Neurocrine Biosciences Presents New KINECT®-HD Data Showing Consistent Efficacy Across 19 Subgroups and Improvements in Aspects of Emotional Health With INGREZZA® (valbenazine) Capsules

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- Data Support Positive Impact of INGREZZA in People With Huntington's Disease Chorea
- Findings Presented at the 2024 Annual Meeting of the Huntington Study Group

SAN DIEGO, Nov. 7, 2024 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today presented subgroup analyses and data from the KINECT®-HD study showing the impact of INGREZZA® (valbenazine) capsules on emotional health and psychiatric stability in patients with chorea associated with Huntington's disease. The subgroup analysis showed consistent efficacy in reducing chorea compared to placebo across all identified subgroups, categorized by demographics and baseline assessment scores. A separate data analysis showed improvements in some aspects of emotional health with no worsening of psychiatric symptoms. This research will be shared at the 2024 Annual Meeting of the Huntington Study Group in Cincinnati.

"In addition to physical symptoms, Huntington's disease significantly affects emotional and psychological health, often leading to increased anxiety and irritability or anger," said Eiry W. Roberts, M.D., Chief Medical Officer, Neurocrine Biosciences. "These data not only support the consistent efficacy of INGREZZA in reducing chorea across various subgroups but also its potential positive impact on emotional health in patients because of the reduced movements."

Efficacy of Valbenazine for Chorea Associated with Huntington's Disease: Subgroup Analyses of KINECT®-HD Results

This analysis was conducted to assess the effects of INGREZZA (n=64) versus placebo (n=61) in subgroups of participants from the Phase 3 KINECT-HD study using the Unified Huntington's Disease Rating Scale (UHDRS®) Total Maximal Chorea (TMC) score. Participants in the study were randomized 1:1 to receive placebo or INGREZZA, with a starting dose of 40 mg that was increased up to 80 mg over an 8-week period as tolerated, for a total treatment period of 12 weeks. In the full analysis set, least-squares mean (LSM) changes for TMC score indicated significantly greater chorea improvements for INGREZZA versus placebo, with an LSM difference at maintenance of -3.2 (95% confidence interval (CI): -4.4 to -2.0; $P < 0.0001$). To further assess INGREZZA efficacy, TMC changes were analyzed in subgroups categorized by demographics (sex, age and body mass index) and baseline assessment scores (Clinical Global Impression of Severity, Patient Global Impression of Severity, Anosognosia Scale, UHDRS Total Functional Capacity, UHDRS Total Motor Score and UHDRS TMC).

TMC changes favored INGREZZA over placebo in all 19 subgroups, with the LSM difference (LSMD; 95% CI) ranging from -4.5 (-6.6 to -2.4) to -1.6 (-4.1 to 0.8). The 95% CIs for all subgroup LSMDs encompassed the primary endpoint LSMD of -3.2.

Effects of Valbenazine on Emotional Health and Psychiatric Stability in Adults with Huntington's Disease

This separate post hoc analysis of the Phase 3 KINECT-HD study was conducted to evaluate emotional health and psychiatric stability in participants taking INGREZZA (n=64) or placebo (n=61) utilizing the Huntington's Disease Health Index (HD-HI) Emotional Health subscale. Mean score changes from baseline (CFB) to Week 10 and Week 12 were analyzed in "affected" participants (those with a baseline item score of at least 2). Safety assessments included adverse events of special interest (AESIs), the Hospital Anxiety and Depression Scale (HADS) and the Columbia-Suicide Severity Rating Scale (C-SSRS).

Results showed that some aspects of emotional health appeared to improve with INGREZZA in affected participants. The largest score changes with INGREZZA compared to placebo at Week 12 were:

- Anger: -1.7 (INGREZZA; n=17) versus -0.2 (placebo; n=22)
- Feeling of being overwhelmed: -1.7 (n=20) versus -0.4 (n=27)
- Fluctuating mood: -1.5 (n=15) versus -0.4 (n=23)
- Reduced enjoyment with activities: -1.5 (n=25) versus -0.4 (n=26)
- Emotional outbursts: -1.5 (n=15) versus -0.6 (n=23)
- Frustration: -1.3 (n=25) versus -0.4 (n=28)
- Anxiety: -1.4 (n=25) versus -0.5 (n=30)

In the safety population (N=127), 5 participants (3 INGREZZA, 2 placebo) reported AESIs related to depression or suicidal ideation. HADS and

C-SSRS shifts from baseline indicated no worsening in anxiety symptoms, depression symptoms or suicidal ideation with INGREZZA.

Additional Neurocrine Biosciences posters presented at the 2024 Annual Meeting of the Huntington Study Group include:

- Huntington's Disease Health Index (HD-HI) Correlations with Clinical Measures: An Analysis of KINECT®-HD Baseline Data
- Somnolence-Related Events Over Time with Valbenazine Treatment for Chorea Associated with Huntington's Disease
- Efficacy of Once-Daily Valbenazine in Adults with Chorea Associated with Huntington's Disease: Effect Size Over Time

About Chorea Associated with Huntington's Disease (HD)
Huntington's disease (HD) 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 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 and the treatment of chorea associated with Huntington's disease (HD). Only INGREZZA offers a therapeutic dose from day one with no required titration.

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 is always one capsule, once daily and can be taken 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 effect 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 **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 September 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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