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Intra-Cellular Therapies Announces Additional Results From Phase I/II Clinical Trial for ITI-007 in Healthy Geriatric Subjects and Patients With Dementia

NEW YORK, Nov. 21, 2014 (GLOBE NEWSWIRE) -- Intra-Cellular Therapies, Inc. (Nasdaq:ITCI), a biopharmaceutical company focused on the development of therapeutics for central nervous system (CNS) disorders, today presented additional results from ITI-007-200, a Phase I/II clinical trial designed to evaluate the safety, tolerability and pharmacokinetics of low doses of its lead drug candidate, ITI-007, in healthy geriatric subjects (trial Part 1) and in patients with dementia, including Alzheimer's disease (trial Part 2). Secondary endpoints explored the effects of ITI-007 on measures of cognitive function. The additional data showing clinical signals for ITI-007 to improve cognition are being presented at the Clinical Trials on Alzheimer's Disease (CTAD) conference being held in Philadelphia, Nov 20-22.

This trial marks an important milestone in the expansion of the Company's CNS platform. The ITI-007-200 trial results to date indicate that ITI-007 is safe and well-tolerated across a range of low doses, has linear- and dose-related pharmacokinetics and improves cognition in the elderly. These results further position the drug as a development candidate for the treatment of behavioral disturbances in patients with dementia and other neuropsychiatric and neurological conditions. The Company plans to initiate a Phase 2 clinical program evaluating ITI-007 in patients with behavioral disturbances associated with dementia and related disorders, including Alzheimer's disease, in 2015.

"Cognitive deficits are a hallmark of dementia, and the data presented today provide clinical evidence that ITI-007 can improve cognitive measures of learning and memory," said Dr. Sharon Mates, Chief Executive Officer and Chairman. "Patients with dementia also suffer from agitation, heightened aggression, depression, sleep disorders, "sundowning" and psychosis, behaviors which often lead to early institutionalization. We believe ITI-007 will reduce the behavioral disturbances associated with dementia in the elderly with a beneficial effect on cognition and with a favorable safety profile that does not increase the risk of cardiovascular events or falls due to motor impairment. We believe the broad therapeutic benefit of ITI-007 will substantially improve patient lives and the lives of their families and caregivers."

About the Phase I/II Clinical Trial

The ITI-007-200 clinical trial was conducted in two parts. Part 1 was a randomized, double-blind, placebo-controlled multiple ascending dose evaluation of ITI-007 in healthy geriatric subjects. In each of 3 cohorts in Part 1, approximately ten subjects were randomized to receive ITI-007 (N=8) or placebo (N=2) orally once daily in the morning for seven days; doses of ITI-007 up to and including 30 mg were evaluated in three cohorts in Part 1. In Part 2, eight patients with dementia were randomized to receive 9 mg ITI-007 (N=5) or placebo (N=3) orally once a day in the evening for seven days. The primary objectives of the study were to evaluate the safety, tolerability and pharmacokinetics of ITI-007 in the elderly and in the target dementia patient population. Secondary measures were included to explore the effects of ITI-007 on cognition and agitation.

The Hopkins Verbal Learning Test-R (HVLT-R) was used to assess cognition in healthy geriatric subjects and dementia patients. The HVLT-R consists of three learning trials (T1, T2, T3) during which the clinician reads a word list of 12 semantically related words and the subject is asked to immediately recall as many of the words as possible. By repeating the trial three times in a row, the number of words recalled increases over the three trials, thereby demonstrating a learning effect. After a delay, the subject is again asked to recall as many words as possible (free recall). In the modified version of the HVLT-R used in the ITI-007-200 trial, the subject was given an extra chance to recall the word list after given a cue to the semantic theme of the word list (cued recall). Lastly, a word recognition test was administered during which the clinician reads a list of 24 words containing the original 12 words (target words) and 12 new words and the subject is asked to recognize words from the original list (target words) by answering 'yes' or 'no' after each word.

In the ITI-007-200 trial, this entire HVLT-R was conducted at baseline, before drug is administered, with the learning trials administered in the evening before bedtime and the delayed recall and recognition tests administered the following morning before breakfast. The present results demonstrated impaired verbal learning and memory (recall and recognition memory) by dementia patients relative to healthy geriatric subjects. Moreover, the data indicated that healthy geriatric subjects treated with ITI-007 for one week experienced an improvement in verbal learning and memory relative to placebo-treated subjects. Dementia patients treated with ITI-007 showed enhanced recognition memory, making fewer false positive errors (i.e., responding 'yes' to non-target words) than patients treated with placebo.

Other secondary endpoints in the ITI-007-200 trial included the assessment of agitation. However, none of the study participants experienced agitation at baseline or during the study, therefore no signals on this behavioral endpoint could be assessed.

The ITI-007-200 trial was designed primarily to measure safety with the cognitive endpoints included to ensure that ITI-007 did not worsen cognition in an already vulnerable patient population without statistical power to demonstrate efficacy. The present results confirmed no cognitive impairment by ITI-007 and, moreover, demonstrated clinical signals for improved cognition with only one week of treatment with ITI-007 in both healthy geriatric subjects and patients with dementia. The Company believes the results are encouraging and suggestive of a meaningful clinical outcome, which deserves further investigation.

