&D facilities costs, laboratory supply costs and depreciation of scientific equipment. All such costs are expensed as R&D when incurred. These expenses result from our independent R&D efforts, as well as efforts associated with collaborations, in-licenses and third-party funded research arrangements, including event-based milestones.

Asset Acquisitions. We account for acquisitions of an asset that does not (or a group 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 asset (or assets) acquired on the basis of its (or 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 in-process research and development, or 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 when services are performed or goods are delivered and are included in selling, general and administrative expense in our consolidated statements of income. We incurred advertising costs related to INGREZZA and ONGENTYS of $139.8 million for 2021, $64.8 million for 2020 and $40.6 million for 2019.

Share-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 3 to 4 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 6 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 (benefit) is computed under the asset and liability method. Significant estimates are required in determining our income tax provision (benefit). 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. Prior to 2020, we recorded a valuation allowance that fully offset our deferred tax assets. 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. Refer to Note 9 to the consolidated financial statements for more information.

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.

Convertible debt instruments that may be settled entirely or partly in cash may, in certain circumstances where the borrower has the ability and intent to settle in cash, be accounted for under the treasury stock method. In December 2021, we entered into the First Supplemental Indenture, dated as of May 2, 2017, by and between the Company and U.S. Bank National Association, as Trustee, or the 2017 Indenture, pursuant to which we irrevocably elected to settle the principal amount of the 2.25% 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, and consistent with historical practice, only the shares required to settle any conversion premium would be considered dilutive under the treasury stock 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 2019-12. On January 1, 2021, we adopted Accounting Standards Update, or ASU, 2019-12, *Income Taxes (Topic 740): Simplifying the Accounting for Income Taxes*, using the modified retrospective transition method. ASU 2019-12 simplifies the accounting for income taxes by removing certain exceptions to the general principles in Topic 740 and amends existing guidance to improve consistent application of Topic 740. The adoption of ASU 2019-12 did not result in a cumulative-effect adjustment to retained earnings. The comparative prior period information continues to be reported under the accounting standards in effect during those periods. The impact of the adoption is expected to be immaterial to our financial position, results of operations and cash flows on an ongoing basis.

Recently Issued Accounting Pronouncements.

ASU 2020-06. In August 2020, the FASB issued 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 removes the separation models for convertible instruments with cash or beneficial conversion features. Instead, entities will account for convertible debt instruments wholly as debt, unless certain other conditions are met. The adoption of ASU 2020-06 is expected to prospectively reduce reported interest expense and increase reported net income, and result in a reclassification of certain conversion feature balance sheet amounts from stockholders' equity to liabilities as it relates to the 2024 Notes. ASU 2020-06 is effective for fiscal years beginning after December 15, 2021, including interim periods within those fiscal years. We will adopt ASU 2020-06 on January 1, 2022 using the modified retrospective transition method, which allows for a cumulative-effect adjustment in the period of adoption and does not require restatement of prior period amounts. Under this transition method, the cumulative effect of the accounting change is expected to increase the carrying amount of the 2024 Notes by $42.2 million, reduce deferred tax liabilities by $10.0 million, reduce the accumulated deficit by $74.6 million, reduce additional paid-in capital by $106.8 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 $10.9 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. We are responsible for all development, manufacturing, and commercialization costs. 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. In addition, we have entered into a 2-year research collaboration with Heptares that, unless extended by the parties, is scheduled to expire in December 2023.

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. 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.

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. 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.

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.

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 6 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.

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.

In connection with the agreement, we paid Xenon $30.0 million upfront and purchased approximately 1.4 million shares of Xenon common stock (at $14.196 per share) for $20.0 million. 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 for the 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.

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.

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.

In connection with the agreement, we paid Voyager $115.0 million upfront and purchased approximately 4.2 million shares of Voyager common stock (at $11.9625 per share) for $50.0 million. 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.

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 1 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.

In connection with the FDA's approval for ONGENTYS for Parkinson's disease in April 2020, we paid BIAL a regulatory milestone of $20.0 million, which was expensed as R&D in 2020. In connection with the FDA's acceptance of the NDA for opicapone for Parkinson's disease in 2019, we paid BIAL a regulatory milestone of $10.0 million, which was expensed as R&D in 2019.

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 9 months' written notice to BIAL. BIAL may terminate the agreement in the event we fail to meet the minimum sales requirements for any 2 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. MTPC is responsible for all development, manufacturing and commercialization costs of valbenazine in such markets.

Under the terms of the license agreement, we may be entitled to receive potential future payments of up to $55.0 million upon the achievement of certain event-based milestones and would be entitled to receive royalties at tiered percentage rates on MTPC's future net sales of valbenazine for the longer of 10 years or the life of the related patent rights.

In connection with MTPC's submission of a filing for marketing authorization for valbenazine for the treatment of tardive dyskinesia in Japan in April 2021, we received a regulatory milestone of $15.0 million, which was recognized as collaboration revenue in 2021.

We are currently conducting the KINECT-HD study, a placebo-controlled Phase III study of valbenazine in adult Huntington disease patients with chorea. In connection with our performance of the study, we recognized non-cash collaboration revenue of $5.7 million for 2021, $2.6 million for 2020 and $0.9 million for 2019. As of December 31, 2021, $1.0 million of revenue is being deferred in connection with our continuing performance obligations under the collaboration and will be recognized as non-cash collaboration revenue over the remaining study period using an input method according to costs incurred to-date relative to estimated total costs associated with the study.

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.

Under the terms of the license agreement, we may be entitled to receive potential future payments of up to $366.0 million upon the achievement of certain event-based milestones and will continue to receive royalties at tiered percentage rates on AbbVie's quarterly net sales of elagolix for the longer of 10 years or the life of the related patent rights.

AbbVie launched ORILISSA® (elagolix tablets) in the United States in August 2018 as an FDA-approved oral medication for the management of moderate to severe endometriosis pain in women. In June 2020, AbbVie launched ORIAHNN® (elagolix, estradiol and norethindrone acetate capsules and elagolix capsules) in the United States as an FDA-approved oral medication for the management of heavy menstrual bleeding associated with uterine fibroids in pre-menopausal women. We recognized elagolix royalty revenue of $22.3 million for 2021, $19.2 million for 2020 and $14.3 million for 2019.

In connection with the FDA's approval for AbbVie's ORIAHNN for uterine fibroids in May 2020, we received a regulatory milestone of $30.0 million, which was recognized as collaboration revenue in 2020. In connection with the FDA's acceptance of AbbVie's NDA for ORIAHNN for uterine fibroids in 2019, we received a regulatory milestone of $20.0 million, which was recognized as collaboration revenue in 2019.

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. Debt Securities

The following table summarizes the amortized cost, unrealized gain and loss recognized in accumulated other comprehensive income (loss) and fair value of debt securities available-for-sale at December 31, 2021, aggregated by major security type and contractual maturity:

		December 31, 2021				December 31, 2020			
(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	$ 204.8	$ —	$ —	$ 204.8	$ 82.2	$ —	$ —	$ 82.2
Corporate debt securities	0 to 1 years	128.2	—	(0.1)	128.1	299.3	1.4	—	300.7
Securities of government-sponsored entities	0 to 1 years	37.6	—	—	37.6	230.9	0.1	—	231.0
		$ 370.6	$ —	$ (0.1)	$ 370.5	$ 612.4	$ 1.5	$ —	$ 613.9
Corporate debt securities	1 to 3 years	$ 358.9	$ —	$ (1.5)	$ 357.4	$ 144.8	$ 0.4	$ —	$ 145.2
Securities of government-sponsored entities	1 to 3 years	204.3	—	(1.0)	203.3	81.9	0.1	(0.1)	81.9
		$ 563.2	$ —	$ (2.5)	$ 560.7	$ 226.7	$ 0.5	$ (0.1)	$ 227.1

As of December 31, 2021, our security portfolio consisted of 164 debt securities available-for-sale, including 136 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. We did not recognize an allowance for credit losses as of December 31, 2021 or 2020.

The following table summarizes debt securities available-for-sale in an unrealized loss position for less than 12 months, aggregated by major security type. There were no debt securities available-for-sale in an unrealized loss position for longer than 12 months as of December 31, 2021 or 2020.

	December 31, 2021		December 31, 2020	
(in millions)	Fair Value	Unrealized Loss	Fair Value	Unrealized Loss
Corporate Debt Securities	$ 428.6	$ (1.6)	$ —	$ —
Securities of government-sponsored entities	230.5	(1.0)	95.0	(0.1)
	$ 659.1	$ (2.6)	$ 95.0	$ (0.1)

4. Fair Value Measurements

Investments, which were measured at fair value on a recurring basis, consisted of the following:

	December 31, 2021				December 31, 2020			
		Fair Value Measurements Using				Fair Value Measurements Using		
(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	$ 340.8	$ 340.8	$ —	$ —	$ 187.1	$ 187.1	$ —	$ —
Restricted cash:								
Certificates of deposit	3.2	3.2	—	—	3.2	3.2	—	—
Debt securities available-for-sale:								
Commercial paper	204.8	—	204.8	—	82.2	—	82.2	—
Corporate debt securities	485.5	—	485.5	—	445.9	—	445.9	—
Securities of government-sponsored entities	240.9	—	240.9	—	312.9	—	312.9	—
Equity securities:								
Equity securities–biotechnology industry	63.7	52.7	—	11.0	38.2	—	—	38.2
	$ 1,338.9	$ 396.7	$ 931.2	$ 11.0	$ 1,069.5	$ 190.3	$ 841.0	$ 38.2

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)	2021	2020	2019
Balance at beginning of period	$ 38.2	$ 55.9	$ —
Purchases [1]	4.6	—	68.9
Unrealized gain (loss) included in earnings	20.9	(17.7)	(13.0)
Transfers out of Level 3 [2]	(52.7)	—	—
Balance at end of period	$ 11.0	$ 38.2	$ 55.9

(1) In September 2021, we purchased 0.3 million shares of Xenon's common stock, valued at $4.6 million on the date of purchase, in connection with the European Union’s approval of the clinical trial application for NBI-921352.

(2) In the fourth quarter of 2021, our equity security investment in Xenon was transferred from Level 3 to Level 1 as the associated holding period restriction expired.

As of December 31, 2021, the discount for lack of marketability used in the valuation analysis of our Voyager equity security investment was 2.5%. Unrealized gains and losses on equity security investments are included in other income (expense), net.

5. Convertible Senior Notes

On May 2, 2017, we completed a private placement of $517.5 million in aggregate principal amount of the 2024 Notes and entered into the 2017 Indenture with respect to the 2024 Notes. The net proceeds from the issuance of the 2024 Notes were approximately $502.8 million, after deducting commissions and the offering expenses payable by us. The 2024 Notes accrue interest at a fixed rate of 2.25% per year, payable semiannually in arrears on May 15 and November 15 of each year, and mature on May 15, 2024.

In November 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 recognized 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.

We may redeem for cash all or part of the 2024 Notes if the last reported sale price (as defined in the 2024 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, 2021) 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, 2021) on each applicable trading day;

(ii) during the 5 business-day period immediately after any 5 consecutive trading-day period (the measurement period) in which the trading price (as defined in the 2024 Indenture) per $1,000 principal amount of the 2024 Notes for each trading day of the measurement period was less than 98% of the product of the last reported sale price of 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 may convert their 2024 Notes at any time.

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 2024 Indenture), in either cash or shares of our common stock. In the event of conversion, holders would forgo all future interest payments, any unpaid accrued interest, and the possibility of further stock price appreciation. Upon the receipt of conversion requests, the settlement of the 2024 Notes will be paid pursuant to the terms of the 2024 Indenture.

The initial conversion rate for the 2024 Notes is 13.1711 shares of common stock per $1,000 principal amount, which is equivalent to an initial conversion price of approximately $75.92 per share of our common stock. At the initial conversion rate, settlement of the 2024 Notes for shares of our common stock would approximate 5.0 million shares. The conversion rate will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. The initial conversion price of the 2024 Notes represented a premium of approximately 42.5% to the closing sale price of $53.28 per share of our common stock on the Nasdaq Global Select Market on April 26, 2017, the date that we priced the private offering of the 2024 Notes.

If we undergo a fundamental change, as defined in the 2024 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 2024 Indenture) occurs prior to January 15, 2024, we will, 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.

While the 2024 Notes were classified as a long-term liability as of December 31, 2021, the future convertibility and associated balance sheet classification will be monitored at each quarterly reporting date and analyzed dependent upon market prices of our common stock during the prescribed measurement periods. In the event that we have the election to redeem the 2024 Notes or the holders of the 2024 Notes have the election to convert the 2024 Notes at any time during the prescribed measurement period, the 2024 Notes would then be considered a current obligation and classified as such.

We are required to separately account for the liability and equity components of the 2024 Notes. The liability component of the instrument was valued in a manner that reflects the market interest rate for a similar nonconvertible instrument at the date of issuance. The initial carrying value of the liability component of $368.3 million was calculated using a 7.5% assumed borrowing rate. The equity component of $149.2 million, representing the conversion option, was determined by deducting the fair value of the liability component from the par value of the 2024 Notes and recorded in additional paid-in capital on the consolidated balance sheet on the issuance date. The equity component is treated as a discount on the liability component of the 2024 Notes, which is currently being amortized over the 7-year term of the 2024 Notes using the effective interest rate method. The equity component is not re-measured as long as it continues to meet the conditions for equity classification. As of December 31, 2021, the remaining period over which the discount on the liability component will be amortized was approximately 2.4 years. We plan to adopt ASU 2020-06 on January 1, 2022 using the modified retrospective transition method. Among other changes, ASU 2020-06 removes the separation models for convertible instruments with cash or beneficial conversion features. Refer to Note 1 to the consolidated financial statements for more information.

We allocated the total transaction costs of approximately $14.7 million related to the issuance of the 2024 Notes to the liability and equity components of the 2024 Notes based on their relative values. Transaction costs attributable to the liability component are amortized to interest expense over the 7-year term of the 2024 Notes, and transaction costs attributable to the equity component are netted with the equity component in stockholders’ equity.

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

The 2024 Notes, net of discounts and deferred financing costs, consisted of the following:

	December 31,	
(in millions)	**2021**	**2020**
Principal	$ 381.2	$ 381.3
Deferred financing costs	(2.9)	(4.0)
Debt discount, net	(43.2)	(59.4)
Net carrying amount	$ 335.1	$ 317.9

The 2024 Notes were recorded at the estimated value of a similar non-convertible instrument on the date of issuance and accretes to the face value of the 2024 Notes over their 7-year term. The fair value of the 2024 Notes, which was estimated utilizing market quotations from an over-the-counter trading market (Level 2), was $464.7 million as of December 31, 2021 and $514.3 million as of December 31, 2020.

6. Other Balance Sheet Details

Inventory consisted of the following:

(in millions)	December 31, 2021	December 31, 2020
Raw materials	$ 11.2	$ 16.6
Work in process	3.6	2.4
Finished goods	15.7	9.0
Total inventory	$ 30.5	$ 28.0

Property and equipment, net, consisted of the following:

(in millions)	December 31, 2021	December 31, 2020
Tenant improvements	$ 34.9	$ 29.5
Scientific equipment	51.6	39.2
Computer equipment	18.1	13.9
Furniture and fixtures	5.9	3.7
	110.5	86.3
Less accumulated depreciation	(51.9)	(41.7)
Total property and equipment, net	$ 58.6	$ 44.6

Accounts payable and accrued liabilities consisted of the following:

(in millions)	December 31, 2021	December 31, 2020
Accrued employee related costs	$ 50.6	$ 38.2
Revenue-related reserves for discounts and allowances	62.7	34.6
Accrued development costs	32.4	32.9
Current branded prescription drug fee	28.6	23.6
Accounts payable and other accrued liabilities	51.5	39.4
Total accounts payable and accrued liabilities	$ 225.8	$ 168.7

The following table provides 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, 2021	December 31, 2020
Cash and cash equivalents	$ 340.8	$ 187.1
Restricted cash	3.2	3.2
Total cash, cash equivalents and restricted cash	$ 344.0	$ 190.3

7. Earnings Per Share

Earnings per share were calculated as follows:

(in millions, except per share data)	Year Ended December 31, 2021	2020	2019
Net income - basic and diluted	$ 89.6	$ 407.3	$ 37.0
Weighted-average common shares outstanding:			
Basic	94.6	93.1	91.6
Effect of dilutive securities:			
Stock options	1.8	2.4	2.6
Restricted stock units	0.3	0.5	0.4
2024 Notes	1.1	1.8	1.1
Diluted	97.9	97.8	95.7
Earnings per share:			
Basic	$ 0.95	$ 4.38	$ 0.40
Diluted	$ 0.92	$ 4.16	$ 0.39

Shares which have been excluded from diluted per share amounts because their effect would have been anti-dilutive were 4.1 million for 2021, 2.5 million for 2020 and 2.1 million for 2019.

8. Share-Based Compensation

In May 2011, we adopted the 2011 Equity Incentive Plan, as amended, or the 2011 Plan. The 2011 Plan authorized 21 million shares of common stock for issuance and allowed for the grant of stock options, stock appreciation rights, restricted stock awards, restricted stock unit awards, or RSUs, performance stock awards, performance-based restricted stock units, or PRSUs, and certain other awards. During 2020, the 2011 Plan was merged into the 2020 Plan (defined below). As a result, there were no shares of common stock remaining available for future grant under the 2011 Plan.

In May 2018, we adopted the 2018 Employee Stock Purchase Plan, or ESPP, pursuant to which 0.3 million shares of common stock are authorized for issuance. As of December 31, 2021, 0.1 million shares of common stock remain available for future grant under the 2018 ESPP.

In May 2020, we adopted the 2020 Equity Incentive Plan, or the 2020 Plan. The 2020 Plan authorized 3.3 million shares of common stock for issuance and allows for the grant of stock options, stock appreciation rights, restricted stock awards, RSUs, performance stock awards, PRSUs and certain other awards. The 2011 Plan was merged into the 2020 Plan and, as a result, all remaining shares in the 2011 Plan were transferred into the 2020 Plan. As of December 31, 2021, 5.4 million shares of common stock remain available for future grant under the 2020 Plan.

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

(in millions)	Year Ended December 31, 2021	2020	2019
Selling, general and administrative expense	$ 85.8	$ 66.3	$ 49.5
Research and development expense	48.4	33.7	25.8
Total share-based compensation expense	$ 134.2	$ 100.0	$ 75.3

Share-based compensation expense by award-type follows:

(in millions)	Year Ended December 31, 2021	2020	2019
Stock options	$ 60.5	$ 47.5	$ 36.5
RSUs	62.5	44.2	30.5
PRSUs	7.6	5.3	5.6
ESPP	3.6	3.0	2.7
Total share-based compensation expense	$ 134.2	$ 100.0	$ 75.3

As of December 31, 2021, unrecognized share-based compensation expense by award-type and the weighted-average period over which such expense is expected to be recognized, as applicable, were as follows:

(dollars in millions)	Unrecognized Expense	Weighted-Average Recognition Period
Stock options	$ 101.7	2.5 years
RSUs	$ 150.5	2.2 years

Stock Options. Typically, stock options have a 10-year term and vest over a 3 to 4-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 $45.02 for 2021, $45.67 for 2020 and $41.74 for 2019.

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,		
	2021	2020	2019
Risk-free interest rate	0.6 %	1.4 %	2.4 %
Expected volatility of common stock	45.9 %	48.5 %	54.8 %
Dividend yield	0.0 %	0.0 %	0.0 %
Expected option term	5.2 years	5.3 years	5.4 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.

A summary of activity related to stock options follows:

(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, 2020	6.8	$ 62.98		
Granted	1.8	$ 110.74		
Exercised	(0.7)	$ 28.02		
Canceled	(0.2)	$ 103.30		
Outstanding at December 31, 2021	7.7	$ 76.38	6.5 years	$ 136.4
Exercisable at December 31, 2021	5.2	$ 63.53	5.5 years	$ 134.7

The total intrinsic value of stock options exercised was $58.0 million for 2021, $40.2 million for 2020 and $64.3 million for 2019. Cash received from stock option exercises was $20.7 million for 2021, $23.5 million for 2020 and $27.3 million for 2019.

Restricted Stock Units. RSUs typically vest over a 4-year period. The fair value of RSUs is based on the closing sale price of our common stock on the date of issuance. RSUs may be subject to a deferred delivery arrangement at the election of eligible employees.

A summary of activity related to RSUs follows:

(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, 2020	1.5	$ 89.60		
Granted [1]	1.2	$ 104.95		
Released	(0.6)	$ 82.22		
Canceled	(0.1)	$ 101.71		
Unvested at December 31, 2021	2.0	$ 99.96	1.3 years	$ 174.1

[1] In August 2021, our board of directors approved an equity grant of approximately 0.5 million RSUs, which will vest over a 2-year period, to our full-time employees other than our executive officers.

The total fair value of RSUs that vested was $64.3 million for 2021, $49.7 million for 2020 and $36.1 million for 2019.

Performance-Based Restricted Stock Units. PRSUs vest based on the achievement of certain predefined Company-specific performance criteria and expire 3 to 4 years from the grant date. The fair value of PRSUs is estimated based on the closing sale price of our common stock on the date of grant. Expense recognition for PRSUs commences when attainment of the performance-based criteria is determined to be probable.

A summary of activity related to PRSUs follows:

(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, 2020	0.2	$ 102.90		
Granted	0.2	$ 114.68		
Unvested at December 31, 2021	0.4	$ 109.31	1.2 years	$ 30.9

As of December 31, 2021, unrecognized share-based compensation expense for PRSUs was $32.0 million. The total fair value of PRSUs that vested was $13.5 million for 2020. No PRSUs vested during 2021 or 2019.

Employee Stock Purchase Plan. Under the 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.

9. Income Taxes

Components of income tax expense (benefit) for continuing operations were as follows:

	Year Ended December 31,		
(in millions)	2021	2020	2019
Current:			
Federal	$ —	$ —	$ —
State	6.3	10.1	9.5
Total current taxes	6.3	10.1	9.5
Deferred:			
Federal	5.9	(287.5)	—
State	(0.4)	(23.2)	—
Total deferred taxes	5.5	(310.7)	—
Provision for (benefit from) income taxes	$ 11.8	$ (300.6)	$ 9.5

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)	**2021**	**2020**	**2019**
Federal income taxes at 21%	$ 21.3	$ 22.4	$ 9.8
State income tax, net of federal benefit	6.2	5.5	4.0
Non-deductible expenses	0.2	0.6	0.8
Branded prescription drug fee	4.8	4.9	3.7
Share-based compensation expense	(11.3)	(6.7)	(12.8)
Officer compensation	7.0	3.7	3.1
Change in tax rate	0.2	3.3	(4.1)
Expired tax attributes	0.6	1.1	1.2
Research credits	(22.0)	(39.0)	(10.4)
Change in valuation allowance	5.0	(296.3)	13.9
Other	(0.2)	(0.1)	0.3
Provision for (benefit from) income taxes	$ 11.8	$ (300.6)	$ 9.5

Significant components of our deferred tax assets as of December 31, 2021 and 2020 are listed below.

	December 31,	
(in millions)	**2021**	**2020**
Deferred tax assets:		
Net operating losses	$ 90.3	$ 111.4
Research and development credits	129.7	109.6
Capitalized research and development	17.9	24.7
Share-based compensation expense	38.9	29.8
Operating lease assets	29.3	25.2
Intangible assets	86.1	86.7
Other	21.6	23.9
Total deferred tax assets	413.8	411.3
Deferred tax liabilities:		
Convertible senior notes	(9.9)	(13.8)
Operating lease liabilities	(23.3)	(19.9)
Other	(10.7)	(8.4)
Total deferred tax liabilities	(43.9)	(42.1)
Net of deferred tax assets and liabilities	369.9	369.2
Valuation allowance	(54.8)	(49.8)
Net deferred tax assets	$ 315.1	$ 319.4

As of December 31, 2021, our deferred tax assets were primarily the result of federal net operating loss carry forwards, capitalized research costs, acquired intangible assets and tax credit carryforwards. As of December 31, 2021 and 2020, we recorded a valuation allowance of $54.8 million and $49.8 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, 2021, management determined there was sufficient positive evidence to conclude that it is more likely than not deferred tax assets of $315.1 million are realizable. The recorded valuation allowance of $54.8 million consisted primarily of state net operating loss and credit carryforwards for which management could not conclude it is more likely than not to be realized.

As of December 31, 2021, we had federal and state income tax net operating loss carryforwards of $421.1 million and $329.9 million, respectively. The federal net operating losses will begin to expire in 2028, unless previously utilized.

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.

In addition, we had federal and state R&D tax credit carryforwards of $107.3 million and $66.3 million, respectively. A portion of the federal R&D tax credit carryforwards expired in 2021. The remaining federal R&D tax credits will continue to expire beginning in 2022, unless previously utilized. The California R&D tax credits carry forward indefinitely and the R&D tax credits related to other states will begin to expire in 2022, 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, 2021.

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.

Our policy is to recognize interest or penalties related to income tax matters in income tax expense. Interest and penalties related to income tax matters were not material for 2021, 2020 or 2019.

We are subject to taxation in the United States and various state jurisdictions. Our tax years for 2001 for federal and since inception for California and forward are subject to examination by federal and state tax authorities due to the carryforward of unutilized net operating losses and R&D tax credits.

A summary of activity related to unrecognized tax benefits follows:

	Year Ended December 31,		
(in millions)	**2021**	**2020**	**2019**
Balance at January 1	$ 60.8	$ 63.9	$ 54.8
Increase (decrease) related to prior year tax positions	0.6	(5.7)	0.3
Increase related to current year tax positions	4.9	3.9	9.5
Settlements related to prior year tax positions	—	(0.2)	—
Expiration of the statute of limitations for the assessment of taxes	(1.7)	(1.1)	(0.7)
Balance at December 31	$ 64.6	$ 60.8	$ 63.9

We excluded those deferred tax assets that are not more-likely-than-not to be sustained under the technical merits of the tax position. Such unrecognized tax benefits totaled $4.9 million for current year tax positions, as reflected in the table above.

As of December 31, 2021, we had $57.4 million of unrecognized tax benefits that, if recognized and realized, would affect the effective tax rate, subject to the valuation allowance. We do not expect a significant change in our unrecognized tax benefits in the next twelve months.

10. Leases

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

The following tables present supplemental operating lease information.

(in millions)	Year Ended December 31, 2021	2020	2019
Operating lease cost	$ 15.3	$ 10.1	$ 8.1
Cash paid for amounts included in the measurement of operating lease liabilities	$ 12.6	$ 8.6	$ 7.7

(in millions, except weighted average data)	December 31, 2021	2020
Weighted average remaining lease term	8.8 years	10.3 years
Weighted average discount rate	5.2 %	5.6 %
Restricted cash related to letters of credit issued in lieu of cash security deposits	$ 3.2	$ 3.2

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

(in millions)	December 31, 2021
Year ending December 31, 2022	$ 17.0
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
Thereafter	70.4
Total operating lease payments	154.3
Less accreted interest	32.5
Total operating lease liabilities	121.8
Less current operating lease liabilities included in other current liabilities	16.5
Noncurrent operating lease liabilities	$ 105.3

11. 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 $8.1 million for 2021, $6.7 million for 2020 and $4.9 million for 2019.

12. Subsequent Events

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 6-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.

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 5 years each.

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, 2021. 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, 2021, 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, 2021, 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, 2021, 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, 2021 and 2020, 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, 2021, and the related notes and our report dated February 11, 2022 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 11, 2022

Item 9B. *Other Information*

On February 8, 2022, we entered into a lease agreement, or the Lease, with Gemdale Aperture Phase I, LLC for the lease of approximately 535,000 gross square feet of office, laboratory and ancillary space, or the Premises, on a 15.72-acre campus located at 6040 Edgewood Bend Court, San Diego, California 92130, or the Property, for our future principal executive offices, and laboratory space for research and development and related uses. The Premises will be delivered to us in two phases, with the initial Premises consisting of two buildings containing a total of approximately 240,000 gross square feet, or Phase 1, and the subsequent premises consisting of two buildings containing a total of approximately 295,000 gross square feet, or Phase 2. We also have the option to expand into a to-be-constructed fifth building, which would contain approximately 121,000 gross square feet, subject to the terms set forth in the Lease. Subject to certain conditions set forth in the Lease, we also have a right of first refusal to purchase the Property.

The commencement date for Phase 1 is expected to occur on or around March 28, 2023, or the Phase 1 Commencement Date, and the commencement date for Phase 2 is expected to occur on or around February 1, 2025. The Lease will have an initial term of approximately 13 years and 7 months, commencing on the Phase 1 Commencement Date, unless terminated earlier, or the Term. We have two options to extend the Term by five years each. Base rent for each of Phase 1 and Phase 2 will be abated for 10 months following the Phase 1 Commencement Date and Phase 2 Commencement Date, respectively. Following the abatement period for Phase 1, the base rent payable for Phase 1 will be $6.00 per gross square foot, or approximately $1.4 million per month, which amount will increase by 3% per year over the Term. Following the abatement period for Phase 2, the per gross square foot base rent payable for Phase 2 will be equal to the per gross square foot base rent being paid for the Phase 1 Premises at such time. We will also enter into a letter of credit equal to base rent due for the Premises during the last month of the initial Term.

Upon vacating our current principal executive offices at 12780 El Camino Real, San Diego, California 92130, we intend to sublet such facilities.

The foregoing description of the material terms of the Lease is qualified in its entirety by reference to the full text of the Lease, a copy of which will be filed as an exhibit to a subsequent filing with the SEC.

