Neurocrine Biosciences Presents Phase III Data Analysis Demonstrating that Opicapone Added to Levodopa Resulted in a Significant and Sustained Increase in ON Time without Troublesome Dyskinesia in Parkinson's Disease Patients with Motor Fluctuations

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- More than 60% of Patients Treated with Once-Daily Opicapone 50 mg Experienced an Increase in Total ON Time of One Hour or Longer

- Data Analysis from the BIPARK-1 and BIPARK-2 Phase III Studies Highlighted as an Oral Presentation at the 2019 American Academy of Neurology Annual Meeting

SAN DIEGO, May 5, 2019 /PRNewswire/ -- Neurocrine Biosciences, Inc. (NASDAQ: NBIX) today announced the presentation of a data analysis from two Phase III studies of opicapone, a novel, once-daily, oral, selective, peripherally-acting catechol-O-methyltransferase (COMT) inhibitor for the treatment of Parkinson's disease. The analysis found that treatment with opicapone 50 mg, added to levodopa, resulted in a significant and sustained increase in ON time without troublesome dyskinesia[1], in Parkinson's disease patients with motor fluctuations. In addition, more than 60% of patients treated with once-daily opicapone 50 mg achieved greater than or equal to a one-hour increase from baseline in total ON time at week 14/15. The analysis, which included data from more than 900 patients in the double-blind, placebo-controlled Phase III BIPARK-1 and BIPARK-2 studies, was highlighted as an oral session at the 2019 American Academy of Neurology (AAN) Annual Meeting in Philadelphia. Parkinson's disease is a chronic, progressive and debilitating neurodegenerative disorder that affects approximately one million people in the U.S.

"The analysis of data from these two Phase III trials showed that adding once-daily opicapone to levodopa significantly increased ON time without troublesome dyskinesia, a common concern for patients with Parkinson's disease," said Peter LeWitt, M.D., the lead author and director of the Parkinson's Disease and Movement Disorders Program at the Henry Ford Hospital in Detroit. "We believe this data will translate into real-world benefits for Parkinson's disease patients on levodopa therapy who experience motor fluctuations, which can be disruptive and impact the patient's quality of life."

Opicapone is in development in the U.S. for adjunctive use with levodopa for the treatment of Parkinson's disease. Levodopa is effective for treating motor symptoms, but troublesome side effects may develop with chronic use of levodopa and progression of disease. These side effects include involuntary movements (dyskinesia) and fluctuations between "ON time," periods when the medication is working and Parkinson's disease symptoms are controlled, and "OFF time," when the medication isn't working and motor and non-motor symptoms return.

"Managing Parkinson's disease is complex and challenging because symptoms worsen as the disease progresses and first-line treatments such as levodopa begin to lose effectiveness over time, placing an increasing burden on patients and caregivers," said Eiry W. Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences. "Based on the Phase III data analysis, we believe once-daily opicapone has the potential to prolong the clinical effects of levodopa and help patients achieve symptom control so they can better cope with this debilitating disease."

The data presentation highlighted statistically significant increases in absolute ON time without troublesome dyskinesia from baseline (± standard error, hours) to the week 14/15 endpoint in both the BIPARK-1 (1.9±0.2 hours; p=0.002 for opicapone 50 mg [n=107] vs. 0.9±0.2 hours for placebo [n=110]) and BIPARK-2 (1.7±0.3 hours; p=0.025 for opicapone 50 mg [n=124] vs. 0.9±0.3 hours for placebo [n=122]) studies. The improvements in ON time without troublesome dyskinesia were sustained in all patients treated with opicapone (all doses) in the one-year long-term open-label extension studies, with an average increase from baseline (± standard error, hours) of 2.0±2.6 hours in BIPARK-1 (n=494) and 1.8±3.2 hours for BIPARK-2 (n=339). In addition, a significantly higher percentage of patients treated with opicapone 50 mg had an increase in total ON time of an hour or longer at week 14/15 in both BIPARK-1 (65.2%, n=115; p<0.01) and BIPARK-2 (61.9%, n=147; p<0.01).

Pooled safety data from the double-blind opicapone-treated population (n=631) showed that 17.4% patients treated with opicapone

(all doses) reported dyskinesia as a treatment-emergent adverse event (TEAE) versus 6.2% in placebo-treated patients (n=257). Only 1.9% of opicapone-treated patients discontinued treatment due to a TEAE of dyskinesia and only 0.3% experienced dyskinesia as a serious TEAE. Other TEAEs included constipation (5.2% and 1.9%), insomnia (4.4% and 1.6%) and dry mouth (4.1% and 1.2%) in opicapone- and placebo-treated patients, respectively.

