Intra-Cellular Therapies Highlights New CAPLYTA Bipolar Depression Data Presentations at the American College of Neuropsychopharmacology 61st Annual Meeting

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NEW YORK, Dec. 08, 2022 (GLOBE NEWSWIRE) -- Intra-Cellular Therapies, Inc. (Nasdaq: ITCI), a biopharmaceutical company focused on the development and commercialization of therapeutics for central nervous system (CNS) disorders, today announced four data presentations at the American College of Neuropsychopharmacology (ACNP) 61st Annual Meeting highlighting the therapeutic use of CAPLYTA for the treatment of bipolar I and II depression.

“At ACNP, we presented new analyses from our bipolar depression program which further support the efficacy and safety profile of lumateperone in both acute and long-term treatment across a broad patient population with bipolar I and bipolar II disorder as monotherapy and as adjunctive therapy,” said Dr. Suresh Durgam, Executive Vice President and Chief Medical Officer of Intra-Cellular Therapies.

Monday December 5:

Poster M78: “**Metabolic Profile of Lumateperone in Late-Phase Clinical Trials for the Treatment of Major Depressive Episodes Associated With Bipolar I or Bipolar II Disorder**”

This poster presents a comprehensive weight and metabolic analysis of more than 1,200 patients that participated in our lumateperone late-stage bipolar depression program: two 6-week monotherapy and one 6-week adjunctive therapy placebo-controlled studies and a 6-month open label extension (OLE) safety study. The results demonstrate that in patients with bipolar I or bipolar II disorder experiencing a major depressive episode (MDE), lumateperone 42-mg monotherapy or adjunctive therapy had a favorable cardiometabolic profile for both acute and long-term treatment.

The results confirm the favorable effects of lumateperone 42mg on body weight and morphology as demonstrated by minimal and similar to placebo mean changes from baseline in weight, BMI (kg/m2) and waist circumference in short-term studies and no increases seen in these parameters in the long-term OLE study.

In addition, potentially clinically significant (PCS) weight changes (defined as ≥7% change from baseline) were assessed. In the short-term studies, no patients treated with lumateperone had PCS weight gain during treatment and, in the long-term OLE study, PCS weight loss was more common than PCS weight gain (6.0% vs 3.4%).

Consistent with prior analyses, mean changes in key cardiometabolic parameters including fasting glucose, insulin, total cholesterol and triglycerides, were all similar to placebo. There were no clinically significant changes in these parameters in the long-term OLE study.

Poster V19: “**Efficacy of Lumateperone in Pooled Short-Term Late-Phase Clinical Trials for the Treatment of Major Depressive Episodes Associated With Bipolar II Disorder**”

This poster describes a pooled analysis of the efficacy of lumateperone 42 mg monotherapy and adjunctive therapy across three short-term, placebo-controlled Phase 3 studies (Studies 401, 404 and 402) in a subgroup of patients with depressive episodes associated with bipolar II disorder. The results demonstrate that in patients with bipolar II disorder experiencing a MDE, lumateperone 42-mg monotherapy or adjunctive therapy significantly improved symptoms of depression and disease severity compared with placebo.

In patients with bipolar II disorder, lumateperone 42 mg significantly improved the Montgomery-Asberg Depression Rating Scale (MADRS) total score from baseline to week 6 compared with placebo. A higher proportion of bipolar II patients on lumateperone had a treatment response (≥50% improvement in MADRS Total score from baseline) compared with placebo. Lumateperone significantly improved illness severity at week 6 as measured by the clinical global impression scales of severity (CGI-BP-S). Further, there was significant improvement on the Quality-of-Life Enjoyment and Satisfaction Questionnaire – Short Form as compared to placebo.

Poster V21: “**Evaluation of Mania and Hypomania in Late-Phase Clinical Trials of Lumateperone in the Treatment of Major Depressive Episodes Associated With Bipolar I or Bipolar II Disorder**”

When treating patients with bipolar depression, switching to mania/hypomania represent important treatment-emergent adverse events (TEAEs) to monitor. This poster presents analyses of measures of mania and hypomania across our short-term, placebo-controlled studies and long-term OLE study of lumateperone in patients with a MDE associated with bipolar I or bipolar II disorder. The poster highlights that the incidence of mania/hypomania events were similar between lumateperone 42 mg and placebo.