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 2022 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2021. 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 2022 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2021. 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 2022 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2021. 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 2022 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2021. 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 2022 Annual Meeting of Stockholders, to be filed pursuant to Regulation 14A with the SEC within 120 days of December 31, 2021. 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, 2021 and 2020

Consolidated Statements of Income and Comprehensive Income for the years ended December 31, 2021, 2020 and 2019

Consolidated Statements of Stockholders' Equity for the years ended December 31, 2021, 2020 and 2019

Consolidated Statements of Cash Flows for the years ended December 31, 2021, 2020 and 2019

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: Reference:	Certificate of Incorporation, as amended 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: Reference:	Bylaws 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: Reference:	Form of Common Stock Certificate Incorporated by reference to the Company's Registration Statement on Form S-1 (Registration No. 333-03172)
4.2	Description: Reference:	Indenture, dated as of May 2, 2017, by and between the Company and U.S. Bank National Association, as Trustee 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
4.4	Description: Reference:	Form of Note representing the Company's 2.25% Convertible Notes due 2024 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: Reference:	Description of Common Stock of the Company 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:	License Agreement dated February 9, 2017 between BIAL– Portela & CA, S.A. and the Company
	Reference:	Incorporated by reference to Exhibit 10.4 of the Company's Quarterly Report on Form 10-Q filed on May 5, 2021
10.5*	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
10.6	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
10.7	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
10.8	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
10.9**	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
10.10**	Description:	Collaboration and License Agreement dated November 22, 2021 between Heptares Therapeutics Limited and the Company

Equity Plans and Related Agreements:

10.11+	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

10.12+	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
10.13+	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
10.14+	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
10.15+	Description:	Neurocrine Biosciences, Inc. 2018 Employee Stock Purchase Plan dated May 30, 2018
	Reference:	Incorporated by reference to Exhibit 99.2 of the Company's Current Report on Form 8-K filed on May 30, 2018
10.16+	Description:	Neurocrine Biosciences, Inc. 2020 Equity Incentive Plan
	Reference:	Incorporated by reference to Exhibit 10.1 of the Company's Quarterly Report on Form 10-Q filed on August 3, 2020
10.17+	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

Agreements with Officers and Directors:

10.18+	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
10.19+	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
10.20+	Description:	Employment Agreement dated November 3, 2014 between the Company and Kyle Gano
		Incorporated by reference to Exhibit 10.16 of the Company's Annual Report on Form 10-K filed on February 6, 2020
10.21+	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
10.22+	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
10.23+	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
10.24+	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

Agreements Related to Real Property:

10.25	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

10.26	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
10.27	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
10.28	Description:	Letter of Credit dated December 3, 2007, issued by Wells Fargo Bank, N.A. for the benefit of Kilroy Realty, L.P., as amended on November 20, 2014 and June 19, 2017
	Reference:	Incorporated by reference to Exhibit 10.3 of the Company's Current Report on Form 8-K filed on December 10, 2007; Exhibit 10.5 of the Company's Annual Report on Form 10-K filed on February 9, 2015; and Exhibit 10.2 of the Company's Quarterly Report on Form 10-Q filed on August 3, 2017
10.29	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

+ 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 11, 2022

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

Date: February 11, 2022

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 11, 2022:

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 4.3

NEUROCRINE BIOSCIENCES, INC.

AND

U.S. BANK NATIONAL ASSOCIATION,

as Trustee

FIRST SUPPLEMENTAL INDENTURE

Dated as of December 20, 2021

2.25% Convertible Senior Notes due 2024

FIRST SUPPLEMENTAL INDENTURE, dated as of December 20, 2021 (this "**Supplemental Indenture**"), among Neurocrine Biosciences, Inc., a Delaware corporation (the "**Company**"), as issuer, and U.S. Bank National Association, a national banking association organized under the laws of the United States of America, as trustee (the "**Trustee**"), to the Indenture, dated as of May 2, 2017 (as supplemented or otherwise modified prior to the date hereof, the "**Indenture**"), between the Company and the Trustee.

WHEREAS, the Company has heretofore executed and delivered the Indenture, pursuant to which the Company issued its 2.25% Convertible Senior Notes due 2024 (the "**Notes**") in the original aggregate principal amount of $517,500,000;

WHEREAS, Section 8.01(G) of the Indenture provides that the Company and the Trustee may amend or supplement the Indenture without the consent of any Holder to irrevocably elect or eliminate any Settlement Method or Specified Dollar Amount; *provided*, *however*, that no such election or elimination will affect any settlement method theretofore elected (or deemed to be elected) with respect to any Note pursuant to Section 5.03(A) of the Indenture;

WHEREAS, in connection with the execution and delivery of this Supplemental Indenture, the Trustee has received an Officer's Certificate and an Opinion of Counsel as contemplated by Sections 8.06, 11.02 and 11.03 of the Indenture; and

WHEREAS, the Company has requested that the Trustee execute and deliver this Supplemental Indenture and have satisfied all requirements necessary to make this Supplemental Indenture a valid instrument in accordance with its terms.

WITNESSETH:

NOW THEREFORE, in consideration of the foregoing and for other good and valuable consideration, the receipt of which is hereby acknowledged, the Company covenants and agrees with the Trustee as follows for the equal and ratable benefit of the Holders:

ARTICLE 1

DEFINITIONS

Section 1.01. *Definitions in the Supplemental Indenture*. Unless otherwise specified herein or the context otherwise requires:

(a) a term defined in the Indenture has the same meaning when used in this Supplemental Indenture unless the definition of such term is amended or supplemented pursuant to this Supplemental Indenture;

(b) the terms defined in this Article and in this Supplemental Indenture include the plural as well as the singular; and

(c) unless otherwise stated, a reference to a Section or Article is to a Section or Article of this Supplemental Indenture.

ARTICLE 2

SETTLEMENT METHOD

Section 2.01. *Irrevocable Elimination of Physical Settlement*. In accordance with Section 8.01(G) of the Indenture, the Company hereby irrevocably elects to eliminate Physical Settlement; *provided* that this election shall not affect any Settlement Method heretofore elected (or deemed to be elected).

Section 2.02. *Amendment*

The definition of "Specified Dollar Amount" in Section 1.01 of the Indenture is hereby amended and restated in its entirety to read as follows:

"Specified Dollar Amount" means, with respect to the conversion of a Note to which Combination Settlement applies, the maximum cash amount per $1,000 principal amount of such Note deliverable upon such conversion (excluding cash in lieu of any fractional share of Common Stock); *provided* that the Specified Dollar Amount shall in no event be less than $1,000.

ARTICLE 3

MISCELLANEOUS

Section 3.01. *Ratification of Indenture*. The Indenture, as supplemented by this Supplemental Indenture, is in all respects ratified and confirmed, and this Supplemental Indenture shall be deemed part of the Indenture in the manner and to the extent herein and therein provided.

Section 3.02. *Trustee Not Responsible for Recitals*. The recitals herein contained are made by the Company and not by the Trustee, and the Trustee assumes no responsibility for the correctness thereof. The Trustee makes no representation as to the validity or sufficiency of this Supplemental Indenture. All of the provisions contained in the Indenture in respect of the rights, privileges, immunities, powers, and duties of the Trustee shall be applicable in respect of the Supplemental Indenture as fully and with like force and effect as though set forth in full herein.

Section 3.03 *Successors*. All agreements of the Company and the Trustee in this Supplemental Indenture will bind their respective successors.

Section 3.04. *Governing Law*. THIS SUPPLEMENTAL INDENTURE AND ANY CLAIM, CONTROVERSY OR DISPUTE ARISING UNDER OR RELATED TO THIS SUPPLEMENTAL INDENTURE SHALL BE GOVERNED BY, AND CONSTRUED IN ACCORDANCE WITH, THE LAWS OF THE STATE OF NEW YORK.

Section 3.05. *Headings, Etc.* The titles and headings of the articles and sections of this Supplemental Indenture have been inserted for convenience of reference only, are not to be considered a part hereof, and shall in no way modify or restrict any of the terms or provisions hereof.

Section 3.06. *Execution in Counterparts*. This Supplemental Indenture may be executed in any number of counterparts, each of which shall be an original, but such counterparts shall together constitute but one and the same instrument. The exchange of copies of this Supplemental Indenture and of signature pages by facsimile or PDF transmission shall constitute effective execution and delivery of this Supplemental Indenture as to the parties hereto and may be used in lieu of the original Supplemental Indenture for all purposes. Signatures of the parties hereto transmitted by facsimile or PDF shall be deemed to be their original signatures for all purposes.

Section 3.07. *Severability*. In the event any provision of this Supplemental Indenture, or any portion thereof, shall be invalid, illegal or unenforceable, then (to the extent permitted by law) the validity, legality or enforceability of the remaining provisions, or any portion thereof, shall not in any way be affected or impaired.

Section 3.08. *Waiver of Jury Trial*. EACH OF THE COMPANY AND THE TRUSTEE HEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF OR RELATING TO THIS SUPPLEMENTAL INDENTURE OR THE TRANSACTIONS CONTEMPLATED HEREBY.

[Signature Page Follows]

IN WITNESS WHEREOF, the parties hereto have caused this Supplemental Indenture to be duly executed as of the day and year first above written.

NEUROCRINE BIOSCIENCES, INC.

By: _____
Name: Matthew C. Abernethy
Title: Chief Financial Officer

U.S. BANK NATIONAL ASSOCIATION,
as Trustee
By: _____
Name: Benjamin Krueger
Title: Vice President

CERTAIN CONFIDENTIAL INFORMATION CONTAINED IN THIS DOCUMENT, MARKED BY [***], HAS BEEN OMITTED BECAUSE IT IS BOTH (I) NOT MATERIAL AND (II) IS THE TYPE THAT NEUROCRINE BIOSCIENCES, INC. TREATS AS PRIVATE OR CONFIDENTIAL

Dated 22 November 2021

HEPTARES THERAPEUTICS LIMITED (1)

AND

NEUROCRINE BIOSCIENCES, INC. (2)

COLLABORATION AND LICENSE AGREEMENT

CONTENTS

THIS COLLABORATION AND LICENSE AGREEMENT (the "**Agreement**") is entered into as of 22 November 2021 (the "**Execution Date**").

PARTIES

(1) **HEPTARES THERAPEUTICS LIMITED**, a company organized under the laws of England having company number 06267989 and having its principal place of business at the Steinmetz Building, Granta Park, Great Abington, Cambridge, Cambridgeshire, CB21 6DG, United Kingdom ("**Heptares**"); and

(2) **NEUROCRINE BIOSCIENCES, INC.**, a company organized under the laws of Delaware and having its principal place of business at 12780 El Camino Real, San Diego, California 92130 ("**Neurocrine**").

In this Agreement, Neurocrine and Heptares are collectively referred to as the "**Parties**" and each individually a "**Party**".

BACKGROUND

(A) Heptares owns or controls certain Patents and Know-How which may be useful in Developing, manufacturing and Commercializing compounds.

(B) Neurocrine has expertise in the Development, manufacture and Commercialization of pharmaceutical products.

(C) Prior to the Effective Date Heptares has discovered and developed a number of selective muscarinic M1, M4 and M1/M4 receptor agonist compounds for the treatment of various neurological and psychiatric diseases and conditions. One such M4 receptor agonist compound is planned to commence Phase II Clinical Trials and a second is planned to commence Phase I Clinical Trials. The Parties desire to enter into a collaboration and license agreement to further Develop and Commercialize all selective muscarinic M1, M4 and M1/M4 receptor agonist compounds controlled by Heptares or its Affiliates.

(D) Heptares and its Affiliates will retain the right to Develop and Commercialize and otherwise Exploit all M1 Target Agonists (including the M1 Lead Candidate) in all indications in Japan and Neurocrine will have options to co-develop and co-commercialize such M1 Target Agonists in Japan with Heptares.

NOW, THEREFORE, in consideration of the respective covenants set forth herein, the Parties agree as follows:

1 DEFINITIONS

1.1 As used in this Agreement, the following terms shall have the meanings set forth below:

Acting Improperly	the meaning set forth in clause 10.1(a);
Affiliate	any person which directly or indirectly controls, is controlled by or is under common control with the Party in question at the relevant time. As used in this definition of **Affiliate** the term "control" shall mean, as to any person, (a) direct or indirect ownership of fifty percent (50%) or more (or such lesser percentage which is the maximum allowed to be owned by a foreign corporation in a particular jurisdiction) of the voting interests or other ownership interests in the person in question; or (b) possession, directly or indirectly, of the power to direct or cause the direction of management or policies of the person in question (whether through ownership of securities or other ownership interests, by contract or otherwise);
Agreement	the meaning set forth in the Preamble;
[***]	the research, development and license agreement between Heptares and [***];
[***]	the letter agreement [***] between Heptares and [***], in the form agreed to in advance by Neurocrine;
[***]	the letter from [***] to Heptares [***] giving notice of termination of the [***];
Alliance Manager	the meaning set forth in clause 3.9;
Anti-Corruption Laws	the U.S. Foreign Corrupt Practices Act, as amended, the UK Bribery Act 2010, as amended, and any other applicable anti-corruption laws and laws for the prevention of fraud, racketeering, money laundering or terrorism;
Arising IP	all Arising Know-How and Arising Patents;
Arising Know- How	any and all Know-How conceived, generated or developed by or on behalf of either Party or jointly by the Parties in the performance of the Research and Development Programs or any other obligations under this Agreement or exercise of rights under this Agreement, in all cases excluding Heptares Platform Improvements;
Arising Patents	any and all Patents that claim or cover Arising Know-How;
Auditor	the meaning set forth in clause 5.10(b);
Bankruptcy Code	the meaning set forth in clause 8.6(b);
[***]	[***];
Blocking Third Party Patent Right	with respect to any country, a Patent in such country controlled by a Third Party that is reasonably necessary or useful to Exploit any Compound or Licensed Product;
Business Day	any Monday, Tuesday, Wednesday, Thursday or Friday that is not a public holiday in London, England or San Diego, California, USA;
Calendar Quarter	a period of three (3) consecutive months corresponding to the calendar quarters commencing on the first day of January, April, July or October;
Calendar Year	a period of twelve (12) consecutive months corresponding to the calendar year commencing on the first day of January;
cGCP	current Good Clinical Practices as specified in the United States Code of Federal Regulations, ICH Guideline E6, or equivalent Laws of an applicable Governmental Authority of any other relevant country where a clinical trial is being conducted;
cGMP	current Good Manufacturing Practices as specified in the United States Code of Federal Regulations, ICH Guideline Q7A, or equivalent Laws of an applicable Governmental Authority of any other relevant country at the time of manufacture;
Clinical Compounds	the compounds known as [***];
Clinical Trial	any of a Phase I Clinical Trial, Phase II Clinical Trial, Phase III Clinical Trial or a clinical trial conducted after the obtaining of Regulatory Approval;

CMO	Contract Manufacturing Organisation;
Combination Products	products in forms suitable for human or veterinary applications that contain a Compound together with one or more other active ingredients that are sold either as a fixed dose/unit or as separate doses/units in a single package or for a single invoice price and separately packaged;
Commercialize	any and all activities (whether before or after Regulatory Approval for a product) directed to commercially manufacturing, obtaining pricing and reimbursement approvals and regulatory activities pertaining to same, promotion, marketing, importing, distribution or sale (and offer for sale or import or export for sale) for a product. "**Commercializing**" and "**Commercialization**" shall have corresponding meanings;
Commercially Reasonable Efforts	efforts that [***] and taking into account other relevant factors including [***];
Committee Deadlock	the meaning set forth in clause 3.6;
Competitive Product	any Target Agonist;
Compounds	all (a) Heptares Existing Compounds and (b) new Target Agonists discovered, identified or developed as a result of carrying out the Research and Development Programs, and in each case any derivative of the foregoing and any [***] of any such new Target Agonist or Heptares Existing Compounds;

Confidential Information all secret, confidential or proprietary information, Know-How, whether provided in written, oral, graphic, video, computer or other form, provided by or on behalf of one Party (the "Disclosing Party") or its Affiliates to the other Party (the "Receiving Party") or its Affiliates pursuant to this Agreement, including information relating to the Disclosing Party's existing or proposed research, development efforts or Patent applications, business or Exploitation of any Compound or Licensed Product and any other materials that have not been made available by the Disclosing Party to the general public. All information disclosed by a Party under the following agreements between the Parties including: [***] (collectively, the "CDAs") will be deemed such Party's Confidential Information hereunder. Notwithstanding the foregoing sentences, Confidential Information shall not include any information or materials that:

(a) were already known to the Receiving Party (other than under an obligation of confidentiality) at the time of disclosure by the Disclosing Party to the extent such Receiving Party has documentary evidence to that effect;

(b) were generally available to the public or otherwise part of the public domain at the time of its disclosure to the Receiving Party through no breach of this Agreement by the Receiving Party;

(c) became generally available to the public or otherwise part of the public domain after its disclosure, other than through any act or omission of a Party in breach of this Agreement;

(d) were subsequently lawfully disclosed to the Receiving Party by a Third Party who is not bound by any obligation of confidentiality with respect to such information; or

(e) were independently discovered or developed by or on behalf of the Receiving Party without the use of the Confidential Information belonging to the Disclosing Party and the Receiving Party has documentary evidence to that effect;

for purposes hereof, Confidential Information constituting (i) the Licensed Know-How that is specific to the Compounds and Licensed Products shall be deemed to be the Confidential Information of Neurocrine (and Neurocrine shall be the Disclosing Party and Heptares shall be the Receiving Party with respect thereto) and (ii) the existence, scope and terms and conditions of this Agreement shall be the Confidential Information of both Parties (and both Parties shall be the Receiving Party and the Disclosing Party with respect thereto);

specific aspects or details of Confidential Information shall not be deemed to be within the public domain or in the possession of the Receiving Party merely because the Confidential Information is embraced by more general information in the public domain or in the possession of the Receiving Party. Further, any combination of Confidential Information shall not be considered in the public domain or in the possession of the Receiving Party merely because individual elements of such Confidential Information are in the public domain or in the possession of the receiving Party unless the combination and its principles are in the public domain or in the possession of the Receiving Party;

Consumer Price Index the consumer price index (all items) (United Kingdom) as published by the Office for National Statistics for the United Kingdom, or such other index as may be published in substitution;

Control and its correlative terms, "**Controlled**" or "**Controls**" shall mean, with respect to any intellectual property right or other intangible property, that a Party owns or has a license or sublicense to such item or right (other than by operation of the licenses in this Agreement), and has the ability to grant access, license or sublicense in or to such right without violating the terms of any agreement or other arrangement with any Third Party. Notwithstanding the foregoing, except for intellectual property in-licensed by Heptares as of the Effective Date (including under the [***] and the [***]), Third Party intellectual property shall only be considered "**Controlled**" by a Party, if [***];

Crystal Structure an X-ray structure determination of a receptor, typically within the following parameters: [***];

Development	discovery and research activities and any and all activities, including non-clinical, pre-clinical and clinical trials, post approval studies, supporting manufacturing, production process development and formulation and related regulatory activities, directed to obtaining and maintaining Regulatory Approval for a product. "**Develop**" and "**Developing**" shall have corresponding meanings;
Development Costs	[***] costs incurred at [***] in performing the activities under the Research and Development Plans;
Development Plan	the meaning set forth in clause 4.9(c);
Discontinued Patent	the meaning set forth in clause 7.1;
Dispute Auditor	the meaning set forth in clause 5.10(d);
Distributor	any Third Party appointed by Neurocrine or any of its Affiliates or its or their Sublicensees to distribute, market and sell Licensed Product(s), with or without packaging rights, in one or more countries in the Territory, in circumstances where the person purchases its requirements of Licensed Product(s) from Neurocrine or its Affiliates or its or their Sublicensees;
Effective Date	means with respect to this Agreement the date of the expiration or termination of any applicable waiting period under the HSR Act;
EMA	the European Medicines Agency and any successor or replacement agency;
EU	the European Union as at the Effective Date;
European Major Markets	the UK, Germany, France, Spain and Italy;
Existing Patents	the meaning set forth in clause 9.2(b);
Exploit	to make, have made, import, use, sell or offer for sale, including to Develop, Commercialize, register, hold or keep (whether for disposal or otherwise), have used, export, transport, distribute, promote, market or have sold or otherwise dispose of. "**Exploitation**" means the act of Exploiting a compound, product or process;
FDA	the US Food and Drug Administration, and any successor or replacement agency;
Field	all human and non-human diagnostic, prophylactic and therapeutic uses;
First Option	the meaning set forth in clause 2.4;
First Option Information Package	the meaning set forth in clause 2.4;
Force Majeure Event	the meaning set forth in clause 12.4;
Formulation	any pharmaceutical formulation (1) used in a commercial dosage form of a Licensed Product to attenuate its pharmacokinetics (e.g., minimizing Cmax, extending half-life, etc.) and (2) leading to an Arising Patent that is listed in the FDA Orange Book and any equivalent of such Patent in any other country other than the US;
FTE	a full-time equivalent person year consisting of a total of [***] hours of work per Calendar Year directed to scientific, medical, technical, research, clinical and regulatory activities under the Research and Development Plans; overtime, and work on weekends, holidays, and the like [***];
FTE Rate	Heptares' at cost FTE rate which is $[***] per annum and [***];
Future Affiliate	any Affiliate that becomes an Affiliate of Heptares after the Execution Date as a result of Heptares or its parent company, Sosei Group Corporation, being acquired by or merging with a Third Party.
GAAP	with respect to a Party or its Affiliates or its or their sublicensees, US generally accepted accounting principles, International Financial Reporting Standards or such other similar national standards as such Party, Affiliate or sublicensee adopts, in each case, consistently applied;
Generic Penetration	the meaning set forth in clause 5.4(b);

Generic Product	with respect to a Licensed Product, any pharmaceutical or biological product that is distributed by a Third Party under a Regulatory Approval approved by a Regulatory Authority [***] including any product authorized for sale (a) in the U.S. pursuant to [***], (b) in the EU pursuant to [***] or (c) in any other country or jurisdiction pursuant to [***]. A Licensed Product distributed under an NDA or foreign equivalent Drug Approval Application held by Neurocrine (i.e., an authorized generic product) will not constitute a Generic Product with respect to such Licensed Product;
Global Major Markets	the US, European Major Markets, and Japan;
Governmental Authority	any court, tribunal, arbitrator, agency, legislative body, commission, official or other instrumentality of (a) any government of any country, (b) a federal, state, province, county, city or other political subdivision thereof or (c) any supranational body;
Government Official	(a) any person employed by or acting on behalf of a government, government-controlled agency or entity or public international organization, (b) any political party, party official or candidate, (c) any person who holds or performs the duties of an appointment, office or position created by custom or convention or (d) any person who holds himself out to be the authorized intermediary of any of the foregoing;
Hatch-Waxman Act	the U.S. "Drug Price Competition and Patent Term Restoration Act" of 1984, including as set forth at 21 U.S.C. §355(b)(2)(A)(iv) or (j)(2)(A)(vii)(IV);
Heptares Existing Compounds	any and all Target Agonists (i) claimed or covered by the Heptares Existing Compound Patents or (ii) discovered, identified or developed by or on behalf of Heptares or any of its Affiliates prior to the Effective Date, including the Clinical Compounds and the Nonclinical Compounds;
Heptares Existing Compound IP	Heptares Existing Compound Know-How and Heptares Existing Compound Patents;
Heptares Existing Compound Know-How	any and all Know-How relating to the Heptares Existing Compounds that is Controlled by Heptares or any of its Affiliates as of the Effective Date;
Heptares Existing Compound Patents	the Patents filed [***];
Heptares Muscarinic Assay	an [***] assay that measures [***];
Heptares Platform	Heptares' proprietary platform covering [***];
Heptares Platform Improvement	the meaning set forth in clause 2.2(b);
Heptares Platform IP	all Patents and Know-How owned or Controlled by Heptares before the Effective Date or after the Effective Date during the Term that cover or comprise the Heptares Platform or Heptares Platform Improvements, but excluding (a) any Patents that claim or cover a Target Agonist (including its manufacture or use) and (B) any Know-How that specifically relates to a Target Agonist (including its manufacture or use);
Heptares Retained Rights	the right of Heptares and its Affiliates to continue to Develop and Commercialize and otherwise Exploit either alone or with or for the benefit of a Third Party, subject to Neurocrine's rights under this Agreement, all M1 Target Agonists (including the M1 Lead Candidate) in all indications in Japan. Such right shall include the right to carry out Clinical Trials of M1 Target Agonists in all indications throughout the Territory for the purpose of supporting Development, Commercialization and Exploitation of M1 Target Agonists (including the M1 Lead Candidate) in all indications in Japan, subject to the oversight and approval of the JSC in accordance with clause 3.2;
Heptares Retained Rights IP	means all Know-How conceived, generated or developed by or on behalf of Heptares or any of its Affiliates or licensees in exercising the Heptares Retained Rights and all Patents Controlled by Heptares or its Affiliates that claim or cover such Know-How;
HSR Act	means the Hart Scott Rodino Antitrust Improvements Act of 1976, as amended, and the rules and regulations promulgated thereunder.
HSR Filing	the meaning set forth in clause 12.12(a).
[***]	the compound known by that reference number and having the structure as described in Schedule 4;

[***]	the compound known by that reference number and having the structure described in Schedule 4;
[***]	the compound known by that reference number and having the structure described in Schedule 4;
[***]	the compound known by that reference number and having the structure described in Schedule 4;
[***]	the compound known by that reference number and having the structure described in Schedule 4;
[***]	the compound known by that reference number and having the structure described in Schedule 4;
[***] Research and Development Plan	the plan and associated budget attached at Schedule 1 as amended in accordance with clause 4.2;
[***]Research and Development Program	the program for the Development of [***], to be conducted by the Parties pursuant to the [***] Research and Development Plan during the Research Term;
[***] Research and Development Plan	the plan and associated budget to be prepared by the Parties as amended in accordance with clause 4.2;
[***] Research and Development Program	the program for the Development of [***], to be conducted by the Parties pursuant to the [***] Research and Development Plan during the Research Term;
[***] Research and Development Plan	the plan and associated budget to be prepared by the Parties as amended in accordance with clause 4.2;
[***] Research and Development Program	the program for the Development of [***], to be conducted by the Parties pursuant to the [***] Research and Development Plan during the Research Term;
[***] Research and Development Plan	the plan and associated budget to be prepared by the Parties as amended in accordance with clause 4.2;
[***] Research and Development Program	the program for the Development of [***], to be conducted by the Parties pursuant to the [***] Research and Development Plan during the Research Term;
[***] Research and Development Plan	the plan and associated budget to be prepared by the Parties as amended in accordance with clause 4.2;
[***] Research and Development Program	the program for the Development of [***], to be conducted by the Parties pursuant to the [***] Research and Development Plan during the Research Term;
IND	any Investigational New Drug application, as defined in Title 21 of the Code of Federal Regulations, on file with the FDA before commencement of Clinical Trials, or any comparable filing with any relevant Regulatory Authority in any country or jurisdiction in the Territory;
IND Acceptance	with respect to an IND submitted to the FDA, either (a) [***] days after submission of such IND to the FDA, if at such time the FDA has confirmed in writing that it has no comments to such IND, or (b) if the FDA indicates during such [***]-day period that it will have comments to the IND, [***].
Indemnification Claim Notice	the meaning set forth at clause 11.3;
Indemnified Party	the meaning set forth at clause 11.3;

Indemnifying Party	the meaning set forth at clause 11.3;
Indemnitee	the meaning set forth at clause 11.3;
Indication	each separate and distinct disease, disorder, illness, health condition, or interruption, cessation or disruption of a bodily function, system, tissue type or organ, for which a separate IND must be submitted and a Regulatory Approval by the submission of a new or supplemental NDA is required. [***];
Infringement	the meaning set forth at clause 7.6;
Initiation	of a Clinical Trial shall mean the first dosing of the first patient in the relevant Clinical Trial of a Compound or Licensed Product, as applicable;
Joint Patent	any Patent that claims or covers Arising Know-How owned jointly by the Parties pursuant to clause 7.11;
JPT	the meaning set forth in clause 3.8;
Joint Steering Committee or **JSC**	the meaning set forth in clause 3.1;
Know-How	all technical, scientific, regulatory and other know-how and information, trade secrets, knowledge, technology, methods, processes, practices, formulae, instructions, skills, techniques, procedures, experiences, ideas, concepts, designs, drawings, assembly procedures, computer programs, apparatuses, specifications, data, results and other material, (whether or not patented or patentable) in written, electronic or any other form now known or hereafter developed;
Knowledge	the actual knowledge of, in the case of Heptares, [***], based on such individuals' good faith understanding of the facts and information in their possession or control after reasonable inquiry, including reasonable inquiry of Third Parties;
Launch	on a Licensed Product-by-Licensed Product and country-by-country basis, the first invoiced commercial sale which is a Net Sale by Neurocrine, its Affiliates or their respective Sublicensees of such Licensed Product after grant of Regulatory Approval in such country for such Licensed Product;
Law	all laws, statutes, ordinances, rules, regulations, writs, judgments, decrees, injunctions (whether preliminary or final), orders and other pronouncements having the effect of law of any Governmental Authority;
Licensed IP	the Licensed Know-How and Licensed Patents;
Licensed Know-How	all Know-How owned or Controlled as of the Effective Date or during the Term by Heptares or its Affiliates (excluding (i) any Know-How owned or Controlled by any Future Affiliate as of the date such Future Affiliate becomes an Affiliate of Heptares; or (ii) any additional Know-How owned or Controlled by any Future Affiliate after the date on which such Future Affiliate becomes an Affiliate of Heptares if such Know-How is created without the use of or access to the Heptares Platform IP, Neurocrine Background IP, Neurocrine Patents, or the Licensed IP, except to the extent such Know—How is used by Heptares or any of its Affiliates in the Development of, or otherwise incorporated in, any Compound or Licensed Product) that is necessary or reasonably useful for the Exploitation of Compounds or Licensed Products in the Field in the Territory. Licensed Know-How shall include all Heptares Existing Compound Know-How, any Know-How in the Heptares Retained Rights IP and Heptares' interest in Arising Know-How, but excludes the Heptares Platform IP;
Licensed Patents	any and all Patents that are owned or Controlled by Heptares or its Affiliates as of the Effective Date or during the Term (excluding (i) any Patents owned or Controlled by any Future Affiliate as of the date such Future Affiliate becomes an Affiliate of Heptares; or (ii) any additional Patents owned or Controlled by any Future Affiliate after the date on which such Future Affiliate becomes an Affiliate of Heptares if such Patents cover only inventions made without the use of or access to the Heptares Platform IP, Neurocrine Background IP, Neurocrine Patents, or the Licensed IP, except to the extent such Patents are used by Heptares or any of its Affiliates in the Development of, or otherwise incorporated in, any Compound or Licensed Product) that are necessary or reasonably useful for the Exploitation of Compounds or Licensed Products in the Field in the Territory. Licensed Patents shall include all Heptares Existing Compound Patents, all Patents in the Heptares Retained Rights IP and Heptares' interest in Arising Patents (including any Joint Patents) but shall exclude the Heptares Platform IP;
Licensed Products	any and all pharmaceutical products containing a Compound as an active ingredient, including Combination Products, in any and all formulations, forms, presentations, dosages and formulations;
Losses	the meaning set forth in clause 11.1;

M1	the meaning set forth in the definition of Target;
M1/M4	the meaning set forth in the definition of Target;
M4	the meaning set forth in the definition of Target;
M1 Lead Candidate	[***] or such other M1 Target Agonist selected by Neurocrine (which may be selected from one of the other advanced lead M1 Target Agonists including the Compounds known as [***];
M1 Lead Candidate Research and Development Plan	the plan and associated budget to be prepared by the Parties as amended in accordance with clause 4.2;
M1 Lead Candidate Research and Development Program	the program for the selection and Development of a M1 Lead Candidate, to be conducted by the Parties pursuant to the M1 Lead Candidate Research and Development Plan during the Research Term;
M1 Target Agonist	(i) M1 Target Agonists include the compounds identified as such on Schedule 4; (ii) any Small Molecule that [***].
M1/M4 Dual Target Agonist	(i) M1/M4 Dual Target Agonists include the compounds identified as such on Schedule 4; (ii) any Small Molecule that [***].
M4 Target Agonist	(i) M4 Target Agonists include the compounds identified as such on Schedule 4; (ii) any Small Molecule that [***].
Materials	any tangible chemical or biological material, including any small molecules, DNA, RNA, clones, cells, and any expression product, progeny, derivative or other improvement thereto, along with any tangible chemical or biological material;
MHLW	Ministry of Health, Labour and Welfare of Japan and any successor or replacement;
Milestone Events	the meaning set forth in clause 5.2(a);
Milestone Payments	the meaning set forth in clause 5.2(a);
NDA	a New Drug Application filed with the FDA in conformance with applicable Laws, or the foreign equivalent of any such application in any other country filed with a Regulatory Authority to obtain marketing approval for a pharmaceutical product including a marketing authorisation application (MAA) filed with the EMA or equivalent filed with the MHRA in the UK;

Net Sales with respect to a Licensed Product for any period, the net sales of such Licensed Product in such period reported by [***];

for example, such net sales may consist of [***], less deductions calculated in accordance with [***] for:

(a) [***];
(b) [***];
(c) [***];
(d) [***];
(e) [***];
(f) [***];
(g) [***];
(h) [***];
(i) [***];
(j) [***]; and
(k) [***]

For the purposes of determining Net Sales, a Licensed Product shall be deemed to be sold when [***].

