Neurocrine Biosciences Presents Interim Data Demonstrating Robust and Sustained Improvements in Chorea Associated With Huntington's Disease Through Week 104 Irrespective of Antipsychotic Use

September 30, 2024

- KINECT®-HD2 Is the First Prospective Clinical Trial to Include Patients Taking Antipsychotic Medication in a Study Evaluating a Vesicular Monoamine Transporter 2 (VMAT2) Inhibitor for the Treatment of Huntington's Disease Chorea
- Findings Presented at the 2024 MDS International Congress of Parkinson's Disease and Movement Disorders®

SAN DIEGO, Sept. 30, 2024 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced interim results from the ongoing open-label KINECT®-HD2 study of INGREZZA® (valbenazine) capsules for the long-term treatment of adults with chorea associated with Huntington's disease. Robust and sustained improvements in chorea associated with Huntington's disease were observed through Week 104 in patients, irrespective of concomitant antipsychotic therapy use. These results (Poster #1465) will be presented on September 30 during the 2024 MDS International Congress of Parkinson's Disease and Movement Disorders® in Philadelphia.

"The data from this study reinforce the long-term clinical safety of INGREZZA observed to date, showing sustained improvement in chorea regardless of antipsychotic use during the study," said Eiry W. Roberts, M.D., Chief Medical Officer, Neurocrine Biosciences. "This is an important finding given that approximately a third of patients living with Huntington's disease chorea are prescribed antipsychotic medications for neuropsychiatric symptoms without receiving treatment for the chorea that may significantly disrupt daily life."

The effect of INGREZZA on chorea over time was assessed using mean changes from baseline in the Unified Huntington's Disease Rating Scale Total Maximal Chorea (TMC) score and response status ("much improved" or "very much improved") for Clinical Global Impression of Change and Patient Global Impression of Change.

Data from this interim analysis of KINECT-HD2 suggest robust and sustained improvements in Huntington's disease (HD) chorea with INGREZZA treatment:

- INGREZZA improved HD chorea as early as Week 2 (TMC change from baseline: -3.4) at the starting dose of 40 mg and at Week 4 (-4.6) with doses up to 60 mg. Efficacy was sustained from Week 8 (-5.7) to Week 104 (-5.2) at the maintenance dose of up to 80 mg.
- These improvements were consistent regardless of presence or absence of concomitant antipsychotic treatment.
- At Week 6 and at each visit thereafter, more than half of participants and investigators rated symptoms as "much improved" or "very much improved." At Week 104, this response status was achieved in 75.9% of participants based on self-report and 73.6% of participants based on clinician assessment.
- The most common treatment-emergent adverse events at the time of the analysis were consistent with those observed in KINECT-HD, including falls, somnolence and fatigue.

Additional presentations by Neurocrine Biosciences include:

- Somnolence-Related Events Over Time with Valbenazine Treatment for Chorea Associated with Huntington's Disease (Poster #1445)
- Treatment Effect Sizes of Once-Daily Valbenazine for Tardive Dyskinesia and for Chorea Associated with Huntington's Disease: A Post-Hoc Analysis of Phase 3 Clinical Trial Data (Poster #1466)

About Chorea Associated with Huntington's Disease
Huntington's disease is a hereditary progressive neurodegenerative disorder in which the loss of certain neurons within the brain causes motor, cognitive and psychiatric symptoms. Symptoms generally appear between the ages of 30 and 50 years and worsen over a 10- to 25-year period. Most people with HD experience chorea, an abnormal involuntary movement disorder, characterized by irregular and unpredictable movements. Chorea can affect various body parts and interfere with motor coordination, gait, swallowing and speech. HD is estimated to affect approximately 41,000 adults in the U.S., with more than 200,000 at risk of inheriting the disease.

About KINECT®-HD

KINECT®-HD was a Phase 3, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy of valbenazine as a once-daily treatment to reduce chorea associated with Huntington's disease (HD) and evaluate the safety and tolerability of valbenazine in patients with HD. The study enrolled 128 adults 18 to 75 years of age who were diagnosed with motor-manifest HD and who had sufficient chorea symptoms to meet study protocol criteria.

KINECT-HD used the Unified Huntington's Disease Rating Scale (UHDRS®) Total Maximal Chorea (TMC) score as the primary efficacy endpoint. The secondary endpoints included Clinical Global Impression of Change (CGI-C) response status and Patient Global Impression of Change (PGI-C) response status for valbenazine treatment. Treatment with valbenazine resulted in a placebo-adjusted mean reduction in the TMC score of 3.2 units ($P < 0.0001$), indicating a substantial improvement in chorea. Secondary endpoints of CGI-C response status and PGI-C response status were also statistically significant and supported the improvements in TMC score that were seen over the 12-week study period.

Treatment-emergent adverse events in this study were generally consistent with the known safety profile of valbenazine. The most common adverse reactions in patients with HD included somnolence and sedation, urticaria, rash and insomnia.

