New INGREZZA® (valbenazine) Analysis Published in the Journal of Affective Disorders Demonstrates Sustained Improvement in Tardive Dyskinesia Symptoms in Patients with Primary Mood Disorders

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INGREZZA Significantly Reduced the Symptoms of Involuntary Movements in Patients with Bipolar or Major Depressive Disorder in Post-Hoc Analysis

Patients Treated with INGREZZA Able to Remain on Existing Psychiatric Medications

SAN DIEGO, Jan. 16, 2019 /PRNewswire/ -- Neurocrine Biosciences, Inc. (NASDAQ: NBIX) today announced that a new analysis of INGREZZA® (valbenazine) capsules, published in the *Journal of Affective Disorders*[1], demonstrated sustained improvement in tardive dyskinesia (TD) symptoms in patients with primary mood disorders. In the post-hoc analysis, INGREZZA significantly reduced involuntary movements associated with TD in patients with a primary mood disorder, such as bipolar and major depressive disorder, and was generally well tolerated with no clinically meaningful changes to psychiatric stability. INGREZZA is the first U.S. Food and Drug Administration (FDA) approved treatment for adults with TD, a movement disorder that is characterized by uncontrollable, abnormal and repetitive movements of the face, torso and/or other body parts.

"Patients with mood disorders, such as bipolar and major depression, are typically high functioning and the abnormal movements associated with their tardive dyskinesia can be burdensome and lead to social isolation. For these patients, it is important that they are able to manage their involuntary movements while maintaining psychiatric stability with their primary mood disorder," said Roger S. McIntyre, Professor of Psychiatry and Pharmacology at the University of Toronto and Head of the Mood Disorders Psychopharmacology Unit at the University Health Network in Toronto. "The data analysis examining this patient population indicates that treatment with INGREZZA did not affect the stability of their underlying psychiatric disorder and significantly improves the severity of tardive dyskinesia."

TD is associated with prolonged use of medications that block dopamine receptors in the brain such as antipsychotics, which are commonly prescribed to treat schizophrenia, bipolar disorder and depression. The abnormal and involuntary movements of TD can impact patients socially, emotionally and physically, causing patients to feel embarrassed or judged by others or withdraw from society and isolate themselves.

"With the increased use of antipsychotics in patients with mood disorders such as bipolar and major depressive disorder, it is important that we understand and analyze the efficacy and tolerability of INGREZZA in reducing the involuntary movements associated with tardive dyskinesia in these patients," said Eiry W. Roberts, M.D., Chief Medical Officer of Neurocrine Biosciences. "Data from our analysis of mood disorder patients who have tardive dyskinesia show that once-daily INGREZZA is an effective and well-tolerated treatment option that allows patients to remain on their existing medications with no clinically meaningful changes in psychiatric stability."

The pooled post-hoc analysis examined data from 114 patients with primary mood disorders and TD from the double-blind, placebo-controlled Phase II KINECT 2 (six weeks) and Phase III KINECT 3 studies (six weeks) and 77 patients from the long-term KINECT 3 extension study (48 weeks). Of the mood disorder patients, 60.5 percent had a primary diagnosis of bipolar disorder and 37.7 percent had a diagnosis of depression/major depression. In the analysis, treatment with INGREZZA significantly improved TD symptoms across both 40 mg and 80 mg doses at week six, with improvements sustained through week 48.

At week six, a significant improvement in the Abnormal Involuntary Movement Scale (AIMS) score was seen in the INGREZZA mood disorder treatment group versus placebo (40 mg/day, -3.1, $p<0.01$; 80 mg/day, -3.5, $p<0.001$; placebo, -0.09). The improvement from baseline was sustained through 48 weeks of treatment (40 mg/day, -4.2; 80 mg/day, -5.8). After long-term treatment with INGREZZA 40 mg/day or 80 mg/day, almost half (46.5 percent) of patients had at least a 50 percent improvement in their AIMS total score from baseline. INGREZZA was generally well tolerated and patients had no notable worsening of psychiatric symptoms. The only treatment-emergent adverse event (TEAE) reported in ≥10 percent of all INGREZZA-treated patients in the double-blind population was somnolence (11.4 percent). In the long-term extension study, the only TEAE reported in ≥10 percent of all INGREZZA-treated patients was headache (10.4 percent).

KINECT 2, KINECT 3 and KINECT 3 Extension Study Designs

The post-hoc analysis in patients with primary mood disorders was conducted on data pooled from two six-week, double-blind, placebo-controlled trials (KINECT 2, KINECT 3; 114 mood patients) and a 48-week, long-term extension study (KINECT 3 extension; 77 mood patients) of once-daily treatment with INGREZZA (40 mg or 80 mg) in adults with TD.

KINECT 2 was a Phase II, randomized, double-blind, placebo-controlled, dose-titration study in which 102 patients with TD and underlying schizophrenia, schizoaffective disorder or mood disorder received six weeks of a titrated dose of once-daily INGREZZA (25-75 mg escalated in 25 mg increments depending on TD symptoms and tolerability) or placebo. The primary endpoint for KINECT 2 was change in Abnormal Involuntary Movement Scale (AIMS) score from baseline to week six.