In the event that a Licensed Product is sold in any country and Calendar Quarter in the form of a Combination Product, Net Sales of such Combination Product in such Calendar Quarter shall be adjusted by multiplying actual Net Sales of such Combination Product in such country and Calendar Quarter calculated pursuant to the foregoing definition of Net Sales by the fraction A/(A+B), where A is the average invoice price in such country and Calendar Quarter of any Licensed Product that contains the same Compound(s) as such Combination Product as its sole active ingredient(s), if sold separately in such country and Calendar Quarter and B is the average invoice price in such country and Calendar Quarter of each product that contains active ingredient(s) other than the Compound(s) contained in such Combination Product as its sole active ingredient(s), if sold separately in such country and Calendar Quarter; provided that the invoice price in a country for each Licensed Product that contains only the Compound(s) and each product that contains solely active ingredient(s) other than the Compound(s), included in the Combination Product shall be for a quantity comparable to that used in such Combination Product and of substantially the same class, purity and potency or functionality, as applicable. If either such Licensed Product that contains the Compound(s) as its sole active ingredient or a product that contains the active ingredient(s) (other than the Licensed Product), in the Combination Product as its sole active ingredient(s) is not sold separately in a particular country and Calendar Quarter, [***].

Subject to the above, Net Sales shall be calculated in accordance with [***];

Neurocrine Background IP all Patents or Know-How that are Controlled by Neurocrine or its Affiliates as at the Effective Date or during the Research Term as are necessary or reasonably useful for Heptares to perform activities under the Research and Development Programs;

Neurocrine Patent any Patent that claims or covers Arising Know-How owned solely by Neurocrine pursuant to clause 7.11;

Nonclinical Compounds (a) the compounds known as [***];

Party Representatives the meaning set forth in clause 10.1;

Patents	all patents or patent applications, including any continuations, continuations-in-part, divisions, provisional or any substitute applications, PCT applications, any patent issued with respect to any such patent applications, any reissue, re-examination, renewal or extension (including any supplementary protection certificate) of any such patent, and any confirmation patent or registration patent or patent of addition based on any such patent, and all foreign counterparts of any of the foregoing;
Patent Challenge	the meaning set forth in clause 8.7;
Payment	the meaning set forth in clause 5.7;
Phase I Clinical Trial	as to a specific Licensed Product, a first clinical study conducted in humans;
Phase II Clinical Trial	as to a specific Licensed Product for a specific Indication, a clinical study in patients conducted in accordance with cGCP which may use a variety of study designs and is intended to confirm efficacy, evaluate safety and efficacy in target patient populations, and/or inform the design or endpoints for a subsequent trial, as described in ICH Guideline E8, General Considerations for Clinical Trials; A Phase II Clinical Trial may be carried out in two stages;
Phase III Clinical Trial	as to a specific Licensed Product for a specific Indication, a clinical study conducted in humans in accordance with cGCP to demonstrate or confirm the therapeutic benefit of the Licensed Product in such Indication and to provide an adequate basis for obtaining Regulatory Approval, as described in ICH Guideline E8, General Considerations for Clinical Trials;
PMDA	the Pharmaceuticals and Medical Devices Agency in Japan or any successor organisation thereto;
Product Trademark	the meaning set forth in clause 8.8(b)(viii);
Receptor Model	a set of co-ordinates representing the 3D structure of a receptor, [***];
Regulatory Approval	any and all approvals (excluding pricing and reimbursement approvals), licenses, registrations or authorizations of any Regulatory Authority, necessary to commercially develop, make, test, distribute, sell or market a product in a country, including any: (a) approval for a product (including any supplements and amendments thereto); (b) pre- and post-approval marketing approvals or authorizations (including any manufacturing approval or authorization related thereto); (c) labelling approval; and (d) technical, medical and scientific licenses;
Regulatory Authority	any national, supranational, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity (including the FDA, the EMA, PMDA and MHLW and any other agencies in any country) regulating or otherwise exercising authority with respect to the research, development, manufacture, distribution, marketing, storage, transportation, use or sale of pharmaceutical products;
Regulatory Exclusivity Period	with respect to each Licensed Product in any country in the Territory, a period of exclusivity (other than Patent exclusivity) granted or afforded by Law or by a Regulatory Authority in such country that confers exclusive marketing rights with respect to such Licensed Product in such country or prevents another party from using or otherwise relying on the data supporting the approval of the NDA for such Licensed Product without the prior written consent of the NDA-holder including regulatory data exclusivity and orphan drug designations;
Research and Development Plans	the [***] Research and Development Plan, the [***] Research and Development Plan, the [***] Research and Development Plan, M1 Lead Candidate Research and Development Plan, the [***] Research and Development Plan and the [***] Research and Development Plan;
Research and Development Programs	the [***] Research and Development Program, the [***] Research and Development Program, [***] Research and Development Program, the M1 Lead Candidate Research and Development Program, the [***] Research and Development Program and the [***] Research and Development Program;

Research Term	the period from the Effective Date until the second anniversary of the Effective Date or such later date as maybe agreed by the Parties through the JSC;
Reversion IP	on a Reversion Product-by-Reversion Product basis, all Patents and Know-How that at the Termination Date are Controlled by Neurocrine or its Affiliates and are necessary or are then being used by Neurocrine for the Exploitation of such Reversion Product;
Reversion Product	any Compound or Licensed Product (excluding a Combination Product involving the combination of a Compound with a proprietary product or compound owned or controlled by Neurocrine or its Affiliates, unless agreed otherwise by the Parties in writing) in relation to which this Agreement is terminated;
Royalty Payment	the meaning set forth in clause 5.3;
Royalty Term	the meaning set forth in clause 5.3(c);
Second Licensed Product	the meaning set forth in clause 5.2(f)(i);
Second Option	the meaning set forth in clause 2.4;
Second Option Information Package	the meaning set forth in clause 2.4;
Senior Officer	the Chief Executive Officer of Sosei Group Corporation and the Chief Business Development and Strategy Officer of Neurocrine, or the functional successor in their respective organizations;
Small Molecule	a molecule of molecular weight of less than [***];
StaR	[***];
Sublicensee	an Affiliate or Third Party to which Neurocrine has granted a sublicense under clause 2.1 to develop, make, have made, use, sell offer for sale, import or commercialize a Licensed Product, but excluding Distributors and wholesalers and resellers and Third Parties conducting Development, manufacturing or Commercialization on behalf of Neurocrine or its Affiliates;
Successful	with respect to a Clinical Trial, that the results of such Clinical Trial (a) meet the pre-specified primary endpoint(s) set forth in the protocol for such Clinical Trial and (b) do not indicate a safety finding that either [***];
Successful Completion of a Carcinogenicity Program	with respect to studies approved by the FDA to identify a [***];
Successful Completion of a Long-Term Toxicity Program	with respect to animal studies, that the results of such animal studies [***];
[***] Agreements	shall mean: • [***] • [***] • [***] • [***]
[***] Assigned Patent	the Patents assigned to Heptares pursuant to the assignment between [***] and Heptares Therapeutics Limited [***], which include the following Patents: • [***] • [***] • [***] • [***]
Target	each of muscarinic receptor subtype 1 ("**M1**"), muscarinic receptor subtype 4 ("**M4**"), or both muscarinic receptor subtype 1 and muscarinic receptor subtype 4, where, for clarity, each receptor is targeted ("**M1/M4**"); M1, M4 and M1/M4 collectively, the "**Targets**";
Target Agonists	M1 Target Agonists, M4 Target Agonists and M1/M4 Dual Target Agonists.

Term	the meaning set forth in clause 8.1;
Termination Date	the date on which any termination of this Agreement becomes effective;
Territory	worldwide (save for Japan in relation to the Heptares Retained Rights unless Neurocrine exercises its First Option or Second Option pursuant to clause 2.4);
Third Licensed Product	the meaning set forth in clause 5.2(f)(i);
Third Party	any person who is not a Party or an Affiliate of a Party;
Third Party Claim	the meaning set forth in clause 11.1;
Third Party Payments	the meaning set forth in clause 5.4(a);
US	the United States of America, including all of its territories and possessions;
USD or $	United States Dollars;
Valid Claim	(a) a claim of an issued and unexpired patent included within the Licensed Patents which has not been abandoned, cancelled or held permanently revoked, unenforceable or invalid by a decision of a court or other governmental agency of competent jurisdiction unappealed within the time allowed for appeal, or which has not been admitted to be invalid or unenforceable through reissue or disclaimer or otherwise; or (b) a claim of a pending patent application included within the Licensed Patents which claim was filed and is being prosecuted in good faith and has not been cancelled, withdrawn from consideration, abandoned or finally disallowed without the possibility of appeal or refiling of the application; provided that such prosecution has not been on-going for more than [***] years from such claim's [***];
VAT	(a) in relation to any jurisdiction within the EU, the tax imposed by the Council Directive on the common system of value added tax (2006/112) and any national legislation implementing that directive together with legislation supplemental thereto and the equivalent tax (if any) in that jurisdiction; and (b) in any other country or jurisdiction, any other value added, goods and services or similar tax chargeable on the supply or deemed supply of goods or services under applicable legislation; but, in each event, excluding any US sales tax.

Unless the context of this Agreement otherwise requires:

(a) Words referring to a particular gender include every gender; words using the singular or plural number also include the plural or singular number, respectively;

(b) the terms "hereof," "herein," "hereby," and other similar words refer to this entire Agreement;

(c) the words "include", "includes", and "including" when used in this Agreement shall be deemed to be followed by the words "without limitation", unless otherwise specified;

(d) the term "clause" refers to the specified clause of this Agreement; and

(e) references to any "person" include individuals, sole proprietorships, partnerships, limited partnerships, limited liability partnerships, corporations, limited liability companies, business trusts, joint stock companies, trusts, incorporated associations, joint ventures or similar entities or organisations, and the successors and permitted assigns of that person. Whenever this Agreement refers to a number of days, unless otherwise specified, such number shall refer to calendar days.

2 LICENSE

2.1 Licenses granted by Heptares

Subject to the terms and conditions of this Agreement, Heptares grants to Neurocrine, and Neurocrine hereby accepts:

(a) an exclusive (save as to allow Heptares to carry out the Research and Development Programs in accordance with this Agreement and to allow Heptares to exercise the Heptares Retained Rights), royalty-bearing, sublicensable (through multiple tiers) license to and under the Licensed IP to Exploit Compounds and Licensed Products in the Field in the Territory.

(b) a non-exclusive, sublicensable to subcontractors in accordance with clause 4.5, license to and under the Heptares Platform IP for Neurocrine to conduct activities under the Research and Development Programs.

(c) a non-exclusive, sublicensable (through multiple tiers but solely in conjunction with a license to Exploit a Compound or Licensed Product) license to and under the Heptares Platform IP to the extent necessary to Exploit Compounds and Licensed Products in the Field in the Territory.

2.2 Provision of Licensed Know-How

(a) Within [***] days of the Effective Date, Heptares shall provide Neurocrine with copies, or where applicable, samples of the Licensed Know-How existing at the Effective Date, including Word, Excel and PDF versions of study reports, raw datasets, TLFs, CSRs, INDs or other applications or communications with any Regulatory Authority, any Regulatory Approval, etc. in a manner reasonably agreeable to Neurocrine. To assist with the transfer of such Licensed Know-How, Heptares will make its personnel reasonably available to Neurocrine as requested by Neurocrine and Heptares will provide up to [***] of assistance in connection with this transfer from Heptares' FTEs in the aggregate at no cost to Neurocrine. If such assistance is provided at Neurocrine's facilities, [***].

(b) Thereafter, at a reasonable frequency during the Term, at no additional cost or expense to Neurocrine, Heptares shall provide all Licensed Know-How that has not previously been provided to Neurocrine (whether under this Agreement or otherwise) for use solely in accordance with the license granted under clause 2.1. Heptares shall be under no obligation to disclose Know-How within the Heptares Platform IP unless it is necessary or reasonably useful to Exploit Compounds. If the Parties agree that any such Know-How should be transferred to Neurocrine in connection with the performance of the Research and Development Programs, any Know-How conceived, generated or developed by Neurocrine (solely or jointly with Heptares) using such transferred Know-How that is an improvement to the Heptares Platform and does not relate specifically to Compounds (a "**Heptares Platform**

Improvement") shall be owned by Heptares. Any Know-How that is an improvement to the Heptares Platform and does not relate specifically to Compounds and that is conceived, generated or developed solely by Heptares shall also be deemed to be a Heptares Platform Improvement and shall be owned by Heptares.

2.3 **Heptares Retained Rights**

Subject to the terms of clause 2.4, Heptares and its Affiliates retain the exclusive right under the Licensed IP to exercise the Heptares Retained Rights, and Neurocrine shall have no rights under the Licensed IP or the Heptares Platform IP to Exploit Compounds or Licensed Products that are M1 Target Agonists in Japan. Heptares shall not conduct any Clinical Trial under the Heptares Retained Rights without the JSC's approval of the design of such Clinical Trial. Heptares shall, and shall ensure that its Affiliates and licensees will, exercise the Heptares Retained Rights in compliance with all applicable Laws and in accordance with professional and ethical standards customary in the pharmaceutical and biotechnology industry.

2.4 **Neurocrine Option**

Heptares shall keep Neurocrine regularly updated with regard to its progress in exercising the Heptares Retained Rights through the JSC, by providing to Neurocrine every [***] months a report summarising in reasonable detail Heptares' Development activities and plans under the Heptares Retained Rights. In addition, if Neurocrine has any concerns regarding any such report, Neurocrine will provide details of such concerns to Heptares and at Neurocrine's reasonable request, Heptares shall make available appropriate personnel to meet with Neurocrine to discuss such concerns. Heptares shall provide to Neurocrine the proposed protocol for the first proof of concept Phase II Clinical Trial for the first M1 Target Agonist being Developed by or on behalf of Heptares or its Affiliate in Japan together with a plan and budget for the remainder of the development program for such first M1 Target Agonist in Japan (the **"First Option Information Package**"). Following receipt of the First Option Information Package Neurocrine will have a period of [***] days to exercise an option **(**the **"First Option")**, by notice in writing to Heptares [***]. If Neurocrine exercises the First Option the Parties will agree in good faith within [***] days an amendment to this Agreement as necessary to reflect the exercise by Neurocrine of the First Option, including on matters such as [***]. If Neurocrine does not exercise the First Option and Heptares does not [***] Neurocrine will have the second option (the **"Second Option"**), following Neurocrine's receipt from Heptares of [***] (the "**Second Option Information Package**") [***]. Neurocrine shall have a period of [***] days from the date of its receipt of the Second Option Information Package to exercise the Second Option by notice in writing to Heptares. If Neurocrine exercises the Second Option the Parties will agree in good faith within [***] days an amendment to this Agreement as necessary to reflect the exercise by Neurocrine of the Second Option, including on matters such as [***].

Whether or not Neurocrine exercises the First Option or the Second Option, Neurocrine will have (i) the right to access and use the Heptares Retained Rights IP and (ii) a right to cross reference (to the extent permitted by applicable Law) all Regulatory Approvals (including filings for such approvals) for M1 Target Agonists Controlled by Heptares, its Affiliates or licensees in Japan in each case for the purposes of Exploiting Licensed Products outside Japan in accordance with this Agreement. Heptares will have (i) the right to access and use the Licensed IP and all Arising IP and (ii) a right to cross reference (to the extent permitted by applicable Law) all Regulatory Approvals (including filings for such approvals) for M1 Target Agonists Controlled by Neurocrine, its Affiliates or Sublicensees outside Japan in each case for the purposes of Exploiting M1 Target Agonists in Japan in accordance with this Agreement. The Parties will also negotiate in good faith applicable terms to govern Clinical Trials conducted jointly by the Parties for the benefit of the Compounds and Licensed Products in the Territory and the M1 Target Agonists in Japan.

2.5 **License to Neurocrine Background IP and Arising IP**

Subject to the terms and conditions of this Agreement, Neurocrine grants to Heptares, and Heptares hereby accepts, a non-exclusive, royalty-free license to and under (a) the Neurocrine Background IP for the sole purpose of carrying out the Research and Development Programs in accordance with the Research and Development Plans and (b) Neurocrine's interest in the Arising IP for the purposes of Heptares exercising the Heptares Retained Rights. Neurocrine shall, as reasonably requested by Heptares from time to time, disclose to Heptares all Know-How forming part of Arising IP owned by Neurocrine to the extent reasonably necessary or useful for exercising the Heptares Retained Rights. Heptares may grant sublicenses under this license to subcontractors appointed in accordance with clause 4.5 and shall be entitled to sub-license such rights granted under clause (b) through multiple tiers in connection with its exercise of the Heptares Retained Rights. Any such sublicense shall be granted on terms that are consistent with the terms of this Agreement. Heptares shall provide a copy of each such sublicense agreement with a Third Party, which may be redacted of any terms not

required to confirm consistency with the terms of this Agreement, to Neurocrine and shall be responsible for ensuring that each such sublicensee complies with the terms of this Agreement.

2.6 **Heptares Exclusivity**

Subject to clause 2.7, during the Term, Heptares shall not and shall procure that its Affiliates shall not, directly or indirectly (including by licensing, authorising or enabling a Third Party) Exploit any Competitive Product. For clarity Heptares' exercise of the Heptares Retained Rights shall not be a breach of this Clause 2.6.

2.7 **Competitive Transactions**

Clause 2.6 shall not apply to a Third Party that is not an Affiliate of Heptares at the Effective Date but subsequently becomes an Affiliate as a result of a merger with or acquisition of Heptares occurring after the Effective Date (each a "**Competitive Transaction**"), provided however that if at the time of such Competitive Transaction the Third Party counterparty (that becomes an Affiliate) is Developing or Commercializing a Competitive Product or if such Affiliate thereafter commences Developing or Commercializing a Competitive Product, then such Affiliate may continue to Develop and Commercialize such Competitive Product but may not, directly or indirectly use or practice under any of the Heptares Platform, Heptares Platform IP, Heptares Platform Improvements, or Licensed IP, including Heptares Existing Compound Patents, Arising IP, Neurocrine Background IP or Reversion IP in connection therewith.

2.8 **Retention of Rights**

(a) Except as expressly provided herein, Heptares grants no other right or license, including any rights or licenses to the Licensed IP, the Heptares Platform IP or any other Patent or intellectual property rights not otherwise expressly granted herein.

(b) Except as expressly provided herein, Neurocrine grants no other right or license, including any rights or licenses to the Neurocrine Background IP, Arising IP or any other Patent or intellectual property rights not otherwise expressly granted herein.

2.9 **Sublicensing**

Neurocrine shall be entitled to grant to its Affiliates or one or more Third Parties a sublicense of the rights granted to Neurocrine under clause 2.1 and clause 2.4 without the prior written consent of Heptares. Any such sublicense shall be granted on terms that are consistent with the terms of this Agreement. Neurocrine shall provide a copy of each such sublicense agreement with a Third Party Sublicensee, which may be redacted of any terms not required to confirm consistency with the terms of this Agreement, to Heptares and shall be responsible for ensuring that each such Sublicensee complies with the terms of this Agreement.

2.10 **[***]**

[***]

2.11 **[***] Assigned Patent**

Neither Party shall without the consent of the other Exploit a Compound or Licensed Product that is claimed by the [***] Assigned Patent.

2.12 **Confirmatory Patent License**

Heptares shall, if requested to do so by Neurocrine, immediately enter into confirmatory license agreements substantially in the form reasonably requested by Neurocrine for purposes of recording the licenses granted under this Agreement with such patent offices in the Territory as Neurocrine considers appropriate.

2.13 **Preservation of Licenses**

Heptares shall not, and if any Licensed IP or Heptares Platform IP is owned by or transferred to an Affiliate in accordance with this Agreement (which transfer to an Affiliate may be done only with the prior written consent of Neurocrine, which may not be unreasonably withheld), shall procure that its Affiliates shall not, (a) encumber the Licensed IP (including the Heptares Retained Rights IP) or the Heptares Platform IP in a manner which is inconsistent with the rights and licenses granted to Neurocrine under this Agreement; (b) transfer or assign any of the Licensed IP (including the Heptares Retained Rights IP) or the Heptares Platform IP to an Affiliate or Third Party, unless such transfer or assignment is subject to the rights of and obligations to Neurocrine under this Agreement (and for clarity any assignment of this Agreement is subject to clause 12.1); or (c) grant any rights or licenses under the Licensed IP (including the Heptares Retained Rights IP) or the Heptares Platform IP that are inconsistent with the rights and licenses granted to Neurocrine under this Agreement.

2.14 **Third Party Technology**

(a) If either Party becomes aware of any Third Party's Patents or Know-How that are necessary or useful to Develop, manufacture or Commercialize in the Field any Compound or Licensed Product (collectively, "**Third Party Technology**"), such Party shall promptly notify the other Party, and the Parties shall promptly thereafter meet to discuss such Third Party Technology.

(b) Neurocrine shall have the first right (but no obligation) to attempt to obtain a license to any Third Party Technology, and shall notify Heptares in writing prior to initiating licensing negotiations for any such Third Party Technology. If Neurocrine obtains such license for any Third Party Technology that is necessary or useful to Exploit M1 Target Agonists in Japan, Heptares will have the right to obtain a sublicense thereunder (if permitted under such license agreement provided that Neurocrine shall use its reasonable efforts to obtain the right to grant such a sublicense) to practice the Heptares Retained Rights, subject to the Parties' agreement on [***] to such Third Party Technology. If Neurocrine elects not to obtain any such license, then Heptares shall have the right (but no obligation) to negotiate and enter into a license agreement with such Third Party with respect to such Third Party Technology; provided that Heptares shall not enter into any such license unless the Third Party Technology so licensed, to the extent otherwise within the scope of the definition of Licensed IP, would be Controlled by Heptares (assuming the Parties' agreement on cost allocation); and provided further that Heptares shall notify Neurocrine in writing prior to initiating licensing negotiations for any such Third Party Technology, and prior to entering into such license agreement, Heptares shall provide Neurocrine with a copy thereof and reasonable opportunity to comment thereon and shall consider all such comments of Neurocrine in good faith, and shall not enter into such license agreement without Neurocrine's prior written approval, which shall not be unreasonably withheld.

(c) If Heptares enters into any agreement with a Third Party after the Execution Date under which it Controls Third Party Technology (provided that Heptares shall use its reasonable efforts when obtaining such a license to include the right to grant sublicenses under any such license) that is necessary or useful to Develop, manufacture or Commercialize any Compound or Licensed Product, then if Neurocrine desires to obtain a sublicense thereunder, the Parties shall negotiate in good faith and determine an allocation between the Parties of any payments thereunder that are owed to such Third Party on account of Neurocrine's Development, manufacture or Commercialization of Licensed Products.

3 GOVERNANCE

3.1 **Establishment of JSC**

Within [***] days of the Effective Date, the Parties shall establish a Joint Steering Committee (the "**Joint Steering Committee**" or "**JSC**") for the Research and Development Programs and to provide a forum for communication between the Parties with regard to the Heptares Retained Rights. The JSC shall consist of [***] members appointed by each Party neither of whom may be a Senior Officer. The initial members of the JSC will be nominated by the Parties promptly following the Effective Date. Such representatives shall be individuals suitable in seniority and experience and having delegated authority to make decisions of the JSC with respect to matters within the scope of the JSC's responsibilities. [***] will appoint one of its representatives as the chair of the JSC. The JSC shall operate in accordance with the provisions of clauses 3.2 through 3.8, and shall have no authority to alter or amend the terms and conditions of this Agreement, including any payment conditions or terms, periods for performance, or obligations of the Parties. A Party may change one or more of its

representatives serving on the JSC at any time upon written notice to the other Party. At its meetings, the JSC shall discuss the matters described below and such other matters as are reasonably requested by either Party's Alliance Manager. The JSC shall continue throughout the Term of the Agreement.

3.2 **Responsibilities of JSC**

The JSC shall, during the Research Term and thereafter perform the following functions:

(a) facilitate communication between the Parties;

(b) discuss and review activities relating to the Research and Development Programs;

(c) discuss any matters relating to manufacturing activities as further described in Clause 4.11;

(d) review and approve any initial Research and Development Plan (including the budget) not prepared as of the Effective Date and any updates or amendments to the Research and Development Plans (including the budgets);

(e) establish JPTs and resolving disputes arising from such JPTs;

(f) provide a forum for communication between the Parties regarding the Heptares Retained Rights and for coordinating the activities of Heptares in its exercise of the Heptares Retained Rights with the activities of Neurocrine in relation to the Compounds and Licensed Products in the Territory;

(g) provide a forum for communication between the Parties for Regulatory Approval and Commercialization of Compounds and Licensed Products by Neurocrine in the Territory and applications for Regulatory Approval and Commercialization of M1 Target Agonists by Heptares in Japan;

(h) approve the design of Clinical Trials proposed to be conducted in or outside of Japan by Heptares as part of Heptares exercising the Heptares Retained Rights, review and approve any proposed publications of Heptares resulting from the Heptares Retained Rights and establish a process for sharing of data and information relating to those trials, which may include, for example, agreeing provisions so that (1) feedback received from a Regulatory Authority by a Party in respect of any such trial shall be shared with the other Party, and (2) the Party not conducting the Clinical Trial shall have full access to the clinical study report and all data arising from it, including clinical datasets, for inclusion in the case of Neurocrine, a Neurocrine regulatory filing for a Regulatory Approval for a Licensed Product in the Territory or, in the case of Heptares, a Heptares regulatory filing for a Regulatory Approval for a Licensed Product in Japan (to the extent within the Heptares Retained Rights);

(i) provide a forum for Neurocrine to [***];

(j) provide a forum for the Parties to exercise their oversight responsibilities as set forth in Section 4.10;

(k) provide a forum for Neurocrine to [***];

(l) determining whether in the case of a Licensed Product that contains an M1 Target Agonist, either an IND should be filed for such a Licensed Product or a Clinical Trial application for such Licensed Product should be filed in Europe;

(m) discuss and resolve matters referred from the IP Committee pursuant to clause 7.5; and

(n) perform such other functions as are specifically designated for the JSC in this Agreement or as the Parties otherwise agree in writing.

3.3 **Meetings**

The JSC shall meet at least [***] during the Research Term and every [***] months thereafter during the Term, or at a frequency determined by the JSC, and JSC meetings can be called at other times by agreement between the Parties for any reason including if it is necessary to resolve Committee Deadlocks in accordance with clause 3.6. JSC meetings may be conducted by telephone, video-conference or in person, with at least one meeting per year being in person (where practicable). Any in-person JSC meetings shall be held on an alternating basis between Heptares' and Neurocrine's facilities, unless otherwise agreed by the Parties. Each Party shall be responsible for its own expenses in attending such meetings. As appropriate, the JSC may invite a reasonable number of non-voting employees, consultants and scientific advisors to attend its meetings as non-voting observers; provided that such invitees are bound by appropriate confidentiality obligations. Each Party may also call for special meetings of the JSC to discuss particular matters requested by such Party. The Alliance Managers shall provide the members of the JSC with no less than [***] Business Days' notice of each regularly scheduled meeting and, to the extent reasonably practicable under the circumstances, no less than [***] Business Days' notice of any special meetings called by either Party.

3.4 **Minutes**

Minutes will be kept of all JSC meetings by chair of the JSC (or his or her designees) and sent to all members of the JSC by facsimile or e-mail for review and approval within [***] days after each such meeting. The JSC shall formally accept the minutes of the previous meeting at or before the next meeting of the JSC. Minutes will be deemed approved unless any member of the JSC objects to the accuracy of such minutes by providing written notice to the other members of the JSC prior to the next meeting of the JSC. Minutes shall list action items and shall designate any issues that need to be resolved by the JSC or applicable resolution process. In the event of any objection to the minutes that is not resolved by mutual agreement of the Parties, such minutes will be amended to reflect such unresolved dispute.

