# Intra-Cellular Therapies Announces Publication Highlighting ITI-214 Mechanism of Action and Describing Positive Results in Preclinical Models of Heart Failure

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*Data indicates ITI-214 acts by a novel mechanism of action via modulation of the adenosine $A_{2B}$ receptor signaling pathway*

*ITI-214 increases cardiac contractility without increasing intracellular calcium*

*These data may represent an important therapeutic advancement for the treatment of heart failure*

*The publication describing these results is now available online in the journal Circulation*

NEW YORK, July 23, 2018 (GLOBE NEWSWIRE) -- Intra-Cellular Therapies, Inc. (Nasdaq:ITCI) today announced the online publication of a report in the journal *Circulation* describing the mechanism of action of its phosphodiesterase (PDE) Type 1 inhibitor, ITI-214, and its potential use for the treatment of heart failure. In these preclinical studies, Johns Hopkins researchers in collaboration with ITCI scientists demonstrated that ITI-214 improved cardiac output through a different mechanism of action than available therapies for the treatment of heart failure. These studies suggest that ITI-214 may represent a novel approach for the treatment of human heart failure.

ITI-214 has completed four Phase 1 clinical studies and was shown to be safe and generally well tolerated, and is currently in a Phase 1/2 clinical study for the treatment of Parkinson's disease and a Phase 1/2 clinical study in heart failure. The heart failure study is assessing the impact of ITI-214 on cardiovascular function in humans and will help determine if the positive preclinical findings seen in animal models are translatable to humans.

"Our results demonstrate that ITI-214, unlike other pharmacological approaches, increases heart contractility through a novel mechanism of action that may lead to efficacious and safer therapies for patients," said David Kass, M.D., the Abraham and Virginia Weiss Professor of Cardiology at Johns Hopkins University School of Medicine and principal investigator of the study.

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 existing heart failure drugs, ITI-214 did not cause calcium levels to rise in rabbit 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.

Therefore, the pharmacological profile of ITI-214 introduces a new mechanism of action for the treatment of heart failure that is different from ß-adrenergic agonism and PDE3 inhibition.

"ITI-214 offers a potential new treatment for heart failure with a novel mechanism of action that may provide an effective and safer alternative to existing therapies," said Sharon Mates Ph.D., Chairman and CEO of Intra-Cellular Therapies, Inc.

**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, dozens of 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. As the clinical lead compound in the Company's PDE1 portfolio, ITI-214 has been found to be generally well tolerated with a favorable safety profile in four Phase 1 clinical trials, in healthy volunteers as well as patients with schizophrenia. 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. 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.

**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 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; the potential for ITI-214 to represent a novel approach for the treatment of human heart failure; that ITI-214 could potentially offer an effective and safer alternative heart failure treatment to existing therapies; that ITI-214 offers a potential new treatment for heart failure with a novel mechanism of action that may provide an effective and safer alternative to existing therapies 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.

CONTACT:

Intra-Cellular Therapies, Inc.
Juan Sanchez, M.D.
Vice President, Corporate Communications and Investor Relations
646-440-9333

Burns McClellan, Inc.
Lisa Burns
Justin Jackson (Media)
jjackson@burnsmc.com
212-213-0006

Primary Logo

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