Across short-term trials, the incidence of mania/hypomania TEAEs were rare, and if occurred, were mild or moderate in severity and similar between lumateperone and placebo. These TEAEs were also rare and mild or moderate in severity in the long-term OLE study. There were no notable changes from baseline in mean Young Mania Rating Scale (YMRS) Total score in short-term, placebo-controlled studies and the long-term OLE study. Mean changes in CGI-BP-S Mania subscore were similar between lumateperone and placebo in short term trials and remained clinically stable throughout the long-term OLE study.

Wednesday December 7:

Poster W79: “**Lumateperone in the Treatment of Major Depressive Episodes Associated With Bipolar I or Bipolar II Disorder: Evaluation of**

Extrapyramidal and Motor Symptoms in Late-Phase Clinical Trials"

Lumateperone is a simultaneous modulator of serotonin, dopamine, and glutamate neurotransmission with low D2 receptor occupancy (39%) at the recommended dose of 42mg. Elevated levels of dopamine D2 occupancy are known to be associated with increases in extrapyramidal symptoms (EPS).

This poster describes the incidence of EPS across our short-term, placebo-controlled studies and long-term OLE study of lumateperone in patients with a MDE associated with bipolar I or bipolar II disorder. The incidence of EPS-related TEAEs was low and mild or moderate in severity across short-term trials and the long-term OLE study. The use of concomitant benztropine and propranolol was rare. There were no notable changes (no increases) from baseline in clinician-rated motor scale scores (BARS, AIMS, or SAS). The incidence of treatment-emergent parkinsonism and akathisia in the short-term, placebo-controlled studies was similar to placebo and was minimal in the OLE. In patients with bipolar I or bipolar II disorder experiencing a MDE, lumateperone 42-mg had a favorable EPS profile in both acute and long long-term treatment.

CAPLYTA® (lumateperone) is indicated in adults for the treatment of schizophrenia and depressive episodes associated with bipolar I or II disorder (bipolar depression) as monotherapy and as adjunctive therapy with lithium or valproate.

Important Safety Information

Boxed Warnings:

- **Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. CAPLYTA is not approved for the treatment of patients with dementia-related psychosis.**
- **Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adults in short-term studies. All antidepressant-treated patients should be closely monitored for clinical worsening, and for emergence of suicidal thoughts and behaviors. The safety and effectiveness of CAPLYTA have not been established in pediatric patients.**

Contraindications: CAPLYTA is contraindicated in patients with known hypersensitivity to lumateperone or any components of CAPLYTA. Reactions have included pruritus, rash (e.g., allergic dermatitis, papular rash, and generalized rash), and urticaria.

Warnings & Precautions: Antipsychotic drugs have been reported to cause:

- **Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis**, including stroke and transient ischemic attack. See Boxed Warning above.
- **Neuroleptic Malignant Syndrome (NMS)**, which is a potentially fatal reaction. Signs and symptoms include: high fever, stiff muscles, confusion, changes in breathing, heart rate, and blood pressure, elevated creatinine phosphokinase, myoglobinuria (and/or rhabdomyolysis), and acute renal failure. Patients who experience signs and symptoms of NMS should immediately contact their doctor or go to the emergency room.
- **Tardive Dyskinesia**, a syndrome of uncontrolled body movements in the face, tongue, or other body parts, which may increase with duration of treatment and total cumulative dose. TD may not go away, even if CAPLYTA is discontinued. It can also occur after CAPLYTA is discontinued.
- **Metabolic Changes**, including hyperglycemia, diabetes mellitus, dyslipidemia, and weight gain. Hyperglycemia, in some cases extreme and associated with ketoacidosis, hyperosmolar coma or death, has been reported in patients treated with antipsychotics. Measure weight and assess fasting plasma glucose and lipids when initiating CAPLYTA and monitor periodically during long-term treatment.
- **Leukopenia, Neutropenia, and Agranulocytosis (including fatal cases)**. Complete blood counts should be performed in patients with pre-existing low white blood cell count (WBC) or history of leukopenia or neutropenia. CAPLYTA should be discontinued if clinically significant decline in WBC occurs in absence of other causative factors.
- **Decreased Blood Pressure & Dizziness**. Patients may feel lightheaded, dizzy or faint when they rise too quickly from a sitting or lying position (orthostatic hypotension). Heart rate and blood pressure should be monitored and patients should be warned with known cardiovascular or cerebrovascular disease. Orthostatic vital signs should be monitored in patients who are vulnerable to hypotension.
- **Falls**. CAPLYTA may cause sleepiness or dizziness and can slow thinking and motor skills, which may lead to falls and, consequently, fractures and other injuries. Patients should be assessed for risk when using CAPLYTA.
- **Seizures**. CAPLYTA should be used cautiously in patients with a history of seizures or with conditions that lower seizure threshold.
- **Potential for Cognitive and Motor Impairment**. Patients should use caution when operating machinery or motor vehicles until they know how CAPLYTA affects them.
- **Body Temperature Dysregulation**. CAPLYTA should be used with caution in patients who may experience conditions that may increase core body temperature such as strenuous exercise, extreme heat, dehydration, or concomitant anticholinergics.
- **Dysphagia**. CAPLYTA should be used with caution in patients at risk for aspiration.