3.5 **Decision Making within JSC**

Decisions of the JSC shall be made by unanimous vote, with each Party having one (1) vote. In order to make any decision, the applicable JSC must have present (in person or via telephone or videoconference) and voting at least one representative of each Party.

3.6 **Referral to Senior Officers**

If the JSC cannot resolve a matter within its responsibilities by consensus (a "**Committee Deadlock**"), then either Party may escalate such Committee Deadlock to the Senior Officers for further consideration; provided that such escalation and further consideration shall not prevent a Party from exercising its casting vote on the JSC or implementing any decision of the JSC following such escalation. Either Party shall have the right to select a Third Party who has experience of issues that are relevant to the disputed issue to present their views to the Senior Officer of the other Party who shall in good faith listen and consider such views. If the Senior Officers are unable to resolve a Committee Deadlock, including a Committee Deadlock regarding the approval of a proposed amended budget for a Research and Development Plan or the allocation of the budget to activities under the Research and Development Plans, then [***]. [***] shall also not have final decision making authority with regard to [***]. [***] shall not, when exercising its final decision making authority [***].

3.7 Limitation of Powers

The JSC is not a substitute for the rights of the Parties under this Agreement and is intended to coordinate and facilitate the activities of the Parties. The JSC will not be involved with the day-to-day management of activities to be performed by a Party under this Agreement. The JSC will have no power to amend this Agreement.

3.8 **Joint Project Teams**.

The JSC shall establish a separate joint project team for each Research and Development Program (each a "**JPT**"). Each JPT will consist of an equal number of appropriate representatives from each Party. The JPTs will provide a forum for communication between the Parties regarding each Research and Development Program and for making day-to-day operational decisions regarding each Research

and Development Program. All such decisions shall be made by consensus of the members of the applicable JPT and any disputes shall be referred to the JSC for resolution. The JPTs shall meet at a frequency established by the JSC.

3.9 Alliance Managers

Each Party shall designate an individual to serve as the main point of contact for such Party to exchange information, facilitate communication and coordinate the Parties' activities under this Agreement (each, an "**Alliance Manager**"). The Alliance Managers shall on no less frequently than [***] provide oral reports to the JSC (or designate an appropriate representative to attend meetings and provide such reports on the Alliance Manager's behalf); provided, however, that the Alliance Managers shall not be counted as members of the JSC (and shall not vote on matters discussed at any JSC meeting). Each Party may change its designated Alliance Manager from time to time upon written notice to the other Party.

4 DEVELOPMENT AND DILIGENCE

4.1 The Research and Development Programs

(a) The Parties shall conduct the activities designated to them in the Research and Development Plans to Develop the Clinical Compounds and Nonclinical Compounds.

(b) Following the completion of each Research and Development Program, as between Neurocrine and Heptares, Neurocrine shall have responsibility and sole decision-making authority for progressing the Development and Commercialization of the applicable Licensed Products (except with respect to the Heptares Retained Rights) including the Clinical Compounds and the Nonclinical Compounds.

4.2 Research and Development Plans

The Research and Development Plan and associated budget for Heptares' activities under the Research and Development Plan and plan for Neurocrine's activities in relation to [***] at the Execution Date is attached at Schedule 1. The Parties have agreed to the initial budget for Heptares' activities under the Research and Development Plan set out in Schedule 1 for the Development Costs for the Development activities planned in the first [***] months following the Effective Date. Within [***] days following the Effective Date, the Parties will mutually agree, through the JSC (and during such [***] day period [***] shall not have final decision making authority with regard to any proposed amendment), on an amendment to such initial Research and Development Plan and budget so that such Research and Development Plan and budget shall be divided into separate sections one for each of [***] (and each such section shall be considered a separate Research and Development Plan for the purposes of this Agreement). Such final Research and Development Plans shall cover Heptares' activities and budgets; and Neurocrine's activities under the Research and Development Plans for the remaining period of the Research Term. If a Party believes that the Research and Development Plans (including the budget included therein) should be amended, that Party shall propose such amendment to the other Party and the matter shall be discussed at the JSC. The terms of, and activities set forth in, the Research and Development Plans shall at all times be conducted in compliance with all applicable Laws and in accordance with professional and ethical standards customary in the pharmaceutical and biotechnology industry, taking into account, where applicable, each Party's health care compliance policies and applicable standard operating procedures.

4.3 Heptares Research and Development Efforts

During the Research Term, Heptares shall carry out the activities allocated to it under the Research and Development Plans in accordance with good scientific standards and practices and in compliance in all material respects with the requirements of applicable Laws and regulations. Heptares will allocate to each Research and Development Plan the number of FTEs set out in each such plan. Heptares will carry out the Research and Development Programs in conformity with standard pharmaceutical and biotechnology industry practices and the terms and conditions of this Agreement and will prepare and maintain, or will cause to be prepared and maintained, complete and accurate laboratory notebooks and other written records, accounts, notes, reports and data with respect to such activities and, upon Neurocrine's written request and at its expense, will send legible copies of the aforesaid to Neurocrine. For the avoidance of doubt, Heptares shall have no obligation to devote any efforts or resources in connection with the Heptares Retained Rights. Nothing in this Agreement

(including any results generated under the Heptares Retained Rights) shall impose or create any obligation on Heptares to develop M1 Target Agonists (including the selected M1 Lead Candidate) in any indications in Japan.

4.4 **Neurocrine Research and Development Efforts**

During the Research Term, Neurocrine will perform the activities allocated to it under the Research and Development Plans in accordance with good scientific standards and practices and in compliance in all material respects with the requirements of applicable Laws and regulations. Neurocrine shall carry out the Research and Development Programs in conformity with standard pharmaceutical and biotechnology industry practices and the terms and conditions of this Agreement. Neurocrine will prepare and maintain, or will cause to be prepared and maintained, complete and accurate laboratory notebooks and other written records, accounts, notes, reports and data with respect to such activities.

4.5 **Subcontracts**

Either Party may perform its Development under the Research and Development Programs pursuant to this Agreement through one or more Third Party subcontractors, provided that (i) Heptares obtains Neurocrine's prior written approval of any such subcontractor, which approval shall not be unreasonably withheld, (ii) such Party engages each Third Party subcontractor through a written agreement consistent with the terms and conditions of this Agreement, (iii) no rights of either Party under this Agreement are diminished or otherwise adversely affected as a result of such subcontracting, (iv) the subcontractor undertakes the obligations of confidentiality and non-use regarding Confidential Information which are substantially the same as those undertaken by the Parties pursuant to clause 6 hereof, and (v) except for academic and non-profit institutions engaged by Neurocrine, the subcontractor agrees that any intellectual property developed in the course of the work hereunder (other than improvements to the subcontractor's background technology that do not relate specifically to a Compound or Licensed Product) shall be licensed or assigned to the Party engaging the subcontractor or such Party's designee, so as to permit license or re-assignment as required by the terms and conditions of this Agreement. The Party engaging any such Third Party subcontractor shall be responsible for all compensation due to the Third Party subcontractor (or its employees or agents) arising from such subcontracting, including by operation of local Law on account of any inventive contributions of the subcontractor's employees or agents with respect to any intellectual property developed in the course of the work hereunder.

4.6 **Materials**

Each Party will, during the Research Term, as a matter of course and as described in the Research and Development Plans or upon the other Party's reasonable written request, furnish to each other samples of Materials which it Controls and which are necessary for the other Party to carry out the Research and Development Plans. Each Party will use such Materials only in accordance with the Research and Development Plans and otherwise in accordance with the terms and conditions of this Agreement. Except with the prior written consent of the supplying Party, the Party receiving any Materials will not distribute or otherwise allow the release of Materials to any Third Party; provided that the Parties may transfer Compounds or other Materials to Third Parties appointed as subcontractors in accordance with clause 4.5; provided that in addition to obligations of confidentiality and non-use of information, each such Third Party agrees to use the Materials solely for the performance of activities for the transferring Party and not to transfer them to any other Third Party. Except as otherwise provided in this Agreement, all Materials will remain the sole property of the supplying Party, will be used in compliance with all applicable Laws, and will be used with prudence and appropriate caution in any experimental work because not all of their characteristics may be known.

4.7 **Reports**

The Parties shall keep each other reasonably informed as to the progress achieved and results, discoveries and technical developments made in the course of performing activities under the Research and Development Programs. Each Party shall prepare and provide to the other Party a written report every Calendar Quarter that (a) summarizes the activities performed by such Party under each Research and Development Program and (b) identifies any issues or circumstances of which it is aware that may prevent or adversely affect in a material manner future work under the Research and Development Programs. The Parties may agree that minutes or presentations from JSC meetings may be used to satisfy this reporting requirement. The JSC shall determine the key information to be exchanged and the mechanisms for exchanging further information as required.

4.8 **Development Costs**

(a) [***] shall be responsible for its costs incurred in conducting activities in connection with the Research and Development Programs in accordance with the Research and Development Plans.

(b) Neurocrine shall reimburse Heptares for the Development Costs incurred by Heptares in carrying out the Research and Development Programs provided that such Development Costs are in accordance with the budget agreed by the Parties and forming part of the applicable Research and Development Plan [***]. Heptares shall invoice Neurocrine within [***] days of the end of each Calendar Quarter during the Research Term for the Development Costs incurred by Heptares in connection with such activities in the prior Calendar Quarter in an appropriate level of detail consistent with Heptares' standard invoice format. Heptares shall include with each invoice documentation for any out-of-pocket costs in excess of fifty thousand USD ($50,000) and any other supporting documentation for the invoiced costs will be provided by Heptares upon the reasonable request of Neurocrine. Such invoices shall be paid by Neurocrine within [***] days of receipt of invoice. If Heptares anticipates that the costs to undertake any activities under the Research and Development Plans will exceed the applicable budget, Heptares shall notify the JSC, which will determine whether to adjust the budget accordingly. Heptares shall not be responsible for conducting any activities allocated to Heptares in the Research and Development Plans if the budget for those activities has not been approved.

4.9 **Ongoing Development and Commercialization**

(a) Neurocrine shall use Commercially Reasonable Efforts to Develop and obtain Regulatory Approvals for (a) at least one Licensed Product that is an M4 Target Agonist, and (b) at least one Licensed Product that is an M1 Target Agonist or an M1/M4 Dual Target Agonist in each case in each of the Global Major Markets.

(b) Subject to obtaining the required Regulatory Approvals, use Commercially Reasonable Efforts to Commercialize (a) at least one Licensed Product that is an M4 Target Agonist, and (b) at least one Licensed Product that is an M1 Target Agonist or an M1/M4 Dual Target Agonist in each case in each of the Global Major Markets.

(c) Promptly following the end of the Research Term, Neurocrine shall prepare a development plan setting out the activities that Neurocrine plans to carry out for the further development of Licensed Products and estimated timelines for completion of such activities (the "**Development Plan**") and shall provide a copy of the same to Heptares. Neurocrine shall consider in good faith and take into account the comments of Heptares on the content of the Development Plan.

(d) Neurocrine shall provide to Heptares every [***] months a report summarizing in reasonable detail Neurocrine’s Development activities and plans with respect to Licensed Products. In addition, if Heptares has any concerns regarding the report, Heptares will provide details of such concerns to Neurocrine and at Heptares’ reasonable request, Neurocrine shall make available appropriate personnel to meet with Heptares to discuss such concerns. The Parties shall work together to align on a report to be provided to [***] for the purposes of complying with Heptares' reporting obligations under the [***].

4.10 **Regulatory Matters**

Subject to the remaining provisions of this clause, Neurocrine shall, unless the Parties agree otherwise, own, and be responsible for preparing, seeking, submitting and maintaining, all regulatory filings and Regulatory Approvals for Licensed Products in the Territory, including (i) preparing any regulatory submissions necessary for carrying out the activities set out in the Research and Development Plans and (ii) preparing all reports necessary as part of a regulatory filing or Regulatory Approval. On a Target Agonist-by-Target Agonist basis until such time as Neurocrine has completed the first Successful Phase II Clinical Trial for a Licensed Product containing an M1 Target Agonist, an M4 Target Agonist or an M1/M4 Dual Target Agonist, Neurocrine shall consult with and shall provide Heptares with an opportunity to review and comment on all substantive, non-administrative regulatory submissions with respect to each such Licensed Product reasonably in advance of when Neurocrine intends to submit such regulatory submissions to a Regulatory Authority. Heptares shall provide its comments within [***] Business Days, or such other period of time agreed to by the Parties, and

Neurocrine shall consider such comments in good faith. Neurocrine shall promptly provide Heptares with a copy, in electronic form, of all substantive, non-administrative regulatory submissions related to Licensed Products that are sent to or received from a Regulatory Authority during such period. Neurocrine shall use good faith efforts during the Research Term to invite one or more representatives of Heptares to any meeting or substantive telephone conference call with a Regulatory Authority with respect to any matter related to Licensed Products or any Research and Development Program during such period to observe and participate in any such meeting or conference call. Until the first Regulatory Approval of any Licensed Product, Neurocrine shall promptly furnish the JSC with copies of all minutes from any substantive meetings with a Regulatory Authority with respect to any IND related to a Research and Development Program. The Parties may agree through the JSC that Heptares shall carry out certain activities relating to Phase I Clinical Trials of M1 and M1/M4 Nonclinical Compounds ("**Phase I Activities**"). If the Parties agree that Heptares shall carry out the Phase I Activities the Parties shall also discuss and agree the protocol design and budgets for the Phase I Activities and Heptares will conduct such studies as approved by the JSC which budgets shall be used to update the applicable Research and Development Plan. Any regulatory submissions that are required to be made to a Regulatory Authority with respect to such clinical activities and any correspondence or meetings with any such Regulatory Authority with regard to such clinical activities provided that, subject to applicable Law, [***] shall have final decision making authority with regard to the foregoing. [***] shall not, when exercising its final decision making authority in relation to any Clinical Trial of which Heptares is the sponsor, exercise such a right in a manner that would cause Heptares to be in breach of applicable Law. Heptares shall, unless the Parties agree otherwise, own, and be responsible for (i) preparing, seeking, submitting and maintaining, all regulatory filings and Regulatory Approvals, and (ii) carrying out all Clinical Trials, in each case as part of exercising the Heptares Retained Rights. Heptares shall prepare and file such filings and Regulatory Approvals and carry out such Clinical Trials in consultation with Neurocrine. Each Party shall keep the other regularly informed with regard to the progress of and results of any Clinical Trial that it carries out in relation to a Licensed Product.

4.11 **Manufacturing**

Except as otherwise agreed by the Parties or set forth herein, Neurocrine shall be responsible for all manufacture and supply of Compounds and Licensed Products for use in the Territory, including all pre-clinical requirements of Licensed Products necessary to carry out the [***] Research and Development Program and the M1 Lead Candidate Research and Development Program. As between the Parties, and subject to the oversight of the JSC, Heptares shall be responsible for transferring to Neurocrine or its designee the cGMP batches of Licensed Product incorporating [***] and [***] manufactured on behalf of Heptares prior to the Execution Date. Heptares shall also be responsible for manufacturing an additional CMC batch of [***]. Promptly following the Effective Date, Heptares will transfer to Neurocrine or its designee the cGMP batches of Licensed Product incorporating [***] and [***] which have been manufactured for Heptares by a Third Party CMO prior to the Execution Date. The costs of any manufacturing activities that Heptares carries out in accordance with this clause will be included in the Development Costs and will be reimbursed by Neurocrine. Within [***] days of the Effective Date the Parties will agree a plan for the technology transfer of the manufacturing process for each Licensed Product to Neurocrine. The timing of such transfer will differ for each Licensed Product depending on when it is intended that Neurocrine will take over the responsibility to manufacture the Licensed Product. Once such plan is agreed the Parties will carry out the transfer of the manufacturing process for each Licensed Product in accordance with such plan. Such transfer shall include, if requested by Neurocrine, Heptares using commercially reasonable efforts to effect assignments of any agreements with any Third Party CMO or other service provider entered into by Heptares to the extent that such agreements exclusively relate to such Licensed Product. Neurocrine shall be responsible for all other manufacturing activities relating to Licensed Products. Heptares has used prior to the Execution Date and shall be free to use after the Execution Date a Third Party CMO to manufacture Licensed Products. Heptares' obligations under this Agreement to manufacture Licensed Products shall be qualified by and shall be subject to the terms of each such agreement with the applicable Third Party CMO, and unless resulting from Heptares' acts or omissions, Heptares shall not be responsible for any failure by a Third Party to supply Licensed Product or for any other liability arising from the use of any Licensed Product manufactured by such a Third Party.

If requested by Heptares, Neurocrine will, where Neurocrine is Developing the same Compound or Licensed Product, negotiate in good faith and agree the terms of a supply agreement to govern the supply of such Compounds and Licensed Products to Heptares by Neurocrine for the purposes of the exercise by Heptares of the Heptares Retained Rights, at a supply price equal to Neurocrine's fully-burdened cost plus (i) [***] percent ([***]%) for clinical supply or (ii) [***] percent ([***]%) for commercial supply. Heptares shall also be entitled at its option and cost to manufacture or have manufactured by a Third Party CMO any M1 Target Agonists anywhere in the Territory as required by

Heptares to exercise the Heptares Retained Rights.

4.12 **Pharmacovigilance**

Not later than the start of the first Clinical Trial by or on behalf of Heptares in the exercise of the Heptares Retained Rights the Parties will negotiate in good faith and enter into a safety data exchange agreement to govern the Parties' obligations to each other with regard to the exchange of safety data relating to the Licensed Products. Neurocrine will be responsible for creating and maintaining the global safety database for the Licensed Products. With respect to each Research and Development Program, Neurocrine shall be responsible for the monitoring and reporting of safety information, if any, related to such Research and Development Program to all relevant Regulatory Authorities. Neurocrine shall provide copies of such safety information to Heptares to the extent any such filings or any interaction with a Regulatory Authority requires information relating to Compounds or Development activities undertaken by Heptares pursuant to this Agreement and Heptares shall provide such assistance as Neurocrine may reasonably request in connection with the preparation of such filings or provision of information to the Regulatory Authority at Neurocrine’s cost.

4.13 **Compliance with Laws**

Each Party shall perform its responsibilities under this Agreement, including the manufacture of products, in accordance with all applicable Laws. Promptly following the Effective Date, the Parties shall negotiate in good faith and enter into a data processing agreement to govern the sharing between the Parties of any personal data (as defined in the EU General Data Protection Regulation) including any applicable clinical data, in accordance with applicable Law.

5 FINANCIAL PROVISIONS

5.1 **Upfront Payments**

In partial consideration of the rights granted under clause 2.1, within ten (10) days of the Effective Date of this Agreement, Neurocrine shall pay Heptares a one-time lump sum payment of one hundred million USD ($100,000,000) in upfront cash which shall be non-refundable and non-creditable against other payments due hereunder. Such payment shall be made by means of wire transfer of immediately available funds to an account designated in advance in writing by Heptares to Neurocrine.

5.2 Milestone Payments

(a) As additional consideration for the grant of rights under this Agreement, and on the terms and subject to the conditions set forth herein, Neurocrine shall make the following one-time payments set forth in clauses 5.2(b) – 5.2(e) to Heptares (collectively the "**Milestone Payments**") after the achievement by or on behalf of Neurocrine of the corresponding event set forth below (collectively, the "**Milestone Events**"). Neurocrine will notify Heptares in writing promptly, but in any event no later than (i) [***] days following the achievement of a Milestone Event in clause 5.2(b)-(d) and (ii) [***] days following the end of the Calendar Quarter in which a Milestone Event in clause 5.2(e) is achieved. Neurocrine shall pay to Heptares the Milestone Payment corresponding to such Milestone Event within [***] days of receipt of an invoice issued by Heptares in respect of such Milestone Payment following achievement of such Milestone Event. Such payment shall be made by means of wire transfer of immediately available funds to an account designated in advance in writing by Heptares to Neurocrine.

(b) Clinical Compound Milestone Payments applying to Licensed Products incorporating [***] (to

be paid only one time for [***] per milestone event):

Milestone Event	Disease State or Indication		
	[***]	**[***]**	**[***]**
[***]	$[***]	-	-
[***]	$[***]	$[***]	$[***]
[***]	$[***]	-	-
[***]	$[***]	-	-
[***]	$[***]	$[***]	$[***]
[***]	$[***]	$[***]	$[***]
[***]	$[***]	$[***]	$[***]
[***]	$[***]	$[***]	$[***]
[***]	$[***]	$[***]	$[***]
[***]	$[***]	$[***]	$[***]
[***]	$[***]	$[***]	$[***]
Total	**$[***]**	**$[***]**	**$[***]**

(c) Clinical Compound Milestone Payments applying to Licensed Products incorporating either [***] (to be paid only one time on first achievement of the milestone event by either [***] so that if the same milestone event is achieved in relation to both [***] the Milestone Payment shall only be paid once in relation to the first such Licensed Product that achieves the milestone event):

Milestone Event	Amount
[***][1]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
[***]	$[***]
Total	**$[***]**

[1] [***].

(d) Nonclinical Compound Milestone Payments applying to [***] Licensed Products incorporating

[***]:

Milestone Event	[***]	
	[***]	**[***]**
[***]	$[***]	$[***]
[***]	$[***]	$[***]
[***]	$[***]	$[***]
[***]	$[***]	-
[***]	$[***]	-
[***]	$[***]	$[***]
[***]	$[***]	$[***]
[***]	$[***]	$[***]
[***]	$[***]	$[***]
[***]	$[***]	$[***]
[***]	$[***]	$[***]
[***]	$[***]	$[***]
[***]	$[***]	$[***]
Total (including Japan)	**$[***]**	**$[***]**
Total (excluding Japan)	**$[***]**	**$[***]**

[***].

(e) Neurocrine shall make the following one-time payments to Heptares upon the first achievement of annual (Calendar Year) Net Sales milestones for each Licensed Product for up to but no more than [***] Licensed Products. Sales of [***] will not count towards the sales milestones in the table below:

Milestone Event	Amount
Annual Net Sales in the Territory Exceed $[***]	$[***]
Annual Net Sales in the Territory Exceed $[***]	$[***]
Annual Net Sales in the Territory Exceed $[***]	$[***]
Annual Net Sales in the Territory Exceed $[***]	$[***]
Total	**$[***]**

The total sales milestones payable under this clause 5.2(e) shall not exceed $1.0625 billion.

(f) Payments due under the milestones set out in clause 5.2(d) shall be triggered as follows where applicable:

(i) [***]

(ii) [***]

(iii) [***]

(iv) [***]

(v) [***]

5.3 **Royalty Payments**

On a Licensed Product-by-Licensed Product and country-by-country basis, Neurocrine shall pay Heptares a royalty on Net Sales of Licensed Products in the Territory as set forth below ("**Royalty**

Payment"). The Royalty Payment shall be payable on a country-by-country and Licensed Product-by-Licensed Product basis from the date of Launch of a Licensed Product by Neurocrine in a particular country until the later of:

(a) the expiration of the last Valid Claim in such country covering the new chemical entity of such Licensed Product, or the Formulation or use of such Licensed Product in an Indication for which such Licensed Product obtained Regulatory Approval in such country;

(b) expiration or termination of the Regulatory Exclusivity Period for such Licensed Product in such country; and

(c) [***] years following the date of Launch of such Licensed Product in such country,

(the "**Royalty Term**").

Neurocrine shall have no obligation to pay any royalty with respect to Net Sales of any Licensed Product in any country after the Royalty Term for such Licensed Product in such country has expired; provided that if and only to the extent that the obligation of Heptares to pay a royalty to [***] in respect of any Licensed Product as defined in [***] in a country extends beyond the Royalty Term in which case Neurocrine shall continue to pay Heptares only the royalty on Net Sales of such Licensed Product and Amendment Letter Product in such country at the rate (as may be reduced) set forth in [***] until the date that such obligation ceases instead of the royalty rates calculated as set forth below. Heptares represents and warrants to Neurocrine that [***]. Heptares shall provide Neurocrine prompt written notice (in any event within [***] days) of [***].

The Royalty Payments for Licensed Products shall be paid as a percentage of Net Sales in the Territory in each Calendar Year as follows depending on whether the Licensed Product incorporates a Clinical Compound or a Nonclinical Compound:

Annual Net Sales in the Territory:	Clinical Compound Royalty Rate	Nonclinical Compound Royalty Rate
Less than $[***]	[***]%	[***]%
Greater than or equal to $[***] and less than $[***]	[***]%	[***]%
Greater than or equal to $[***] and less than $[***]	[***]%	[***]%
Greater than or equal to $[***]	[***]%	[***]%

For clarity, these royalty rates are tiered and are based on the aggregate of Net Sales in the Territory in a given Calendar Year, such that, for example, if Net Sales of Licensed Product [***] in a given Calendar Year, the royalty payable for such Calendar Year is [***].

5.4 **Reduction of Royalty**

(a) Blocking Third Party Patent Rights. If, during the Term, Neurocrine determines, in its reasonable judgment, that it is necessary to obtain rights under any Blocking Third Party Patent Rights in order to Exploit a Licensed Product in accordance with this Agreement, then Neurocrine shall promptly notify Heptares. In the event a license or acquisition of Blocking Third Party Patent Rights is obtained, and any amounts are paid by Neurocrine or its Affiliate or Sublicensee to any Third Party to license or acquire such Blocking Third Party Patent Rights ("**Third Party Payments**"), Neurocrine shall have the right to reduce the Royalty Payments otherwise payable to Heptares under clause 5.3 in a given period by up to [***] percent ([***]%) of the Third Party Payments made in such period, subject to clause 5.4(d) below.

(b) Generic Products. On a Licensed Product-by-Licensed Product basis, if in any country in the Territory during the Royalty Term for a Licensed Product unit sales of all Generic Products in such country in a Calendar Quarter as a percentage of the sum of unit sales of such Licensed Product (including all such Generic Products) in such country ("**Generic Penetration**") are at least [***] percent ([***]%), the royalty rates in clause 5.3 shall be reduced by [***] percent ([***]%) until the end of the Royalty Term for such Licensed Product in such country, subject to

clause 5.4(d) below.

(c) No Valid Claim. The royalty rates set out in clause 5.3 shall be reduced by [***] percent ([***]%) in any country in the Territory where there is not a Valid Claim covering the new chemical entity of such Licensed Product, or the Formulation or the use of such Licensed Product in an Indication for which such Licensed Product obtained Regulatory Approval in such country, subject to clause 5.4(d) below.

(d) Maximum Royalty Adjustment. The royalty payable with respect to Net Sales of a Licensed Product sold by Neurocrine or its Affiliates or Sublicensees in any country of the Territory in any Calendar Quarter shall not as a result of adjustments made pursuant to clauses 5.4(a), 5.4(b) and 5.4(c) be less than [***] percent ([***]%) of the Royalty Payments payable pursuant to clause 5.3 prior to such adjustments thereof. Credits not exhausted in any Calendar Quarter may be carried into future Calendar Quarters.

5.5 **Heptares Third Party Payments**

The Parties acknowledge and agree that Heptares shall remain responsible for, and shall promptly discharge, any and all payments payable to [***] (or its successor-in-interest) in connection with [***].

5.6 **Royalty Payments and Statement**

Neurocrine shall within [***] days of the end of each Calendar Quarter provide to Heptares a flash report showing the estimated Net Sales made in such Calendar Quarter and an estimate of the royalties payable to Heptares in respect of such estimated Net Sales. Neurocrine shall pay to Heptares the Royalty Payment quarterly in accordance with this clause 5.6 by means of wire transfer of immediately available funds to an account designated in advance in writing by Heptares to Neurocrine. Neurocrine shall calculate all amounts payable to Heptares pursuant to clause 5.3 as adjusted pursuant to clause 5.4 at the end of each Calendar Quarter, which amounts shall be converted to USD, in accordance with clause 5.9. Neurocrine shall pay to Heptares the royalty amounts due with respect to a given Calendar Quarter within [***] days after the end of such Calendar Quarter. Each payment of royalties due to Heptares shall be accompanied by a report setting forth for such Calendar Quarter the following information for Licensed Product: (a) the amount of gross sales and Net Sales of Licensed Product on a Licensed Product-by-Licensed Product and country-by-country basis (including such amounts expressed in local currency and converted to USD); and (b) a calculation of the amount of royalties due to Heptares on account of Net Sales of Licensed Product.

5.7 **Taxes**

The milestones, royalties and other amounts payable by Neurocrine to Heptares pursuant to this Agreement (each, a "**Payment**") shall be paid free and clear of any and all taxes, except for any withholding taxes required by applicable Law. Except as provided in this clause 5.7 and subject to clause 5.8, Heptares shall be solely responsible for paying any and all taxes (other than withholding taxes required by applicable Law to be deducted from Payments and remitted by Neurocrine) levied on account of, or measured in whole or in part by reference to, any Payments it receives. Neurocrine shall deduct or withhold from the Payments any taxes that it is required by applicable Law to deduct or withhold. Notwithstanding the foregoing, if Heptares is entitled under any applicable tax treaty to a reduction of rate of, or the elimination of, applicable withholding tax, it may deliver to Neurocrine or the appropriate Governmental Authority (with the assistance of Neurocrine to the extent that this is reasonably required and is expressly requested in writing) the prescribed forms necessary to reduce the applicable rate of withholding tax or to relieve Neurocrine of its obligation to withhold such tax and Neurocrine shall apply the reduced rate of withholding tax or dispense with withholding tax, as the case may be; provided that Neurocrine has received evidence, in a form satisfactory to Neurocrine, of Heptares' delivery of all applicable forms (and, if necessary, its receipt of appropriate governmental authorization) prior to the time that the Payments are due. If, in accordance with the foregoing, Neurocrine withholds any amount, it shall pay to Heptares the balance when due, make timely payment to the proper taxing authority of the withheld amount and send to Heptares proof of such payment within [***] days following such payment. If any such withholding tax is assessed against, or paid (but in each case not withheld), by Neurocrine, then Heptares will pay the relevant amount of such withholding tax to Neurocrine. In the event that a Governmental Authority retroactively determines that a payment made by Neurocrine to Heptares under this Agreement should have been subject to withholding taxes (or to additional withholding taxes), and Neurocrine remits such withholding taxes to the Governmental Authority, including any interest and penalties that may be imposed thereon, at the option of Neurocrine, then Heptares will pay the relevant amount of any withholding tax (excluding any interest and penalties thereon which shall be payable by Neurocrine) to

Neurocrine.

