Intra-Cellular Therapies Presents Data on Antitumor Effects of Phosphodiesterase I Inhibition in a Preclinical Colorectal Cancer Model at the 2021 American Association for Cancer Research (AACR) Annual Meeting

April 12, 2021

Our research has demonstrated that the phosphodiesterase type 1 (PDE1) enzyme modulates the immune system by reducing macrophage and microglial activity with demonstrated effects in neuroinflammatory conditions, cancer and cardiac diseases.

Preclinical findings describing the antitumor effects of PDE1 Inhibitors when administered in conjunction with checkpoint inhibitor immunotherapy are being presented at the American Association for Cancer Research (AACR) virtual annual meeting.

Our PDE1 platform consists of a portfolio of PDE I inhibitors that are being developed for cancer and other diseases.

NEW YORK, April 12, 2021 (GLOBE NEWSWIRE) -- Intra-Cellular Therapies, Inc. (Nasdaq: ITCI) today announced a poster presentation on its PDE1 inhibitor program at the ongoing 2021 American Association for Cancer Research (AACR) Virtual Annual Meeting, which is being held from April 10 - 15, 2021. Details of the poster presentation are as follows:

Title: Effects of ITI-214, a Potent and Selective Phosphodiesterase Type 1 Inhibitor, on Tumor Myeloid Cellular Composition, Tumor Volume and Survival in Mouse Models of Colorectal Cancer When Combined with an Anti-PD-1 Checkpoint Inhibitor (Poster 1243).
Session Category: Experimental and Molecular Therapeutics
Session Title: Novel Antitumor Agents

The poster describes results from preclinical studies demonstrating that the Company's selective PDE1 inhibitor, lenrispodun (ITI-214), alters the tumor microenvironment and exhibits compelling anti-tumor activity when combined with a programmed cell death-1 (PD-1) immune checkpoint inhibitor in an animal model of colorectal cancer.

In previous studies we have shown the ability of our PDE1 inhibitors to reduce neuroinflammation. In these studies we discovered a novel intracellular pathway by which the PDE1 enzyme controls the functions of certain immune cells called microglia (brain resident macrophage-like cells). We have shown that inhibition of the activity of these cells by PDE1 inhibitors reduces inflammation in the brain (O'Brien et al., 2018).

Based on our understanding of the role of PDE1 in regulating the function of microglia and macrophages, we hypothesized that PDE1 inhibitors would block the recruitment of immunosuppressive cells (macrophages, monocytes) into the tumor microenvironment (TME) of certain cancers. By inhibiting PDE1, host immune responses may be potentiated leading to inhibition of tumor growth.

At AACR we are reporting on pre-clinical studies demonstrating that lenrispodun alone decreased the numbers of infiltrating macrophages and increased the numbers of natural killer cells in the TME. These effects serve to prevent tumors from evading the host immune system and thereby potentiate the tumor killing activity of checkpoint inhibitors. When lenrispodun and an anti-PD-1 antibody were combined, tumor volumes were significantly reduced and tumor-free survival was significantly increased in a mouse model of colon carcinoma. Importantly, the effect of combining an anti-PD-1 immune checkpoint inhibitor and lenrispodun treatment produced a complete response in about 50% (7/15) of treated mice as compared to 10% (1/10) in anti-PD-1 alone treated mice, 20% (1/5) in the lenrispodun alone group and 0% (0/9) in the control group. This translated into a statistically significant effect on survival for the combination treatment group as compared to control (p=0.001).

Tumor associated macrophages can promote tumor growth in certain cancers. Our experiments indicate PDE1 inhibition prevents the migration and accumulation of monocytes and macrophages in the tumor microenvironment and could represent a novel and broadly applicable approach to the treatment of immune responsive cancers. We are currently evaluating our PDE1 inhibitors in other cancer models and are developing potential biomarkers that may assist in the translation of these data to the treatment of human cancers.

Phosphodiesterase type 1 (PDE1) inhibitor Portfolio

Our PDE1 inhibitor program is focused on diseases in which the PDE1 enzyme is over-expressed and/or abnormal immune cell function contributes to disease pathology providing opportunities to pursue innovative treatments for multiple diseases including Parkinson's disease, heart failure and other diseases.

Lenrispodun is a potent and selective PDE1 Inhibitor and is the lead compound in the Company's PDE1 portfolio. Lenrispodun is in development for the treatment of symptoms associated with Parkinson's disease and for the treatment of heart failure. Lenrispodun has been generally well tolerated with a favorable safety profile in six Phase 1 clinical trials. Lenrispodun works by blocking the breakdown of cyclic nucleotides (cAMP, cGMP), thus allowing these molecules to build up in the cells and to exert important functions.

Previous studies have described the mechanism of action of lenrispodun in the brain. The mechanism of action of ITI-214 and our other PDE1 inhibitors suggests therapeutic potential across a variety of diseases including neurological and, cardiovascular diseases and cancer.

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.

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; 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 or 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; the COVID-19 pandemic may negatively impact the conduct of, and the timing of enrollment, completion and reporting with respect to, our clinical trials; any other impacts on our business as a result of or related to the COVID-19 pandemic; 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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