Intra-Cellular Therapies Announces Positive Topline Results from Study 402 Evaluating Lumateperone as Adjunctive Therapy in Patients with Bipolar Depression

September 9, 2020

Lumateperone 42 mg achieved statistically significant results in primary and key secondary endpoints in Study 402. Company expects to submit supplemental new drug application (sNDA) to the U.S. Food and Drug Administration (FDA) in late 2020 or early 2021.

Lumateperone 42 mg met the primary endpoint of change from baseline at Week 6 on the Montgomery-Åsberg Depression Rating Scale (MADRS) total score versus placebo (p=0.0206).

Lumateperone 42 mg also met the key secondary objective on the Clinical Global Impression Scale for Bipolar for Severity of Illness- Depression subscale (CGI-BP-S) (p=0.0082).

Favorable safety and tolerability profile observed, consistent with all prior lumateperone trials. Rates of akathisia, restlessness, extrapyramidal symptoms and changes in weight were similar to placebo.

This study, in conjunction with our previously reported positive Phase 3 monotherapy study, Study 404, forms the basis for our sNDA for the treatment of bipolar depression in patients with Bipolar I or II disorder as monotherapy and adjunctive therapy.

Conference call scheduled today at 8:00 a.m. ET

NEW YORK, Sept. 09, 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 positive topline results from its Phase 3 clinical trial (Study 402) evaluating lumateperone as adjunctive therapy to lithium or valproate in the treatment of major depressive episodes associated with Bipolar I or Bipolar II disorder. In Study 402, once daily lumateperone 42 mg met the primary endpoint for improvement in depression as measured by change from baseline versus placebo on the MADRS total score (p=0.0206; effect size = 0.27). Lumateperone 42 mg also met the key secondary endpoint, the CGI-BP-S Depression Score (p=0.0082; effect size = 0.31). The lower lumateperone dose, 28 mg, showed a trend for a dose-related improvement in symptoms of depression but the results did not reach statistical significance. Lumateperone demonstrated a favorable safety profile and was generally well-tolerated in the trial. The most commonly reported adverse events that were observed at a rate greater than or equal to 5% and at least twice the rate of placebo were somnolence, dizziness, and nausea. Rates of akathisia, restlessness, extrapyramidal symptoms, and changes in weight were similar to placebo. This trial, in conjunction with our previously reported positive Phase 3 monotherapy study, Study 404, forms the basis for our sNDA for the treatment of bipolar depression in patients with Bipolar I or II disorder as monotherapy and adjunctive therapy which we expect to submit to the FDA in late 2020 or early 2021.

“Our program now has confirmatory evidence of efficacy and a favorable safety and tolerability profile of lumateperone in bipolar depression; we look forward to submitting our supplemental NDA to expand lumateperone’s label to include a second major neuropsychiatric disorder,” said Dr. Sharon Mates, Chairman and CEO of Intra-Cellular Therapies. “With this clinical milestone, lumateperone has shown further potential to benefit patients suffering from a range of serious mental health conditions in addition to schizophrenia.”

“Bipolar disorders are serious and complex mental health conditions that affect millions of people, and depression is the most common presentation of these disorders. In this study, lumateperone demonstrated a robust effect, which is particularly significant considering patients were maintained on lithium or valproate,” 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. “Lumateperone is the first treatment to demonstrate efficacy for bipolar depression as monotherapy and as adjunctive therapy to mood stabilizers in a study population including both Bipolar I and Bipolar II patients. This will be welcome news to the psychiatric community as there is a tremendous need for improved treatment options.”

About Study 402

Study 402 was conducted globally in five countries including in the U.S. A total of 529 patients with moderate to severe major depressive episodes associated with either Bipolar I or Bipolar II disorder were randomized 1:1:1 to lumateperone 42 mg, 28 mg or placebo, while being maintained on lithium or valproate as mood stabilizers.