5.8 **VAT**

Notwithstanding anything contained in clause 5.7, this clause 5.8 shall apply with respect to VAT. All Payments or other consideration are exclusive of VAT. If any VAT is chargeable in respect of any Payments or other consideration, the paying Party (being the Party making the payment or providing the other consideration), shall pay VAT which is accountable to a tax authority by the payee Party (being the recipient of the payments or other consideration) at the applicable rate in respect of any such Payments following the receipt of a VAT invoice in the appropriate form in compliance with applicable Law issued by the payee in respect of those Payments or other consideration, such VAT to be payable on the later of the due date of the payment of the Payments (or provision of other consideration) to which such VAT relates and [***] days after the receipt by the paying Party of the applicable invoice relating to that VAT payment. The Parties shall issue valid invoices for all goods and services supplied under this Agreement consistent with the applicable Law governing such VAT, and to the extent any invoice is not initially issued in an appropriate form, the Parties shall cooperate to provide such information or assistance as may be necessary to enable the issuance of such invoice consistent with the applicable Law governing such VAT. Where under the terms of this Agreement one Party is liable to indemnify or reimburse the other Party (or an Affiliate of that other Party) in respect of any costs, charges or expenses, the payment shall only include an amount equal to any VAT thereon not otherwise recoverable by the other Party (or its Affiliate), subject to that Party or representative member using all reasonable efforts to recover such amount of VAT as may be practicable.

5.9 **Currency Exchange**

All payments to either Party under this Agreement shall be made by deposit of USD in the requisite amount to such bank account as the receiving Party may from time to time designate by written notice to the paying Party. For the purpose of calculating any sums due under, or otherwise reimbursable pursuant to, this Agreement (including the calculation of Net Sales expressed in currencies other than USD), Neurocrine shall convert any amount expressed in a foreign currency into USD equivalents using its, its Affiliate's or Sublicensee's standard conversion methodology consistent with GAAP.

5.10 **Records Retention; Financial Audit; Consolidation Reporting**

(a) Record Retention. Each Party shall and shall cause its Affiliates and its and their Sublicensees to, keep complete and accurate financial books and records pertaining to the Development and Commercialization of Licensed Products hereunder (including with respect to Neurocrine, Net Sales of Licensed Products and with respect to Heptares, Development Costs) to the extent required to calculate and verify all amounts payable hereunder. Each Party shall, and shall cause its Affiliates and its and their Sublicensees to, retain such books and records until the later of (a) [***] years after the end of the period to which such books and records pertain and (b) the expiration of the applicable tax statute of limitations (or any extensions thereof) or for such longer period as may be required by applicable Law.

(b) Financial Audit. Each Party shall have the right to have an independent certified public accounting firm of internationally recognized standing reasonably acceptable to the other Party ("**Auditor**") to have access during normal business hours, upon reasonable prior written notice, to such of the records of the other Party and its Affiliates as may be required to verify the accuracy of the calculation of Development Costs, Milestone Payments, Net Sales and Royalty Payments due for any year, no more frequently than once per year. The same records may be audited only once. All information subject to review under this clause 5.10(b) is subject to the confidentiality provisions of clause 6 and the auditing Party shall cause the Auditor to enter into a reasonably acceptable confidentiality agreement with the audited Party obligating such firm to retain all such financial information in confidence pursuant to such confidentiality agreement. The Auditor shall disclose to the auditing Party only the amounts which the Auditor believes to be due and payable hereunder to such Party or, in the case of Development Costs, to have been due and payable hereunder to the audited Party and shall provide a copy of the same to the audited Party, and shall disclose no other information revealed in such audit. Any and all records of the audited Party and its Affiliates examined by such Auditor shall be deemed the audited Party's Confidential Information, which may not be disclosed by said Auditor to any Third Party or (except for the information expressly sought to be confirmed by the auditing Party as set forth in this clause 5.10(b)) to the auditing Party. The auditing Party shall bear all costs of such audit, unless the audit reveals a discrepancy in its favour of more than [***] percent ([***]%), in which case the audited Party shall bear the cost of the audit.

(c) Payment of Additional Amounts. If, based on the results of any audit conducted under clause 5.10(b), additional payments are owed to the auditing Party or the auditing Party was overcharged for Development Costs under this Agreement, then the audited Party shall make such additional payments or refund Development Costs within [***] days after the Auditor's written report is delivered to the Parties, with interest calculated thereon in accordance with clause 5.12. If the results of the audit show that the audited Party over-reported and overpaid amounts due or the audited Party undercharged Development Costs, then the auditing Party shall refund excess amounts or pay additional Development Costs within [***] days after the Auditor's written report is delivered. If the report is contested by either, the Parties shall follow the dispute resolution procedures described in clause 5.10(d).

(d) Audit Dispute. In the event of a dispute with respect to any audit under clause 5.10(b), Heptares and Neurocrine shall work in good faith to resolve the disagreement. If the Parties are unable to reach a mutually acceptable resolution of any such dispute within [***] days, the dispute shall be submitted for resolution to a certified public accounting firm jointly selected by each Party's certified public accountants or to such other person as the Parties shall mutually agree (the "**Dispute Auditor**"). The decision of the Dispute Auditor shall be final and the costs of such dispute resolution as well as the initial audit shall be borne between the Parties in such manner as the Auditor shall determine. Not later than [***] days after such decision and in accordance with such decision, the Parties shall make reconciling payments as described in Section 5.10(c).

5.11 **Payment Details**

Any payments due to be paid by Neurocrine to Heptares shall be made to the account details set out below:

[***]

or such other account as Heptares shall designate before any such payment is due.

5.12 **Interest on Late Payments**

If any payment due to either Party under this Agreement is not paid when due, then such paying Party shall pay interest thereon (before and after any judgment) at an annual rate (but with interest accruing on a daily basis) of [***]% above the [***] rate, as adjusted from time to time on the first [***] business day of each month, such interest to run from the date on which payment of such sum became due until payment thereof in full together with such interest.

6 CONFIDENTIALITY

6.1 **Protection of Confidential Information**

The Receiving Party shall not disclose or disseminate Confidential Information of the Disclosing Party to any Third Party, unless expressly permitted hereunder, and shall not use such Confidential Information for any purpose other than in performing the Receiving Party's obligations or exercising the Receiving Party's rights hereunder. In addition, the Receiving Party shall take reasonable steps to protect the Confidential Information of the Disclosing Party from unauthorized use or disclosure, which steps shall be no less than those the Receiving Party takes to protect its own confidential and/or proprietary material of a similar nature. The foregoing obligations shall apply equally to all copies, extracts and summaries of the Disclosing Party's Confidential Information.

6.2 **Certain Permitted Disclosures**

(a) Disclosure Required by Law. Notwithstanding the foregoing, each of Heptares and Neurocrine may disclose Confidential Information of the other Party to a Third Party to the extent such disclosure is made in response to a valid order of a court of competent jurisdiction or other supra-national, federal, national, regional, state, provincial and local governmental or regulatory body of competent jurisdiction or, if in the reasonable opinion of the Receiving Party's legal counsel, such disclosure is otherwise required by Law, including by reason of filing with securities regulators; provided, however, that if a Party is required by Law to make any such disclosure of the Disclosing Party's Confidential Information, to the extent it may

legally do so it shall give reasonable advance notice to the Disclosing Party of such disclosure to permit the Disclosing Party to use its reasonable efforts to secure confidential treatment of such Confidential Information prior to disclosure (whether through protective orders or otherwise); and provided, further, that the Confidential Information disclosed in response to such court or governmental order shall be limited to that information which is legally required to be disclosed in response to such court or governmental order.

(b) Disclosure to Certain Third Parties. The Receiving Party may disclose such of the Disclosing Party's Confidential Information to its Affiliates, and its and their respective employees and permitted subcontractors who have a need to know such Confidential Information and who are bound by written obligations of confidentiality and non-use at least as stringent as those by which the Receiving Party is bound hereunder.

(c) Exploitation of Compounds and Licensed Products by Neurocrine. Neurocrine and its Affiliates and its and their Sublicensees may disclose the Confidential Information of Heptares that is specific to Compounds or Licensed Products to the extent that such disclosure is made to its or their attorneys, auditors, advisors, consultants, contractors, existing or prospective collaboration partners, licensees, sublicensees, any Regulatory Authorities or other Third Parties for use by such persons as may be reasonably necessary or useful in connection with the Exploitation of Compounds or Licensed Products (including in connection with any filing, application or request for Regulatory Approval by or on behalf of Neurocrine or any of its Affiliates or its or their Sublicensees) or otherwise in connection with the performance of its obligations or exercise of Neurocrine's rights as contemplated by this Agreement, provided that each recipient (other than Regulatory Authorities) is bound by written obligations of confidentiality and non-use at least as stringent as those by which the Receiving Party is bound hereunder.

(d) Exploitation of Compounds and Licensed Products by Heptares. Heptares and its Affiliates and its and their licensees and sublicensees may disclose the Confidential Information of Neurocrine that is specific to Compounds or Licensed Products to the extent that such disclosure is made to its or their attorneys, auditors, advisors, consultants, contractors, existing or prospective collaboration partners, licensees, sublicensees, any Regulatory Authorities or other Third Parties for use by such persons as may be reasonably necessary or useful in connection with and to the extent that Heptares has a license to use such Confidential Information for the Heptares Retained Rights (including in connection with any filing, application or request for Regulatory Approval by or on behalf of Heptares or any of its Affiliates or its or their licensees or sublicensees) or otherwise in connection with the performance of its obligations or exercise of Heptares' rights as contemplated by this Agreement, provided that each recipient (other than Regulatory Authorities) is bound by written obligations of confidentiality and non-use at least as stringent as those by which the Receiving Party is bound hereunder.

(e) Patent Filings. Neurocrine may disclose Confidential Information of Heptares to a Third Party to the extent such disclosure is made by or on behalf of Neurocrine to a patent authority as may be reasonably necessary or useful for purposes of obtaining or enforcing a Patent covering a Compound or a Licensed Product.

(f) Disclosure to Investors and Acquirers. The Receiving Party may disclose such of the Disclosing Party's Confidential Information to potential or actual investors or acquirers as may be necessary in connection with their evaluation of such potential or actual investment or acquisition; provided, however, that such persons shall be bound by written obligations of confidentiality and non-use at least as stringent as those by which the Receiving Party is bound under this clause 6 (provided that the term of the obligations may be shorter but not less than [***] years).

6.3 Return of Confidential Information. Upon expiration or termination of this Agreement, the Receiving Party shall promptly return, or at the Disclosing Party's request, destroy or delete, all of the Disclosing Party's Confidential Information except to the extent that the Receiving Party has a continuing license to use such Confidential Information, provided that the Receiving Party may retain one copy for its legal files, subject to its continuing obligations under this clause 6.

6.4 Unauthorized Use. If either Party becomes aware or has knowledge of any unauthorized use or disclosure of the Disclosing Party's Confidential Information, it shall promptly notify the Disclosing Party of such unauthorized use or disclosure.

6.5 **Public Disclosure**

(a) Neither Party shall use the name, logo or trademark of the other Party or of any director, officer, employee or agent of the other Party or any adaptation thereof in any advertising, promotional or sales literature, publicity or in any document employed to obtain funds or financing without the prior written approval of the Party or individual whose name is to be used. The restrictions imposed by this clause 6.5 shall not prohibit either Party from making any disclosure identifying the other Party that is required by applicable Law or the rules of a stock exchange on which the securities of the disclosing Party are listed (or to which an application for listing has been submitted). As exceptions to the foregoing:

(i) The Parties shall issue a joint press release substantially in the form set out at Schedule 3. Neither Party shall issue any other public announcement, press release or other public disclosure regarding this Agreement or its subject matter, or shall publicly disclose the terms of this Agreement, without the other Party's prior written consent, except for any such disclosure that is in the opinion of the disclosing Party's or its Affiliate's counsel, required by applicable Law or the rules of a stock exchange on which the securities of the disclosing Party or its Affiliate are listed (or to which an application for listing has been submitted). In the event a Party or its Affiliate is, in the opinion of its legal counsel, required to make such a public disclosure, such Party shall, or shall procure that its Affiliate shall, submit the proposed disclosure (including, if applicable, a proposed redacted version of this Agreement to be filed with a regulator or stock exchange) in writing to the other Party as far in advance as reasonably practicable so as to provide a reasonable opportunity to comment thereon. Neither Party shall be required to seek the permission of the other Party to repeat any information regarding the terms of this Agreement or any amendment to this Agreement that has already been publicly disclosed by such Party or its Affiliate or by the other Party or its Affiliate, in accordance with this clause 6.5, provided that such information remains accurate as of such time and provided the frequency and form of such disclosure are reasonable.

(b) Publications. Neurocrine shall be free to publicly disclose research, development and commercial information (including with respect to regulatory matters) regarding the Compounds and Licensed Products, provided that during the Research Term, any publication of Heptares Existing Compound Know-How shall be subject to prior review by Heptares for issues of patentability and protection of its Confidential Information, in a manner consistent with applicable Law and industry practices. Any proposed public disclosure of research, development and commercial information (including with respect to regulatory matters) regarding M1 Target Agonists in connection with the Heptares Retained Rights shall be subject to the review and approval of the JSC, provided that during the Research Term, any publication of Heptares Existing Compound Know-How shall be subject to prior review by Neurocrine for issues of patentability in a manner consistent with applicable Law and industry practices.

6.6 Subject to limited disclosure in accordance with clauses 6.2 and 6.5, the content and terms of this Agreement shall be considered Confidential Information of the Parties and shall remain subject to the obligations set out in clause 6.1.

7 INTELLECTUAL PROPERTY

7.1 **Preparation, Filing, Prosecution and Maintenance of Patents**

Neurocrine shall have the right and the obligation as provided in this clause 7.1 and subject to the remaining provisions of this clause 7.1, at its cost through the use of internal or outside counsel as it may reasonably determine, to prepare, file, prosecute and maintain the Licensed Patents in the Territory and the Neurocrine Patents and Joint Patents worldwide, and to be responsible for any related interference, re-issuance, re-examination and opposition; provided that if Neurocrine proposes to make any new filing (of a patent application or any other substantive communication) for a Patent in the Licensed Patents in the Territory or the Neurocrine Patents or Joint Patents worldwide, Neurocrine shall provide a draft of any such proposed filing to Heptares for review and comment and will consider Heptares' comments in good faith. Neurocrine shall prosecute and maintain the Licensed Patents (including Joint Patents) and the Neurocrine Patents in at least the US and EU, in each case consistent with Neurocrine's patent strategy for Patents owned by Neurocrine. Heptares shall prosecute and maintain the Licensed Patents (including Joint Patents) and the Neurocrine Patents that cover M1 Target Agonists in Japan, in each case consistent with Heptares' patent strategy for Patents owned by Heptares, and provided that if Heptares proposes to make any new filing (of a

patent application or any other substantive communication) for any such Patent in Japan, Heptares shall provide a draft of any such proposed filing to Neurocrine for review and comment and will consider Neurocrine's comments in good faith provided that Heptares shall not make any such proposed filing if Neurocrine believes that such filing would be reasonably likely to have a material adverse effect on the Development and Commercialization of any Licensed Product in the Territory or on any of the Licensed Patents or any of the Neurocrine Patents in the Territory. In the event Neurocrine decides that it is no longer interested in prosecuting or maintaining any particular Patent(s) from among the Licensed Patents (including Joint Patents) or any Neurocrine Patents in a particular country (each a "**Discontinued Patent**") and Neurocrine is not and has not filed a continuation or divisional application to such Discontinued Patent, Neurocrine shall notify Heptares and provide Heptares with an opportunity to assume, at Heptares' expense, control of the prosecution and/or maintenance of such Discontinued Patent.

7.2 **Patent Term Extension and Supplementary Protection Certificate**

As between the Parties, Neurocrine shall have the sole right to make decisions regarding and to apply for (in each case in consultation with Heptares) patent term extensions, including supplementary protection certificates and any other extensions that are now or become available in the future, wherever applicable, for Licensed Patents (including Joint Patents) and Neurocrine Patents in any country save for any such Patents that cover M1 Target Agonists in Japan. Heptares shall retain the sole right to apply for (in each case in consultation with Neurocrine), patent term extensions, including supplementary protection certificates and any other extensions that are now or become available in the future, wherever applicable, for Licensed Patents (including Joint Patents) and Neurocrine Patents that cover M1 Target Agonists in Japan. Each Party shall provide prompt and reasonable assistance, as requested by the other Party, including by taking such action as is required under any applicable Law to obtain such extension or supplementary protection certificate.

7.3 **Patent Listings**

As between the Parties, Neurocrine shall have the sole right to make all filings with Regulatory Authorities in the Territory with respect to Licensed Patents (including Joint Patents) and Neurocrine Patents, including as required or allowed in the US, in the FDA's Orange Book or other international equivalents (save in relation to Licensed Patents (including Joint Patents) and Neurocrine Patents that cover M1 Target Agonists in Japan, where Heptares shall retain such right).

7.4 **Information Exchange with Heptares**

Neurocrine shall keep Heptares reasonably apprised of material developments regarding the preparation, filing, maintenance and prosecution of Licensed Patents in the Territory and Neurocrine Patents, shall provide Heptares with a reasonable opportunity to comment and make requests regarding the same and shall take such requests into account. Heptares shall keep Neurocrine reasonably apprised of material developments regarding the preparation, filing, maintenance and prosecution of Licensed Patents (including Joint Patents) and Neurocrine Patents that cover M1 Target Agonists in Japan, shall provide Neurocrine with a reasonable opportunity to comment and make requests regarding the same and shall not make any filing if Neurocrine believes that such filing would be reasonably likely to have a material adverse effect on the Development and Commercialization of any Licensed Product in the Territory or on any of the Licensed Patents or any of the Neurocrine Patents in the Territory. Neurocrine shall also provide to Heptares an updated list of the Licensed Patents every six months from the Effective Date which details the current status of each Licensed Patent. Heptares shall cooperate with Neurocrine to the extent reasonably necessary for Neurocrine to prosecute the Licensed Patents in the Territory, including the execution and delivery of documents at Neurocrine's reasonable cost.

7.5 **IP Committee**. Within [***] days after the Effective Date, the Parties shall establish a joint IP committee by each Party designating one of its representatives as a member of such committee ("**IP Committee**"). Each member shall have the appropriate background and expertise to contribute to the IP Committee. Each Party may change its representative on the IP Committee from time to time by notice to the other Party. The IP Committee shall meet as often as the IP Committee shall decide and shall act as a forum for discussing matters relating to clauses 7.1-7.4 above. The members of the IP Committee may decide to refer matters on which they cannot agree to the JSC for discussion and resolution.

7.6 **Infringement of the Patents**

In the event that either Party learns of any infringement of any Licensed Patents (including Joint Patents) or Neurocrine Patents under this Agreement or any certification filed under the Hatch-Waxman Act or declaratory judgment action claiming that any Licensed Patents or Neurocrine Patents are invalid or unenforceable or claiming that any such Patents would not be infringed by the making, use, offer for sale, sale or import of a product for which an application under the Hatch-Waxman Act is filed or any equivalent or similar certification or notice in any jurisdiction worldwide (each an "**Infringement**"), such Party shall promptly, but in all cases within [***] days of any notice of Infringement, inform the other Party and shall provide the other Party with reasonable evidence of such Infringement of which it is aware. Neurocrine shall have the sole right, but not the obligation, to initiate and litigate at its sole cost and expense any Infringement action against any party believed to be infringing the Licensed Patents (including Joint Patents) or Neurocrine Patents, except that Heptares shall have the first right, but not the obligation, to initiate and litigate at its sole cost and expense any Infringement action against any party believed to be infringing the Licensed Patents or Neurocrine Patents that cover the M1 Target Agonists in Japan provided that Heptares shall not take any such action if Neurocrine believes that taking such action would be reasonably likely to have a material adverse effect on the Development and Commercialization of any Licensed Product in the Territory or on any of the Licensed Patents or any of the Neurocrine Patents in the Territory. In the event the Party having such right ("the **Enforcing Party**") elects to initiate such proceeding, the Enforcing Party shall have the sole right to direct the litigation, to name the other Party in any such litigation proceeding as a party, and to elect when, whether and on what terms to settle such litigation at its cost and to receive any awards. The other Party shall cooperate fully in any Infringement action pursuant to this clause 7.6, including by being named as a necessary party to, such action at the Enforcing Party's cost and subject to the other Party being indemnified by the Enforcing Party in respect of all costs and liabilities associated with being so named. In the event that the Enforcing Party elects not to initiate such proceeding to enforce Licensed Patents, Heptares Existing Compound Patents or Arising Patents owned solely by Heptares, the other Party shall have the right to initiate and litigate the claim of Infringement at other Party's sole cost and expense, and to name the Enforcing Party in any such litigation proceeding as a party, and to elect when, whether and on what terms to settle such litigation and to receive any awards; provided that, if the Enforcing Party has notified the other Party that it had elected not to initiate such proceedings because it reasonably believed that such proceedings would be detrimental or prejudicial to the Enforcing Party's rights under this Agreement, the other Party shall not have the right to initiate or litigate any proceedings with respect to such Infringement. In any event, the Party not directing such proceeding shall reasonably assist the Party directing such proceeding and cooperate in any such litigation at the request and expense of the Party directing the proceeding. Each Party may at its own expense and with its own counsel join any proceeding initiated and directed by the other Party under this clause 7.6. Heptares shall (at Neurocrine's request and expense) use its reasonable efforts to cause [***] to (a) reasonably assist Heptares and Neurocrine and cooperate in any such litigation with respect to any Licensed Patent licensed to Heptares pursuant to the [***] and (b) join such litigation if [***] is deemed to be a necessary party to such litigation, in each case to the extent provided in and subject to the terms of the [***]. Before taking any action under this clause 7.6, the Party seeking to initiate the action shall give written notice to the other Party informing it of the steps it considers need to be taken and the Parties shall, before any such action is initiated, discuss in good faith the manner, timing and the Party responsible for initiating such action(s). Any damages awarded to Neurocrine or to Heptares that are attributable to loss of sales or profits with respect to Licensed Products in the Territory shall, [***].

7.7 **Defence of Claims Brought by Third Parties**

Subject to clause 7.8 in respect of the Heptares Platform and to clause 11, if a Third Party initiates a proceeding claiming that any patent owned by or licensed to such Third Party is infringed by the Exploitation of a Compound or Licensed Product under this Agreement, the Party against which the claim has been brought shall have the right, but not the obligation, to defend against such proceeding at its sole cost and expense. In the event such Party elects to defend against such proceeding, that Party shall have the sole right to direct the defence and to elect when, whether and on what terms to settle such claim. In the event a proposed settlement involves Neurocrine obtaining a license under Blocking Third Party Patent Rights, the provisions of clause 5.4(a) shall apply. The other Party shall reasonably assist the defending Party in the defence of such proceeding and cooperate in any such litigation at the request and expense of the defending Party, including, if requested by the defending Party, joining such action, and executing all papers and performing such acts as the defending Party may reasonably require. The other Party may at its own expense and with its own counsel join any defence initiated and directed by the defending Party under this clause 7.7. Each Party shall provide the other with prompt written notice of the commencement of any such proceeding, or of any allegation of infringement of which a Party becomes aware and that is of the type described in this clause 7.7, and such Party shall promptly furnish the other with a copy of any Third Party notice communicating the alleged infringement and with copies of all pleadings and evidence served or filed in any suit or proceeding relating to such Third Party infringement claim.

7.8 **Heptares Platform IP**

Heptares shall own the Heptares Platform and the Heptares Platform IP. Heptares shall also own all Heptares Platform Improvements, whether or not created, invented, identified or synthesised by Heptares, Neurocrine or jointly by Heptares and Neurocrine during the Term. At the request of Heptares and at Heptares' expense, Neurocrine shall, and shall procure that any of its employees, agents and subcontractors shall, do all acts and things (including making declarations, oaths and providing assistance in relation to the supply of information for any patent applications) and execute all documents that may be reasonably necessary under the Laws of any country for ensuring that all rights in any Heptares Platform Improvements are assigned to Heptares together with the right to sue for past infringement and recover damages. Heptares will be solely responsible, at its expense, for the preparation, filing, prosecution, maintenance and enforcement of all Patents within the Heptares Platform IP including, without limitation, any related interference, re-issuance, re-examination and opposition proceedings. Heptares will be solely responsible for defending any proceedings initiated by a Third Party claiming that the Heptares Platform IP are invalid or any patent owned by or licensed to such Third Party is infringed by use of the Heptares Platform or any Heptares Platform Improvement to identify, generate or optimise compounds.

7.9 **Ownership of Neurocrine Background IP**

As between the Parties, Neurocrine shall own all Neurocrine Background IP.

7.10 **Ownership of Heptares Existing Compound IP**

As between the Parties, Heptares shall own the Heptares Existing Compound IP.

7.11 **Ownership of Arising IP**

Ownership of all Arising IP shall be based on inventorship, as determined in accordance with the rules of inventorship under United States patent laws. Each Party shall solely own all Arising Know-How made solely by its and its Affiliates' employees, agents, or independent contractors, and all Arising Patents that claim or cover such Arising Know-How. The Parties shall jointly own all Arising Know-How that is made jointly by employees, agents, or independent contractors of one Party and its Affiliates together with employees, agents, or independent contractors of the other Party and its Affiliates, and all Arising Patents that claim or cover such Arising Know-How. Except to the extent either Party is restricted by the licenses granted to the other Party or exclusivity or non-compete obligations under this Agreement, each Party shall be entitled to practice, license, assign and otherwise exploit the jointly-owned Arising IP without the duty of accounting or seeking consent from the other Party. Each Party shall promptly disclose to the other Party all Arising Know-How made by such Party to which the other Party has a license hereunder during the Term, including all invention disclosures or other similar documents submitted to such Party by its or its Affiliates' employees, agents or independent contractors relating to such inventions, and shall also respond promptly to reasonable requests from the other Party for additional information relating to such inventions. Each employee, agent or independent contractor of a Party or its respective Affiliates performing work under this Agreement shall, prior to commencing such work, be bound by invention assignment obligations, including: (i) promptly reporting any invention, discovery, process or other intellectual property right; (ii) presently assigning to the applicable Party or Affiliate all of his or her right, title and interest in and to any invention, discovery, process or other intellectual property; (iii) cooperating in the preparation, filing, prosecution, maintenance and enforcement of any patent and patent application; and (iv) performing all acts and signing, executing, acknowledging and delivering any and all documents required for effecting the obligations and purposes of this Agreement. It is understood and agreed that such invention assignment agreement need not reference or be specific to this Agreement.

7.12 **Co-operation**

At the request of Neurocrine or Heptares (as the case may be), the other Party shall, and shall procure that any of its or its Affiliates' employees, agents and subcontractors shall, do all acts and things (including making declarations, oaths and providing assistance in relation to the supply of information for any patent applications) and execute all documents that may be reasonably necessary or useful in connection with the filing, prosecution and maintenance of Patents under this clause 7.

7.13 **Trademarks for Licensed Product**

Neurocrine shall be solely responsible for developing, selecting, searching, registering and maintaining, and shall be the exclusive owner of, all trademarks, trade dress, logos, slogans, designs, copyrights and domain names used on and/or in connection with Licensed Products provided that Heptares shall be responsible for the foregoing for Licensed Products that are M1 Target Agonists for use in all indications in Japan. Upon Heptares' request, the Parties shall negotiate and enter into a trademark license agreement pursuant to which Neurocrine will grant Heptares an exclusive, payment free, sub-licensable license under any trademarks and trade dress used by or on behalf of Neurocrine exclusively in connection with the Licensed Products, for the purposes of exercising the Heptares Retained Rights.

7.14 **Trademarks for Heptares Platform**

Heptares shall be solely responsible for developing, selecting, searching, registering and maintaining, and shall be the exclusive owner of, all trademarks, trade dress, logos, slogans, designs, copyrights and domain names used on and/or in connection with the Heptares Platform, Heptares Platform IP and Heptares Platform Improvements.

7.15 **Joint Research Agreement**

This Agreement is a joint research agreement within the meaning of pre-AIA 35 U.S.C. § 103(c) and AIA 35 U.S.C. § 102(c).

8 TERM AND TERMINATION

8.1 **Term**

Unless terminated earlier pursuant to this clause 8 the term of this Agreement shall commence on the Effective Date (except for clauses 6, 9.3 and 12.12, which shall commence on the Execution Date) and shall continue in full force and effect on a Licensed Product-by-Licensed Product and country-by-country basis until the expiration of the Royalty Term in such country (the "**Term**"). Upon expiration of the Royalty Term, on a Licensed Product-by-Licensed Product and country-by-country basis the license granted to Neurocrine pursuant to clause 2.1 shall be a fully paid, irrevocable, perpetual license.

8.2 **Termination at Will by Neurocrine**

Neurocrine shall have the right to terminate this Agreement for any reason or no reason:

(a) in its entirety or on a Target-by-Target basis during the Research Term on one hundred and eighty (180) days' written notice to Heptares; and

(b) following the end of the Research Term, in its entirety or on a Target-by-Target basis, on ninety (90) days' prior written notice to Heptares.

Neurocrine shall remain liable to pay (a) any Milestone Payments that have become due for payment and/or (b) Royalty Payments on Net Sales by Neurocrine (in accordance with GAAP), in each case (a) and (b) on or before the Termination Date.

8.3 **Termination by Heptares**

Heptares shall have the right to terminate this Agreement on a Target-by-Target basis on one hundred and twenty (120) days' written notice to Neurocrine if after the end of the Research Term, for a continuous period of not less than three hundred and sixty five (365) days, no material Development activities have been undertaken by or on behalf of Neurocrine on (a) any Compound or Licensed Product that is an M4 Target Agonist or (b) Compounds or Licensed Products that are M1 Target Agonists and Compounds or Licensed Products that are M1/M4 Dual Target Agonists; provided that, (i) if the absence of material Development Activities relates to one of (a) or (b) but not both (a) and (b)

the rights of Heptares set out in this clause shall apply only to the Target Agonist in relation to which no such material Development activities have been undertaken and (ii) at least three (3) months prior to providing notice of the termination, Heptares shall notify Neurocrine of its concerns and the Parties shall discuss in good faith the reasons why Neurocrine is not undertaking such material Development activities and its plans for recommencing such activities and if there is a dispute regarding Heptares' right to terminate under this clause the Parties shall refer the matter to the dispute resolution provisions of clause 8.5; provided that Heptares shall not have the right to terminate this Agreement pursuant to this clause 8.3 if: (A) Neurocrine recommences material Development activities during either the one hundred and twenty (120) day notice period or the [***] months period prior to such notice period or (B) Neurocrine is acting in accordance with activities that have been approved by Heptares at the JSC, in either case the Heptares notice of termination shall be withdrawn automatically and shall be void ab initio.

