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Intra-Cellular Therapies Announces the Results of a Phase I Pet Study For ITI-007 for the Treatment of Schizophrenia and other Psychiatric Disorders.

Key Targets are Critical to Drug Treatment of Neuropsychiatric and Related Disorders

Intra-Cellular Therapies, Inc. (ITI) announced at a recent conference on neuropsychiatric diseases the results from a recently completed Phase I clinical study demonstrating ITI-007, the Company's lead antipsychotic drug, interacts with important targets in the living human brain. These key targets are critical to drug action in many neuropsychiatric and related disorders. Using positron emission tomography (PET) to image receptor interactions, ITI-007 produced dose-related and long-lasting occupancy of three key targets of psychotropic drug action: the serotonin 5-HT2A and dopamine D2 receptors, as well as the serotonin reuptake transporter (SERT). At low doses, ITI-007 selectively occupies 5-HT2A receptors in the brains of normal healthy volunteers. At a dose of 10 mg, neocortical 5-HT2A receptors are fully occupied and the first evidence is seen of D2 receptor occupancy in the basal ganglia. This 10 mg dose has been shown previously to be particularly effective in improving sleep in patients with sleep maintenance problems.

As the dose of ITI-007 is increased, dose-dependent and progressively increasing amounts of D2 occupancy are achieved, reaching 40% peak occupancy in the basal ganglia at the 40 mg dose (the highest dose tested in this study). At this dose, ITI-007 also demonstrates significant occupancy of the SERT. Moreover, when these targets are occupied in the presence of fully saturated 5-HT2A receptors, effects should be amplified.

"We are pleased to have demonstrated ITI-007's potent interactions with key brain targets in humans," stated Sharon Mates, Chief Executive Officer of Intra-Cellular Therapies. "The simultaneous occupancy of these targeted receptors is unprecedented for antipsychotic drugs. We believe that these results will translate into a reduced need to impose high doses of drugs on patients suffering from schizophrenia and other disorders."

ITI-007 rapidly penetrates the brain after oral administration and interacts with molecular targets important in a variety of central nervous system disorders. Taken together, these data suggest that ITI-007 exhibits a unique and beneficial pharmacological profile useful for the treatment of schizophrenia, mood disorders and insomnia.

Summary of the Phase I Receptor Occupancy Results
This Phase I trial was a single-center, open-label study in sequential groups of healthy volunteers (N = 2 to 4 at each dose). At the lowest dose tested (10 mg), ITI-007 fully occupied cortical 5-HT2A receptors (up to 92% displacement of [11C]-MDL100907 in the prefrontal cortex) with measurable occupancy of D2 receptors (up to 16% displacement of [11C]-raclopride) in the human basal ganglia. This is consistent with the approximate 60-fold separation between the 5-HT2A receptor and D2 receptor binding affinities previously measured in vitro. Moreover, at the highest dose evaluated, 40 mg, ITI-007 showed similar occupancy for D2 receptors (up to 39% occupancy) and for SERTs (up to 31% occupancy) in the human basal ganglia.

Given the unique pharmacological profile of ITI-007 that includes potent 5-HT2A receptor antagonism, pre-synaptic partial agonism and post-synaptic antagonism of D2 receptors, and functional mesolimbic/mesocortical selectivity of dopaminergic and glutamatergic interactions, ITI-007 is predicted to exhibit antipsychotic efficacy at low levels of D2 receptor occupancy. However, the positive safety profile of ITI-007 allows for the exploration of higher doses and higher levels of receptor occupancies. Further, the ability of ITI-007 to interact with SERTs, an important target of antidepressant drug action, expands the therapeutic utility of this unique drug.

ITI-007 was safe and well-tolerated in healthy volunteers at all doses evaluated. No serious adverse events were reported. Pharmacokinetic analyses confirmed good exposure to ITI-007. There was a significant correlation between ITI-007 receptor occupancy and ITI-007 plasma levels. Important for a centrally mediated drug, the brain residency time for ITI-007 far outlasted its plasma half-life confirming rapid and long-lasting effects in brain.

ABOUT ITI-007

ITI-007 is the Company's first-in-class 5-HT2A receptor antagonist/dopamine receptor phosphoprotein modulator (DPPM)/serotonin reuptake inhibitor for the treatment of schizophrenia. As a DPPM, ITI-007 has dual properties; it acts as a post-synaptic antagonist and as a pre-synaptic partial agonist. ITI-007 also exhibits mesocortical and mesolimbic selectivity as evidenced by regionally selective increases in dopamine release and phosphorylation of glutamatergic NMDA NR2B receptors in response to dopamine D1 receptor activation. The combination of ITI-007's high-potency blockade of 5-HT2A receptors and unique dopamine receptor activity should allow a personalized approach to patient treatment for schizophrenia by making it

possible for the first time to select a clinical dose capable of saturating 5-HT2A receptors while permitting the "dialing in" of an optimal amount of dopamine receptor modulation by simple dose adjustments using a single drug. The ability to optimize the level of dopamine receptor modulation holds promise for the reduction of psychotic symptoms without incurring high levels of dopamine antagonism that cause motor disturbances and other deleterious side effects. In addition, the wide separation of affinity at 5-HT2A and D2 receptors may allow for administration of the appropriate amount of dopamine modulation for antipsychotic maintenance therapy and the treatment of bipolar disorders. The additional serotonin reuptake inhibition allows the potential for antidepressant efficacy.

ITI-007 has a low propensity to interact with receptors that mediate deleterious cardiovascular events, sedation and rapid and significant weight gain.

At low doses, ITI-007 is sleep promoting without having sedative properties and should not exhibit adverse effects during the night (e.g. falls, amnesia) or next day hangover effects that are commonly associated with other sleep medications. In a Phase II clinical trial, ITI-007 showed robust, dose-related and statistically significant increases in deep, slow wave sleep and decreases in the duration of wake time after sleep onset in patients with insomnia. ITI-007 is expected to have a strong safety profile with no addiction liability. This compound is being evaluated for the treatment of sleep disorders in various patient populations with sleep maintenance problems and in other sleep disorders such as sleep disorders in depression, other mood disorders, Alzheimer's disease and schizophrenia.

ABOUT INTRA-CELLULAR THERAPIES

Intra-Cellular Therapies, Inc. (ITI) is a biopharmaceutical company developing novel drugs for the treatment of diseases and disorders of the Central Nervous System (CNS). Building on the science generated from the Nobel Prize winning laboratory of Dr. Paul Greengard at The Rockefeller University, the Company develops compounds that have the potential to treat a wide range of diseases associated with the CNS, including schizophrenia, sleep disorders, Parkinson's and Alzheimer's disease, cognitive deficits in schizophrenia, depression and female sexual dysfunction, and other disorders pertaining to Women's Health. To aid in the development process, ITI incorporates its CNSProfile™, a state-of-the-art platform that allows the Company to choose compounds with the strongest potential to succeed in these difficult to treat diseases.

ABOUT CNSProfile™

Intra-Cellular Therapies has developed a state-of-the-art technology platform, CNSProfile™, capable of generating a unique molecular signature for drug compounds. Specifically, CNSProfile measures the levels of phosphoproteins, proteins chemically linked at specific sites to phosphates. This profile provides the Company with a proprietary and unique window into the intracellular action of CNS drugs or drug candidates. Intra-Cellular Therapies uses this platform in its drug discovery and development efforts of proprietary compounds and also to evaluate in-licensing opportunities.

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