Lumateperone 42 mg met the primary endpoint by demonstrating a statistically significant improvement compared to placebo at week 6 (trial endpoint), as measured by change from baseline on the MADRS total score. In the intent-to-treat (ITT) study population, the least squares (LS) mean reduction from baseline for lumateperone 42 mg was 16.9 points, versus 14.5 points for placebo (LS mean difference = 2.4 points; effect size = 0.27, p=0.0206).

Lumateperone 42 mg also met the key secondary endpoint of statistically significant improvement on the CGI-BP-S Depression Score (p=0.0082; effect size = 0.31).

Lumateperone 28 mg showed a trend for a dose-related improvement in symptoms of depression. Though not formally tested against placebo since it did not separate on the primary endpoint, lumateperone 28 mg demonstrated a statistically significant improvement versus placebo on the CGI-BP-S.

Lumateperone was generally well-tolerated with a favorable safety profile in the trial. Adverse events were mostly mild to moderate and similar to

those seen in prior studies in bipolar depression and schizophrenia, with no new adverse events observed. These findings provide further evidence supporting lumateperone's favorable safety and tolerability profile across different patient populations.

Conference Call and Webcast Details

Intra-Cellular Therapies will host a live conference call and webcast today at 8:00 a.m. ET, during which management will discuss the topline results of Study 402. The live webcast and subsequent replay may be accessed by visiting the Company's website at www.intracellulartherapies.com. Please connect to the Company's website at least 5-10 minutes prior to the live webcast to ensure adequate time for any necessary software download. Alternatively, please call 1-(844) 835-6563 (U.S.) or 1-(970) 315-3916 (international) to listen to the live conference call. The conference ID number for the live call is 2980818. Please dial in approximately 10 minutes prior to the call.

About Lumateperone

Pharmacodynamics studies have shown lumateperone acts as a potent antagonist with high binding affinity at serotonin 5-HT2A receptors, as an antagonist with moderate binding affinity at postsynaptic D2 receptors, an inhibitor of the reuptake of serotonin transporter (SERT) with moderate biding affinity, and a partial agonist with moderate affinity at D1 receptors (which may contribute to the indirect activation of AMPA and NMDA receptors). These receptors 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 compared to D2 receptors.

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

About Bipolar Depression

Bipolar I and Bipolar II disorder are serious, highly prevalent psychiatric conditions, affecting approximately 6 million adults in the United States, or about 2.8% of the U.S. population.

These disorders are characterized by recurrent episodes of mania or hypomania interspersed with episodes of major depression known as Bipolar depression. Bipolar I and Bipolar II each represent about half of the overall population of patients with bipolar disorder.

Bipolar depression is the most common clinical presentation of bipolar disorder. These episodes tend to last longer, recur more often, and are associated with a worse prognosis than the manic/hypomanic episodes. Bipolar depression remains a significantly underserved medical need, with only a few FDA-approved treatment options available. These treatments are commonly associated with tolerability issues.

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, tolerability and efficacy of our product candidates; the potential for lumateperone to receive FDA approval for treatment of bipolar depression in patients with Bipolar I or II disorder as monotherapy and adjunctive therapy; our expectation that we will submit an sNDA, based on Study 402 and Study 404, for the treatment of bipolar depression in patients with Bipolar I or II disorder as monotherapy and adjunctive therapy to the FDA in late 2020 or early 2021; the potential for lumateperone to represent an advancement for the treatment of bipolar depression; 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: we may encounter issues or other challenges in commercializing CAPLYTA for the treatment of schizophrenia, including but not limited to negative impacts from the COVID-19 pandemic, ongoing pricing negotiations with certain payors that have not finalized their assessments, and performance of our sales activity, and that results achieved in CAPLYTA in the treatment of schizophrenia 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; there can be no guarantee that the sNDA for lumateperone for the treatment of bipolar depression will be submitted within the target timelines or that the sNDA will be approved by the FDA without a request for the submission of additional information or at all; 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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