8.4 **Material Breach**

In the event of a material breach of this Agreement, the non-breaching Party shall have the right to terminate this Agreement in its entirety (if the breach is material to the Agreement as a whole) by written notice to the breaching Party specifying the nature of such breach in reasonable detail. Such termination shall become effective [***] days from receipt of such notice by the breaching Party, except that such period shall be [***] days in the event the basis of the alleged material breach is a failure to make payment(s) under this Agreement, unless the breaching Party has cured such breach within such [***] or [***] day period (as applicable). Notwithstanding the foregoing: (a) except in the event the basis of the alleged material breach is a failure to make payment(s) under this Agreement, such [***]-day cure period shall be extended for an additional [***] days or such longer period as is reasonably required to cure such breach if the breaching Party is employing ongoing, good faith efforts to cure such alleged material breach; (b) in the event the basis of the alleged material breach is a failure to make payment(s) under this Agreement and the alleged breaching Party (i) notifies the non-breaching Party, during such thirty (30)-day cure period, of a bona fide dispute regarding whether such payment(s) are due; and (ii) pays the undisputed portion of such payment(s) on or before providing such notice, such [***]-day cure period shall be tolled pending resolution of such dispute pursuant to clause 8.5, and in the event the dispute is finally resolved against the Party allegedly in material breach, the applicable cure period shall commence upon such final resolution; and (c) in the event the basis of the alleged material breach is other than a failure to make payment(s) under this Agreement and the alleged breaching Party notifies the non-breaching Party, during such [***]-day cure period, of a bona fide dispute regarding the alleged breach, such [***]-day cure period shall be tolled pending resolution of such dispute pursuant to clause 8.5, and in the event the dispute is finally resolved against the Party allegedly in material breach, the applicable cure period shall commence upon such final resolution.

8.5 **Dispute Resolution**

Any dispute arising out of an allegation of material breach of this Agreement or any other dispute, controversy or claim that may arise out of or in connection with this Agreement, will be resolved as follows:

(a) the Senior Officers will meet to attempt to resolve the dispute by good faith negotiations. If the Senior Officers cannot resolve the dispute within [***] days after a Party requests such negotiations, then each Party will attempt in good faith to settle the dispute by mediation pursuant to clause 8.5(b);

(b) the mediation of any dispute is to be administered in the United Kingdom by the Centre for Effective Dispute Resolution ("**CEDR**") or such other mediator as may be mutually agreed to by the Parties. If mediation is unsuccessful, the Parties may initiate arbitration in accordance with clause 12.3; and

(c) notwithstanding anything to the contrary in this Agreement, if either Party in its sole judgment believes that any such breach or dispute could cause it irreparable harm, such Party shall be entitled to seek equitable relief from a court of competent jurisdiction in order to avoid such irreparable harm and will not be required to follow the procedures set forth in this clause 8.5.

8.6 **Insolvency**

(a) Either Party may terminate this Agreement if, at any time (i) the other Party files in any court or agency pursuant to any statute or regulation of any state or country a petition in bankruptcy or

insolvency or for reorganization (save for solvent reorganization or solvent reconstruction) or for an arrangement or for the appointment of a receiver or trustee of the Party or of substantially all of its assets, (ii) the other Party proposes a written agreement of composition or extension of substantially all of its debts, (iii) the other Party is served with an involuntary petition against it, filed in any insolvency proceeding, and such petition is not dismissed within [***] days after the filing thereof, (iv) the other Party proposes to be a party to any dissolution or liquidation or (v) the other Party makes an assignment of substantially all of its assets for the benefit of creditors.

(b) All rights and licenses granted under or pursuant to any clause of this Agreement are for the purposes of Section 365(n) of Title 11, United States Code (the "**Bankruptcy Code**") licenses of rights to "intellectual property" as defined in Section 101(56) of the Bankruptcy Code (and any equivalent provisions under the bankruptcy or insolvency laws of any other relevant jurisdiction). The Parties shall retain and may fully exercise all of their respective rights and elections under the Bankruptcy Code provided that they comply with the terms of this Agreement.

8.7 **Patent Challenge**

If a Party or its Affiliate directly commences, or knowingly assists a Third Party (save where such assistance is ordered by a court, patent office or other tribunal) to commence any interference or opposition proceeding, challenges the validity or enforceability in any patent office or court proceedings of, or opposes any extension of or the grant of a supplementary protection certificate with respect to a Patent licensed to such Party by the other Party hereunder ("**Patent Challenge**"), the other Party may terminate such Party's license to the applicable Patent on sixty (60) days' written notice stating its intention to terminate the license if the Patent Challenge has not been stopped within such period, provided that (a) a Party may not terminate a license pursuant to this clause 8.7 if the Patent Challenge had been commenced by an Affiliate of the other Party prior to such Affiliate becoming an Affiliate of such other Party; and (b) a Party shall not have the right to terminate a license if such Patent Challenge is a defence to any claim that the Exploitation of a compound which is not a Compound or Licensed Product infringes a Patent.

8.8 **Effect of Expiration or Termination of this Agreement**

(a) Accrued Obligations. Expiration or termination of this Agreement for any reason shall not release either Party from any obligation or liability which, at the time of such expiration or the Termination Date, has already accrued to the other Party or which is attributable to a period prior to such expiration or the Termination Date.

(b) Termination by Neurocrine at Will or by Heptares for Material Breach, Insolvency or by Heptares pursuant to clauses 8.3 and 8.7. If (i) this Agreement is terminated in its entirety by Neurocrine pursuant to clause 8.2 or by Heptares pursuant to clause 8.3, 8.4, or 8.6, then the following provisions shall apply to this Agreement in its entirety and to all Compounds, Licensed Products, Arising Patents, and Licensed Patents or (ii) if this Agreement is terminated on a Target-by-Target basis by Neurocrine pursuant to clause 8.2 or on a Target-by-Target basis or Licensed Patent-by-Licensed Patent basis by Heptares pursuant to clause 8.3 or 8.7, then clause (ix) shall apply, but this Agreement shall remain in full force and effect with respect to all other Compounds, Licensed Products and Licensed Patents:

(i) the license and rights granted to Neurocrine under clause 2.1 and to Heptares under clause 2.5(a) (but not clause 2.5(b)) shall terminate;

(ii) Neurocrine shall reimburse Heptares for all Third Party committed and non-cancelable Development Costs provided such commitments have been made pursuant to an approved Research and Development Plan and budget;

(iii) except as otherwise expressly provided herein all rights and obligations of each Party hereunder will cease with respect to all Compounds or Licensed Products including all rights, licenses and sublicenses granted by a Party to the other hereunder, provided that clause 5 will survive with regard to any outstanding payment obligations accrued as of the Termination Date;

(iv) Neurocrine and its Affiliates will immediately cease all activity using the Heptares

Platform;

(v) subject to clause 8.8(d), Neurocrine shall grant Heptares an exclusive, worldwide, sublicensable (through multiple tiers of sublicensees), royalty-bearing (as set out in this sub-clause) license under the Reversion IP solely to Exploit Reversion Products after the Termination Date in the Field in the Territory; provided that in consideration for such license, on a Reversion Product-by-Reversion Product basis, Heptares shall pay Neurocrine

(A) a royalty of (i) [***] percent ([***]%) of Net Sales of any such Reversion Product if the Termination Date occurs [***], (ii) [***] percent ([***]%) of Net Sales of any such Reversion Product if the Termination Date occurs [***], (iii) [***] percent ([***]%) of Net Sales of any such Reversion Product if the Termination Date occurs [***]. The terms of clauses 5.3 and 5.4 shall apply to the payment of any such royalty except that (i) all references to Neurocrine shall be replaced by Heptares and vice versa, (ii) the royalty rate shall be the applicable rate set out above and (iii) [***]. If the Agreement is terminated by Heptares pursuant to clauses 8.4 or 8.6, the royalty rates set out in this subsection shall be reduced by [***] percent ([***]%);

(vi) Neurocrine will at Heptares' cost (A) transfer to Heptares any IND and Regulatory Approval (or filing therefor) related solely to any Reversion Products, in each case which are Controlled by Neurocrine or its Affiliates at the Termination Date, (B) provide access to Know-How Controlled by Neurocrine and its Affiliates that are licensed to Heptares under clause 8.8(b)(v) above and (C) to the extent owned and possessed by Neurocrine or its Affiliates, transfer to Heptares all tangible chemical or biological material embodying the Reversion Products and reasonable quantities of other Materials Controlled by Neurocrine and its Affiliates that are licensed to Heptares under this clause;

(vii) Neurocrine shall, and shall procure that its Affiliates shall, at Heptares' request and cost, for a reasonable period not exceeding [***] days following the Termination Date, provide Heptares with such assistance as Heptares may reasonably require in order to transfer the ongoing Development, manufacture and Commercialization of any Reversion Products to Heptares, to the extent contemplated by this clause 8.8(b);

(viii) Neurocrine shall grant Heptares an exclusive, worldwide, sublicensable (through multiple tiers of sublicensees) license under any trademark (if any) registered by or on behalf of Neurocrine that is owned by Neurocrine or its Affiliates and used exclusively to Exploit a Reversion Product as at the Termination Date ("**Product Trademark**"); provided that Neurocrine may, at its election, instead of granting such exclusive license, transfer such trademark to Heptares;

(ix) If the termination applies to a particular Target or class of Target Agonists or, in the case of clause 8.7 a Licensed Patent that covers a particular Target or class of Target Agonists, then notwithstanding anything to the contrary in this clause 8.8, (A) the above provisions and other relevant provisions of this clause 8 will apply to the particular Target or class of Target Agonists in relation to which this Agreement has been terminated, (B) if any Licensed Patent and/or Arising Patent relates to both a Compound or Licensed Product for which this Agreement is terminated and a Compound or Licensed Product for which this Agreement remains in effect, then Neurocrine shall retain all rights with respect to prosecution, maintenance, defense and enforcement of such Licensed Patents and/or Arising Patents as set forth in clauses 7.1, 7.2, 7.3, 7.4, 7.6 and 7.7, except that Neurocrine shall have no obligation to defend or enforce any Licensed Patent and/or Arising Patents with respect to any Reversion Product and Heptares may do so provided that Neurocrine shall have the right to participate in any such action or proceeding to protect its interest in any Compound or Licensed Product to which Neurocrine retains a license under this Agreement, and (C) the Parties will agree in good faith any necessary amendments to this clause to take account of any such partial termination including to address any instance where a terminal disclaimer occurs between any US patent in the Agreement and a US patent that has been terminated to ensure that the patents that are still in the Agreement remain enforceable, as well as take account of any overlap between Reversion Products that are claimed in the Licensed Patents where such same patents also claim Licensed Products that are not subject to the termination; and

(x) If the Agreement is terminated as contemplated by this clause 8.8 in relation to M1 Target Agonists the provisions of clause 2.4 shall terminate and any provisions in clause 3.6 giving [***] final decision making or approval rights in relation to the exercise of the Heptares Retained Rights shall terminate (except as such provisions apply to any Compound or Licensed Product to which [***] retains a license under this Agreement, in which case it shall continue in effect) or in clause 7 giving Neurocrine the prosecution, defence or enforcement of Licensed Patents (including Joint Patents) covering M1 Target Agonists shall terminate (except in the case described in clause (ix) above with respect to Licensed Patents covering M1 Target Agonists and any Compound or Licensed Product to which Neurocrine retains a license under this Agreement, in which case it shall continue in effect). Additionally if after the end of the Research Term, for a continuous period of not less than three hundred and sixty five (365) days, no material Development activities have been undertaken by or on behalf of Neurocrine on Compounds or Licensed Products that are M1 Target Agonists, the provisions in clause 3.6 giving [***] final decision making or approval rights in relation to the exercise of the Heptares Retained Rights shall terminate (except as such provisions apply to any Compound or Licensed Product to which [***] retains a license under this Agreement, in which case it shall continue in effect) or in clause 7 giving Neurocrine the prosecution, defence or enforcement of Licensed Patents (including Joint Patents) covering M1 Target Agonists shall terminate (except in the case described in clause (ix) above with respect to Licensed Patents covering M1 Target Agonists and any Compound or Licensed Product to which Neurocrine retains a license under this Agreement, in which case it shall continue in effect).

(c) Termination by Neurocrine for Material Breach or Insolvency. If Neurocrine terminates this Agreement in its entirety pursuant to clause 8.4 or 8.6, then the following provisions shall apply to this Agreement in its entirety and to all Compounds, Licensed Products and Patents:

(i) the license and rights granted to Neurocrine under clause 2.1 and to Heptares under clause 2.5(a) (but not clause 2.5(b)) shall terminate;

(ii) Neurocrine shall reimburse Heptares for all Third Party committed and non-cancelable Development Costs provided such commitments have been made pursuant to an approved Research and Development Plan and budget.

(iii) except as otherwise expressly provided herein all rights and obligations of each Party hereunder will cease with respect to all Compounds or Licensed Products including all rights, licenses and sublicenses granted by a Party to the other hereunder, provided that clause 5 will survive with regard to any outstanding payment obligations accrued as of the Termination Date;

(iv) Neurocrine and its Affiliates will immediately cease all activity using the Heptares Platform;

(v) Neurocrine shall, at Heptares' request, negotiate a royalty-bearing license from Neurocrine to Heptares under the Reversion IP and Product Trademarks for the Exploitation of Reversion Products;

(vi) The prosecution of all Licensed Patents and, to the extent they are subject to a license granted pursuant to clause 8.8(c)(v), Arising Patents shall be transferred to Heptares, including the rights contained in clause 7.2; and

(vii) From the Termination Date, Neurocrine and its Affiliates and Sublicensees shall not Exploit Reversion Products in a country.

(d) Termination by Neurocrine for Patent Challenge. If this Agreement is terminated by Neurocrine on a Licensed Patent-by-Licensed Patent basis by Neurocrine pursuant to clause 8.7, then the license and rights granted to Heptares under clause 2.5 shall terminate, but this Agreement shall otherwise remain in full force and effect with respect to all other Compounds, Licensed Products and Licensed Patents.

(e) Notwithstanding any other provision in this clause 8.8, if there are any Clinical Trials being conducted at the Termination Date, Neurocrine shall be entitled to continue Exploiting

Compounds and Products to the extent and for the period necessary to effect an orderly transfer or wind down of such Clinical Trials in a timely manner and in accordance with all Laws.

8.9 **Survival**

Upon the expiration or termination of this Agreement for any reason, all rights and obligations of the Parties under this Agreement (or with respect to a particular Target or class of Target Agonists, or Licensed Patent that covers a Target or class of Target Agonists, in relation to which this Agreement has been terminated, as applicable) shall terminate. Notwithstanding any provision herein to the contrary, the rights and obligations of the Parties set forth in the Preamble, clause 1 (Definitions), clause 2.5(b), clause 2.8 (Retention of Rights), clause 5 (Financial Provisions) (solely with respect to payment obligations that have accrued prior to the effective date of such expiration or termination), clause 5.10 (Record Retention; Financial Audit; Consolidation Reporting), clause 6 (Confidentiality), clause 7.8 (Heptares Platform IP), clause 7.9 (Ownership of Neurocrine Background IP), clause 7.10 (Ownership of Heptares Existing Compound IP), clause 7.11 (Ownership of Arising IP), clause 7.12 (Co-operation), clause 7.14 (Trademarks for Heptares Platform), clause 8.1 (Term), last sentence with respect to any fully paid, irrevocable, and perpetual license, clause 8.5 (Dispute Resolution), clause 8.8 (Effect of Expiration or Termination of this Agreement) and any clauses referenced therein as continuing in effect, this clause 8.9 (Survival), clause 8.10 (Effect of Termination on Sublicenses), clause 8.11 (Termination not Sole Remedy), clause 11 (Indemnification), clause 12.1 (Assignment), clause 12.2 (Governing Law), clause 12.3 (Arbitration), clause 12.6 (No Agency), clause 12.8 (Entire Agreement; Amendment), clause 12.9 (Illegality, Non-enforceability), clause 12.11 (Notices), clause 12.13 (Further Assurances), clause 12.14 (No Strict Construction), clause 12.15 (Headings) and clause 12.17 (Non-Exclusive Remedies) and shall survive the expiration or termination of this Agreement for any reason.

8.10 **Effect of termination on Sublicenses**

If this Agreement terminates for any reason, any Sublicensee that is not an Affiliate of Neurocrine will, from the Termination Date, automatically and without any additional consideration become a direct licensee of Heptares with respect to the rights sublicensed to the Sublicensee by Neurocrine under this Agreement; so long as (a) such Sublicensee is not in breach of its sublicense agreement, (b) such Sublicensee agrees in writing to comply with all of the terms of this Agreement to the extent applicable to the rights originally sublicensed to it by Neurocrine, and (c) such Sublicensee agrees to pay directly to Heptares such Sublicensee's payments under this Agreement to the extent applicable to the rights sublicensed to it by Neurocrine. The foregoing shall not apply if a Sublicensee provides written notice to Heptares that it does not wish to receive and retain the rights afforded to it pursuant to this clause 8.10. At Neurocrine's request, Heptares will enter into a standby license with any Sublicensee confirming the benefits conferred on such Sublicensee by this clause 8.10.

8.11 **Termination Not Sole Remedy**

Termination is not the sole remedy under this Agreement and, whether or not termination is effected, all other remedies at equity or law shall remain available to the Parties.

8.12 **Right to Offset**

Neurocrine will have the right to offset any damages awarded to Neurocrine on account of a breach of this Agreement by Heptares against any payments owed by Neurocrine to Heptares under this Agreement.

8.13 **Right to Terminate in Relation to HSR**

Either Party may terminate this Agreement by notice in writing to the other Party if the expiration or termination of any applicable waiting period under the HSR Act with respect to this Agreement has not been satisfied (or if permitted by applicable Law, waived) on or before one hundred and twenty (120) days following the Execution Date (the "Outside Date"). If a Party terminates this Agreement pursuant to this clause 8.13, then this Agreement shall be of no further force or effect, except that the rights and obligations of the Parties set forth in clauses 6 and 12.12 and this clause 8.13, and any relevant definitions in clause 1 (Definitions), shall survive such termination of this Agreement.

9 REPRESENTATIONS, WARRANTIES AND COVENANTS

9.1 Mutual Representations

As of the Execution Date, each of Heptares and Neurocrine represents, warrants and, as applicable, covenants to the other Party that:

(a) such Party is an entity duly organized, validly existing and in good standing under the Laws of the state or country (as applicable) of its organization, is qualified to do business and is in good standing as a foreign entity in each jurisdiction in which the conduct of its business or the ownership of its properties requires such qualification and failure to have such would prevent it from performing its obligations under this Agreement, and has full power and authority to enter into this Agreement and to carry out the provisions hereof;

(b) such Party is duly authorized, by all requisite action, to execute and deliver this Agreement and the effective delivery and performance of this Agreement by such Party does not require any shareholder action or approval, and the person executing this Agreement on behalf of such Party is duly authorized to do so by all requisite action;

(c) except pursuant to clause 12.12, no consent, approval, order or authorization of, or registration, qualification, designation, declaration or filing with, any Governmental Authority is required on the part of such Party in connection with the valid effective delivery and performance of this Agreement by it;

(d) such Party (i) has not employed (and, to its knowledge, has not used a contractor or consultant that has employed) and (ii) in the future shall not employ (or, to its Knowledge, use any contractor or consultant that employs) any person debarred by the FDA or subject to a similar sanction of EMA or foreign equivalent, or any person which is the subject of an FDA debarment investigation or proceeding (or similar proceeding of EMA or foreign equivalent), for the conduct of its activities under this Agreement;

(e) this Agreement is a legal and valid obligation binding upon such Party and enforceable in accordance with its terms except as enforceability may be limited by (i) bankruptcy, insolvency, reorganization, moratorium or similar Laws affecting the enforcement of creditors' rights; and (ii) equitable principles of general applicability; and

(f) the delivery and performance by it of this Agreement and its compliance with the terms and provisions of this Agreement does not and shall not conflict with or result in a breach of any of the terms or provisions of (a) any other contractual or other obligations of such Party, (b) the provisions of its operating documents or bylaws, or (c) any order, writ, injunction or decree of any Governmental Authority entered against it or by which it or any of its property is bound.

9.2 Heptares' Additional Representations, Warranties and Covenants

Heptares represents and warrants that as at the Execution Date:

(a) it has full right and authority to grant the rights granted under this Agreement, and is sole owner or exclusive licensee of all Licensed Know-How (except as provided in the [***]), free of any encumbrance, lien or claim of ownership by any Third Party;

(b) all Licensed Patents in existence as of the Execution Date ("**Existing Patents**") are (i) set forth on Schedule 2 and identified by owner, serial number, filing date, country, and status, (ii) subsisting, (iii) solely and exclusively owned by (except as indicated on Schedule 2) or, if indicated on Schedule 2, licensed to Heptares, free of any encumbrance, lien or claim of ownership by any Third Party, (iv) being diligently prosecuted in the respective patent offices, and (v) filed and maintained properly and correctly and all applicable fees have been paid on or before the due date for payment, and the claims included in any issued patents included in the Existing Patents are in full force and effect as of the Execution Date;

(c) Heptares does not have Knowledge of any fact or circumstance that would cause it to reasonably conclude that any of the Licensed Patents is, or will be upon issuance, invalid or

unenforceable;

(d) the inventorship of each Licensed Patent is properly identified on each granted patent and on relevant documents filed at the US Patent Office;

(e) Heptares has disclosed to the US Patent Office in writing (i) all information that is (A) known to any individual associated with the filing or prosecution (as defined in 37 C.F.R. § 1.56(c)) of the Licensed Patents and (B) material to patentability of the Licensed Patents (as defined in 37 C.F.R. § 1.56(b)), or that would be considered material to patentability as defined in 37 C.F.R. § 1.56(b) but for an exception under 35 U.S.C. § 102(b) and (ii) and each piece of such information has been disclosed in every relevant U.S. Licensed Patent;

(f) Heptares is not aware of any reference or prior art that would preclude the issuance of any claim in a Licensed Patent;

(g) Heptares has no Knowledge of any claim, whether or not brought or asserted by any person alleging that (i) the Existing Patents are invalid or unenforceable or (ii) the conception, development, reduction to practice, disclosing, copying, making, assigning or licensing of the Existing Patents or the Exploitation of the Compounds or Licensed Products as contemplated herein, violates, infringes, constitutes misappropriation or otherwise conflicts or interferes with, or would violate, infringe or otherwise conflict or interfere with, any intellectual property rights of a Third Party; or (iii) any challenges or disputes exist relating to the inventorship, ownership, scope, duration, priority or right to use any of any of the Existing Patents;

(h) to Heptares' Knowledge, no person is infringing or threatening to infringe or misappropriating or threatening to misappropriate the Existing Patents or Licensed Know-How;

(i) to Heptares' Knowledge, the Exploitation of the Compounds in accordance with the terms of this Agreement will not infringe the intellectual property rights of any Third Party;

(j) to Heptares' Knowledge, Heptares and its Affiliates do not own or Control any Patent, other than the Licensed Patents, that is necessary or, to Heptares' reasonable belief as of the Execution Date, reasonably useful to carry out the Development or other Exploitation of Compounds and Licensed Products in accordance with the terms of this Agreement;

(k) to Heptares' Knowledge, the documents, data and information that are included in the Licensed Know-How transferred to Neurocrine pursuant to clause 2.2(a) constitute all of the Know-How owned or Controlled by Heptares that is reasonably necessary for the Development, manufacture or other Exploitation of Compounds and Licensed Products in accordance with the terms of this Agreement;

(l) except as set out in the [***] and the [***] Agreements, Heptares has not previously assigned, transferred, conveyed, or granted any license or other rights to its right, title and interest in any Patents or Know-How licensed hereunder, in any way that would materially conflict with or limit the scope of any of the rights or licenses granted to Neurocrine hereunder, and Heptares has to its Knowledge disclosed to Neurocrine all Know-How, Patents and regulatory materials arising under or as a result of the [***] and the [***] Agreements, including, without limitation, all [***] for any Compounds and Licensed Products generated by [***] pursuant to the [***];

(m) Heptares has disclosed to Neurocrine all regulatory filings, materials and communications related to the Compounds and Licensed Products Controlled by, owned by or otherwise in the possession of Heptares or its Affiliates;

(n) Heptares owns all Know-How generated by Third Party service providers in connection with the Development or manufacture of Compounds and Licensed Products;

(o) Heptares has disclosed to Neurocrine a complete list of all Target Agonists identified, discovered or developed by or on behalf of Heptares or its Affiliates;

(p) there are no pending, and to Heptares' Knowledge, no threatened, adverse actions, suits or proceedings (including interferences, reissues, reexaminations, cancellations, oppositions,

nullity actions, invalidation actions or post-grant reviews) against Heptares involving the Licensed IP or any Compound or Licensed Product;

(q) all discovery, research, Development and manufacture of Compounds and Licensed Products by or on behalf of Heptares and its Affiliates prior to the Execution Date was conducted in accordance with all applicable Laws, including cGCP and cGMP;

(r) the materials transferred to Neurocrine under clause 4.11 will have been manufactured, stored, packaged and shipped in accordance with all applicable Laws, including cGMP, and will comply with the applicable specifications;

(s) neither Heptares nor its Affiliates, nor any of its or their respective directors, officers, employees or agents has (i) committed an act, (ii) made a statement or (iii) failed to act or make statement, in any case ((i), (ii) or (iii)), that (x) would be or create an untrue statement of material fact or fraudulent statement to the FDA or any other Regulatory Authority with respect to the research, Development and manufacture of any Compound or Licensed Product or (y) could reasonably be expected to provide a basis for the FDA or any other Regulatory Authority to invoke its policy respecting “Fraud, Untrue Statements of Material Facts, Bribery and Illegal Gratuities”, set forth in 56 Fed. Reg. 46191 (September 10, 1991) and any amendments thereto or any analogous laws or policies, with respect to the research, Development and manufacture of any Compound or Licensed Product; and

(t) Heptares has disclosed to Neurocrine all information it has Knowledge of or in its Control related to the Licensed IP, Compounds or Licensed Products that Heptares and its agents uses or has used in connection with, and which in each case Heptares reasonably believes would be material to, the Licensed IP or the Development and Commercialization of Compounds and Licensed Products as contemplated by this Agreement, and all such information is complete and accurate; and (ii) Heptares and its agents has not failed to disclose any information it has Knowledge of or in its or its Affiliate’s Control related to the Licensed IP, Compounds or Licensed Products that would cause the information actually disclosed to Neurocrine to be misleading or incomplete in any material respect.

9.3 **Heptares Covenant**

Heptares agrees that all activities performed by Heptares in relation to the discovery, research Development and manufacture of Compounds and Licensed Products in the period between the Execution Date and the Effective Date shall be conducted in accordance with all applicable Laws, including cGCP and cGMP. Heptares agrees, on behalf of itself and its Affiliates, not to take any action or fail to take any action in the period between the Execution Date and the Effective Date that would cause or be reasonably likely to cause any of the representations and warranties by Heptares set forth in clause 9.1 or 9.2 to be untrue in any material respect if made as of the Effective Date.

9.4 **No Other Warranties**

Except as expressly set forth in this Agreement, neither Party makes any warranties or conditions, express, implied, statutory or otherwise, with respect to the subject matter of this Agreement.

10 ANTI-BRIBERY AND ANTI-CORRUPTION

10.1 Each Party agrees, on behalf of itself, its officers, directors and employees and on behalf of its Affiliates, agents, representatives, consultants and subcontractors hired in connection with the subject matter of this Agreement (together with the Party, the "**Party Representatives**") that for the performance of its obligations under this Agreement:

(a) The Party Representatives shall not directly or indirectly pay, offer or promise to pay, authorize the payment of any money or give, offer or promise to give, or authorize the giving of anything else of value, to: (i) any Government Official in order to influence official action; (ii) any person (whether or not a Government Official) (A) to influence such person to act in breach of a duty of good faith, impartiality or trust ("**Acting Improperly**"), (B) to reward such person for Acting Improperly or (C) where such person would be acting improperly by receiving the money or other thing of value; (iii) any person (whether or not a Government Official) while knowing or having reason to know that all or any portion of the money or other thing of value will be paid,

offered, promised or given to, or will otherwise benefit, a Government Official in order to influence official action for or against either Party in connection with the matters that are the subject of this Agreement; or (iv) any person (whether or not a Government Official) to reward that person for Acting Improperly or to induce that person to Act Improperly.

10.2 The Party Representatives shall not, directly or indirectly, solicit, receive or agree to accept any payment of money or anything else of value in violation of the Anti-Corruption Laws.

10.3 The Party Representatives shall comply with the Anti-Corruption Laws and shall not take any action that will, or would reasonably be expected to, cause the other Party or its Affiliates to be in violation of any such laws or policies.

10.4 Each Party represents and warrants to the other that as of the Effective Date, such Party and its Party Representatives have not taken any action that if conducted after the Effective Date would violate clauses 10.1 through 10.3;

10.5 Each Party shall promptly provide the other with written notice upon becoming aware of any breach or violation by a Party or other Party Representative of any representation, warranty or undertaking set forth in clauses 10.1 through 10.4 above.

11 INDEMNIFICATION

11.1 Heptares

Heptares shall defend, indemnify and hold Neurocrine, its Affiliates and its and their respective directors, officers, employees and agents, at Heptares' cost and expense, harmless from and against any and all losses, costs, damages, liabilities, fees or expenses (including reasonable attorneys' fees and expenses) ("**Losses**") incurred in connection with or arising out of any Third Party claims, suits, investigations or demands ("**Third Party Claim**"):

(a) arising out of or in connection with the exercise of the Heptares Retained Rights;

(b) resulting from the Exploitation of any Reversion Product;

(c) arising out of or in connection with any breach by Heptares of this Agreement, including the warranties or covenants contained in clause 2.10, clause 9 or clause 10 herein; or

(d) arising out of or in connection with any negligence or wilful misconduct of Heptares or its Affiliates or of its or their respective directors, officers, employees or agents in the exercise of any of Heptares' rights or the performance of any of its obligations under this Agreement,

in each case except to the extent that such Losses are subject to indemnification by Neurocrine pursuant to clause 11.2 below (or would be subject to indemnification if the claim were made against Heptares).