About ITI-007

ITI-007 is our lead product candidate, whose mechanisms of action, we believe, have the potential to yield a first-in-class antipsychotic therapy and, at lower doses, a first-in-class therapy for the behavioral disturbances associated with dementia. In our pre-clinical and clinical trials to date, ITI-007 combines potent serotonin 5-HT2A receptor antagonism, dopamine receptor phosphoprotein modulation (DPPM), glutamatergic modulation and serotonin reuptake inhibition into a single drug candidate. At dopamine D2 receptors, ITI-007 has been demonstrated to have dual properties and to act as both a post-synaptic antagonist and a pre-synaptic partial agonist. ITI-007 has also been demonstrated to stimulate phosphorylation of glutamatergic NMDA NR2B, or GluN2B, receptors in a mesolimbic specific manner.

At the lowest dose studied to date (1 mg), ITI-007 has been demonstrated to act primarily as a potent 5-HT2A serotonin receptor antagonist. As the dose is increased, additional benefits are derived from the engagement of additional drug targets, including modest dopamine receptor modulation and modest inhibition of serotonin transporters. We believe that combined interactions at these receptors may provide additional benefits above and beyond selective 5-HT2A antagonism for treating agitation, aggression and sleep disturbances in diseases that include dementia, Alzheimer's disease and autism spectrum disorders, while avoiding many of the side effects associated with more robust dopamine receptor antagonism. As the dose of ITI-007 is further increased, leading to moderate dopamine receptor modulation, inhibition of serotonin transporters, and indirect glutamate modulation, these actions complement the complete blockade of 5-HT2A serotonin receptors. In this dose range, we believe that ITI-007 may be useful in treating the symptoms associated with schizophrenia, bipolar disorder, major depressive disorder and other neuropsychiatric diseases.

About Behavioral Disturbances in Dementia, Including Alzheimer's Disease

It has been estimated that 44.4 million people worldwide were living with dementia in 2013 including over five million patients with Alzheimer's disease in the United States. This number is expected to nearly double to 75.6 million by 2030 and to 135.5 million by 2050. While the diagnostic criteria for Alzheimer's disease and other dementias mostly focus on the related cognitive deficits, it is often the behavioral and psychiatric symptoms that are most troublesome for caregivers and lead to poor quality of life for patients. Several behavioral symptoms are quite prevalent in patients with dementia, including patients with Alzheimer's disease. Rates of depression in Alzheimer's disease are estimated to be up to 87%, although most estimates are between 30% and 50%. Agitation and aggression are present in approximately 60% of patients. Sleep disturbances, particularly as an increased likelihood of day-night reversal, are present in up to approximately 60% of patients. In view of the potential multiple effects of ITI-007 on aggression, agitation, sleep disorders and depression, and its safety profile to date, we believe that ITI-007 may provide a novel therapy for treating the behavioral disturbances accompanying dementia, including Alzheimer's disease.

The FDA has not approved any drug to treat the behavioral symptoms of dementia, including Alzheimer's disease. As symptoms progress and become more severe, physicians often resort to off-label use of antipsychotic medications in these patients. Current antipsychotic drugs are associated with a number of side effects, which can be problematic for elderly patients with dementia. In addition, antipsychotic drugs may exacerbate the cognitive disturbances associated with dementia. There is a large unmet medical need for a safe and effective therapy to treat the behavioral symptoms in patients with dementia, including Alzheimer's disease.

About Intra-Cellular Therapies

Intra-Cellular Therapies (the "Company") is developing novel drugs for the treatment of neuropsychiatric and neurodegenerative disease and other disorders of the central nervous system ("CNS"). The Company is developing its lead drug candidate, ITI-007, for the treatment of schizophrenia, behavioral disturbances in dementia, bipolar disorder and other neuropsychiatric and neurological disorders. The Company is also utilizing its phosphodiesterase platform and other proprietary chemistry platforms to develop drugs for the treatment of cognitive deficits in schizophrenia and other CNS disorders. The Company is also developing inhibitors against additional targets for CNS indications such as Alzheimer's disease, Parkinson's disease and depression and non-CNS indications such as cardiovascular 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 progress and timing of our drug discovery and development programs; our beliefs about the potential uses and benefits of ITI-007 for the treatment of behavioral disturbances associated with dementia, including Alzheimer's disease; our plans for the future testing of a range of low doses of ITI-007; and our research and development efforts and plans under the caption "About Intra-Cellular Therapies, Inc." 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: our current and planned clinical trials for ITI-007 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 reliance on collaborative partners and other third-parties for development and commercialization of our product candidates; and the other risk factors discussed under the heading "Risk Factors" contained in our Annual Report on Form 10-K for the year ended December 31, 2013 filed with the Securities and Exchange Commission, as well as any updates to those risk factors filed from time to time in our periodic and current reports. 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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