Intra-Cellular Therapies Highlights Lumateperone Bipolar Depression Data Presentations at the 2022 International Society for Bipolar Disorders (ISBD) Experience

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NEW YORK, June 13, 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 data presentations at the 2022 International Society for Bipolar Disorders (ISBD) Experience held virtually June 10-12, 2022.

Three posters were presented on Saturday June 11, 2022 during the “In the Spotlight: Live Posters 2” session:

Oral Poster titled “Lumateperone (ITI-007) in the Treatment of Bipolar Depression: Efficacy Across Symptoms”

Oral Poster titled “Effect of Lumateperone (ITI-007) on Quality of Life and Functional Disability in the Treatment of Bipolar Depression”

Oral Poster titled “Metabolic Syndrome in Bipolar Depression with Lumateperone (ITI-007): A Post Hoc Analysis of 2 Randomized, Placebo-Controlled Trials”

“At ISBD, we shared additional analyses from our lumateperone bipolar depression program including findings consistent with broad antidepressant effects, marked improvements in patients’ daily functioning, and further evidence of a favorable metabolic profile. We are very pleased with the feedback we receive from the scientific and medical community about the efficacy and safety profile of CAPLYTA,” said Dr. Suresh Durgam, Executive Vice President and Chief Medical Officer of Intra-Cellular Therapies.

Lumateperone (ITI-007) in the Treatment of Bipolar Depression: Efficacy Across Symptoms

This poster presents additional analysis from Study 404[1]. This Phase 3 study established the efficacy and safety of lumateperone 42 mg monotherapy in patients with bipolar I or bipolar II depression. In this study, lumateperone 42 mg met the primary endpoint for improvement in depression as measured by change from baseline versus placebo on the Montgomery-Åsberg Depression Rating (MADRS) total score ($p<0.0001$). Statistically significant greater MADRS improvement compared with placebo was found for lumateperone in patients with both bipolar I ($p<0.0001$) and bipolar II disorder ($p<0.001$). Lumateperone 42 mg also met the key secondary endpoint, the CGI-BP-S Total Score ($p<0.0001$).

This poster describes a post-hoc analysis of this study evaluating the shift in severity of depression symptoms as assessed by the MADRS single-item scores. Lumateperone 42 mg treatment compared to placebo significantly improved ($p<0.05$ to <0.0001) each of the 10 MADRS symptom items at day 43. Data presented also included the categorical shift in severity of these MADRS single-item scores showing a higher percentage of lumateperone patients than placebo patients shifting from severe to moderate/mild or no illness.

About the Montgomery-Åsberg Depression Rating Scale (MADRS)

The MADRS is a 10-item, validated rating scale used to diagnose and rate the severity of depressive episodes and is an accepted regulatory endpoint in clinical trials of depression.

The scale includes questions on the following items: 1. Apparent sadness; 2. Reported sadness; 3. Inner tension; 4. Reduced sleep; 5. Reduced appetite; 6. Concentration difficulties; 7. Lassitude; 8. Inability to feel; 9. Pessimistic thoughts; and 10. Suicidal thoughts. Each item can be scored 0 (no abnormality) to 6 (severe) with the potential overall score ranging from 0 to 60.

Effect of Lumateperone (ITI-007) on Quality of Life and Functional Disability in the Treatment of Bipolar Depression

This poster expands upon published data which highlights the effects of lumateperone on quality-of-life secondary endpoint in Study 404, a Phase 3 clinical trial evaluating lumateperone as monotherapy for the treatment of patients with Bipolar I or Bipolar II disorder experiencing a major depressive episode (bipolar depression). In this Study, lumateperone 42 mg met both primary and key secondary endpoints and these results were published in The American Journal of Psychiatry[2].

The analysis presented at ISBD investigated lumateperone’s improvements in functional disability and quality of life as measured by the prespecified secondary outcome measure, the Quality-of-Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-Q-SF)[2]. Results showed lumateperone 42 mg treatment resulted in a mean 10.1-point improvement from baseline in the Q-LES-Q-SF Total score to Day 43 while placebo showed a 7.3-point improvement (ES; 0.36; $p= 0.0012$, nominal).

This poster also described a post-hoc analysis of the individual items of the Q-LES-Q-SF. Significant improvement was seen in 8 of 14 items of the Q-LES-Q-SF at Day 43 and all items improved numerically. There were marked improvements ($p<0.01$ to <0.05, nominal) in items representing the ability to function in daily life, family relationships, social relationships, household activities, leisure time activities, sexual drive, mood, and overall sense of well-being.

About the Quality-of-Life Enjoyment and Satisfaction Questionnaire-Short Form (Q-LES-Q-SF)

The Q-LES-Q-SF is a well-established and validated self-administered questionnaire designed to measure a patient’s satisfaction and enjoyment in different areas of daily functioning. Each question is rated from 1 (Very Poor) to 5 (Very Good). The raw total score ranges from 14 to a maximum of 70. Scores are added together and reported as percentage of the maximum possible score.

Metabolic Syndrome in Bipolar Depression with Lumateperone (ITI-007): A Post Hoc Analysis of 2 Randomized, Placebo-Controlled Trials
This poster describes a pooled analysis of Studies 404 and 401 comparing the incidence of and shifts in metabolic syndrome (MetSy) with lumateperone 42 mg as monotherapy and placebo in the treatment of bipolar depression in patients with bipolar I and bipolar II disorder. In this pooled analysis, the rates of MetSy were similar between lumateperone and placebo at baseline and remained stable at end of treatment (6 weeks) for both groups. More patients who received lumateperone compared with placebo improved from having MetSy at baseline to no longer meeting MetSy criteria at end of treatment.

In our clinical trials, CAPLYTA has consistently shown a favorable safety profile with changes in weight, fasting glucose, total cholesterol, and triglycerides similar to placebo. In our longer-term open label studies, patients with bipolar depression were stable with respect to weight with no weight gain from baseline at 6-months, while patients with schizophrenia lost an average of about 7 pounds at one year. The pooled analysis presented at ISBD further highlight the favorable placebo-like metabolic profile of lumateperone 42mg.

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. CAPLYTA is available in 42 mg capsules.

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 (10.5 mg) or moderate CYP3A4 inhibitors (21 mg).

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 (21 mg).

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, our expectations regarding the commercialization of CAPLYTA; 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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[1]*Calebrese JR, et al. Efficacy and Safety of Lumateperone for Major Depressive Episodes Associated With Bipolar I or Bipolar II Disorder: A Phase 3 Randomized Placebo-Controlled Trial.: Am Journal Psychiatry; Am J Psychiatry. 2021 Dec;178(12):1098-1106. doi: 10.1176/appi.ajp.2021.20091339.*

[2]*Endicott J, Nee J, Harrison W, Blumenthal R. Quality of Life Enjoyment and Satisfaction Questionnaire: A New Measure. Psychopharmacology Bulletin 1993; 29:321-326*

Source: Intra-Cellular Therapies Inc.