11.2 Neurocrine

Neurocrine shall defend, indemnify and hold Heptares, its Affiliates and its and their respective directors, officers, employees and agents, at Neurocrine's cost and expense, harmless from and against any and all Losses incurred in connection with or arising out of any Third Party Claims:

(a) resulting from (i) the conduct of the activities by or on behalf of the Parties or their Affiliates under each Research and Development Program (excluding breach, negligence or wilful misconduct of Heptares or its Affiliates in conducting activities under any Research and Development Program) and (ii) the Exploitation of Licensed Products by Neurocrine, its Affiliates or Sublicensees during the Term;

(b) arising out of or in connection with any breach by Neurocrine of this Agreement, including the

warranties or covenants contained in clauses 9.1 and 10 herein; or

(c) arising out of or in connection with any negligence or wilful misconduct of Neurocrine or its Affiliates or of its or their respective directors, officers, employees or agents in the exercise of any of its rights or the performance of any of its obligations under this Agreement,

in each case except to the extent that such Losses are subject to indemnification by Heptares pursuant to clause 11.1 above (or would be subject to indemnification if the claim were made against Neurocrine).

11.3 **Notice of Claim**

All indemnification claims in respect of any person seeking indemnification under clause 11.1 or 11.2 (collectively, the "**Indemnitees**" and each an "**Indemnitee**") shall be made by the corresponding Party (the "**Indemnified Party**"). The Indemnified Party shall give the indemnifying Party (the "**Indemnifying Party**") prompt written notice (an "**Indemnification Claim Notice**") of any Losses or the discovery of any fact upon which such Indemnified Party intends to base a request for indemnification under clause 11.1 or 11.2, but in no event shall the Indemnifying Party be liable for any Losses that result from any delay by the Indemnified Party in providing such notice. Each Indemnification Claim Notice must contain a description of the claim and the nature and amount of such Loss (to the extent that the nature and amount of such Loss are known at such time). Together with the Indemnification Claim Notice, the Indemnified Party shall furnish promptly to the Indemnifying Party copies of all notices and documents (including court papers) received by any Indemnitee in connection with the Third Party Claim. The Indemnifying Party shall not be obligated to indemnify the Indemnified Party to the extent any admission or statement made by the Indemnified Party materially prejudices the defence of such Third Party Claim. Where required the Indemnifying Party shall promptly send a copy of the Indemnification Claim Notice to its relevant insurers and shall permit them to exercise their rights of subrogation and hereafter in this clause 11. "**Indemnifying Party**" shall be deemed to include any such insurers.

11.4 The obligations of an Indemnifying Party under this clause 11 shall be governed by and contingent upon the following:

(a) at its option, the Indemnifying Party may assume control of the defence of any Third Party Claim (which, for the avoidance of doubt, shall include the conduct of all dealings with such Third Party) by giving written notice to the Indemnified Party within [***] days after the Indemnifying Party's receipt of an Indemnification Claim Notice. The assumption of control of the defence of a Third Party Claim by the Indemnifying Party shall not be construed as an acknowledgement that the Indemnifying Party is liable to indemnify any Indemnitee in respect of the Third Party Claim, nor shall it constitute a waiver by the Indemnifying Party of any defences it may assert against any Indemnified Party's claim for indemnification.

(b) upon the assumption of the control of the defence of a Third Party Claim by the Indemnifying Party:

(i) subject to the provisions of clause 11.4(c), it shall have the right to and shall assume sole control and responsibility for dealing with the Third Party and the Third Party Claim, including the right to settle the claim on any terms the Indemnifying Party chooses, but at all times in accordance with the provisions of clauses 11.4(c) and 11.4(d);

(ii) if it chooses, the Indemnifying Party may appoint as counsel in the defence of the Third Party Claim any law firm or counsel selected by the Indemnifying Party; and

(iii) except as expressly provided in clause 11.4(c), the Indemnifying Party shall not be liable to the Indemnified Party for any legal expenses subsequently incurred by such Indemnified Party or any Indemnitee in connection with the analysis, defence, or settlement of the Third Party Claim. In the event that it is ultimately determined that the Indemnifying Party is not obligated to indemnify, defend or hold harmless an Indemnitee from and against the Third Party Claim, the Indemnified Party shall reimburse the Indemnifying Party for any and all costs and expenses (including lawyers' fees and costs of suit) and any Losses incurred by the Indemnifying Party in its defence of the Third Party Claim with respect to such Indemnified Party or

Indemnitee.

(c) without limiting the remainder of this clause 11.4, any Indemnitee shall be entitled to participate in, but not control, the defence of a Third Party Claim by having its views regularly solicited by the Indemnifying Party and, where proceedings are commenced, to retain counsel of its choice for such purpose; provided that such retention shall be at the Indemnitee's own expense unless (i) the Indemnifying Party has failed to assume the defence and retain counsel in accordance with clause 11.4(a) and 11.4(b)(ii) (in which case the Indemnified Party shall control the defence), (ii) the interests of the Indemnitee and the Indemnifying Party with respect to such Third Party Claim are sufficiently adverse to prohibit the representation by the same counsel of both Parties under any legal requirement, ethical rules or equitable principles or (iii) the employment thereof has been specifically authorised in writing by the Indemnifying Party.

(d) with respect to any Losses relating solely to the payment of money to the Third Party to settle the Third Party Claim and that will not result in the Indemnified Party or the Indemnitee becoming subject to injunctive relief, and as to which the Indemnifying Party shall have acknowledged in writing the obligation to indemnify the Indemnitee under clause 11.4(a), the Indemnifying Party shall have sole authority to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Losses, without the prior written consent of the Indemnified Party. With respect to all other Losses or where the Indemnified Party will be subject to injunctive relief, where the Indemnifying Party has assumed the defence of a Third Party Claim in accordance with clause 11.4(a), the Indemnifying Party must not consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Losses, unless it obtains the prior written consent of the Indemnified Party (which consent shall not be unreasonably withheld or delayed).

(e) if the Indemnifying Party chooses not to take control of the defence or prosecute any Third Party Claim, the Indemnified Party shall retain control of the defence thereof, but no Indemnified Party or Indemnitee shall admit any liability with respect to, or settle, compromise or discharge, any such Third Party Claim without the prior written consent of the Indemnifying Party, which consent shall not be unreasonably withheld or delayed. The Indemnifying Party shall not be liable for any settlement or other disposition of Losses by an Indemnified Party or an Indemnitee under such a Third Party Claim that is reached without the written consent of the Indemnifying Party which consent will not be unreasonably withheld or delayed.

(f) if the Indemnifying Party chooses to control the defence of any Third Party Claim, the Indemnified Party shall, and shall cause each other Indemnitee to, reasonably cooperate in the defence thereof and shall furnish such records, information and testimony, provide such witnesses and attend such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested in connection therewith. Such cooperation shall include access during normal business hours by the Indemnifying Party to, and reasonable retention by the Indemnified Party of, records and information that are reasonably relevant to such Third Party Claim, and making the Indemnified Party, the Indemnitees and its and their employees and agents available on a mutually convenient basis to provide additional information and explanation of any records or information provided, and the Indemnifying Party shall reimburse the Indemnified Party for all of its related reasonable out-of-pocket expenses.

11.5 Except as expressly provided above, the reasonable and verifiable costs and expenses, including fees and disbursements of counsel, incurred by the Indemnified Party where it participates in the defence under clause 11.4(c) shall be reimbursed on a quarterly basis by the Indemnifying Party, without prejudice to the Indemnifying Party's right to contest the Indemnified Party's right to indemnification and subject to refund in the event the Indemnifying Party is ultimately held not to be obligated to indemnify the Indemnified Party.

11.6 **Insurance**

Each Party shall have and maintain, at its sole cost and expense, an adequate liability insurance or self-insurance program (including product liability insurance) to protect against potential liabilities and risk arising out of activities to be performed under this Agreement and upon such terms (including coverages, deductible limits and self-insured retentions) as are customary in the pharmaceutical industry generally for the activities to be conducted by such Party under this Agreement. Such liability insurance or self-insurance program shall insure against all types of liability, including personal injury, physical injury or property damage arising out of such Party's activities hereunder. This clause 11.6 shall not create any limitation on the Parties' liability under this Agreement. Such insurance information shall be kept in confidence in the same manner as any other Confidential Information

disclosed by the Parties hereunder.

11.7 **Consequential Damages**

In no event shall either Party or any of its Affiliates or Sublicensees or licensees be liable for special, indirect, incidental, punitive, treble or consequential damages or indirect lost profits, whether based on contract, tort or any other legal theory; provided, however, that this limitation shall not limit (a) the indemnification obligation of such Party in respect of amounts actually awarded against an Indemnified Party as a part of a Third Party Claim under the provisions of this clause 11 and (b) a Party's liability for breach of its obligations under clause 6.

11.8 Nothing in this Agreement shall exclude or limit a Party's liability for death or personal injury caused by its negligence or for fraud.

12 MISCELLANEOUS

12.1 **Assignment**

This Agreement, or any of the rights and obligations under this Agreement, may not be assigned or otherwise transferred by either Party without the prior written consent of the other Party; provided, however, that either Party may assign this Agreement, or any of the rights and obligations under this Agreement, without the consent of the other Party (a) to any of its Affiliates, if the assigning Party guarantees the full performance of its Affiliates' obligations hereunder, or (b) to any person acquiring all or substantially all of its assets or business to which this Agreement relates, whether by merger, acquisition, sale of assets or otherwise. In all cases, the assigning Party shall provide the other Party with prompt written notice of any such assignment and the permitted assignee shall assume the obligations of the assigning Party hereunder in writing. No assignment of this Agreement shall act as a novation or release of either Party from responsibility for the performance of any accrued obligations. This Agreement shall be binding upon successors and permitted assigns of the Parties. Any assignment not in accordance with this clause 12.1 will be null and void.

12.2 **Governing Law**

This Agreement and any dispute or claim arising out of or in connection with it (whether contractual or non-contractual in nature such as claims in tort, from breach of statute or regulation or otherwise) shall be governed by and construed in accordance with the laws of England, excluding any conflicts or choice of law rule or principle that might otherwise refer construction or interpretation of this Agreement to the substantive law of another jurisdiction; provided that any dispute with respect to infringement, validity, or enforceability of any Patent, shall be governed by and construed and enforced in accordance with the laws of the jurisdiction in which such Patent is issued or published.

12.3 **Arbitration**

Subject to clause 8.5, any dispute or claim arising out of or in connection with this Agreement, including any question regarding its existence, validity or termination shall be referred to and finally resolved by arbitration under the Rules of Arbitration of the International Chamber of Commerce which only are deemed incorporated into this clause 12.3. The seat, or legal place, of arbitration shall be London. The language to be used in the arbitration procedures shall be English. The arbitration proceedings including any outcome shall be confidential except (i) to the extent that disclosure may be required of a Party to fulfill a legal duty, protect or pursue a legal right, or enforce or challenge an award in bona fide legal proceedings before a state court or other judicial authority, (ii) with the consent of all Parties, (iii) where needed for the preparation or presentation of a claim or defense in this arbitration, (iv) where such information is already in the public domain other than as a result of a breach of this clause, or (v) by order of the arbitral tribunal upon application of a Party. Nothing in this clause 12.3 will preclude either Party from seeking equitable interim or provisional relief from a court of competent jurisdiction including a temporary restraining order, preliminary injunction or other interim equitable relief, concerning a dispute either prior to or during any arbitration if necessary to protect the interests of such Party or to preserve the status quo pending the arbitration proceeding. The number of arbitrators shall be three (3) of which each Party shall appoint one (1), the arbitrators so appointed will select the third and final arbitrator. The arbitrators shall have experience of pharmaceutical licensing disputes.

12.4 **Force Majeure**

Neither Party shall be liable to the other for any failure or delay in the fulfilment of its obligations under this Agreement (other than the payment of monies due and owing to a Party under this Agreement), when any such failure or delay is caused by fire, flood, earthquakes, explosions, sabotage, terrorism, pandemics, epidemics, civil commotions, riots, invasions, wars, peril of the sea or requirements of Governmental Authorities (each, a "**Force Majeure Event**"). In the event that either Party is prevented from discharging its obligations under this Agreement on account of a Force Majeure Event, the performing Party shall notify the other Party forthwith, and shall nevertheless make every endeavour, in the utmost good faith, to discharge its obligations, even if in a partial or compromised manner.

12.5 **Expenses**

Except as otherwise expressly provided herein or mutually agreed, all costs and expenses incurred in connection with this Agreement and the transactions contemplated hereby shall be borne by the Party incurring such costs and expenses.

12.6 **No Agency**

Nothing herein contained shall be deemed to create an agency, joint venture, amalgamation, partnership or similar relationship between Heptares and Neurocrine. Notwithstanding any of the provisions of this Agreement, neither Party shall at any time enter into, incur, or hold itself out to Third Parties as having authority to enter into or incur, on behalf of the other Party, any commitment, expense, or liability whatsoever, and all contracts, expenses and liabilities undertaken or incurred by one Party in connection with or relating to the Development of Compound or the Exploitation of Licensed Product shall be undertaken, incurred or paid exclusively by that Party, and not as an agent or representative of the other Party. All persons employed by a Party will be the employees of such Party and not of the other Party and all costs and obligations incurred by reason of any such employment shall be for the account and expense of such first Party.

12.7 **No Third Party Beneficiaries**

Except for any rights and immunities granted in this Agreement to any Affiliates, the Contracts (Rights of Third Parties) Act 1999 shall not apply to this Agreement. No person who is not a party to this Agreement (including any employee, officer, agent, representative or subcontractor of either Party) shall have the right (whether under the Contracts (Rights of Third Parties) Act 1999 or otherwise) to enforce any provision of this Agreement which expressly or by implication confers a benefit on that person without the express prior agreement in writing of the Parties, which agreement must refer to this clause 12.7.

12.8 **Entire Agreement; Amendment**

This Agreement (including all schedules and exhibits hereto) sets forth and constitutes the entire agreement and understanding between the Parties with respect to the subject matter hereof and supersedes all prior agreements or understandings, promises, misrepresentations and representations, whether oral or written, with respect to such matters, including the CDAs, which are hereby terminated in their entirety. Each Party confirms that it is not relying on any representations, misrepresentations or warranties of the other Party except as specifically set forth in this Agreement. This Agreement may be amended or modified only by a writing signed by both Parties. No release or discharge shall be binding upon the Parties unless in a writing signed by both Parties.

12.9 **Illegality; Non-Enforceability**

If the whole or any part of this Agreement is or becomes or is declared illegal, invalid or unenforceable in any jurisdiction for any reason (including both by reason of the provisions of any legislation and also by reason of any decision of any court or Governmental Authority which either has jurisdiction over this Agreement or has jurisdiction over any of the Parties):

(a) in the case of the illegality, invalidity or un-enforceability of the whole of this Agreement, it shall terminate in relation to the jurisdiction in question; or

(b) in the case of the illegality, invalidity or un-enforceability of part of this Agreement, that part shall be severed from this Agreement in the jurisdiction in question and that illegality, invalidity or un-enforceability shall not in any way whatsoever prejudice or affect the remaining parts of this Agreement which shall continue in full force and effect provided that the said remaining parts continue to satisfy the commercial intentions of the Parties and provided that the remaining parts do constitute a substantial part of this Agreement.

12.10 **Extension; Waiver**

At any time, either Heptares or Neurocrine may (a) with respect to obligations owed to it or the performance of other acts for its benefit, extend the time for the performance of such obligations or such other acts to be performed hereunder by the other, (b) waive any inaccuracies in the representations and warranties of the other contained herein or in any document delivered pursuant hereto, (c) waive compliance with any of the conditions to the obligations of the other contained herein and (d) waive the benefit of any other right hereunder, the other Party's failure to perform, or a breach by the other Party of, its obligations under this Agreement. Any agreement on the part of either Party to any such extension or waiver shall be valid only if set forth in an instrument executed by such Party. No such waiver shall be operative as a waiver of any other right hereunder or of any breach or failure by the other Party whether of a similar nature or otherwise. The failure of any Party to assert any of its rights under this Agreement or otherwise shall not constitute a waiver of such rights.

12.11 **Notices**

All communications, including notices, requests, demands, waivers, consents or approvals, required to be made under this Agreement shall be effective upon receipt, and shall be sent to the addresses set out below, or to such other addresses as may be designated by one Party to the other by notice pursuant hereto, by (a) internationally recognized overnight courier; (b) prepaid registered or certified mail, return receipt requested; or (c) an electronic copy of such communication to be sent by email as follows:

If to Heptares, as follows: [***]

With a copy to: [***]

If to Neurocrine, as follows: [***]

With a copy to: [***]

This clause 12.11 is not intended to govern the day-to-day business communications necessary between the Parties in performing their obligations under the terms of this Agreement, which may be made by any means mutually agreeable to the Parties.

12.12 **HSR Act**

(a) Heptares and Neurocrine shall as soon as reasonably practicable, but in any event within [***] Business Days after the Execution Date, file a Notification and Report Form (an "**HSR Filing**") pursuant to the HSR Act and each Party shall use commercially reasonable efforts to obtain early termination or expiration of the waiting period under the HSR Act, including by requesting early termination of the HSR waiting period. In connection with obtaining any necessary approvals under the HSR Act, each Party shall promptly and in good faith respond to any request for additional information by the U.S. Federal Trade Commission and U.S. Department of Justice in connection with such notification and otherwise cooperate in good faith with each other and such Governmental Authority, provided that no Party shall have any obligation to (i) litigate any action or claim filed by a Governmental Authority in state or federal court alleging violation of any antitrust or other laws, (ii) sell, divest, hold separate or license any of their assets or lines of business, or (iii) change or modify any course of conduct or otherwise make any commitments to any Governmental Authority regarding future operations of Neurocrine's or Heptares' business. For the avoidance of doubt, Neurocrine shall be responsible for paying any filing fees required in connection with such HSR Act filing.

(b) For any HSR Filings required, neither Neurocrine nor Heptares shall, and each shall use reasonable best efforts to cause their respective Affiliates not to, directly or indirectly take any action, including, directly or indirectly, acquiring or investing in any person or acquiring, leasing or licensing any assets, or agreement to do any of the foregoing, if doing so would reasonably be expected to impose any material delay in the obtaining of, or significantly increase the risk of not obtaining, any required approval under the HSR Act. Neurocrine and Heptares will promptly provide the other with copies of all substantive written communications (and memoranda setting forth the substance of all substantive oral communications) between each of them, any of their subsidiaries and their respective agents, representatives and advisors, on the one hand, and any Governmental Authority, on the other hand, with respect to this Agreement. Without limiting the foregoing, Neurocrine and Heptares shall: (i) promptly inform the other of any communication to or from the U.S. Federal Trade Commission or the U.S. Department of Justice regarding the Agreement; (ii) permit each other to review in advance any proposed substantive written communication to any such Governmental Authority and incorporate reasonable comments thereto; (iii) give the other prompt written notice of the commencement of any legal proceeding with respect to the Agreement; (iv) not agree to participate in any substantive meeting or discussion with any such Governmental Authority in respect of any filing, investigation or inquiry concerning this Agreement unless, to the extent reasonably practicable, it consults with the other Party in advance and, to the extent permitted by such Governmental Authority, gives the other Party the opportunity to attend; (v) keep the other reasonably informed as to the status of any such legal proceeding; and (vi) promptly furnish each other with copies of all correspondence, filings (except for filings made under the HSR Act) and written communications between such Party and their Affiliates and their respective agents, representatives and advisors, on one hand, and any such Governmental Authority, on the other hand, in each case, with respect to this Agreement; provided that materials required to be supplied pursuant to this clause may be redacted (1) to remove references concerning valuation, (2) as necessary to comply with contractual arrangements, (3) as necessary to comply with applicable Law, and (4) as necessary to address reasonable privilege or confidentiality concerns; provided further, that a Party may reasonably designate any competitively sensitive material provided to another party under this clause as “Outside Counsel Only”.

12.13 **Further Assurances**

Each Party shall perform, or caused to be performed, all further acts and things and execute and deliver such further documents as may be necessary or as the other Party may reasonably require to implement or give effect to this Agreement.

12.14 **No Strict Construction**

This Agreement shall be construed as if it were drafted jointly by the Parties.

12.15 **Headings**

The headings herein are for convenience purposes only and shall not be used to interpret any of the provisions hereof.

12.16 **Counterparts**

This Agreement may be executed in any number of counterparts, each of which shall be deemed an original and all of which taken together shall be deemed to constitute one and the same instrument. This Agreement may be executed electronically. An executed signature page of this Agreement delivered by PDF format via email shall be as effective as an original executed signature page.

12.17 **Non-Exclusive Remedies**

The remedies set forth in this Agreement shall be in addition to, and shall not be to the exclusion of, any other remedies available to the Parties at Law, in equity or under this Agreement.

IN WITNESS WHEREOF, this Agreement has been signed by the duly authorized representatives of the Parties on the day and year first before written.

SIGNED by Chris Cargill
for and on behalf of
HEPTARES THERAPEUTICS LIMITED

/s/ Chris Cargill

SIGNED by Kyle Gano
for and on behalf of
NEUROCRINE BIOSCIENCES, INC.

/s/ Kyle Gano

SCHEDULE 3

Press Release

PRESS RELEASE

Sosei Heptares and Neurocrine Biosciences Announce Collaboration to Develop Novel Muscarinic Receptor Agonists for Schizophrenia and Other Neuropsychiatric Disorders

- *Neurocrine Biosciences anticipates initiating a Phase 2 study with the selective M4 agonist HTL-0016878 in schizophrenia in 2022 and Phase 1 studies for a dual M1/M4 and selective M1 agonist in 2023*
- *Sosei Heptares receives US$100 million upfront, ongoing R&D funding, and up to US$2.6 billion in potential development, regulatory and commercial milestone payments, plus tiered sales royalties*

Tokyo, Japan, Cambridge, UK, and San Diego, CA, USA November 22 2021 – Neurocrine Biosciences, Inc. (Nasdaq: NBIX) and Sosei Group Corporation ("Sosei Heptares"; TSE: 4565) announce the signing of a strategic collaboration and licensing agreement to develop novel muscarinic receptor agonists, which Neurocrine Biosciences intends to study in the treatment for schizophrenia, dementia and other neuropsychiatric disorders.

Under the terms of the agreement, Neurocrine Biosciences gains development and commercialization rights to a broad portfolio of novel clinical and preclinical subtype-selective muscarinic M4, M1 and dual M1/M4 receptor agonists discovered by Sosei Heptares in development for the treatment of major neurological disorders. The most advanced program, HTL-0016878, is a selective M4 agonist. Neurocrine Biosciences plans to submit an Investigational New Drug (IND) application and initiate a placebo-controlled Phase 2 study with HTL-0016878 as a potential treatment for schizophrenia in 2022.

Sosei Heptares retains the rights to develop M1 agonists in Japan in all indications, with Neurocrine Biosciences receiving co-development and profit share options.

Muscarinic receptors are central to brain function and validated as drug targets in psychosis and cognitive disorders. Sosei Heptares has discovered selective muscarinic M4, M1 and M1/M4 dual agonists that offer the potential to deliver therapeutic effects while avoiding both the harmful side effects caused by non-selective agonists and efficacy issues experienced in some older patients caused by positive allosteric modulators that require cooperativity of diminishing levels of acetylcholine. Sosei Heptares achieved this through application of its world leading G protein-coupled receptor (GPCR) stabilized receptor platform (StaR®) and subsequent translational medicine studies.

PRESS RELEASE

"Our partnership collaboration with Sosei Heptares to advance their selective muscarinic agonist portfolio leverages the strengths of both our organizations with one goal in mind, to bring important medicines to patients who need better treatment options," **said Kevin Gorman, Ph.D., Chief Executive Officer at Neurocrine Biosciences.** "We continue to add potential best-in-class compounds to our growing pipeline, which further positions Neurocrine Biosciences as a leading neuroscience-focused biopharmaceutical company."

Shinichi Tamura, President and CEO of Sosei Heptares, added: "We are delighted to partner with Neurocrine Biosciences to advance our selective muscarinic receptor agonist portfolio. The deal highlights the significant potential value within this portfolio and brings to bear the substantial expertise of the Neurocrine team, which is highly experienced in developing and commercializing novel products for patients with neurological and psychiatric diseases globally. It also enables Sosei Heptares to retain rights in Japan, where we are confident that we can make important progress leveraging our own expertise to advance novel candidates that aim to address this major unmet need. Overall, the deal is a great example of our strategy to combine our drug design and early development capabilities with those of later stage development and commercialization partners, while also providing significant funding to expand and advance our own pipeline."

Collaboration Details

Under the terms of the agreement, Neurocrine Biosciences will be responsible for development costs associated with the programs globally, except for M1 agonists being developed in Japan. The agreement will be subject to the following terms:

- **Upfront License Payment**: Sosei Heptares will receive a total of US$100 million in upfront cash.
- **Development and Regulatory Milestones**: Sosei Heptares is eligible to receive up to approximately US$1.5 billion related to the successful progression of licensed candidates through to regulatory approval.
- **Commercial Milestones**: Sosei Heptares is eligible to receive up to US$1.1 billion upon achieving certain global sales milestones of any products developed under the partnership.
- **Product Royalties**: Sosei Heptares is eligible to receive tiered royalties ranging from high single digit to mid-teen percentage on future net sales of any products developed under the partnership.
- **R&D Collaboration**: The R&D collaboration will be conducted jointly by Neurocrine Biosciences and Sosei Heptares to advance preclinical candidates through Phase 1 clinical studies. The R&D collaboration will be funded by Neurocrine Biosciences.
- **Sosei Heptares M1 Agonist Rights in Japan**: Sosei Heptares retains rights to develop M1 agonists in Japan for any indication, with Neurocrine Biosciences receiving co-development and profit share options.

PRESS RELEASE

This transaction is subject to customary clearances under the Hart-Scott-Rodino Antitrust Improvements Act. Assuming this transaction completes by December 31, 2021, the US$100 million upfront payment will represent a material positive revenue impact to Sosei Heptares and is expected to be recognized as revenue in the fourth quarter of the financial year ending December 31, 2021.

BofA Securities is acting as financial advisor to Sosei Heptares. Gowling WLG and Orrick Herrington & Sutcliffe LLP are serving as legal counsel to Sosei Heptares.

Conference Call and Webcast Information

On Wednesday November 24, 2021, Sosei Heptares will host a conference call and webinar for Japanese investors at 8:00 a.m Japan Standard Time. The live call may be accessed by pre-registration here.

A live audio webcast of the conference call will be available online in the Investors section on the Sosei Heptares website at www.soseiheptares.com. A replay of the webcast will be available on Sosei Heptares' website after the conclusion of the event and will be archived for approximately one month.

About Muscarinic Receptors

Muscarinic receptors are G protein-coupled receptors (GPCRs) found in multiple tissues including the brain, cardiovascular system, and gastrointestinal tract. Selective activation of M4 and M1 receptors in the brain is a clinically validated approach to treating cognitive and neuropsychological symptoms of neurological diseases, including Schizophrenia, dementia associated with Alzheimer's disease, Parkinson's disease, and others. Until now, attempts to develop medicines that selectively target M4 and M1 receptors have been unsuccessful because of side effects caused by the activation of M2 and M3 receptors. Highly selective M4 or M1 agonists that do not activate M2 or M3 therefore are highly sought after and expected to have the potential to address major unmet medical needs with blockbuster potential.

About Programs in the Collaboration Agreement

HTL-0016878

HTL-0016878 ("878") is an oral, investigational M4 selective agonist that has completed multiple Phase 1 studies and Neurocrine Biosciences is preparing to initiate Phase 2 studies in schizophrenia in 2022. As a selective M4 orthosteric agonist, '878 offers the potential for an improved safety profile without the need of combination therapy to minimize side effects and avoids the need of cooperativity with acetylcholine (ACh) when compared to non-selective muscarinic agonists and positive allosteric modulators in development. Studies completed to date have shown '878 to be generally well tolerated.

PRESS RELEASE

Preclinical Programs
The collaboration includes rights to multiple preclinical programs which include selective muscarinic compounds targeting M1, M4 receptors and a dual M1/M4 receptor candidate. In combination with '878, the programs offer the ability to leverage M1 and M4 selectivity to address the unmet need for patients suffering from psychosis and cognitive-related diseases.

After signing a R&D and commercialization partnership in 2016, Allergan returned all program rights to '878 and the preclinical programs to Sosei Heptares in Q1 2021.

– **ENDS** –

About Neurocrine Biosciences
Neurocrine Biosciences is a neuroscience-focused, biopharmaceutical company dedicated to discovering, developing and delivering life-changing treatments for people with serious, challenging and under-addressed neurological, endocrine and psychiatric disorders. The company's diverse portfolio includes FDA-approved treatments for tardive dyskinesia, Parkinson's disease, endometriosis*, uterine fibroids* and clinical programs in multiple therapeutic areas. For nearly three decades, Neurocrine Biosciences has specialized in targeting and interrupting disease-causing mechanisms involving the interconnected pathways of the nervous and endocrine systems. For more information, visit neurocrine.com, and follow the company on LinkedIn. (*in collaboration with AbbVie).

About Sosei Heptares
We are an international biopharmaceutical group focused on the discovery and early development of new medicines originating from our proprietary GPCR-targeted StaR® technology and structure-based drug design platform capabilities. We are advancing a broad and deep pipeline of novel medicines across multiple therapeutic areas, including neurology, immunology, gastroenterology, and inflammatory diseases. We have established partnerships with some of the world's leading pharmaceutical companies and multiple emerging technology companies, including AbbVie, AstraZeneca, Biohaven, Genentech (Roche), GSK, Neurocrine Biosciences, Pfizer, and Takeda. Sosei Heptares is headquartered in Tokyo, Japan with corporate and R&D facilities in Cambridge, UK.

