Neurocrine Biosciences Publishes Analysis Showing Long-Term Efficacy and a Consistent Safety Profile of INGREZZA® (valbenazine) Capsules in Older Adults with Tardive Dyskinesia in The Journal of Clinical Psychiatry

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Post-hoc analysis of higher risk older adults showed substantial and sustained improvements in tardive dyskinesia symptoms with no new treatment-emergent adverse events of clinical concern

SAN DIEGO, April 24, 2025 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today announced publication of a post-hoc analysis from two 48-week studies, the KINECT® 3 extension and KINECT® 4, demonstrating the long-term safety profile and robust efficacy of INGREZZA® (valbenazine) capsules in adults aged 65 years and older with tardive dyskinesia (TD) in *The Journal of Clinical Psychiatry.* This represents the first and only published peer-reviewed analysis of a vesicular monoamine transporter 2 inhibitor for the treatment of TD in older adults (≥65 years), a group at higher risk for TD and associated consequences.

Individuals aged 60 years and older may develop TD after as little as one month of exposure to antipsychotics and other dopamine receptor blocking agents. The involuntary movements of TD can also have a substantial impact on older adults, affecting their balance, gait, ability to swallow and respiratory conditions. The data from this post-hoc analysis show substantial and sustained improvements in TD symptoms in older adults, with no new treatment-emergent adverse events of clinical concern found when compared with younger adults (<65 years).

"This analysis, the first and only of its kind in a peer-reviewed publication, addresses an important gap in research on this potentially vulnerable population," said Eiry W. Roberts, M.D., Chief Medical Officer, Neurocrine Biosciences. "These data show that participants 65 years and older achieved clinically meaningful improvements in tardive dyskinesia symptoms within eight weeks of INGREZZA treatment, with substantial and sustained improvement up to 48 weeks, adding to the breadth of evidence suggesting INGREZZA is uniquely suitable for this patient population."

The pooled post-hoc analysis included 304 participants across studies who received a once-daily dose of INGREZZA (40 mg or 80 mg) for up to 48 weeks. Of the total participants, 55 (18.1%) were 65 years and older. At Week 48, efficacy and safety outcomes were analyzed by dose (40 mg, 80 mg) and age (<65 years, ≥65 years).

The efficacy of INGREZZA was assessed using mean changes from baseline in the Abnormal Involuntary Movement Scale (AIMS) total score, AIMS response thresholds (≥30% and ≥50% improvement from baseline) and response threshold for Clinical Global Impression of Change-Tardive Dyskinesia (CGI-TD) and Patient Global Impression of Change (PGIC), defined as a score ≤2 ("much improved" or "very much improved"). At baseline, participants in both age subgroups had a mean AIMS total score of approximately 12, consistent with moderate to severe severity in one or more body regions. The safety profile of INGREZZA was evaluated through adverse event monitoring and psychiatric symptom scales.

Data from this analysis of participants ≥65 years in the KINECT 3 extension and KINECT 4 studies suggest substantial and sustained improvements in TD symptoms with INGREZZA treatment (all doses):

AIMS threshold ≥30% by Week 48*	**CGI-TD scores ≤2 by Week 48***	**PGIC scores ≤2 by Week 48***
95% on INGREZZA 80 mg	95% on INGREZZA 80 mg	90% on INGREZZA 80 mg
75% on INGREZZA 40 mg	88% on INGREZZA 40 mg	75% on INGREZZA 40 mg

*Post-hoc analysis results not adjusted for multiple comparisons.

Overall, psychiatric stability was maintained through 48 weeks of treatment and INGREZZA was generally well tolerated. The most common treatment-emergent adverse events reported from Weeks 8 to 48 included urinary tract infection and somnolence; each occurred in six of the 55 participants who were 65 years and older.

There were no statistically significant differences between age groups (<65 versus ≥65) for most efficacy and safety outcomes at Week 48.

About the KINECT® 3 Phase 3 Study
KINECT 3 is a Phase 3, randomized, double-blind, placebo-controlled, parallel-group, fixed-dose study in which 234 participants with moderate to severe TD and underlying schizophrenia, schizoaffective disorder or mood disorder (including bipolar disorder or major depressive disorder) received six weeks of once-daily INGREZZA (40 mg or 80 mg capsules) or placebo (participants randomized to 80 mg started on 40 mg for one week). Subsequent to the completion of the six-week placebo-controlled dosing, participants receiving INGREZZA continued on their current dose and placebo participants 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 participants 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 participants who were unable to tolerate the 80 mg dose. Patients were discontinued if the new dose was not tolerated.

The study met its primary endpoint of change-from-baseline in AIMS at Week 6 in the 80 mg once-daily dosing group compared with placebo as assessed by expert central blinded video raters. The mean change from baseline to Week 6 in the AIMS rating was -3.2 for the 80 mg once-daily group as compared with -0.1 in the placebo group (P>0.0001). Sustained TD improvements were seen with INGREZZA 40 mg and 80 mg through Week 48.

INGREZZA was generally well tolerated throughout 48 weeks of treatment. The most common adverse reactions (≥ 5% and twice the rate of placebo) during the six-week, double-blind, placebo-controlled phase was somnolence with the frequency of adverse events being similar among all treatment groups. Treatment-emergent adverse events were consistent with those of prior studies. There were no drug-drug interactions identified in participants who were utilizing a wide range of psychotropic and other concomitant medications, and participants generally remained psychiatrically stable throughout the study.

About the KINECT® 4 Phase 3 Study
KINECT 4 is a Phase 3, open-label study in which 163 participants with moderate to severe TD and underlying schizophrenia, schizoaffective disorder or mood disorder (including bipolar disorder or major depressive disorder) received 48 weeks of open-label treatment with once-daily INGREZZA (40 mg or 80 mg capsules) followed by a four-week washout. Dosing was initiated at 40 mg/day in all participants, with escalation to 80 mg/day at Week 4 based on effectiveness and tolerability. Dose reduction to 40 mg was allowed in participants who could not tolerate the 80 mg dose. Patients were discontinued if the new dose was not tolerated.

Participants experienced TD improvements during long-term treatment as demonstrated by mean change from baseline to Week 48 in AIMS total score (sum of items 1-7, evaluated by site raters) with INGREZZA 40 mg/day (-10.2) or 80 mg/day (-11.0). Consistent with previous studies, INGREZZA was generally well tolerated. After Week 4, treatment-emergent adverse events that occurred in ≥5% of all participants (combined dose groups) were urinary tract infection (8.5%) and headache (5.2%). Changes from baseline in psychiatric stability, vital signs, electrocardiogram parameters and laboratory test values were generally small and not clinically significant.

About Tardive Dyskinesia
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 associated with taking certain kinds of mental health medicines (antipsychotics) that help control dopamine receptors in the brain. Taking antipsychotics commonly prescribed to treat mental illnesses such as major depressive disorder, bipolar disorder, schizophrenia and schizoaffective disorder and other prescription medicines (metoclopramide and prochlorperazine) used to treat gastrointestinal disorders are associated with TD. 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 mild to severe and are often persistent and irreversible. TD is estimated to affect at least 800,000 adults in the U.S.

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 proven across the widest range of patients. It 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 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 **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. 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, classic congenital adrenal hyperplasia, 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** 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 and the value INGREZZA may bring to patients. 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; whether INGREZZA receives adequate reimbursement from third-party payors; risks and uncertainties relating to competitive products and technological changes 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 additional regulatory submissions for INGREZZA 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; risks that post-approval INGREZZA commitments or requirements may be delayed; risks that INGREZZA 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 annual report on Form 10-K for the year ended December 31, 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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