KINECT 3 was a Phase III, randomized, double-blind, placebo-controlled, parallel-group, fixed-dose study in which 234 patients with moderate to severe TD and underlying schizophrenia, schizoaffective disorder or mood disorder received six weeks of once-daily INGREZZA (40 mg or 80 mg) or

placebo (patients randomized to 80 mg started on 40 mg for one week). Following completion of the six-week placebo-controlled dosing, patients receiving INGREZZA continued on their current dose and placebo patients were randomized to receive either once-daily 40 mg or once-daily 80 mg of INGREZZA, through week 48 (42-week blinded treatment extension period; placebo patients randomized to 80 mg started on 40 mg for one week), followed by a four-week drug-free washout. Dose reduction to 40 mg was allowed for patients who were unable to tolerate the 80 mg dose. Patients who were unable to tolerate 40 mg were discontinued from the study. The primary endpoint of KINECT 3 was change from baseline in AIMS at week six in the 80 mg once-daily dosing group compared to placebo, as assessed by expert central blinded video raters.

About Tardive Dyskinesia (TD)
Tardive dyskinesia (TD) 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 caused by 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 and depression and certain anti-nausea medications. In patients with TD, these treatments are thought to result in irregular dopamine signaling in a region of the brain that controls movement. The symptoms of TD can be severe and are often persistent and irreversible. TD is estimated to affect at least 500,000 people in the U.S.

About INGREZZA® (valbenazine) Capsules
INGREZZA, a selective vesicular monoamine transporter 2 (VMAT2) inhibitor, is the first FDA-approved product indicated for the treatment of adults with tardive dyskinesia, a condition associated with uncontrollable, abnormal and repetitive movements of the face, torso and/or other body parts.

INGREZZA is thought to work by reducing the amount of dopamine released in a region of the brain that controls movement and motor function, helping to regulate nerve signaling in adults with tardive dyskinesia. VMAT2 is a protein in the brain that packages neurotransmitters, such as dopamine, for transport and release in presynaptic neurons. INGREZZA, developed in Neurocrine's laboratories, is novel in that it selectively inhibits VMAT2 with no appreciable binding affinity for VMAT1, dopaminergic (including D2), serotonergic, adrenergic, histaminergic, or muscarinic receptors. Additionally, INGREZZA can be taken for the treatment of tardive dyskinesia as one capsule, once-daily, together with psychiatric medications such as antipsychotics or antidepressants.

Important Safety Information

Contraindications
INGREZZA is contraindicated in patients with a history of hypersensitivity to valbenazine or any components of INGREZZA. Rash, urticaria, and reactions consistent with angioedema (e.g., swelling of the face, lips, and mouth) have been reported.

Warnings & Precautions
Somnolence
INGREZZA can cause somnolence. Patients should not perform activities requiring mental alertness such as operating a motor vehicle or operating hazardous machinery until they know how they will be affected by INGREZZA.

QT Prolongation
INGREZZA may prolong the QT interval, although the degree of QT prolongation is not clinically significant at concentrations expected with recommended dosing. INGREZZA should be avoided in patients with congenital long QT syndrome or with arrhythmias associated with a prolonged QT interval. For patients at increased risk of a prolonged QT interval, assess the QT interval before increasing the dosage.

Adverse Reactions
The most common adverse reaction (≥5% and twice the rate of placebo) is somnolence. Other adverse reactions (≥2% and >placebo) include: anticholinergic effects, balance disorders/falls, headache, akathisia, vomiting, nausea, and arthralgia.

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

Please see INGREZZA full Prescribing Information at www.INGREZZA.com/PI.

About Neurocrine Biosciences, Inc.
Neurocrine Biosciences, a San Diego based biopharmaceutical company, is focused on developing treatments for neurological and endocrine related disorders. The company discovered, developed and markets INGREZZA® (valbenazine) capsules, the first FDA-approved product indicated for the treatment of adults with tardive dyskinesia, an involuntary movement disorder. Discovered and developed through Phase II clinical trials by Neurocrine, ORILISSA® (elagolix), the first FDA-approved oral medication for the management of endometriosis with associated moderate to severe pain in over a decade, is marketed by AbbVie as part of a collaboration to develop and commercialize elagolix for women's health. Neurocrine's clinical development programs include opicapone as an adjunctive therapy to levodopa/DOPA decarboxylase inhibitors in Parkinson's disease patients, elagolix for uterine fibroids with AbbVie, valbenazine for the treatment of Tourette syndrome, and NBI-74788 for the treatment of congenital adrenal hyperplasia (CAH). For more information and the latest updates from Neurocrine Biosciences, please visit www.neurocrine.com.

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 INGREZZA and the continued success of the launch of INGREZZA. 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 and uncertainties associated with the commercialization of INGREZZA, including the likelihood of continued revenue and prescription growth of INGREZZA; risks and uncertainties relating to factors that may limit demand for INGREZZA; risks associated with the Company's dependence on third parties for development and manufacturing activities related to INGREZZA, and the ability of the Company to manage these third parties; risks that the FDA or other regulatory authorities may make adverse decisions regarding INGREZZA; risks that clinical development activities may be delayed for regulatory 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 INGREZZA may be precluded from commercialization or continued 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 September 30, 2018. Neurocrine disclaims any obligation to update the statements contained in this press release after the date hereof.

References:

1. McIntyre R., et al. The Effects of Valbenazine on Tardive Dyskinesia in Patients with a Primary Mood Disorder. J. Affective Disorders, 246 (2019), pp. 217-223. https://doi.org/10.1016/j.jad.2018.12.023

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