

Pivotal Study of CAPLYTA™ (lumateperone) for the Treatment of Schizophrenia in Adults Published in JAMA Psychiatry

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NEW YORK, Feb. 20, 2020 (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, announced the publication of results from its CAPLYTA (lumateperone) clinical trial (ITI-007-301) in adult patients with schizophrenia. The article, "Efficacy and Safety of Lumateperone for Treatment of Schizophrenia: A Randomized Clinical Trial" (Correll et al. 2020), was recently published online in JAMA Psychiatry and is available [here](#).

In this trial, CAPLYTA 42 mg met the primary endpoint and demonstrated antipsychotic efficacy with statistically significant superiority over placebo at Week 4 as measured by the change from baseline on the Positive and Negative Syndrome Scale (PANSS) total score (drug-placebo difference = -4.2 points). CAPLYTA 42 mg also met the key secondary endpoint of statistically significant improvement on the Clinical Global Impression Scale for Severity of Illness. CAPLYTA 42 mg showed significant antipsychotic efficacy as early as week 1, which was maintained at every time point throughout the study.

The most commonly reported adverse events occurring for CAPLYTA 42 mg in ≥5% of patients and >2 times the rate in the placebo group were somnolence (CAPLYTA 42 mg, 17.3% vs placebo, 4.0%), sedation (12.7% vs 5.4%), fatigue (5.3% vs 1.3%), and constipation (6.7% vs 2.7%).

No significant differences were observed compared to placebo on metabolic parameters, including weight, cholesterol, triglycerides, glucose and insulin, or on prolactin levels. No extrapyramidal symptoms (EPS)-related TEAEs occurred in 5% or more of patients in any treatment arm.

"Treatment with CAPLYTA 42 mg significantly improved symptoms in patients with acute exacerbation of schizophrenia with a favorable tolerability profile," said Dr. Christoph Correll, Professor of Psychiatry and Molecular Medicine at the Zucker School of Medicine at Hofstra/Northwell, New York. "CAPLYTA represents an important addition to the treatment options of healthcare providers managing this heterogeneous mental condition."

Intra-Cellular Therapies is also presenting today additional analyses of Study ITI-007-301 in a poster at the International Society for CNS Clinical Trials and Methodologies (ISCTM) Annual Scientific Meeting that further demonstrate the strength of the Study 301 results.

This poster presents a post-hoc sensitivity analysis of Study ITI-007-301 that assesses the sensitivity of the prospective Mixed-effect Model for Repeated Measures (MMRM) based analysis, which assumes missing data as missing-at-random (MAR), under the alternative assumption that missing data were missing-not-at-random (MNAR). There was a higher rate of early discontinuations due to lack of efficacy in the placebo group compared with the lumateperone-treated group, suggesting that the MAR assumption that underlies the MMRM analysis may result in an underestimation of the drug-placebo difference by at least 32%. Using 3 other appropriate methods for dealing with imbalances in discontinuations due to lack of efficacy, lumateperone 42 mg was found to have substantially greater benefit compared with placebo than that obtained using the primary MMRM analysis, with drug-placebo differences of -6.2, -6.5, and -7.3 points on the PANSS in these analyses compared with -4.2 points in the primary analysis. Results from these additional sensitivity analyses confirm the efficacy of lumateperone 42 mg compared with placebo in Study '301.

About the ITI-007-301 Clinical Trial

This randomized, double-blind, fixed-dose, placebo-controlled Phase 3 inpatient clinical trial was conducted at 12 sites in the United States with 450 patients randomized (1:1:1) to receive either CAPLYTA 42 mg or 28 mg or placebo once daily in the morning for four weeks. Patients were diagnosed with schizophrenia using DSM-5 criteria and were required to have an acute exacerbation of psychotic symptoms. The pre-specified primary efficacy measure was change from baseline at study endpoint (4 weeks) on the centrally rated PANSS total score. The key secondary endpoint was the centrally rated CGI-S. Trial participants had a mean PANSS score of 89.8 at baseline, indicative of being markedly ill. The 28 mg dose is not an approved dose for CAPLYTA.

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

Important Safety Information

Boxed Warning: 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.

Contraindications: CAPLYTA is contraindicated in patients with known hypersensitivity to lumateperone or any components of CAPLYTA.

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**, which is a potentially fatal reaction. Signs and symptoms include: hyperpyrexia, muscle rigidity, delirium, autonomic instability, elevated creatinine phosphokinase, myoglobinuria (and/or rhabdomyolysis), and acute renal failure. Manage with immediate discontinuation of CAPLYTA and close monitoring.
- **Tardive Dyskinesia**, a syndrome of potentially irreversible, dyskinetic, and involuntary movements which may increase as the duration of treatment and total cumulative dose increases. Discontinue CAPLYTA if clinically appropriate.
- **Metabolic Changes**, including hyperglycemia, diabetes mellitus, dyslipidemia, and weight gain. 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)**. Perform complete blood counts in patients with pre-existing low white blood cell count (WBC) or history of leukopenia or neutropenia. Discontinue CAPLYTA if clinically significant decline in WBC occurs in absence of other causative factors.
- **Orthostatic Hypotension and Syncope**. Monitor heart rate and blood pressure and warn patients with known

cardiovascular or cerebrovascular disease.

- **Falls.** CAPLYTA may cause somnolence, postural hypotension, and motor and/or sensory instability, which may lead to falls and, consequently, fractures and other injuries. Assess patients for risk when using CAPLYTA.
- **Seizures.** Use CAPLYTA cautiously in patients with a history of seizures or with conditions that lower seizure threshold.
- **Potential for Cognitive and Motor Impairment.** Advise patients to use caution when operating machinery or motor vehicles until they know how CAPLYTA affects them.
- **Body Temperature Dysregulation.** Use CAPLYTA 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.** Use CAPLYTA with caution in patients at risk for aspiration.

Drug Interactions: Avoid concomitant use with CYP3A4 inducers and moderate or strong CYP3A4 inhibitors.

Special Populations: Neonates 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. Avoid use in patients with moderate or severe hepatic impairment.

Adverse Reactions: The most common adverse reactions in clinical trials with CAPLYTA vs. placebo were somnolence/sedation (24% vs. 10%) and dry mouth (6% vs. 2%).

[Please see full Prescribing Information including Boxed Warning.](#)

About CAPLYTA (lumateperone)

CAPLYTA is an oral, once daily medicine approved for the treatment of schizophrenia in adults (42mg/day).

The mechanism of action of CAPLYTA in the treatment of schizophrenia is unknown. However, the efficacy of CAPLYTA could be mediated through a combination of antagonist activity at central serotonin 5-HT_{2A} receptors and postsynaptic antagonist activity at central dopamine D₂ receptors.

CAPLYTA was approved for the treatment of schizophrenia in adults by the U.S. Food and Drug Administration in December 2019.

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 safety and efficacy of CAPLYTA and our other product candidates; that CAPLYTA represents an important addition to the treatment options of healthcare providers; 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 launching or 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 indication; 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 once we have launched the product may be different than observed in clinical trials, and may vary among patients; 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 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; 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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