



## Neurocrine Biosciences Announces FDA Approval of Once-Daily ONGENTYS® (opicapone) as an Add-On Treatment for Patients with Parkinson's Disease Experiencing "Off" Episodes

April 27, 2020

- ***ONGENTYS, the First and Only Approved Once-Daily COMT Inhibitor, Decreases "Off" Time and Increases "On" Time Without Troublesome Dyskinesia When Added to Levodopa/Carbidopa in Patients with Parkinson's Disease***
- ***Neurocrine Biosciences Plans to Make ONGENTYS Available to Patients Later This Year***

SAN DIEGO – April 27, 2020 – Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced that the U.S. Food and Drug Administration (FDA) has approved once-daily oral ONGENTYS® (opicapone) 25 mg and 50 mg capsules as an add-on treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing "off" episodes. As the disease progresses, patients taking levodopa/carbidopa may begin to experience "off" time between treatment doses, during which an increase in Parkinson's disease motor symptoms such as tremor, slowed movement and difficulty walking occur. ONGENTYS also increases "on" time without troublesome dyskinesia, the time when the motor symptoms of a patient with Parkinson's disease are better controlled. The company plans to launch ONGENTYS later this year.

"The FDA approval of ONGENTYS represents an important new treatment option for people with Parkinson's disease," said Robert A. Hauser, M.D., Professor of Neurology and Director, University of South Florida Parkinson's Disease and Movement Disorders Center. "As Parkinson's disease progresses, first-line treatments such as levodopa begin to lose effectiveness and the beneficial effects of levodopa begin to wear off more quickly, causing more frequent and often debilitating motor fluctuations in patients. Clinical studies have shown that adding once-daily ONGENTYS to levodopa therapy significantly reduced "off" time, leading to better and more consistent motor symptom control."

Parkinson's disease is the second most common neurodegenerative disorder in the United States after Alzheimer's disease. <sup>1</sup> About one million Americans have Parkinson's disease and each year, an estimated 50,000 people in the United States are newly diagnosed with this chronic, progressive and debilitating neurodegenerative disorder.

"The FDA approval of ONGENTYS provides patients living with Parkinson's disease with an important new treatment option to help manage the disruptive and unpredictable motor fluctuations by decreasing "off" episodes and increasing "on" time without troublesome dyskinesia when taking levodopa/carbidopa," said Kevin C. Gorman, Ph.D., Chief Executive Officer of Neurocrine Biosciences. "At Neurocrine Biosciences, our mission is to relieve patient suffering and we look forward to working with the Parkinson's disease community to make this new therapy available to patients later this year."

ONGENTYS is an oral, selective catechol-O-methyltransferase (COMT) inhibitor that helps block the COMT enzyme which breaks down levodopa, the gold standard therapy for controlling motor symptoms in patients with Parkinson's disease. ONGENTYS protects levodopa by reducing its breakdown in the blood, making more levodopa available to reach the brain, prolonging its clinical effects and helping patients achieve motor symptom control.

"Due to the progressive nature of Parkinson's disease, those living with the condition often struggle to control their motor fluctuations, affecting a wide range of functions, including speech, balance and movement, which adversely impact many aspects of life," said John L. Lehr, President and Chief Executive Officer of the Parkinson's Foundation. "The Parkinson's disease community is encouraged by the FDA approval of a new add-on treatment option to help patients further control symptoms, enabling them to better cope with this progressive disease."

The FDA approval of ONGENTYS is supported by data from 38 clinical studies, including two multinational Phase III clinical studies (BIPARK-1 and BIPARK-2), with more than 1,000 Parkinson's disease patients treated with ONGENTYS. In the BIPARK-1 trial, approximately 600 patients with Parkinson's disease and motor fluctuations received one of three doses of ONGENTYS (5 mg, 25 mg or 50 mg), placebo or 200 mg doses of the COMT inhibitor entacapone for 14 or 15 weeks. In the BIPARK-2 trial, approximately 400 patients received one of two doses of ONGENTYS (25 mg or 50 mg) or placebo for 14 or 15 weeks. Both studies included a one-year open-label extension. Data from both trials showed that ONGENTYS 50 mg significantly reduced "off" time from baseline to week 14 or 15 compared to placebo. "On" time without troublesome dyskinesia also increased from baseline to week 14 or 15 compared to placebo.

