Intra-Cellular Therapies Announces Presentations at the 2024 European College of Neuropsychopharmacology Congress

September 23, 2024

Oral and poster presentations of results from Study 501 evaluating lumateperone 42 mg as an adjunctive therapy to antidepressants for the treatment of major depressive disorder (MDD)

Poster presentations of post-hoc analyses from Study 403 including the prespecified patient population with MDD or bipolar depression with mixed features who also had anxious distress

NEW YORK, Sept. 23, 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 of lumateperone including the results from Phase 3 adjunctive Major Depressive Disorder (MDD), Study 501 at the 37th European College of Neuropsychopharmacology (ECNP) Congress being held September 21 - 24, 2024 in Milan, Italy.

“We are very pleased to present additional lumateperone data across depressive disorders including remarkable positive results from Study 501 evaluating lumateperone 42 mg as an adjunctive therapy to antidepressants for the treatment of MDD at ECNP. The robust efficacy demonstrated by lumateperone, coupled with its favorable safety and tolerability profile, position CAPLYTA to become an important medicine for the treatment of MDD,” said Dr. Suresh Durgam, Executive Vice President and Chief Medical Officer of Intra-Cellular Therapies. “We are on track to submit our lumateperone sNDA for the adjunctive treatment of MDD including the results of Studies 501 and 502 later this year.”

Details of the presentations are as follows:

Study 501 Presentations

Oral presentation: “Adjunctive Lumateperone Significantly Improves Symptoms of Major Depressive Disorder: Topline Results From a Randomised, Double-Blind, Placebo-Controlled Phase 3 Trial.” Monday, September 23, 15:00 - 16:20 CEST.

P2127: “Lumateperone as Adjunctive Therapy in Patients With Major Depressive Disorder: Results From a Randomised, Double-blind, Phase 3 Trial.” Monday, September 23 12:35 - 14:00 CEST.

Study 403 Presentations

P2113: “Lumateperone in the Treatment of Patients With Major Depressive Disorder and Bipolar Disorder With Anxious Distress and Mixed Features.” Monday, September 23 12:35 - 14:00 CEST.

P2096: “Lumateperone in the Treatment of Major Depressive Disorder and Bipolar Depression With Mixed Features: Efficacy Across Symptoms.” Monday, September 23 12:35 - 14:00 CEST.

In Study 501, lumateperone met the primary endpoint of change from baseline at Week 6 on the Montgomery Asberg Depression Rating Scale (MADRS) total score versus placebo with a 4.9-point reduction ($p<0.0001$; Cohen’s d effect size (ES)= 0.61). Statistically significant reductions in depressive symptoms as measured by the MADRS were seen at the earliest time point tested, Week 1, and these improvements continued throughout the course of the trial. Lumateperone also met the key secondary endpoint of change from baseline on the clinician-rated Clinical Global Impression Scale for Severity of Illness (CGI-S) ($p < 0.0001$; ES: 0.67).

On a patient-reported measure, the Quick Inventory of Depressive Symptomatology Self Report scale (QIDS), patients reported robust reduction in their depressive symptoms ($p <0.0001$). Adverse events were similar to those seen in prior studies of lumateperone as a treatment for bipolar depression and schizophrenia. Mean changes in key metabolic parameters including glucose, insulin, triglycerides, and total, LDL and HDL cholesterol were similar between lumateperone and placebo. Importantly, mean changes in weight were also similar to placebo.

In an additional, similarly-designed trial, Study 502, lumateperone 42 mg plus an antidepressant met primary and key secondary efficacy endpoints (MADRS Total Score [LSMD vs placebo=−4.5; ES= 0.56; $P<0.0001$] and CGI-S score [LSMD vs placebo=−0.5; ES= 0.51; $P<0.0001$]) and was generally safe and well tolerated in patients with MDD with inadequate antidepressant response. Details of Study 502 will be presented at upcoming conferences.

Study 403 presentations highlight important analyses of lumateperone’s double-blind placebo-controlled study in patients with either MDD or bipolar depression exhibiting mixed features.

Poster #2113 presents a post-hoc analysis of Study 403 evaluating lumateperone’s efficacy in the prespecified patient population with MDD or bipolar depression with mixed features who also met the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) criteria for anxious distress.

In this analysis, lumateperone significantly improved depression symptoms and severity (MADRS Total score and CGI-S score) compared with placebo. Lumateperone also significantly improved MADRS inner tension single-item score in patients with co-morbid anxious distress. Both anxious distress and mixed features are specified in the DSM-5 and are common in patients with major depressive episodes associated with MDD and bipolar

disorder. Patients with these specifiers have more severe symptoms, more comorbidities, increased suicide risk, and/or poorer treatment response than patients without these specifiers.

Poster #2096 presents a post-hoc analysis of Study 403 individual MADRS items. Treatment with lumateperone significantly improved a broad range of depression symptoms across individual MADRS items.

About Major Depressive Disorder

Major Depressive Disorder (MDD) is a common mood disorder in the U.S. affecting an estimated 21 million adults each year. Depressive disorders are the number two cause of years lived with disability in the world. Symptoms include sadness, hopelessness, helplessness, feelings of guilt, irritability, loss of interest in formerly pleasurable activities, cognitive impairment, disturbed sleep patterns, and suicide ideation or behavior. MDD can cause severe functional impairment, adversely affecting interpersonal relationships, and may impact quality of life. Approximately two-thirds of patients with depression fail to achieve remission with first-line treatment.

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, 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; 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 planned sNDA for the treatment of MDD will be submitted or 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.