Intra-Cellular Therapies Announces the Initiation of Clinical Trials for ITI-LLAI, a Long-Acting Injectable Formulation of Lumateperone for the Treatment of Schizophrenia and for ITI-333, a Novel Treatment for Opioid Use Disorder

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The Company continues expansion of its lumateperone programs with the advancement of a Long-Acting injectable formulation into clinical trials.

ITI-333 introduces a unique pharmacology for the treatment of opioid use disorder.

NEW YORK, Dec. 29, 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, today announced the initiation of clinical programs for the Company's lumateperone long-acting injectable formulation (ITI-LLAI) and for ITI-333, a novel molecule for the treatment of opioid use disorder.

"I am pleased to announce that two important proprietary programs have advanced into human clinical testing, further demonstrating our commitment to patients through the development of novel treatments for schizophrenia, mood disorders and other neuropsychiatric and neurologic disorders," said Dr. Sharon Mates, Chairman and CEO of Intra-Cellular Therapies.

LLAI, Study ITI-007-025: A Phase 1 single ascending dose study of LLAI, a formulation designed to be administered subcutaneously and to maintain therapeutic levels of lumateperone for at least 1 month. This study will evaluate the pharmacokinetics, safety and tolerability of lumateperone LAI in patients with stable symptoms of schizophrenia. Results from this study will inform the dosing strategy for future studies.

Maintaining patients symptomatically stable and functional are the primary objectives of the treatment of schizophrenia. Long-acting injectable antipsychotics provide patients with blood concentrations of active drug that remain within a therapeutic range for an extended period. These formulations represent a treatment option for patients who prefer not to take medication daily or have history of poor adherence to oral treatments as they have the potential to improve adherence and prevent relapse. Oral lumateperone has demonstrated efficacy in treating schizophrenia symptoms with a favorable safety and tolerability profile. A long-acting formulation of lumateperone if successfully developed and approved will provide an additional option for patients.

ITI-333, Study ITI-333-001: A Phase 1 single ascending dose study evaluating the safety, tolerability and pharmacokinetics of ITI-333 in healthy volunteers. ITI333 is a novel compound that uniquely combines activity as an antagonist at serotonin 5-HT2A receptors and a partial agonist at μ-opioid receptors. These combined actions support the potential utility of ITI-333 in the treatment of opioid use disorder and associated comorbidities (e.g., depression, anxiety, sleep disorders) without opioid-like safety and tolerability concerns.

Opioid use disorder is a chronic disorder with over 10 million people in the United States having misused opioids and nearly fifty-thousand persons died from opioid drug overdoses in 2018.

About Lumateperone Long Acting Injectable (LLAI) formulation

The Company is developing a long-acting injectable formulation of lumateperone (LLAI) that is designed for once monthly administration by subcutaneous injection for the treatment of schizophrenia. Nonclinical studies in rodents and monkeys have shown the LLAI formulation is safe and well tolerated in single and once monthly multiple dose studies and sustains plasma lumateperone levels for 28 day or longer after each injection.

Pharmacodynamic studies have shown lumateperone acts as a potent serotonin 5-HT2A receptor antagonist with high binding affinity, as a postsynaptic D2 receptor antagonist with moderate binding affinity, as an inhibitor of the serotonin reuptake transporter (SERT) with moderate binding affinity. Lumateperone also has moderate binding affinity to the D1 receptor (which may contribute to the indirect activation of NMDA and AMPA neurotransmission). These drug targets are believed to play an important role in in schizophrenia, bipolar disorder, depressive disorders and other neuropsychiatric disorders. In vitro studies have shown lumateperone has a ~60-fold greater affinity for 5-HT2A receptors vs D2 receptors.

Lumateperone is being investigated for the treatment of bipolar depression, major depressive disorders and other neuropsychiatric and neurological disorders. Lumateperone is not FDA approved for these disorders. CAPLYTA 42 mg (lumateperone) is approved by the U.S. Food and Drug Administration for the treatment schizophrenia of adults.

About ITI-333

ITI333 is a novel compound that uniquely combines activity as an antagonist at serotonin 5-HT2A receptors and a partial agonist at μ-opioid receptors. These combined actions support the potential utility of ITI-333 in the treatment of opioid use disorder and associated comorbidities (e.g., depression, anxiety, sleep disorders) without opioid-like safety and tolerability concerns. In addition, ITI-333 exhibits analgesic efficacy in acute and chronic preclinical models of pain supporting its potential utility in the management of pain.

ITI333's pharmacology is predominantly driven by high affinity binding to serotonin 5-HT2A (Ki = 8.3 nM) and μ-opioid (Ki = 11 nM) receptors. ITI333 shows modest affinity for dopamine D1 receptors, low affinity for κ-opioid receptors, and no binding to δ-opioid and NOP receptors.

In vivo, ITI-333 elicits potent analgesia in rodents that is blocked by the opioid antagonist, naloxone. Further, ITI-333 mitigates symptoms associated with opioid withdrawal and blocks reinstatement of opioid mediated behaviors; behaviors thought to be associated with a return to opioid use after a

period of abstinence.

ITI-333 possesses low potential for abuse liability. Unlike opioid agonists, ITI-333 is not self-administered, does not develop physical tolerance/dependences and does not impair gastrointestinal and pulmonary function. This pharmacologic profile is unique and supports the study of ITI-333 in humans as a potential treatment for opioid use disorder and pain.

Intra-Cellular Therapies has received a grant from the National Institute on Drug Abuse as part of the NIH Helping to End Addiction Long-term initiative, or HEAL, to support the early clinical development of ITI-333 for the treatment of opioid use disorder.

CAPLYTA™ (lumateperone) is indicated for the treatment of schizophrenia in adults. CAPLYTA is available in 42 mg capsules.

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. 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.
- **Sleepiness and Trouble Concentrating**. 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, moderate or strong CYP3A4 inhibitors and UGT 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 (24% vs. 10%) and dry mouth (6% vs. 2%).
  Please click here to see full Prescribing Information including Boxed Warning.

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.

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 beliefs about the potential utility of our product candidates; our belief that a long-acting injectable formulation of lumateperone could represent an important treatment option for patients; our expectation that we will continue to invest in our drug development pipeline; 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: the COVID-19 pandemic may negatively impact the conduct of, and the timing of enrollment, completion and reporting with respect to, our clinical trials; 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 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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