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Intra-Cellular Therapies Announces Positive Topline Data From 6-Week Open-label Safety Switching Study with Lumateperone in Patients with Schizophrenia

Intra-Cellular Therapies to Host a Conference Call Today at 8:30 a.m. ET

NEW YORK, Sept. 07, 2017 (GLOBE NEWSWIRE) -- Intra-Cellular Therapies, Inc. (NASDAQ:ITCI), a biopharmaceutical company focused on the development of therapeutics for central nervous system (CNS) disorders, today announced positive topline data from the first part of an open-label safety switching study in which 302 patients with stable symptoms of schizophrenia were switched from standard-of-care antipsychotic medications to lumateperone (ITI-007 60 mg) with no dose titration of lumateperone required for a 6-week treatment duration, then switched back to standard-of-care. Many currently available antipsychotic agents are associated with motor side effects and/or weight gain, cardiovascular liabilities, dyslipidemia, and hyperglycemia. In this study, lumateperone was generally well tolerated with a favorable safety profile. Statistically significant improvements from standard-of-care baseline were observed in body weight, cardiometabolic and endocrine parameters in patients with stable symptoms of schizophrenia when switched to lumateperone and worsened again when switched back to standard-of-care medication. Additionally, treatment with lumateperone was not associated with the motor or cardiovascular disturbances often associated with other antipsychotic medications. These data are consistent with previous study results reflecting a safety profile similar to placebo in placebo-controlled trials with lumateperone in patients with acutely exacerbated schizophrenia and extend this favorable safety profile to this stable patient population. Symptoms of schizophrenia did not worsen upon switch to lumateperone from standard-of-care. Rather, statistically significant improvement from baseline was observed in the Positive and Negative Syndrome Scale (PANSS) mean total score. Notably, greater improvements were observed in subgroups of patients with elevated symptomatology such as those with comorbid symptoms of depression and those with prominent negative symptoms.

"Significant weight-gain or other cardiometabolic side effects or motor disturbances may prompt treating physicians to switch antipsychotics as a treatment management strategy," said Dr. Christoph Correll, MD, Professor of Psychiatry and Molecular Medicine, Hofstra Northwell School of Medicine. "This open-label safety switching study showing improvements in important cardiometabolic and motor parameters, was conducted in an outpatient setting representative of common clinical practice. Results confirm in a more generalizable population the safety profile of lumateperone that demonstrated a lack of metabolic, motor and cardiovascular issues in prior large placebo-controlled trials. These new findings are very encouraging as improving psychiatric symptoms without compromising physical health in people with schizophrenia is a very important goal."

"In addition to the favorable safety profile seen in this study, we are encouraged by the efficacy profile of lumateperone in patients with stable symptoms of schizophrenia switched from standard-of-care antipsychotic medication," said Dr. Sharon Mates, Chairman and CEO of ITCI. "The observations of statistically significant symptomatic improvements upon switch from standard-of-care in patients taking lumateperone warrant further investigation, especially in those patients with comorbid symptoms of depression or with prominent negative symptoms who are particularly underserved by currently available treatments."

About the Lumateperone Open-label Safety Switching Study

To assess long-term safety and to observe the impact of switching from standard-of-care antipsychotic medications, the Company is conducting an open-label safety switching study in stable patients with schizophrenia switched to lumateperone (ITI-007 60 mg) from standard-of-care antipsychotic therapy. This study is being conducted in the United States in two parts. The first part has completed clinical conduct and included a 6-week treatment duration with lumateperone followed by a 2-week period where patients are switched back to standard-of-care. This study assesses both the impact of switching to lumateperone from standard-of-care antipsychotics as well as the impact of switching back to standard-of-care antipsychotics from lumateperone. The second part of the study, the Company's long-term safety study in schizophrenia, is enrolling patients for up to 1-year treatment duration with lumateperone following switch from standard-of-care. Clinical conduct of the second part of the long-term safety study of lumateperone is ongoing.

