Intra-Cellular Therapies Presents Data from the CAPLYTA Adjunctive MDD Phase 3 Program at the American College of Neuropsychopharmacology Annual Meeting

December 11, 2024

Presentations complement topline data with new data from two pivotal studies (Studies 501 and 502) evaluating lumateperone as an adjunctive therapy for the treatment of major depressive disorder

Data shows robust remission and response efficacy rates in patients taking CAPLYTA

Robust improvements in anxiety symptoms were also observed in patients taking CAPLYTA as measured by the Generalized Anxiety Disorder Questionnaire (GAD-7)

Pooled safety and tolerability data from Studies 501 and 502 show favorable safety and tolerability profile for CAPLYTA consistent with prior studies

A post-hoc analysis from Study 403 in mixed features shows CAPLYTA significantly improved anhedonia symptoms as measured by the MADRS anhedonia factor score

BEDMINSTER, N.J., Dec. 11, 2024 (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 presentations at the 63rd Annual Meeting of the American College of Neuropsychopharmacology (ACNP) which included new efficacy, safety, and tolerability analyses from its CAPLYTA adjunctive major depressive disorder (MDD) pivotal program.

“We have previously shared positive results from Studies 501 and 502 demonstrating a robust clinical profile of CAPLYTA as an adjunctive treatment in MDD with strong efficacy results in the Montgomery Asberg Depression Rating Scale (MADRS) total score, the Clinical Global Impression Scale for Severity of Illness (CGI-S) and the Quick Inventory of Depressive Symptomatology Self-Report (QIDS-SR-16) scale. We are excited to share new data that further characterize CAPLYTA’s robust efficacy and favorable safety and tolerability profile,” said Dr. Suresh Durgam, Executive Vice President and Chief Medical Officer of Intra-Cellular Therapies. “In addition, the improvements in anhedonia symptoms observed in Study 403 further contribute to enriching CAPLYTA’s profile in the treatment of MDD and bipolar depression.”

Details of the presentations are as follows:

Poster T126 “Lumateperone as Adjunctive Therapy in Patients with Major Depressive Disorder: Results from a Randomized, Double-blind, Phase 3 Trial,” Tuesday, December 10

Poster W85 “Adjunctive Lumateperone in Patients With Major Depressive Disorder: Results From an Additional Randomized, Double-Blind, Phase 3 Trial,” Wednesday, December 11

These poster presentations highlight the efficacy of lumateperone 42mg adjunctive to anti-depressant therapy (ADT) shown in two similarly designed trials (Studies 501 and 502). In these studies, lumateperone 42 mg demonstrated significant and clinically meaningful efficacy over placebo, improving depressive symptoms and disease severity. Lumateperone plus ADT improved depression as measured by both clinician-rated and patient-reported outcomes (MADRS total score, CGI-S score, and QIDS-SR-16 total score). Subject to FDA approval, we believe these results demonstrate lumateperone represents a promising new treatment option for adults with MDD with inadequate response to prior ADT.

In both studies, MADRS response and remission rates were significantly greater with lumateperone compared to placebo. Specifically, in Study 501 the response rates for CAPLYTA were 45.6% vs. 24.0% for placebo ($p<0.0001$) and remission rates were 25.9% vs. 13.6% for placebo ($p<0.001$). In Study 502 the response rates for CAPLYTA were 40.1% vs. 25.3% for placebo ($p<0.01$) and remission rates were 25.0% vs. 13.5% for placebo ($p<0.01$).

In Study 501 anxiety symptoms were measured using the GAD-7 scale. Lumateperone plus ADT significantly improved self-reported anxiety symptoms, as measured by the GAD-7 total score, compared with placebo from baseline to Day 43 (Cohen’s d effect size (ES): 0.43; $p<0.0001$).

Poster W84 “Safety and Tolerability of Lumateperone 42 mg for the Treatment of Major Depressive Disorder: A Pooled Analysis of 2 Randomized Placebo-Controlled Trials,” Wednesday, December 11

A pooled analysis of Studies 501 and 502 demonstrates the safety and tolerability of lumateperone 42 mg plus ADT in patients with MDD who had inadequate response to ADT.

The most common adverse reactions in the lumateperone group (defined as ≥5% of patients and at more than twice the rate of placebo) were dizziness, dry mouth, somnolence, nausea, and fatigue.

In Studies 501 and 502 changes in cardiometabolic parameters, prolactin levels and body morphology with lumateperone were similar to placebo. The risk of extrapyramidal symptoms and motor symptoms with lumateperone was low.

Poster W88 “Lumateperone Treatment for Major Depressive Episodes With Mixed Features in Major Depressive Disorder and Bipolar I or Bipolar II Disorder: A Post Hoc Analysis of Anhedonia,” Wednesday, December 11

The poster reports on a post-hoc analysis from Study 403 evaluating the efficacy of lumateperone 42mg monotherapy in improving the anhedonia factor score in patients with MDD or bipolar depression with mixed features. The results from this analysis support lumateperone to treat the broad range of anhedonia symptoms of a major depressive episode in these patient populations.

Anhedonia, which is diminished interest or pleasure, occurs in approximately 70% of patients with MDD and approximately 50% of patients with bipolar depression. Heightened levels of anhedonia in mood disorders are associated with more severe and recurrent depressive illness, a greater risk of suicidal ideation, and poorer treatment response compared with lower levels of anhedonia.

Lumateperone significantly improved the MADRS anhedonia factor score from baseline to Day 43 compared with placebo in the combined MDD/bipolar depression population with mixed features (least squares mean difference (LSMD)= -3.4; ES= 0.63; p<0.0001) as well as both individual populations of patients with MDD with mixed features (LSMD= -3.4; ES= 0.63; p<0.0001) and bipolar depression with mixed features (LSMD= -3.3; ES= 0.61; p<0.0001).

CAPLYTA® (lumateperone) is indicated in adults for the treatment of schizophrenia and for the treatment of 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. 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.

CAPLYTA is available in 10.5 mg, 21 mg, and 42 mg capsules.

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 the treatment of 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 psychiatric 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, the potential approval of CAPLYTA (lumateperone) for the treatment of major depressive disorder as adjunctive therapy; our expectations regarding the commercialization of CAPLYTA; our plans to conduct clinical or non-clinical trials and the timing of developments with respect to those trials, including enrollment, initiation or completion of clinical conduct, or the availability or reporting of results; plans to make regulatory submissions to the FDA and the timing of such submissions and any product approvals; whether clinical trial results will be predictive of future real-world results; whether CAPLYTA will serve an unmet need; the goals of our development programs; 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; 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; challenges associated with supply and manufacturing activities, which in each case could limit our sales and the availability of our product; 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; there is no guarantee that a generic equivalent of CAPLYTA will not be approved and enter the market before the expiration of our patents; there is no guarantee that our supplemental New Drug Application (sNDA) for the treatment of MDD will be approved, if at all, on the timeline that we expect; 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; impacts on our business, including on the commercialization of CAPLYTA and our clinical trials, as a result of the COVID-19 pandemic, the conflicts in Ukraine, Russia and the Middle East, global economic uncertainty, inflation, higher interest rates or market disruptions; 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.

Contact:

Intra-Cellular Therapies, Inc.
Juan Sanchez, M.D.
Vice President, Corporate Communications and Investor Relations
646-440-9333

Burns McClellan, Inc.
Cameron Radinovic
cradinovic@burnsmc.com
646-930-4406

Source: Intra-Cellular Therapies, Inc.