Neurocrine Biosciences Presents Breadth of Data Demonstrating Holistic Improvements Over Time in Patients With Tardive Dyskinesia Following Treatment With INGREZZA® (valbenazine) Capsules

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- Findings Presented at the 2024 Psych Congress Include Data From More Than 300 Patients

SAN DIEGO, Nov. 4, 2024 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) presented data from more than 300 patients diagnosed with tardive dyskinesia and treated with INGREZZA® (valbenazine) capsules. These data showed significant improvements in functional, social, emotional and health-related quality of life measures in Phase 3 and 4 studies and improvements in functional, social, independence, emotional and physical aspects of patients' lives and antipsychotic adherence in real-world practice. This research was shared at the 2024 Psych Congress in Boston.

"Tardive dyskinesia can have a profound impact on patients that extends well beyond the physical symptoms caused by the movement disorder, affecting functional, social and emotional aspects of everyday life," said Eiry W. Roberts, M.D., Chief Medical Officer, Neurocrine Biosciences. "These data, taken together across clinical studies and real-world patient charts, are one of the largest efforts to examine and characterize the overall impact of treating tardive dyskinesia with INGREZZA and show significant improvements in measures that are important to patients and clinicians."

Impact of INGREZZA on Function, Socialization and Emotionality in Phase 3 Studies

This analysis (Poster #28) was conducted using combined data from 252 patients (n=71 placebo; n=181 INGREZZA) who completed the Phase 3 KINECT®-3 or KINECT®-4 studies. The 11-item Tardive Dyskinesia Impact Scale (TDIS), a validated patient-reported outcome measure, was used to evaluate tardive dyskinesia (TD) symptom impact at baseline through Week 48. TDIS scores range from 0 to 4 for each item, with higher scores indicating greater impact and decreases in scores indicating improvement.

Results showed consistent improvements across all items, suggesting treatment with INGREZZA improved TDIS scores for both physical and socio-emotional domains.

- The most impacted items at baseline were self-consciousness (mean score: 1.99), embarrassment (1.89), mouth noises (1.80), unwanted attention (1.74) and writing (1.29).
- Improvements of 1 point or more from baseline to Week 48 were observed in self-consciousness (mean change -1.24), embarrassment (-1.19) and mouth noises (-1.05).
- Unwanted attention (-1.00) and writing (-0.78) also improved considerably.

Impact of INGREZZA on Health-Related Quality of Life in Phase 4 Study

This analysis (Poster #27) was conducted using data from 127 patients who participated in a double-blind, placebo-controlled, randomized withdrawal Phase 4 study. Following an 8-week treatment period, patients were randomly assigned INGREZZA or placebo for an additional 8 weeks. INGREZZA was then withdrawn for a 4-week washout period. Health-related quality of life (HRQOL) was measured using the EQ-5D-5L, which includes 5 dimensions of health status (mobility, self-care, usual activities, pain/discomfort and anxiety/depression) each scored as: no problems (1); slight problems (2); moderate problems (3); severe problems (4); unable to/extreme problems (5). Lower scores indicate an improvement in health status. A utility index (UI), ranging from 0 to 1, and visual analog scale (VAS), ranging from 0 to 100, were also reported with higher scores indicating better health status.

At the end of the treatment period (Week 16, n = 56), scores for each dimension and UI and VAS scores improved significantly, while scores returned to or were near baseline after the washout period (Week 20):

Measure	Baseline Score	Week 16 Score
Dimensions		
Mobility	1.91	1.57
Self-care	1.69	1.34
Usual activities	1.98	1.59
Pain/discomfort	2.15	1.70
Anxiety/depression	2.03	1.80
UI	0.68	0.80
VAS	73.82	79.57

Real-World Functional, Social, Independence, Emotional, Physical and Antipsychotic Adherence Improvements With INGREZZA

A web-based survey and chart extraction (Poster #29) was conducted among U.S. physicians, nurse practitioners and physician assistants. Participants characterized the burden of diagnosed TD and improvement following at least two months of treatment with INGREZZA with at least one follow-up visit. This interim analysis included 78 clinicians caring for 164 patients. Most patients (82.9%) had mild to moderate TD severity, while 12.2% had severe TD.

At the time of the survey, nearly all patients (93.9%) had experienced TD improvement after starting INGREZZA, irrespective of TD severity.

- TD had an impact on functional ability in 95.1% of patients, with the most commonly impacted areas being emotionality, socialization, activities of daily living and mouth/throat function.
- Among those impacted (n = 156), 94.2% improved in overall functional status.
- 87.8% of all patients experienced improvement in independence.
- For those with available information on antipsychotic adherence (n = 115), more than half (52.2%) experienced improved adherence.

Additional Neurocrine Biosciences posters presented at Psych Congress 2024 include:

- Remission of Tardive Dyskinesia in Patients Receiving Long-Term Valbenazine Treatment (Poster #98)
- Once-Daily Valbenazine for Tardive Dyskinesia or Huntington's Disease Chorea in Patients with Dysphagia or Swallowing Difficulties (Poster #114)
- A Multi-Year Survey on United States Psychiatry Clinicians: Trends on Managing Patients with Tardive Dyskinesia (Poster #48)
- 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 #44)

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 1 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 1 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 six in the 80 mg once-daily dosing group compared to placebo as assessed by expert central blinded video raters. The mean change from baseline to week six in the AIMS rating was -3.2 for the 80 mg once-daily group as compared to -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 (≥ five percent 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 (TEAEs) 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 (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 800,000 people in the U.S.

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 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 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; risks that clinical trial activities may not be predictive of real-world results or of results in subsequent clinical trials; 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, manufacturing, and commercialization 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 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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