



## Neurocrine Biosciences Announces Publication of Phase 3 KINECT®-4 Post Hoc Analysis Demonstrating Clinically Meaningful and Sustained Improvement in Tardive Dyskinesia With Long-Term Use of INGREZZA® (valbenazine) Capsules

May 21, 2024

SAN DIEGO, May 21, 2024 /PRNewswire/ -- [Neurocrine Biosciences, Inc.](#) (Nasdaq: NBIX) today announced the publication of data from a post hoc analysis of the Phase 3 KINECT®-4 study of INGREZZA® (valbenazine) capsules in the [Journal of Clinical Psychopharmacology](#). The analysis assessed long-term outcomes relevant to the real-world management of tardive dyskinesia (TD) and demonstrated that nearly all study participants met the threshold for clinically meaningful improvements in TD symptom severity by Week 48.



"TD is a persistent, debilitating disorder requiring continuous treatment to effectively and sustainably improve symptoms over time," said Eiry W. Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences. "This post hoc analysis, along with previous long-term analyses, demonstrate the reliable, long-term efficacy and tolerability of one-capsule, once-daily INGREZZA to help inform use of this treatment in clinical practice."

The KINECT-4 study implemented an open-label design and on-site assessments of TD severity. The analysis included 103 participants from the Phase 3 KINECT-4 study who completed 48 weeks of treatment with INGREZZA. KINECT-4 was designed to be representative of clinical practice to provide insight into real-world management of TD with INGREZZA.

Key highlights include:

- At Week 4, 55% of participants experienced clinically meaningful improvement in TD symptom severity on the lowest starting dose (40 mg). A clinically meaningful improvement was defined as a reduction of at least 2 points in the Abnormal Involuntary Movement Scale (AIMS) total score used to assess the severity of involuntary movements in different body regions. Ninety-five percent of participants reached this threshold as soon as Week 24, with 97% achieving it by Week 48. TD improvement was sustained throughout treatment, with an AIMS mean total score reduction from baseline to Week 48 of 10.5.
- Eighty-six percent of participants met the response threshold of at least 50% AIMS improvement, and 52% met the higher threshold of at least 70% AIMS improvement at Week 48.
- More than 88% of patients and healthcare professionals rated participants' symptoms as "much improved" or "very much improved" at Week 48, as measured by the Patient Global Impression of Change and Clinical Global Impression of Change-TD, respectively.

Overall, INGREZZA was generally well tolerated. The most common treatment emergent adverse events reported from Weeks 4 to 48 included urinary tract infection (8.5%) and headache (5.2%).

### 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 (TEAEs) 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 (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 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 severe and are often persistent and irreversible. TD is estimated to affect approximately 600,000 people in the United States.

### **About INGREZZA® (valbenazine) Capsules**

INGREZZA is the only one-capsule, once-daily 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).

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 selectively 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. Additionally, INGREZZA can be taken as one capsule, once daily together with most psychiatric medications such as antipsychotics or antidepressants. INGREZZA dosages approved for use are 40 mg, 60 mg and 80 mg capsules. INGREZZA is not approved in any other dosage form.

### **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**

**VMAT2 inhibitors, including INGREZZA and 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](http://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](http://neurocrine.com), and follow the company on [LinkedIn](#), [X \(formerly Twitter\)](#) and [Facebook](#). (\*in collaboration with AbbVie)

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#### **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. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are: risks and uncertainties associated with Neurocrine Biosciences' business and finances in general, as well as risks and uncertainties associated with the commercialization of INGREZZA; risks that clinical trial activities may not be predictive of real-world results or of results in subsequent clinical trials; risks that INGREZZA may be precluded from commercialization by the proprietary rights of third parties, or have unintended side effects or adverse reactions; risks and uncertainties relating to competitive products and technological changes that may limit demand for INGREZZA; risks associated with our dependence on third parties for development and manufacturing activities related to INGREZZA and our product candidates, and our ability to manage these third parties; risks that the FDA or other regulatory authorities may make adverse decisions regarding our products or product candidates; risks that our products, and/or 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; risks associated with potential generic entrants for our products; 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, 2024. Neurocrine Biosciences disclaims any obligation to update the statements contained in this press release after the date hereof.

#### **Reference:**

1. Correll CU, Citrome L, Singer C, Lindenmayer JP, Zinger C, Liang G, Dunayevich E, Marder SR. Sustained treatment response and global improvements with long-term valbenazine in patients with tardive dyskinesia. *J Clin Psychopharmacology*. May 20, 2024. doi:10.1097/JCP.0000000000001860

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