In this first part of the open-label safety switching study, 302 patients with schizophrenia were enrolled and treated for 6 weeks with lumateperone (ITI-007 60 mg) administered orally once daily in the evening. Of the 302 patients enrolled, 218 (72.2%) completed the treatment period. To be eligible for inclusion in the study, patients must have had a clinical diagnosis of schizophrenia according to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5) and be stable with respect to their schizophrenia symptoms. The primary objective was to determine the safety of lumateperone. Safety is measured by treatment-related adverse events, vital signs, electrocardiograms, clinical laboratory values, physical and neurological exams and standardized clinical assessments such as the Simpson Angus Scale (SAS), the Barnes Akathisia Rating Scale

(BARS), the Abnormal Involuntary Movement Scale (AIMS), and the Columbia — Suicide Severity Rating Scale (C-SSRS). Secondary objectives were to determine the effectiveness of lumateperone as measured by change from baseline to improve psychopathology on the Positive and Negative Syndrome Scale (PANSS), improve social functioning as measured by the PANSS Pro-Social Factor and the Personal and Social Performance Scale (PSP), and reduce depression as measured by the Calgary Depression Scale for Schizophrenia (CDSS). Analyses in pre-specified subgroups were performed.

No dose titration was needed for the administration of lumateperone when patients were switched from standard-of-care antipsychotics to lumateperone. Patients could be started on an active dose of ITI-007 60 mg from Day 1. Consistent with good clinical care, patients were tapered down from their previous antipsychotic medication during the screening period or switched to lumateperone from one day to the next if no tapering down of the previous antipsychotic medication was clinically indicated. In this study, the most recent antipsychotic taken prior to screening, in descending order of frequency, included risperidone, quetiapine, aripiprazole, olanzapine, lurasidone, ziprasidone, haloperidol, paliperidone, perphenazine, asenapine, brexpiprazole and iloperidone.

The most frequent drug-related adverse event was somnolence occurring in 6.6% of patients receiving ITI-007 60 mg dosed daily in the evening. The proportion of patients reporting somnolence in this study was lower than that observed with morning dosing in previous lumateperone controlled trials and similar to that seen with placebo in those studies. There were no drug related serious adverse events. The proportion of patients experiencing motor side effects on lumateperone was low: akathisia (0.3%), and extrapyramidal side effects (0.7%). There were no signs of emerging extrapyramidal side effects, akathisia or dyskinesia as measured by the SAS, BARS or AIMS, respectively.

In contrast to many other antipsychotics that cause weight gain, in this study mean body weight, body mass index, and waist circumference change from baseline statistically significantly decreased over 6 weeks of treatment with lumateperone ($p = 0.001$, $p = 0.001$, $p=0.005$, respectively). Lumateperone also demonstrated a favorable cardiometabolic and endocrine safety profile. Prespecified comparisons of mean change from baseline to Day 42 on lumateperone revealed statistically significant reductions in total cholesterol ($p = 0.002$), LDL cholesterol ($p = 0.001$), triglycerides ($p = 0.035$) and prolactin ($p = 0.001$). These key laboratory mean values worsened again when patients who completed treatment with lumateperone returned to standard-of-care, with prolactin ($p<0.001$) and triglycerides ($p=0.01$) reaching statistically significant worsening after only 2 weeks on standard-of-care. There was a trend for improvement in insulin sensitivity with time on lumateperone (glucose levels were unchanged while insulin levels decreased, $p = 0.055$). This trend reversed when subjects were switched back from lumateperone to standard-of-care. The cardiovascular safety of lumateperone was also favorable with no change in multi-positional blood pressure or heart rate, no orthostasis, and no QTc interval prolongation.

The mean PANSS total score, at baseline 62.7, was consistent with a stable schizophrenia population and nonetheless symptoms of schizophrenia generally improved with lumateperone treatment or remained stable upon switch from standard-of-care antipsychotic therapy. Statistically significant improvements were observed in change from baseline of the PANSS total scores in this stable patient population switched from standard-of-care antipsychotic therapy ($p = 0.003$). Mean Clinical Global Impression Scale for Severity of Illness (CGI-S) scores improved in those patients who completed 6 weeks of lumateperone treatment ($p = 0.003$). In this safety study, it is important that patients receiving open-label lumateperone did not worsen when switched from standard-of-care antipsychotic medication. Improvements with lumateperone were seen even in these presumed symptomatically stable patients as demonstrated by a responder analysis for the PANSS total score which indicated greater than 20% of patients improved by at least 20%, a widely accepted standard of clinical meaningfulness in the medical community.

