Neurocrine Biosciences Presents INGREZZA® (valbenazine) Capsules Data on Tardive Dyskinesia Improvement Regardless of Baseline Antipsychotic Use at 2023 Psych Congress Elevate

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SAN DIEGO, June 2, 2023 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) today presented findings from a meta-analysis of three long-term studies evaluating INGREZZA® (valbenazine) capsules that demonstrated substantial and sustained improvements in tardive dyskinesia (TD) in adults with or without concomitant antipsychotic therapy. The data (Poster #4) were presented at 2023 Psych Congress Elevate in Las Vegas.

The analysis of the three studies (KINECT™ 3, KINECT™ 4, and J-KINECT™) demonstrated that treatment with once-daily INGREZZA (40 mg or 80 mg) resulted in substantial and sustained TD improvement through week 48 as measured by the Abnormal Involuntary Movement Scale (AIMS) total score, with no meaningful differences between study completers taking antipsychotics at baseline (AP+) and those who were not (AP-).

Upon withdrawal of INGREZZA, both subgroups experienced a return toward baseline severity of TD symptoms, demonstrating the potentially persistent nature of TD, even in patients no longer taking antipsychotic therapy. Researchers concluded that continuous treatment with INGREZZA to manage TD may be warranted irrespective if they were on concurrent antipsychotic therapy.

"TD may persist even after patients are no longer taking antipsychotic therapy," said Eiry W. Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences. "These data from three long-term studies reinforce the continuing value of INGREZZA in TD management, regardless of antipsychotic status."

Key results from the meta-analysis demonstrated the following:

- Mean baseline AIMS scores within each study ranged from 7.9 to 14.9 in the subgroup taking antipsychotics at baseline (AP+) and from 10.9 to 14.5 in the subgroup not taking antipsychotics at baseline (AP-)
- Mean changes from baseline in AIMS total scores within the combined group were similar between the AP+ and AP- subgroups and indicated substantial TD improvements with INGREZZA 40 mg and 80 mg at week 48 (AP+, -6.1; AP-, -6.5)
- Both AP+ and AP- subgroups within the combined group experienced a return toward baseline severity at week 52, four weeks after INGREZZA 40 mg or 80 mg withdrawal (AP+, -2.1; AP-, -1.4)

Additional presentations include:

- Global Improvements and Psychiatric Stability in Adults With Tardive Dyskinesia and Mood Disorder: Post Hoc Analyses of Two Long-Term Valbenazine Studies (Poster #3)

The full abstracts presented by Neurocrine Biosciences at 2023 Psych Congress Elevate are available on the meeting website and can be accessed by registering.

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 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 four, TEAEs that occurred in ≥5 percent of all participants (combined dose groups) were urinary tract infection (8.5 percent) and headache (5.2 percent). Changes from baseline in psychiatric stability, vital signs, electrocardiogram parameters and laboratory test values were generally small and not clinically significant.

About J-KINECT ™ Phase 2 and 3 Studies
In 2015, Mitsubishi Tanabe Pharma Corporation (MTPC) exclusively licensed the development and commercialization rights for valbenazine in Japan and certain other Asian countries with Neurocrine Biosciences. MTPC conducted J-KINECT, the Phase 2/3, multicenter, randomized, double-blind, placebo-controlled study to confirm the efficacy and safety of valbenazine 40 mg or 80 mg administered once daily for up to 48 weeks in adult patients with moderate or severe tardive dyskinesia (TD). The study showed a significant improvement in the primary efficacy endpoint of the mean change from baseline in the Abnormal Involuntary Movement Rating Scale (AIMS) total score at week 6 of treatment with valbenazine compared to placebo. The persistence of efficacy was also shown in the AIMS total score at week 48. In addition, valbenazine was also well tolerated. The incidence of adverse events was highest in the 80 mg group and included nasopharyngitis, somnolence, schizophrenia worsening, hypersalivation, insomnia and tremor. In 2021, MTPC received approval of valbenazine capsules 40mg for the treatment of TD in Singapore, Thailand, South Korea, and Indonesia, followed by approval in Japan and Malaysia in 2022.

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 (like 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 U.S.

About INGREZZA® (valbenazine) Capsules
INGREZZA, a selective vesicular monoamine transporter 2 (VMAT2) inhibitor, is an FDA-approved product indicated for the treatment of adults with tardive dyskinesia, a condition associated with uncontrollable, abnormal, and repetitive movements of the face, torso, and/or other body parts.

INGREZZA is thought to work by reducing the amount of dopamine released in a region of the brain that controls movement and motor function, helping to regulate nerve signaling in adults with tardive dyskinesia. VMAT2 is a protein in the brain that packages neurotransmitters, such as dopamine, for transport and release in presynaptic neurons. INGREZZA, developed by Neurocrine Biosciences, is novel in that it selectively inhibits VMAT2 with no appreciable binding affinity for VMAT1, dopaminergic (including D2), serotonergic, adrenergic, histaminergic, or muscarinic receptors. Additionally, INGREZZA can be taken for the treatment of tardive dyskinesia 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 Use

INGREZZA® (valbenazine) capsules is a prescription medicine used to treat adults with movements in the face, tongue, or other body parts that cannot be controlled (tardive dyskinesia).

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

IMPORTANT SAFETY INFORMATION

Do not take INGREZZA if you:

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

INGREZZA may cause serious side effects, including:

- **Sleepiness (somnolence).** Do not drive, operate heavy machinery, or do other dangerous activities until you know how INGREZZA affects you.
- **Heart rhythm problems (QT prolongation).** INGREZZA may cause a heart problem known as QT prolongation.

  Symptoms of QT prolongation may include:

  - fast, slow, or irregular heartbeat
  - shortness of breath
  - dizziness or fainting

  Tell your healthcare provider right away if you have a change in your heartbeat (a fast or irregular heartbeat), or if you faint.

- **Abnormal movements (Parkinson-like).** Symptoms include: shaking, body stiffness, trouble moving or walking, or keeping your balance.

Before taking INGREZZA, 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.

The most common side effect of INGREZZA is sleepiness (somnolence). Other side effects include changes in balance (balance problems, dizziness) or an increased risk of falls, headache, feelings of restlessness, dry mouth, constipation, and blurred vision.

These are not all of the possible side effects of INGREZZA. 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.

Please see accompanying INGREZZA full Product Information.

About Neurocrine Biosciences
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, Parkinson'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, 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 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, 2023. Neurocrine Biosciences disclaims any obligation to update the statements contained in this press release after the date hereof.

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