View the complete study results from the Phase 3 KINECT-HD study published in *The Lancet Neurology* online edition. For more information on the KINECT-HD study, please visit HuntingtonStudyGroup.org.

About KINECT®-HD2

KINECT®-HD2 is an ongoing open-label study to evaluate the long-term safety and tolerability, as well as the maintenance of effects, of INGREZZA in patients with chorea associated with Huntington's disease (HD). The maintenance period up to week 156 of treatment enrolled 154 adults 18 to 75 years of age who have been diagnosed with motor-manifest HD and who have sufficient chorea symptoms to meet study protocol criteria. Concomitant antipsychotic use is allowed in the study. For more information on the KINECT-HD2 study, please visit HuntingtonStudyGroup.org or ClinicalTrials.gov.

About INGREZZA® (valbenazine) Capsules and INGREZZA® SPRINKLE (valbenazine) Capsules

INGREZZA is a selective vesicular monoamine transporter 2 (VMAT2) inhibitor approved by the U.S. Food and Drug Administration for the treatment of adults with tardive dyskinesia (TD) and the treatment of chorea associated with Huntington's disease (HD) that is always one capsule, once daily with no complex dose adjustments to get to an effective dose. Only INGREZZA offers a therapeutic dose from day one.

INGREZZA, developed by Neurocrine Biosciences, selectively inhibits VMAT2 with no appreciable binding affinity for VMAT1, dopaminergic (including D2), serotonergic, adrenergic, histaminergic or muscarinic receptors. While the specific way INGREZZA works to treat TD and HD chorea is not fully understood, INGREZZA is unique in that it selectively and specifically targets VMAT2 to inhibit the release of dopamine, a chemical in the brain that helps control movement. INGREZZA is believed to reduce extra dopamine signaling, which may lead to fewer uncontrollable movements.

INGREZZA can be taken as one capsule, once daily together with most stable mental health regimens such as antipsychotics or antidepressants. Only INGREZZA offers the benefit of a sprinkle formulation, INGREZZA® SPRINKLE, for those who experience dysphagia, have difficulty swallowing or prefer not to swallow a pill. INGREZZA and INGREZZA SPRINKLE dosages approved for use are 40 mg, 60 mg and 80 mg capsules.

Important Information

Approved Uses

INGREZZA® (valbenazine) capsules or INGREZZA® SPRINKLE (valbenazine) capsules are prescription medicines used to treat adults with:

- movements in the face, tongue, or other body parts that cannot be controlled (tardive dyskinesia).
- involuntary movements (chorea) of Huntington's disease. INGREZZA or INGREZZA SPRINKLE do not cure the cause of involuntary movements, and do not treat other symptoms of Huntington's disease, such as problems with thinking or emotions.

It is not known if INGREZZA or INGREZZA SPRINKLE is safe and effective in children.

IMPORTANT SAFETY INFORMATION

INGREZZA or INGREZZA SPRINKLE can cause serious side effects in people with Huntington's disease, including: depression, suicidal thoughts, or suicidal actions. Tell your healthcare provider before you start taking INGREZZA or INGREZZA SPRINKLE if you have Huntington's disease and are depressed (have untreated depression or depression that is not well controlled by medicine) or have suicidal thoughts. Pay close attention to any changes, especially sudden changes, in mood, behaviors, thoughts, or feelings. This is especially important when INGREZZA or INGREZZA SPRINKLE is started and when the dose is changed. Call your healthcare provider right away if you become depressed, have unusual changes in mood or behavior, or have thoughts of hurting yourself.

Do not take INGREZZA or INGREZZA SPRINKLE if you:

- are allergic to valbenazine, or any of the ingredients in INGREZZA or INGREZZA SPRINKLE.

INGREZZA or INGREZZA SPRINKLE can cause serious side effects, including:

- **Allergic reactions.** Allergic reactions, including an allergic reaction that causes sudden swelling called angioedema can happen after taking the first dose or after many doses of INGREZZA or INGREZZA SPRINKLE. Signs and symptoms of allergic reactions and angioedema include: trouble breathing or shortness of breath, swelling of your face, lips, eyelids, tongue, or throat, or other areas of your skin, trouble with swallowing, or rash, including raised, itchy red areas on your skin (hives). Swelling in the throat can be life-threatening and can lead to death. Stop taking INGREZZA or INGREZZA SPRINKLE and go to the nearest emergency room right away if you develop these signs and symptoms of allergic reactions and angioedema.