Statistically significant improvements were also seen in the positive symptom subscale scores ($p < 0.001$), general psychopathology subscale scores ($p = 0.014$), and PANSS-derived Prosocial Factor scores ($p < 0.001$) as well as in social functioning as measured by the PSP scale in this stable patient population ($p < 0.001$). Negative symptoms also improved significantly with lumateperone treatment in a subgroup of patients ($N = 36$) with prominent negative symptoms at baseline as measured by the negative symptom subscale ($p = 0.029$) and the Marder Negative Factor ($p = 0.014$). In a subgroup of patients with comorbid symptoms of depression ($N=17$), as measured by a CDSS score of greater than 6, symptoms of depression improved significantly ($p = 0.001$).

While efficacy data in an open label study should be interpreted cautiously due to the absence of a parallel control group, the Company is encouraged by the efficacy findings associated with switching to lumateperone in this study population and believes they warrant further investigation. Further data from this study will be presented at upcoming medical conferences.

In two large placebo-controlled trials in patients with acute schizophrenia, lumateperone has demonstrated a statistically significant reduction of symptoms of psychosis as measured by change from baseline on the PANSS total score compared to placebo with supportive evidence from a third study. In all of these studies lumateperone has been well-tolerated, with a safety profile similar to placebo, and with clinically relevant and statistically significant safety and tolerability advantages when directly compared in two studies with risperidone used as an active control, the most commonly prescribed antipsychotic for the treatment of schizophrenia. These findings include no significant adverse effects on cardiovascular parameters, weight, blood lipids, glucose, prolactin and motor function. The data from the present open label safety study of

patients with stable symptoms of schizophrenia switched from standard-of-care antipsychotic therapy are consistent with and extend previous data with over 1,500 people exposed to date.

Conference Call and Webcast Details

Intra-Cellular Therapies will host a live conference call and webcast today at 8:30 a.m. ET, during which management will discuss the corporate update on the schizophrenia program. 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 81934888. Please dial in approximately 10 minutes prior to the call.

About Intra-Cellular Therapies

Intra-Cellular Therapies is developing novel drugs for the treatment of neuropsychiatric and neurodegenerative diseases and diseases of the elderly, including Parkinson's and Alzheimer's disease. The Company is developing its lead drug candidate, lumateperone (also known as ITI-007), for the treatment of schizophrenia, bipolar disorder, behavioral disturbances in patients with dementia, including Alzheimer's disease, depression and other neuropsychiatric and neurological disorders. Lumateperone, a first-in-class molecule, is in Phase 3 clinical development for the treatment of schizophrenia, bipolar depression and agitation associated with dementia, including Alzheimer's disease. The Company is also utilizing its phosphodiesterase (PDE) platform and other proprietary chemistry platforms to develop drugs for the treatment of CNS and other disorders. The lead molecule in the Company's PDE1 portfolio, ITI-214, is in development for the treatment of symptoms associated with Parkinson's disease.

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 view that the positive efficacy observations in this open label study warrant further investigation; factors that may prompt treating physicians to switch antipsychotics as a treatment management strategy; the effect of lumateperone's safety profile on medication adherence and patient outcomes; further clinical conduct in this switching study; future presentations of data at upcoming medical conferences; our belief that lumateperone, if approved, will be an attractive treatment option for schizophrenia; 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: this switching study was an open label study and its efficacy observations may not be replicated in any future controlled trials; any toxicities discovered in our long-term safety study of lumateperone in patients with schizophrenia and nonclinical studies could delay or prevent our filing of an NDA; the FDA may place our long-term safety study on a clinical hold, which would delay or prevent us from completing the safety study and from filing an NDA; our current and planned clinical trials, other studies for lumateperone, and 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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