BIPARK-1 and BIPARK-2 were conducted by BIAL – Portela & CA, S.A. (BIAL). Neurocrine Biosciences in-licensed opicapone from BIAL and has exclusive development and commercialization rights in the U.S. and Canada.

About the BIPARK-1 Study
BIPARK-1 was a Phase III, randomized, double-blind placebo- and active-controlled study of opicapone as an adjunct to levodopa therapy in which approximately 600 patients with Parkinson's disease and motor fluctuations received once-daily doses of opicapone (5 mg, 25 mg, or 50 mg), placebo or 200 mg of the COMT inhibitor entacapone for 14 to 15 weeks. The primary endpoint was the change from baseline in absolute time in the OFF state, as assessed by patient diaries; the primary analysis followed a hierarchical procedure for each opicapone dose in which superiority compared with placebo in the full analysis set was first tested and then, if positive, non-inferiority to entacapone was tested in the per-protocol set with a margin of 30 minutes. The initial study period was followed by a one-year open-label phase during which all patients received treatment with opicapone. Primary outcomes from the BIPARK-1 study were previously published in *Lancet Neurology*, with the outcomes from the open-label extension phase of the BIPARK-1 study subsequently published in *Neurology*.

About the BIPARK-2 Study
BIPARK-2 was a Phase III, randomized, double-blind placebo-controlled study of opicapone as an adjunct to levodopa therapy in which approximately 400 patients with Parkinson's disease and motor fluctuations received once-daily doses of opicapone (25 mg or 50 mg) or placebo for 14 to 15 weeks. The primary endpoint was the change from baseline in absolute time in the OFF state, as assessed by patient diaries. The initial study period was followed by a one-year open-label phase during which all patients received treatment with opicapone. Primary outcomes from the BIPARK-2 study and the open-label extension were previously published in *JAMA Neurology*.

About Parkinson's Disease
Parkinson's disease is a chronic, progressive and debilitating neurodegenerative disorder that affects approximately one million people in the U.S and six million people worldwide. Parkinson's disease is characterized by a loss of dopamine and its function. Dopamine is a chemical "messenger" that is produced in the brain and is involved in the control of movement. As Parkinson's progresses, dopamine production steadily decreases resulting in slowed movement (bradykinesia), tremor, rigidity, impaired posture and balance, and speech and writing difficulty.

There is no present cure for Parkinson's disease and management consists of controlling the motor symptoms primarily through administration of dopaminergic therapies, including levodopa. While levodopa improves the control of Parkinson's motor symptoms, the disease progresses, and the beneficial effects of levodopa begin to wear off, symptoms worsen and patients experience motor fluctuations.

About Opicapone
Opicapone, an investigational treatment for Parkinson's disease in the U.S., is a novel, once-daily, peripherally-acting, selective catechol-O-methyltransferase (COMT) inhibitor. Opicapone works by prolonging the duration of effect of levodopa through decreasing its conversion rate into 3-O-methyldopa. Discovered by the BIAL laboratories, it is designed to provide patients and physicians with a once-daily option for the treatment of Parkinson's disease.

In June 2016, the European Commission approved ONGENTYS® (opicapone) as an adjunct therapy to preparations of levodopa/DOPA decarboxylase inhibitors (DDCIs) in adult patients with Parkinson's disease and end-of-dose motor fluctuations who cannot be stabilized on those combinations. In February 2017, Neurocrine Biosciences entered into an exclusive licensing agreement with BIAL for the development and commercialization of opicapone in the U.S. and Canada. Opicapone is an investigational drug not approved for use in the U.S. or Canada.

About Neurocrine Biosciences
Neurocrine Biosciences (Nasdaq: NBIX) is a neuroscience-focused, biopharmaceutical company with more than 25 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 and endometriosis* and clinical development programs in multiple therapeutic areas including Parkinson's disease, congenital adrenal hyperplasia and uterine fibroids*. 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, and follow the company on LinkedIn. *(*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. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are: the Company's future financial and operating performance; risks or uncertainties related to the development of the Company's product candidates, including opicapone; risks and uncertainties relating to competitive products and technological changes that may limit demand for opicapone; risks associated with the Company's dependence on BIAL for development and manufacturing activities related to opicapone, and the ability of the Company to manage BIAL; risks that the FDA or other regulatory authorities may make adverse decisions regarding opicapone; 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 that the benefits of the agreement with BIAL 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 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, 2019. Neurocrine disclaims any obligation to update the statements contained in this presentation after the date hereof.

[1] Troublesome dyskinesia was defined as either no dyskinesia or non-troublesome dyskinesia

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