Pooled safety data from the BIPARK-1 and BIPARK-2 studies indicated that the most common adverse reactions across all patients treated with ONGENTYS (incidence at least 4% and greater than placebo) were dyskinesia, constipation, blood creatine kinase increase, hypotension/syncope, and weight decrease.

In June 2016, BIAL – Portela & CA, S.A. (BIAL) received approval from the European Commission for ONGENTYS as an adjunct therapy to preparations of levodopa/DOPA decarboxylase inhibitors in adult patients with Parkinson's disease and end-of-dose motor fluctuations who cannot be stabilized on those combinations. BIAL currently markets ONGENTYS in Germany, United Kingdom, Spain, Portugal and Italy. Neurocrine Biosciences in-licensed opicapone from BIAL in 2017 and has exclusive development and commercialization rights in the U.S. and Canada.

### **About Parkinson's Disease**

Parkinson's disease is a chronic, progressive and debilitating neurodegenerative disorder that affects approximately one million people in the United States and six million people worldwide. Parkinson's disease 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 (bradykinesia), tremor, rigidity, impaired posture and balance, and difficulty with speech and writing.

There is presently no cure for Parkinson's disease and management of the disease consists of the use of treatments that attempt to control motor

symptoms primarily through dopaminergic mechanisms. The current gold standard for treatment of motor symptoms is levodopa/carbidopa. While levodopa/carbidopa improves patients' motor symptoms, as the disease progresses, the beneficial effects of levodopa begin to wear off more quickly. Patients then experience motor fluctuations throughout the day between "on" time, periods when the medication is working and Parkinson's disease symptoms are controlled, and "off" time, when the medication is not working and motor symptoms return.

**About ONGENTYS® (opicapone) Capsules** ONGENTYS is a novel, once-daily, oral, peripheral, selective and reversible catechol-O-methyltransferase (COMT) inhibitor approved by the U.S. Food and Drug Administration (FDA) as an add-on treatment to levodopa/carbidopa in patients with Parkinson's disease experiencing "off" episodes. ONGENTYS inhibits the COMT enzyme, which breaks down levodopa, making more levodopa available to reach the brain.

### **Important Safety Information**

#### **Contraindications**

ONGENTYS is contraindicated in patients with:

- Concomitant use of non-selective monoamine oxidase (MAO) inhibitors.
- Pheochromocytoma, paraganglioma, or other catecholamine secreting neoplasms.

### **Warnings & Precautions**

#### **Cardiovascular Effects with Concomitant Use of Drugs Metabolized by Catechol-O-Methyltransferase (COMT)**

Possible arrhythmias, increased heart rate, and excessive changes in blood pressure may occur with concomitant use of ONGENTYS and drugs metabolized by COMT, regardless of the route of administration (including inhalation). Monitor patients treated concomitantly with ONGENTYS and drugs metabolized by COMT.

#### **Falling Asleep During Activities of Daily Living and Somnolence**

Patients treated with dopaminergic medications and medications that increase levodopa exposure, including ONGENTYS, have reported falling asleep while engaged in activities of daily living, including the operation of motor vehicles, which sometimes has resulted in accidents. If a patient develops daytime sleepiness or somnolence, consider discontinuing ONGENTYS or adjusting other dopaminergic or sedating medications and advise patients to avoid driving and other potentially dangerous activities.

#### **Hypotension/Syncope**

Monitor patients for hypotension and advise patients about the risk for syncope. If these adverse reactions occur, consider discontinuing ONGENTYS or adjusting the dosage of other medications that can lower blood pressure.

#### **Dyskinesia**

ONGENTYS potentiates the effects of levodopa which may result in dyskinesia or exacerbate pre-existing dyskinesia. Reducing the patient's levodopa dosage or the dosage of another dopaminergic drug may reduce dyskinesia that occurs during treatment with ONGENTYS.

#### **Hallucinations and Psychosis**

Consider stopping ONGENTYS if hallucinations or psychotic-like behaviors occur. Patients with a major psychotic disorder should ordinarily not be treated with ONGENTYS.

