Intra-Cellular Therapies Announces Progression to Higher Dose Cohort in ITI-214 Translational Medicine Study in Patients with Heart Failure

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Data indicate ITI-214 at a dose of 30 mg is well tolerated with a favorable safety profile

Study '104 now proceeding to a third cohort at a dose of 90 mg

NEW YORK, Sept. 25, 2019 (GLOBE NEWSWIRE) -- Intra-Cellular Therapies, Inc. (Nasdaq:ITCI) today announced the successful completion of the second dose cohort (single dose of 30 mg administered orally) in Study ITI-214-104 (Study '104), a proof-of-mechanism, translational medicine study of ITI-214, a novel phosphodiesterase-1 (PDE1) inhibitor, in patients with chronic heart failure. Clinical conduct of the third and last cohort, 90 mg, is now ongoing following review of safety and tolerability data from the 30 mg dose cohort, where no safety concerns were identified.

Study '104 is a randomized, double-blind, placebo-controlled study of escalating single doses of ITI-214 to evaluate hemodynamic effects and safety in patients with systolic heart failure. The primary objective of the study is to determine effects of ITI-214 on cardiac contractility and cardiac output in patients already maintained on standard-of-care treatment for chronic heart failure.

Initiation of Study 104 followed findings that ITI-214 improved cardiac output through a different mechanism of action than available heart failure therapies. These findings in a preclinical model of heart failure were published by researchers at Johns Hopkins University and ITCI scientists in the journal *Circulation*. Currently available heart failure drugs that strengthen heart contractions, such as the PDE3 inhibitors (amrinone and milrinone) and ß-adrenergic agonists (dobutamine), increase calcium entry into cardiac muscle cells and have potentially dangerous complications, such as irregular heartbeats. Unlike these drugs, ITI-214 did not cause calcium levels to rise in cardiomyocyte cells and did not interact with the ß-adrenergic signaling pathway. These experimental results demonstrate that ITI-214 exerts its effects via a separate pathway involving adenosine A_{2B} receptor signaling, previously shown to be cardioprotective, and suggest that ITI-214 may represent a novel and potentially safer approach for the treatment of human heart failure.

"We are encouraged by the continuing safety of ITI-214 in patients with heart failure and our progress toward completion of this important mechanistic study," said Sharon Mates Ph.D., Chairman and CEO of Intra-Cellular Therapies, Inc. "We believe ITI-214 offers a potential new treatment for heart failure with a novel mechanism."

About Study ITI-214-104

Study '104 is a randomized, double-blind, placebo-controlled study of escalating single doses of oral ITI-214 to evaluate hemodynamic effects and safety in patients with systolic heart failure (NYHA class II-III heart failure). This single dose ascending Study evaluates three dose cohorts of ITI-214: 10 mg, 30 mg and 90 mg with 12 patients per cohort randomized to ITI-214 or placebo 9:3. The primary objective of the study is to determine effects of ITI-214 on cardiac contractility and cardiac output using echocardiogram with doppler imaging and hemodynamic monitoring in patients already maintained on standard-of-care treatment for chronic heart failure. Secondary objectives include safety and tolerability. This Study is being conducted at Johns Hopkins University and Duke Clinical Research Institute.

About Heart Failure

Heart failure affects about 5.7 million U.S. adults, according to the U.S. Centers for Disease Control and Prevention and contributes to an estimated one in nine deaths. Human heart failure is a chronic condition often marked by weakening of the heart muscle and its subsequent failure to pump enough blood. Currently, drugs are available to treat or manage heart failure symptoms, but drugs that improve the strength of the heart muscle's contractions, carry the risk of dangerous complications such as developing irregular heartbeats. There is no cure. PDE1 inhibition may provide a new approach to treating heart failure that may not have the adverse events currently seen in available drugs.

About ITI-214

ITI-214, is a potent and selective phosphodiesterase type 1 (PDE1) inhibitor. ITI-214 is the lead compound in the Company's PDE1 portfolio and is in development for the treatment of symptoms associated with Parkinson's disease and for the treatment of heart failure. ITI-214 has been found to be generally well tolerated with a favorable safety profile in four Phase 1 clinical trials. ITI-214 works by slowing the breakdown of cyclic nucleotides (cAMP, cGMP), allowing these molecules to build up in the cells and to exert important functions. The PDE1 enzyme is highly active in pathological or disease states, and our PDE1 molecules are designed to reestablish normal function in these disease states through the inhibition of the PDE1 enzyme. ITI-214 may allow precise adjustment of cAMP and/or cGMP in cells in which it is present. In heart disease, excessive PDE1 activity may limit the beneficial effects of cAMP or cGMP, so inhibitors like ITI-214, have the potential to act as a therapy. Previous studies have described the mechanism of action of ITI-214 in the brain. The mechanism of action of ITI-214 suggests therapeutic potential across a variety of neurological and cardiovascular diseases.

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 is under review by the FDA for the treatment of schizophrenia and is in Phase 3 clinical development for the treatment of bipolar depression. Intra-Cellular Therapies 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 and for the treatment of heart failure.

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 therapeutic value, clinical and non-clinical development plans and commercial potential of our drug product candidates; the progress, timing and results of our clinical trials and preclinical studies; our beliefs about the extent to which the results of our clinical trials and preclinical studies to date support new drug application filings for product candidates; the safety and efficacy of our product development candidates; our beliefs about the potential uses and benefits of our drug product candidates; that ITI-214 may represent a novel and potentially safer approach for the treatment of human heart failure; that ITI-214 offers a potential new treatment for heart failure with a novel mechanism 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: our current and planned clinical trials, other studies for our 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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