Drug Interactions: CAPLYTA should not be used with CYP3A4 inducers. Dose reduction is recommended for concomitant use with strong CYP3A4 inhibitors or moderate CYP3A4 inhibitors.

Special Populations: Newborn infants exposed to antipsychotic drugs during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. Breastfeeding is not recommended. Dose reduction is recommended for patients with moderate or severe hepatic impairment.

Adverse Reactions: The most common adverse reactions in clinical trials with CAPLYTA vs. placebo were somnolence/sedation, dizziness, nausea, and dry mouth.

Please click here to see full Prescribing Information including **Boxed Warning**.

About CAPLYTA (lumateperone)

CAPLYTA 42 mg is an oral, once daily atypical antipsychotic approved in adults for the treatment of schizophrenia and depressive episodes associated with bipolar I or II disorder (bipolar depression) as monotherapy and as adjunctive therapy with lithium or valproate. While the mechanism of action of CAPLYTA is unknown, the efficacy of CAPLYTA could be mediated through a combination of antagonist activity at central serotonin 5-HT2A receptors and postsynaptic antagonist activity at central dopamine D2 receptors.

Lumateperone is being studied for the treatment of major depressive disorder, and other neuropsychiatric and neurological disorders. Lumateperone is not FDA-approved for these disorders.

About Intra-Cellular Therapies

Intra-Cellular Therapies is a biopharmaceutical company founded on Nobel prize-winning research that allows us to understand how therapies affect the inner-workings of cells in the body. The company leverages this intracellular approach to develop innovative treatments for people living with complex psychiatric and neurologic diseases. For more information, please visit www.intracellulartherapies.com.

Forward-Looking Statements

This news release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995 that involve risks and uncertainties that could cause actual results to be materially different from historical results or from any future results expressed or implied by such forward-looking statements. Such forward-looking statements include statements regarding, among other things, whether clinical trial results will be predictive of future real-world results; our beliefs about the potential utility of our product candidates; and development efforts and plans under the caption “About Intra-Cellular Therapies.” All such forward-looking statements are based on management's present expectations and are subject to certain factors, risks and uncertainties that may cause actual results, outcome of events, timing and performance to differ materially from those expressed or implied by such statements. These risks and uncertainties include, but are not limited to, the following: there are no guarantees that CAPLYTA will be commercially successful; we may encounter issues, delays or other challenges in commercializing CAPLYTA; the COVID-19 pandemic may negatively impact our commercial plans and sales for CAPLYTA; the COVID-19 pandemic may negatively impact the conduct of, and the timing of enrollment, completion and reporting with respect to, our clinical trials; whether CAPLYTA receives adequate reimbursement from third-party payors; the degree to which CAPLYTA receives acceptance from patients and physicians for its approved indications; challenges associated with execution of our sales activities, which in each case could limit the potential of our product; results achieved in CAPLYTA in the treatment of schizophrenia and bipolar depression following commercial launch of the product may be different than observed in clinical trials, and may vary among patients; any other impacts on our business as a result of or related to the COVID-19 pandemic; challenges associated with supply and manufacturing activities, which in each case could limit our sales and the availability of our product; impacts on our business, including on the commercialization of CAPLYTA and our clinical trials, as a result of the conflict in Ukraine; risks associated with our current and planned clinical trials; we may encounter unexpected safety or tolerability issues with CAPLYTA following commercial launch for the treatment of schizophrenia or bipolar depression or in ongoing or future trials and other development activities; our other product candidates may not be successful or may take longer and be more costly than anticipated; product candidates that appeared promising in earlier research and clinical trials may not demonstrate safety and/or efficacy in larger-scale or later clinical trials or in clinical trials for other indications; our proposals with respect to the regulatory path for our product candidates may not be acceptable to the FDA; our reliance on collaborative partners and other third parties for development of our product candidates; and the other risk factors detailed in our public filings with the Securities and Exchange Commission. All statements contained in this press release are made only as of the date of this press release, and we do not intend to update this information unless required by law.

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