



Intra-Cellular Therapies Announces U.S. FDA Approval of CAPLYTA® (lumateperone) for the Treatment of Bipolar Depression in Adults

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CAPLYTA is the only FDA-approved treatment for depressive episodes associated with bipolar I or II disorder (bipolar depression) in adults as monotherapy and as adjunctive therapy with lithium or valproate.

NEW YORK, Dec. 20, 2021 (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 that the U.S. Food and Drug Administration (FDA) approved CAPLYTA for the treatment of depressive episodes associated with bipolar I or II disorder in adults, as monotherapy and as adjunctive therapy with lithium or valproate.

"CAPLYTA is the only medication approved by the FDA to treat depressive disorders associated with bipolar I or bipolar II as both monotherapy and adjunctive therapy with lithium or valproate. CAPLYTA has shown a consistent favorable profile on weight, cardiometabolic parameters and extrapyramidal symptoms (movement disturbances). We are positioned to launch immediately and are excited to offer CAPLYTA to the millions of patients living with bipolar depression," said Dr. Sharon Mates, Chairman and CEO of Intra-Cellular Therapies. "We thank the patients, healthcare professionals and our Intra-Cellular team for all their contributions that led to this approval."

Bipolar I and bipolar II disorder are serious, highly prevalent psychiatric chronic conditions affecting approximately 11 million adults in the U.S., characterized by recurrent episodes of mania or hypomania interposed with episodes of major depression (bipolar depression). Bipolar I and bipolar II disorder each represent about half of the overall population of patients with bipolar disorder.

Bipolar depression is the most common and debilitating clinical presentation of bipolar disorder. These depressive episodes tend to last longer, recur more often, and are associated with a worse prognosis than the manic/hypomanic episodes. Bipolar depression is a significantly underserved medical need.

"The efficacy, and favorable safety and tolerability profile, make CAPLYTA an important treatment option for the millions of patients living with bipolar I or II depression and represents a major development for these patients. CAPLYTA is approved for a broad range of adult patients including those patients with bipolar II depression who have been underserved with limited treatment options," said Dr. Roger McIntyre, Professor of Psychiatry and Pharmacology at the University of Toronto and Head of the Mood Disorders Psychopharmacology Unit at the University Health Network, Toronto, Canada.

The FDA approval for CAPLYTA's additional indications is based on two positive Phase 3 placebo-controlled bipolar depression studies, which evaluated the effects of CAPLYTA on depression in adult patients with bipolar I or bipolar II disorder both as monotherapy (Study 404) and as adjunctive therapy with lithium or valproate (Study 402). In these studies, the efficacy of CAPLYTA 42 mg was established by demonstrating statistically significant improvements over placebo for the change from baseline in the Montgomery-Asberg Depression Rating scale (MADRS) total score at week 6. CAPLYTA 42 mg also showed a statistically significant improvement in the key secondary endpoint relating to clinical global impression of bipolar disorder in each study.

In addition, CAPLYTA demonstrated a favorable tolerability and safety profile consistent with findings in prior clinical studies in schizophrenia. The most common reported adverse reactions (occurring at a rate of 5% or more and at least twice the rate of placebo) were somnolence/sedation, dizziness, nausea, and dry mouth. Mean changes from baseline in weight, fasting glucose, total cholesterol, triglycerides, and LDL cholesterol were similar between CAPLYTA and placebo.

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.**
- **Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adults in short-term studies. All anti-depressant-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 and moderate or strong 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. Use of CAPLYTA should be avoided in patients with moderate or severe liver problems.

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-HT_{2A} 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 plans to commercialize CAPLYTA for bipolar depression immediately following approval; whether clinical trial results will be predictive of future real-world results; whether CAPLYTA will serve an unmet need; 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; 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.

Contact:

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

Burns McClellan, Inc.
Lisa Burns
cradinovic@burnsmc.com
212-213-0006

MEDIA INQUIRIES:
Sara Franks
Corporate Media Relations W2O Group
sfranks@w2ogroup.com
410-991-4287



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