For more information, please visit https://www.soseiheptares.com/
LinkedIn: @soseiheptaresco | Twitter: @soseiheptaresco | YouTube: @soseiheptaresco

PRESS RELEASE

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PRESS RELEASE

Outline of Neurocrine Biosciences

(1)	Company Name	Neurocrine Biosciences, Inc.		
(2)	Head office	San Diego, California		
(3)	Representative	Kevin C. Gorman, Ph.D., Chief Executive Officer		
(4)	Main Business	Neurocrine Biosciences, Inc. is a neuroscience-focused, biopharmaceutical company dedicated to discovering, developing and delivering life-changing treatments for people with serious, challenging and under-addressed neurological, endocrine and psychiatric disorders. Its diverse portfolio includes FDA approved treatments for tardive dyskinesia, Parkinson's disease, endometriosis, uterine fibroids and clinical programs in multiple therapeutic areas.		
(5)	Capital	(Common Stock + Additional paid-in capital) as at Dec 31, 2020 = $1,849.8m		
(6)	Date of establishment	January 1992		
(7)	Major shareholders and percentage of shares held	**Shareholder (as at June 30, 2021)**	**Shares held**	**% of Outstanding Shares held**
		The Vanguard Group	8,984,621	9.49
		Janus Henderson	8,952,074	9.46
		BlackRock Institutional	8,085,370	8.54
		T. Rowe Price	5,029,259	5.31
(8)	Relationship between Sosei Heptares and Neurocrine Biosciences	Capital	None	
		Personnel	None	
		Business	None	
		Related party status	None	
(9)	Financial position and business performance for the last three years			
Fiscal year (consolidated)		Year ended December 31, 2018	Year ended December 31, 2019	Year ended December 31, 2020
Net assets (USDm)		480.8	636.9	1,126.2
Total assets (USDm)		993.2	1,306.0	1,734.7
Net assets per share (USD)		*5.30*	*6.90*	*12.04*
Total revenues (USDm)		451.2	788.1	1,045.9
Operating income (USDm)		36.8	72.3	163.0
Ordinary income (USDm)*		36.8	72.3	163.0
Net income attributable to owners of the parent (USDm)		21.1	37.0	407.3
Basic net income per share (USD)		*0.23*	*0.40*	*4.38*
Dividend per share (USD)		-	-	-

* = All Operating income is assumed to relate to Ordinary Activities.

Outlook

The expected timing of SGC's recognition of the upfront receipt is Q4 2021.

PRESS RELEASE

Neurocrine Biosciences Forward-looking statements

In addition to historical facts, this press release contains forward-looking statements that involve a number of risks and uncertainties. These statements include, but are not limited to, statements related to the benefits to be derived from transactions with Sosei Group Corporation; our potential milestone and royalty payments to Sosei Heptares; the development of our product candidates and the timing of completion of our clinical, regulatory, and other development activities Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are: the possibility that the transaction with Sosei Heptares is not consummated on the expected timeline or at all or the possibility that regulatory approvals of the proposed transaction will impose conditions or are not obtained; risks and uncertainties associated with the scale and duration of the COVID-19 pandemic and resulting global, national, and local economic and financial disruptions; risks and uncertainties related to any COVID-19 quarantines, shelter-in-place and similar government orders that are currently in place or that may be put in place in the future, including the impact of such orders on our business operations and the business operations of the third parties on which we rely; our future financial and operating performance; risks or uncertainties related to the development of the our product candidates; risks that the FDA or other regulatory authorities may make adverse decisions regarding our product candidates; risks that clinical development activities may not be completed on time or at all; risks that clinical development activities may be delayed for regulatory, manufacturing, or other reasons, may not be successful or replicate previous clinical trial results, may fail to demonstrate that our product candidates are safe and effective, or may not be predictive of real-world results or of results in subsequent clinical trials; risks and uncertainties relating to competitive products and technological changes that may limit demand for a product candidate; risks that the benefits of the agreements with Sosei Heptares may never be realized; risks that our product candidates may be precluded from commercialization by the proprietary or regulatory rights of third parties, or have unintended side effects, adverse reactions or incidents of misuse; and other risks described in our periodic reports filed with the SEC, including without limitation our quarterly report on Form 10-Q for the quarter ended September 30, 2021. Neurocrine disclaims any obligation to update the statements contained in this press release after the date hereof.

Sosei Group Corporation Forward-looking statements

This press release contains forward-looking statements, including statements about the discovery, development, and commercialization of products. Various risks may cause Sosei Group Corporation's actual results to differ materially from those expressed or implied by the forward-looking statements, including: adverse results in clinical development programs; failure to obtain patent protection for inventions; commercial limitations imposed by patents owned or controlled by third parties; dependence upon strategic alliance partners to develop and commercialize products and services; difficulties or delays in obtaining regulatory approvals to market products and services resulting from development efforts; the requirement for substantial funding to conduct research and development and to expand commercialization activities; and product initiatives by competitors. As a result of these factors, prospective investors are cautioned not to rely on any forward-looking statements. We disclaim any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

Neurocrine Biosciences, Inc. 2020 Equity Incentive Plan

Option Grant Notice

Neurocrine Biosciences, Inc. (the "***Company***") has granted to you ("***Participant***") an option to purchase the number of shares of Common Stock set forth below (the "***Option***") under the Neurocrine Biosciences, Inc. 2020 Equity Incentive Plan (the "***Plan***"). The Option is subject to all of the terms and conditions set forth in this Option Grant Notice (the "***Grant Notice***"), the Option Agreement (the "***Agreement***") and the Plan, all of which are available by logging into your E*TRADE account and which are incorporated herein in their entirety. Capitalized terms not explicitly defined in this Grant Notice but defined in the Agreement or the Plan will have the meanings set forth in the Agreement or the Plan, as applicable.

Participant:

Date of Grant:

Vesting Commencement Date:

Number of Shares of Common Stock:

Exercise Price (Per Share):

Total Exercise Price:

Expiration Date:

Type of Grant: You have been granted an Incentive Stock Option. However, due to the $100,000 Rule (as described below), the Option (or a certain portion thereof) may be treated as a Nonstatutory Stock Option. Please log into your E*TRADE account to see the exact details of your grant.

Vesting Schedule: Subject to Section 2 of the Agreement, the Option will vest as follows: [_____].

Exercise Schedule: Same as Vesting Schedule

Participant Acknowledgements: By your electronic acceptance of the Option via your E*TRADE account, you understand and agree that:

- The Option is governed by this Grant Notice, the Agreement and the Plan, all of which are made a part of this document. Unless otherwise provided in the Plan, this Grant Notice and the Agreement may not be modified, amended or revised except in a writing signed by you and a duly authorized officer of the Company.
- If the Option is an Incentive Stock Option, it (plus other outstanding Incentive Stock Options granted to you) cannot be first *exercisable* for more than $100,000 in value (measured by exercise price) in any calendar year. Any excess over $100,000 is a Nonstatutory Stock Option. For purposes of this Grant Notice, such rule is referred to as the "***$100,000 Rule***".
- Copies of this Grant Notice, the Agreement, the Plan and the Prospectus are available via your E*TRADE account and may be viewed and printed by you. You consent to receive this Grant Notice, the Agreement, the Plan, the Prospectus and any other Plan-related documents by electronic delivery and to participate in the Plan through an on-line or electronic system established and maintained by the Company or another third party designated by the Company.
- You have read and are familiar with the provisions of this Grant Notice, the Agreement, the Plan and the Prospectus. In the event of any conflict between the provisions in this Grant Notice, the Agreement or the Prospectus and the provisions of the Plan, the provisions of the Plan will control.
- As of the Date of Grant, this Grant Notice, the Agreement and the Plan set forth the entire understanding between you and the Company regarding the Option and supersede all prior oral and written agreements, promises and/or representations regarding the Option, with the exception of any written employment, offer letter, severance or other agreement, or any written severance plan or policy, in each case that specifies the terms that should govern the Option.

Neurocrine Biosciences, Inc. 2020 Equity Incentive Plan

Option Agreement

Pursuant to the accompanying Option Grant Notice (the "***Grant Notice***") and this Option Agreement (the "***Agreement***"), Neurocrine Biosciences, Inc. (the "***Company***") has granted you an option under the Neurocrine Biosciences, Inc. 2020 Equity Incentive Plan (the "***Plan***") to purchase the number of shares of Common Stock set forth in the Grant Notice at the exercise price set forth in the Grant Notice (the "***Option***"). Capitalized terms not explicitly defined in this Agreement but defined in the Grant Notice or the Plan will have the meanings set forth in the Grant Notice or the Plan, as applicable.

The general terms and conditions applicable to your Option are as follows:

1. **Governing Plan Document.** Your Option is subject to all the provisions of the Plan, including but not limited to the provisions in:
    a. Section 6 of the Plan regarding the impact of a Capitalization Adjustment, dissolution, liquidation, or Transaction on your Option;
    b. Section 9(f) of the Plan regarding the Company's and any Affiliate's (if applicable) retained rights to terminate your Continuous Service notwithstanding the grant of your Option; and
    c. Section 8(c) of the Plan regarding the tax consequences of your Option.

Your Option is further subject to all interpretations, amendments, rules and regulations, which may from time to time be promulgated and adopted pursuant to the Plan. In the event of any conflict between the provisions in this Agreement or the Grant Notice and the provisions of the Plan, the provisions of the Plan will control.

2. **Vesting.**
    a. Subject to the limitations contained in this Agreement, your Option will vest in accordance with the vesting schedule set forth in the Grant Notice, provided that vesting will cease upon the termination of your Continuous Service, except as otherwise explicitly provided in the Plan (in connection with a Transaction or certain terminations of Continuous Service following such Transaction) or this Agreement.
    b. If you are an Employee or Director, in each case as of the date of termination of your Continuous Service, then in the event of a termination of your Continuous Service due to your death or Disability, your Option will become vested, as of the date of such termination, in accordance with the vesting schedule set forth in the Grant Notice as if you had provided an additional six months of Continuous Service as of the date of such termination.
    c. If you are an Employee as of the date of termination of your Continuous Service, then in the event of a termination of your Continuous Service due to your Retirement, your Option will become fully vested as of the date of such Retirement. For purposes of this Agreement, "***Retirement***" means a termination of your Continuous Service upon or after you have reached age 60 with at least 5 years of Continuous Service, provided that you comply with any other requirements in the Company's then-current policy regarding Retirement.
    d. If you are a Director as of the date of a Transaction, then in the event of a Transaction during your Continuous Service, your Option will become fully vested as of the date of such Transaction.
3. **Exercise.**
    a. You may generally exercise the vested portion of your Option (and the unvested portion of your Option if permitted by the Grant Notice) for whole shares of Common Stock at any time during its term by delivery of payment of the exercise price and any Withholding Obligation, as set forth in Section 6, and other required documentation to the Plan Administrator in accordance with the exercise procedures established by the Plan Administrator, which may include an electronic submission. Please review Sections 4(i), 4(j) and 7(b)(v) of the Plan, which may restrict or prohibit your ability to exercise your Option during certain periods.

b. To the extent permitted by Applicable Law, you may pay the exercise price of your Option by cash or check or as follows:

i. pursuant to a "cashless exercise" program, as provided in Section 4(c)(ii) of the Plan, if at the time of exercise the Common Stock is publicly traded;

ii. by delivery of already owned shares of Common Stock, as provided in Section 4(c)(iii) of the Plan, if at the time of exercise the Common Stock is publicly traded; or

iii. subject to approval by the Company and/or the Committee, as applicable, at or prior to the time of exercise, if your Option is a Nonstatutory Stock Option, by a "net exercise" arrangement, as provided in Section 4(c)(iv) of the Plan.

4. Term. You may not exercise your Option before the commencement of its term or after its term expires. The term of your Option commences on the Date of Grant and expires upon the earliest of the following:

a. immediately upon the termination of your Continuous Service for Cause;

b. if you are an Employee as of the date of termination of your Continuous Service, then three months after the termination of your Continuous Service for any reason other than Cause, Disability, death or Retirement;

c. if you are a Director as of the date of termination of your Continuous Service, then three years after the termination of your Continuous Service for any reason other than Cause;

d. if you are a Consultant as of the date of termination of your Continuous Service, then 30 days after the termination of your Continuous Service for any reason other than Cause;

e. if you are an Employee as of the date of termination of your Continuous Service, then 12 months after the termination of your Continuous Service due to your Disability;

f. if you are an Employee as of the date of termination of your Continuous Service, then 18 months after your death if you die during your Continuous Service;

g. if you are an Employee as of the date of termination of your Continuous Service, then 12 months after the termination of your Continuous Service due to your Retirement;

h. immediately upon a Transaction if the Board has determined that your Option will terminate in connection with such Transaction;

i. the Expiration Date set forth in the Grant Notice; or

j. the day before the 10th anniversary of the Date of Grant.

If you are an Employee as of the date of termination of your Continuous Service, then notwithstanding the foregoing, if you die during the period provided in Section 4(b) above, the term of your Option will not expire until the earlier of (i) 18 months after the termination of your Continuous Service, (ii) a Transaction if the Board has determined that your Option will terminate in connection with such Transaction, (iii) the Expiration Date set forth in the Grant Notice, or (iv) the day before the 10th anniversary of the Date of Grant.

In addition, the Post-Termination Exercise Period of your Option may be extended as provided in Section 4(i) of the Plan.

To obtain the federal income tax advantages associated with an Incentive Stock Option, the Code requires that at all times beginning on the date of grant of your Option and ending on the day three months before the date of your Option's exercise, you must be an employee of the Company or an Affiliate, except in the event of your death or Disability. If the Company provides for the extended exercisability of your Option under certain circumstances for your benefit, your Option will not necessarily be treated as an Incentive Stock Option if you exercise your Option more than three months after the date your employment terminates.

5. Transferability. Except as otherwise provided in Section 4(e) of the Plan, your Option is not transferable, except by will or by the applicable laws of descent and distribution, and is exercisable during your life only by you. Notwithstanding the foregoing, by delivering written notice to the Company, in a form satisfactory

to the Company, you may designate a third party who, in the event of your death, will thereafter be entitled to exercise your Option.

6. **Withholding Obligations.**

   a. As provided in Section 8 of the Plan, at the time you exercise your Option, in whole or in part, or at any time thereafter as requested by the Company, you hereby authorize withholding from payroll and any other amounts payable to you, and otherwise agree to make adequate provision for (including by means of a "cashless exercise" pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board to the extent permitted by the Company), any sums required to satisfy the federal, state, local and foreign tax withholding obligations, if any, which arise in connection with your Option (the "***Withholding Obligation***") in accordance with the withholding procedures established by the Company.

   b. Upon your request and subject to approval by the Company and/or the Committee, as applicable, and in compliance with any applicable legal conditions or restrictions, the Company may withhold from fully vested shares of Common Stock otherwise issuable to you upon exercise of your Option a number of whole shares of Common Stock with a Fair Market Value on the date of exercise not in excess of the maximum amount of tax that may be required to be withheld by law (or such other amount as may be permitted while still avoiding classification of your Option as a liability for financial accounting purposes).

   c. You may not exercise your Option unless the Withholding Obligation is satisfied. Accordingly, you may not be able to exercise your Option even though your Option is vested, and the Company will have no obligation to issue any shares of Common Stock subject to your Option, unless and until the Withholding Obligation is satisfied. In the event that the amount of the Withholding Obligation was greater than the amount actually withheld by the Company (or an Affiliate, if applicable), you agree to indemnify and hold the Company (and Affiliate, if applicable) harmless from any failure to withhold the proper amount.

7. **Incentive Stock Option Disposition Requirement.** If your Option is an Incentive Stock Option, you must notify the Company in writing within 15 days after the date of any disposition of any of the shares of Common Stock issued upon exercise of your Option that occurs within two years after the date of grant of your Option or within one year after such shares of Common Stock are transferred upon exercise of your Option.

8. **Transaction.** Your Option is subject to the terms of any agreement governing a Transaction involving the Company, including, without limitation, a provision for the appointment of a stockholder representative that is authorized to act on your behalf with respect to any escrow, indemnities and any contingent consideration.

9. **No Liability for Taxes.** As a condition to accepting your Option, you hereby (a) agree to not make any claim against the Company, or any of its Officers, Directors, Employees or Affiliates related to tax liabilities arising from your Option or other Company compensation and (b) acknowledge that you were advised to consult with your own personal tax, financial and other legal advisors regarding the tax consequences of your Option and have either done so or knowingly and voluntarily declined to do so. Additionally, you acknowledge that your Option is exempt from Section 409A only if the exercise price of your Option is at least equal to the "fair market value" of the Common Stock on the date of grant as determined by the Internal Revenue Service and there is no other impermissible deferral of compensation associated with your Option. Additionally, as a condition to accepting your Option, you agree to not make any claim against the Company, or any of its Officers, Directors, Employees or Affiliates in the event that the Internal Revenue Service asserts that such exercise price is less than the "fair market value" of the Common Stock on the date of grant as subsequently determined by the Internal Revenue Service.

10. **Severability.** If any part of this Agreement, the Grant Notice or the Plan is declared by any court or governmental authority to be unlawful or invalid, such unlawfulness or invalidity will not invalidate any portion of this Agreement, the Grant Notice or the Plan not declared to be unlawful or invalid. Any Section of this Agreement, the Grant Notice or the Plan (or part of such a Section) so declared to be unlawful or

invalid will, if possible, be construed in a manner which will give effect to the terms of such Section or part of a Section to the fullest extent possible while remaining lawful and valid.

11. **Other Documents.** You hereby acknowledge receipt of or the right to receive a document providing the information required by Rule 428(b)(1) promulgated under the Securities Act, which includes the Prospectus. In addition, you acknowledge receipt of the Company's Trading Policy.

Neurocrine Biosciences, Inc. 2020 Equity Incentive Plan

RSU Award Grant Notice

Neurocrine Biosciences, Inc. (the "***Company***") has granted to you ("***Participant***") a restricted stock unit award for the number of restricted stock units ("***RSUs***") set forth below (the "***RSU Award***") under the Neurocrine Biosciences, Inc. 2020 Equity Incentive Plan (the "***Plan***"). The RSU Award is subject to all of the terms and conditions set forth in this RSU Award Grant Notice (the "***Grant Notice***"), the RSU Award Agreement (the "***Agreement***") and the Plan, all of which are available by logging into your E*TRADE account and which are incorporated herein in their entirety. Capitalized terms not explicitly defined in this Grant Notice but defined in the Agreement or the Plan will have the meanings set forth in the Agreement or the Plan, as applicable.

Participant:

Date of Grant:

Vesting Commencement Date:

Number of RSUs:

Vesting Schedule: Subject to Section 3 of the Agreement, the RSU Award will vest as follows: [_____].

Issuance Schedule: One share of Common Stock will be issued for each RSU which vests at the time set forth in Section 4 of the Agreement.

Withholding Obligation: To the fullest extent permitted under the Plan and Applicable Law, any Withholding Obligation (as set forth in Section 6 of the Agreement) will be satisfied through a "Sell to Cover" procedure as described in Section 6 of the Agreement; *provided*, *however*, that in order to effectuate such Sell to Cover, the Company and any applicable broker-dealer may require you to execute certain documents authorizing and directing such Sell to Cover in accordance with the requirements of Rule 10b5-1(c) under the Exchange Act.

Participant Acknowledgements: By your electronic acceptance of the RSU Award via your E*TRADE account, you understand and agree that:

- The RSU Award is governed by this Grant Notice, the Agreement and the Plan, all of which are made a part of this document. Unless otherwise provided in the Plan, this Grant Notice and the Agreement may not be modified, amended or revised except in a writing signed by you and a duly authorized officer of the Company.
- Copies of this Grant Notice, the Agreement, the Plan and the Prospectus are available via your E*TRADE account and may be viewed and printed by you. You consent to receive this Grant Notice, the Agreement, the Plan, the Prospectus and any other Plan-related documents by electronic delivery and to participate in the Plan through an on-line or electronic system established and maintained by the Company or another third party designated by the Company.
- You have read and are familiar with the provisions of this Grant Notice, the Agreement, the Plan and the Prospectus. In the event of any conflict between the provisions in this Grant Notice, the Agreement or the Prospectus and the provisions of the Plan, the provisions of the Plan will control.
- As of the Date of Grant, this Grant Notice, the Agreement and the Plan set forth the entire understanding between you and the Company regarding the RSU Award and supersede all prior oral and written agreements, promises and/or representations regarding the RSU Award, with the exception of any written employment, offer letter, severance or other agreement, or any written severance plan or policy, in each case that specifies the terms that should govern the RSU Award.

Neurocrine Biosciences, Inc. 2020 Equity Incentive Plan

RSU Award Agreement

Pursuant to the accompanying RSU Award Grant Notice (the "***Grant Notice***") and this RSU Award Agreement (the "***Agreement***"), Neurocrine Biosciences, Inc. (the "***Company***") has granted you a restricted stock unit award under the Neurocrine Biosciences, Inc. 2020 Equity Incentive Plan (the "***Plan***") for the number of restricted stock units ("***RSUs***") set forth in the Grant Notice (the "***RSU Award***"). Capitalized terms not explicitly defined in this Agreement but defined in the Grant Notice or the Plan will have the meanings set forth in the Grant Notice or the Plan, as applicable.

The general terms and conditions applicable to your RSU Award are as follows:

1. **Governing Plan Document.** Your RSU Award is subject to all the provisions of the Plan, including but not limited to the provisions in:
    a. Section 6 of the Plan regarding the impact of a Capitalization Adjustment, dissolution, liquidation, or Transaction on your RSU Award;
    b. Section 9(f) of the Plan regarding the Company's and any Affiliate's (if applicable) retained rights to terminate your Continuous Service notwithstanding the grant of your RSU Award; and
    c. Section 8(c) of the Plan regarding the tax consequences of your RSU Award.

Your RSU Award is further subject to all interpretations, amendments, rules and regulations, which may from time to time be promulgated and adopted pursuant to the Plan. In the event of any conflict between the provisions in this Agreement or the Grant Notice and the provisions of the Plan, the provisions of the Plan will control.

2. **Grant of the RSU Award.** The RSU Award represents your right to be issued on a future date a number of shares of Common Stock that is equal to the number of RSUs set forth in the Grant Notice, as adjusted to reflect any Capitalization Adjustment, subject to your satisfaction of the vesting conditions set forth in the Grant Notice and this Agreement. Any additional RSUs that become subject to your RSU Award pursuant to any Capitalization Adjustment will be subject, in a manner determined by the Board, to the same forfeiture restrictions, restrictions on transferability, and time and manner of issuance as applicable to the other RSUs covered by your RSU Award. Your RSU Award was granted in consideration of your services to the Company or an Affiliate.
3. **Vesting.**
    a. Subject to the limitations contained in this Agreement, your RSU Award will vest in accordance with the vesting schedule set forth in the Grant Notice, provided that vesting will cease upon the termination of your Continuous Service, except as otherwise explicitly provided in the Plan (in connection with a Transaction or certain terminations of Continuous Service following such Transaction) or this Agreement. Upon such termination of your Continuous Service, you will forfeit (at no cost to the Company) any RSUs subject to your RSU Award that have not vested as of the date of such termination and you will have no further right, title or interest in such RSUs or the shares of Common Stock to be issued in respect of such RSUs.
    b. If you are an Employee or Director, in each case as of the date of termination of your Continuous Service, then in the event of a termination of your Continuous Service due to your death or Disability, your RSU Award will become vested, as of the date of such termination, in accordance with the vesting schedule set forth in the Grant Notice as if you had provided an additional six months of Continuous Service as of the date of such termination.
    c. If you are a Director as of the date of a Transaction, then in the event of a Transaction during your Continuous Service, your RSU Award will become fully vested as of the date of such Transaction.
4. **Date of Issuance.**
    a. The issuance of any shares of Common Stock in respect of your RSU Award is (i) subject to satisfaction of any Withholding Obligation, as set forth in Section 6, and (ii) intended to comply

with Treasury Regulations Section 1.409A-1(b)(4) and will be construed and administered in such a manner.

b. In the event one or more RSUs subject to your RSU Award vests, the Company will issue to you, on the applicable vesting date, one share of Common Stock for each RSU that vests on such date (and for purposes of this Agreement, such issuance date is referred to as the "***Original Issuance Date***"); *provided*, *however*, that if the Original Issuance Date falls on a date that is not a business day, such shares will instead be issued to you on the next following business day.

c. Notwithstanding the foregoing, if:

i. your RSU Award is otherwise subject to a Withholding Obligation on the Original Issuance Date,

ii. the Original Issuance Date does not occur (x) during an "open window period" applicable to you, as determined by the Company in accordance with the Company's Trading Policy, or (y) on a date when you are otherwise permitted to sell shares of Common Stock on an established stock exchange or stock market (including but not limited to under a previously established written trading plan that meets the requirements of Rule 10b5-1 under the Exchange Act and was entered into in compliance with the Company's policies (a "***10b5-1 Arrangement***")), and

iii. the Company elects, prior to the Original Issuance Date, (x) not to satisfy such Withholding Obligation by withholding shares of Common Stock from the shares of Common Stock otherwise due, on the Original Issuance Date, to you under your RSU Award, (y) not to permit you to enter into a "same day sale" commitment with a broker-dealer in order to satisfy such Withholding Obligation (including but not limited to a commitment under a 10b5-1 Arrangement), and (z) not to permit you to pay such Withholding Obligation in cash,

then the shares of Common Stock that would otherwise be issued to you on the Original Issuance Date will not be issued to you on the Original Issuance Date and will instead be issued to you on the first business day when you are not prohibited from selling shares of Common Stock on an established stock exchange or stock market, but in no event later than December 31 of the calendar year in which the Original Issuance Date occurs (that is, the last day of your taxable year in which the Original Issuance Date occurs), or, if permitted in a manner that complies with Treasury Regulations Section 1.409A-1(b)(4), no later than the date that is the 15th day of the third calendar month of the year following the year in which the shares of Common Stock in respect of your RSU Award are no longer subject to a "substantial risk of forfeiture" within the meaning of Treasury Regulations Section 1.409A-1(d).

d. To the extent your RSU Award is a Non-Exempt Award, the provisions of Section 11 of the Plan will apply.

5. Transferability. Except as otherwise provided in the Plan, your RSU Award is not transferable, except by will or by the applicable laws of descent and distribution.

6. Withholding Obligations.

a. As provided in Section 8 of the Plan, you hereby authorize withholding from payroll and any other amounts payable to you, and otherwise agree to make adequate provision for, any sums required to satisfy the federal, state, local and foreign tax withholding obligations, if any, which arise in connection with your RSU Award (the "***Withholding Obligation***") in accordance with the withholding procedures established by the Company. Additionally, the Company may, in its sole discretion, satisfy all or any portion of the Withholding Obligation by any of the following means or by a combination of such means: (i) causing you to tender a cash payment; (ii) permitting or requiring you to enter into a "same day sale" commitment, if applicable, with a broker-dealer that is a member of the Financial Industry Regulatory Authority (a "***FINRA Dealer***") whereby you irrevocably elect to sell a portion of the shares to be issued in connection with your RSU Award to satisfy the Withholding Obligation and whereby the FINRA Dealer irrevocably commits to forward the proceeds necessary to satisfy the Withholding Obligation directly to the Company

and/or its Affiliates (a "***Sell to Cover***" arrangement); or (iii) such other method permitted under the Plan.

b. Upon your request and subject to approval by the Company and/or the Committee, as applicable, and in compliance with any applicable legal conditions or restrictions, the Company may withhold from the shares of Common Stock otherwise issuable to you in connection with your RSU Award a number of whole shares of Common Stock with a Fair Market Value on the date of issuance not in excess of the maximum amount of tax that may be required to be withheld by law (or such other amount as may be permitted while still avoiding classification of your RSU Award as a liability for financial accounting purposes).

c. Unless the Withholding Obligation is satisfied, the Company will have no obligation to issue to you any shares of Common Stock in respect of your RSU Award. In the event the Withholding Obligation arises prior to the issuance to you of any shares of Common Stock or it is determined after such issuance that the amount of the Withholding Obligation was greater than the amount actually withheld by the Company (or an Affiliate, if applicable), you agree to indemnify and hold the Company (and Affiliate, if applicable) harmless from any failure to withhold the proper amount.

7. **Dividends.** You will receive no dividends or dividend equivalents with respect to your RSU Award; *provided*, *however*, that this sentence will not apply with respect to any shares of Common Stock that are issued to you in connection with your RSU Award after such shares have been issued to you.

8. **Transaction.** Your RSU Award is subject to the terms of any agreement governing a Transaction involving the Company, including, without limitation, a provision for the appointment of a stockholder representative that is authorized to act on your behalf with respect to any escrow, indemnities and any contingent consideration.

9. **No Liability for Taxes.** As a condition to accepting your RSU Award, you hereby (a) agree to not make any claim against the Company, or any of its Officers, Directors, Employees or Affiliates related to tax liabilities arising from your RSU Award or other Company compensation and (b) acknowledge that you were advised to consult with your own personal tax, financial and other legal advisors regarding the tax consequences of your RSU Award and have either done so or knowingly and voluntarily declined to do so.

10. **Severability.** If any part of this Agreement, the Grant Notice or the Plan is declared by any court or governmental authority to be unlawful or invalid, such unlawfulness or invalidity will not invalidate any portion of this Agreement, the Grant Notice or the Plan not declared to be unlawful or invalid. Any Section of this Agreement, the Grant Notice or the Plan (or part of such a Section) so declared to be unlawful or invalid will, if possible, be construed in a manner which will give effect to the terms of such Section or part of a Section to the fullest extent possible while remaining lawful and valid.

11. **Other Documents.** You hereby acknowledge receipt of or the right to receive a document providing the information required by Rule 428(b)(1) promulgated under the Securities Act, which includes the Prospectus. In addition, you acknowledge receipt of the Company's Trading Policy.

* * * *

Exhibit 21.1

NEUROCRINE BIOSCIENCES INC. SUBSIDIARIES

Name of Subsidiary	**Jurisdiction**
Neurocrine Continental, Inc.	Delaware, USA
Neurocrine Europe, Ltd.	Ireland
Neurocrine Therapeutics, Ltd.	Ireland

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, and

(6) Registration Statements (Form S-8 No. 333-240301) pertaining to the 2020 Equity Incentive Plan

of our reports dated February 11, 2022 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, 2021.

/s/ Ernst & Young LLP

San Diego, California
February 11, 2022

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 11, 2022

/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 11, 2022

/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, 2021 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 11, 2022

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, 2021 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 11, 2022

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