- **Sleepiness and tiredness that could cause slow reaction times (somnolence and sedation).** Do not drive a car or operate dangerous machinery until you know how INGREZZA or INGREZZA SPRINKLE affects you. Drinking alcohol and taking other medicines may also cause sleepiness during treatment with INGREZZA or INGREZZA SPRINKLE.
- **Heart rhythm problems (QT prolongation).** INGREZZA or INGREZZA SPRINKLE may cause a heart rhythm problem known as QT prolongation. You have a higher chance of getting QT prolongation if you also take certain other medicines during treatment with INGREZZA or INGREZZA SPRINKLE. Tell your healthcare provider right away if you develop any signs or symptoms of QT prolongation, including: fast, slow, or irregular heartbeat (heart palpitations), shortness of breath, dizziness or lightheadedness, or fainting or feeling like you are going to faint.
- **Neuroleptic Malignant Syndrome (NMS).** NMS is a serious condition that can lead to death. Call a healthcare provider right away or go to the nearest emergency room if you develop these symptoms and they do not have another obvious cause: high fever, stiff muscles, problems thinking, irregular pulse or blood pressure, increased sweating, or very fast or uneven heartbeat.
- **Parkinson-like symptoms.** Symptoms include: body stiffness, drooling, trouble moving or walking, trouble keeping your balance, shaking (tremors), or falls.

Before taking INGREZZA or INGREZZA SPRINKLE, tell your healthcare provider about all of your medical conditions including if you: have liver or heart problems, are pregnant or plan to become pregnant, or are breastfeeding or plan to breastfeed.

Tell your healthcare provider about all the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Make sure you tell all of your healthcare providers that you are taking INGREZZA or INGREZZA SPRINKLE. Taking INGREZZA or INGREZZA SPRINKLE with certain other medicines may cause serious side effects. Especially tell your healthcare provider if you: take digoxin or take or have taken a monoamine oxidase inhibitor (MAOI) medicine. You should not take INGREZZA or INGREZZA SPRINKLE if you are taking, or have stopped taking, a MAOI within the last 14 days.

The most common side effects of INGREZZA or INGREZZA SPRINKLE in people with tardive dyskinesia are sleepiness and tiredness.

The most common side effects of INGREZZA or INGREZZA SPRINKLE in people with chorea associated with Huntington's disease include sleepiness and tiredness, raised itchy red areas on your skin (hives), rash, and trouble getting to sleep or staying asleep.

These are not all of the possible side effects of INGREZZA or INGREZZA SPRINKLE. Call your doctor for medical advice about side effects. You are encouraged to report negative side effects of prescription drugs to the FDA. Visit MedWatch at **https://www.fda.gov/medwatch** or call **1-800-FDA-1088.**

Dosage Forms and Strengths: INGREZZA and INGREZZA SPRINKLE are available in 40 mg, 60 mg, and 80 mg capsules.

Please see full Prescribing Information, including Boxed Warning, and Medication Guide.

About Neurocrine Biosciences, Inc.
Neurocrine Biosciences is a leading neuroscience-focused, biopharmaceutical company with a simple purpose: to relieve suffering for people with great needs, but few options. We are dedicated to discovering and developing life-changing treatments for patients with under-addressed neurological, neuroendocrine and neuropsychiatric disorders. The company's diverse portfolio includes FDA-approved treatments for tardive dyskinesia, chorea associated with Huntington's disease, endometriosis* and uterine fibroids*, as well as a robust pipeline including multiple compounds in mid- to late-phase clinical development across our core therapeutic areas. For three decades, we have applied our unique insight into neuroscience and the interconnections between brain and body systems to treat complex conditions. We relentlessly pursue medicines to ease the burden of debilitating diseases and disorders, because you deserve brave science. For more information, visit neurocrine.com, and follow the company on LinkedIn, X (formerly Twitter) and Facebook. (**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 regarding the potential benefits to be derived from INGREZZA for the treatment of chorea associated with Huntington's disease (HD) and the value INGREZZA may bring to patients with chorea associated with HD. Factors that could cause actual results to differ materially from those stated or implied in the forward-looking statements include, but are not limited to, the following: risks and uncertainties associated with Neurocrine Biosciences' business and finances in general, as well as risks and uncertainties associated with the commercialization of INGREZZA for the treatment of chorea associated with HD; whether INGREZZA receives adequate reimbursement from third-party payors; the degree and pace of market uptake of INGREZZA for the treatment of chorea associated with HD; risks and uncertainties relating to competitive products and technological changes that may limit demand for INGREZZA for the treatment of chorea associated with HD; risks associated with the Company's dependence on third parties for development and manufacturing activities related to INGREZZA for the treatment of chorea associated with HD, and the ability of the Company to manage these third parties; risks that additional regulatory submissions for INGREZZA for the treatment of chorea associated with HD 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 INGREZZA for the treatment of chorea associated with HD; risks that post-approval INGREZZA commitments or requirements may be delayed; risks that INGREZZA for the treatment of chorea associated with HD 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; risks and uncertainties relating to competitive products and technological changes that may limit demand for INGREZZA for the treatment of chorea associated with HD; 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 June 30, 2024. Neurocrine Biosciences disclaims any obligation to update the statements contained in this press release after the date hereof other than required by law.

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