#### **Impulse Control/Compulsive Disorders**

Patients may experience intense urges (e.g., gambling, sexual, spending money, binge eating) and the inability to control them. It is important for prescribers to specifically ask patients or their caregivers about the development of new or increased urges. Re-evaluate the patient's current therapies for Parkinson's disease and consider stopping ONGENTYS if a patient develops such urges while taking ONGENTYS.

#### **Withdrawal-Emergent Hyperpyrexia and Confusion**

A symptom complex resembling neuroleptic malignant syndrome (elevated temperature, muscular rigidity, altered consciousness, and autonomic instability), has been reported in association with rapid dose reduction or withdrawal of drugs that increase central dopaminergic tone. There were no reports of neuroleptic malignant syndrome in ONGENTYS controlled clinical studies. When discontinuing ONGENTYS, monitor patients and consider adjustment of other dopaminergic therapies as needed.

#### **Adverse Reactions**

The most common adverse reactions (incidence at least 4% and greater than placebo) were dyskinesia, constipation, blood creatine kinase increase, hypotension/syncope, and weight decrease.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit MedWatch at [www.fda.gov/medwatch](http://www.fda.gov/medwatch) or call 1-800-FDA-1088.

Please see ONGENTYS full Prescribing Information at [www.neurocrine.com/ongentyspi](http://www.neurocrine.com/ongentyspi).

#### **About Neurocrine Biosciences**

Neurocrine Biosciences is a neuroscience-focused, biopharmaceutical company with 28 years of experience discovering and developing 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 and endometriosis\* and clinical development programs in multiple therapeutic areas including a gene therapy for Parkinson's disease, chorea in Huntington disease, congenital adrenal hyperplasia, epilepsy, uterine fibroids\* and polycystic ovary syndrome\*. Headquartered in San Diego, Neurocrine Biosciences specializes in targeting and interrupting disease-causing mechanisms involving the interconnected pathways of the nervous and endocrine systems. For more information, visit [neurocrine.com](http://neurocrine.com), and follow the company on [LinkedIn](https://www.linkedin.com/company/neurocrine). (\*in collaboration with AbbVie)

#### **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 ONGENTYS; the size of the potential market for ONGENTYS; the value ONGENTYS brings to patients; the timing of ONGENTYS's availability; the ability of Neurocrine Biosciences to ensure patients have access to ONGENTYS; our expectations regarding business and financial impacts of the COVID-19 pandemic, including with respect to ONGENTYS availability and the ONGENTYS commercial supply chain and other business operations; and whether results from ONGENTYS's clinical trial results are indicative of real-world results. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are: risks and uncertainties associated with the scale and duration of the COVID-19 pandemic and resulting global, national, and local economic and financial disruptions; risk 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; risks and uncertainties associated with Neurocrine Biosciences' business and finances in general, as well as risks and uncertainties associated with the commercialization of ONGENTYS; whether ONGENTYS receives adequate reimbursement from third-party payors; the degree and pace of market uptake of ONGENTYS; risks and uncertainties relating to competitive products and technological changes that may limit demand for ONGENTYS; risks that additional regulatory submissions, for ONGENTYS or other product candidates, may not occur or be submitted in a timely manner; risks that the FDA or other regulatory authorities may make adverse decisions regarding ONGENTYS; risks that post-approval ONGENTYS commitments or requirements may be delayed; risks that ONGENTYS may be precluded from commercialization by the proprietary rights of third parties, or have unintended side effects, adverse reactions or incidents of misuse; risks and uncertainties relating to competitive products and technological changes that may limit demand for ONGENTYS; risks associated with the Company's dependence on BIAL for the commercial supply of, and manufacturing activities related to, ONGENTYS, and the ability of the Company to manage BIAL; and other risks described in the Company's periodic reports filed with the Securities and Exchange Commission, including without limitation the Company's quarterly report on Form 10-Q for the quarter ended March 31, 2020. Neurocrine disclaims any obligation to update the statements contained in this presentation after the date hereof.

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**REFERENCES**

1. Parkinson's Disease: Challenges, progress, and promise, 2018; <https://www.ninds.nih.gov/Disorders/All-Disorders/Parkinsons-Disease-Challenges-Progress-and-Promise>