UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Form 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): April 6, 2016

Intra-Cellular Therapies, Inc.
(Exact name of registrant as specified in its charter)

Commission File Number: 001-36274

Delaware	**36-4742850**
(State or other jurisdiction of incorporation)	**(IRS Employer Identification No.)**

430 East 29th Street
New York, New York 10016
(Address of principal executive offices, including zip code)

(646) 440-9333
(Registrant's telephone number, including area code)

Not applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

ITEM 8.01 Other Events.

On April 6, 2016, Intra-Cellular Therapies, Inc. (the "Company") announced additional data from the first Phase 3 clinical trial of its lead drug candidate, ITI-007 (ITI 007-301), and the ITI-007 Positron Emission Tomography ("PET") study in patients with schizophrenia.

The Company's press release announcing additional data from the PET study and the Phase 3 clinical trial of ITI-007-301, and the related posters presented at the 5th Biennial Schizophrenia International Research Society ("SIRS") Conference, are filed as Exhibits 99.1, 99.2, 99.3 and 99.4, respectively, to this Current Report on Form 8-K and are incorporated herein by reference.

ITEM 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press release dated April 6, 2016
99.2	Poster presentation, entitled "ITI-007 Exhibits Unique Pharmacology: Combined Results from Positron Emission Tomography (PET) Studies in Healthy Volunteers and Patients with Schizophrenia"
99.3	Poster presentation, entitled "Positive Phase 3 Clinical Trial of ITI-007 for the Treatment of Schizophrenia: Secondary Endpoints and Subgroup Analyses from a Randomized, Double-Blind, Placebo-Controlled Trial"
99.4	Poster presentation, entitled "Positive Phase 3 Clinical Trial of ITI-007 for the Treatment of Schizophrenia: Safety Results from a Randomized, Double-Blind, Placebo-Controlled Trial"

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

INTRA-CELLULAR THERAPIES, INC.

By: /s/ Lawrence J. Hineline
Lawrence J. Hineline
Vice President of Finance, Chief Financial Officer, Treasurer and Assistant Secretary

Date: April 6, 2016

Exhibit 99.1

Intra-Cellular Therapies Presents Additional ITI-007 Data at the 5th Biennial Schizophrenia International Research Society (SIRS) Conference

NEW YORK, April 6, 2016/GLOBE NEWSWIRE/ — Intra-Cellular Therapies, Inc. (NASDAQ: ITCI), a biopharmaceutical company focused on the development of therapeutics for central nervous system (CNS) disorders, today announced it delivered an oral presentation and presented several posters featuring data on ITI-007, the Company's lead drug candidate at the 5th Biennial Schizophrenia International Research Society (SIRS) Conference being held in Florence, Italy.

The oral presentation and two poster presentations featured additional efficacy and safety data from ITI-007-301, the Company's recently completed Phase 3 clinical trial in patients with schizophrenia. An additional poster presentation featured data from the ITI-007 Positron Emission Tomography (PET) study in patients with schizophrenia. Top-line data from both trials were announced in September 2015 and subsequently presented at the 54th annual meeting of the American College of Neuropsychopharmacology (ACNP) in December 2015.

Poster #S66 entitled "ITI-007 Exhibits Unique Pharmacology: Combined Results from Positron Emission Tomography (PET) Studies in Healthy Volunteers and Patients with Schizophrenia," was presented on Sunday, April 3rd. This PET study highlights ITI-007's unique pharmacological profile via serotonergic, dopaminergic, and glutamatergic pathways. ITI-007 was safe and well-tolerated and demonstrated dose-related occupancy of human brain dopamine D_2 receptors, 5-HT_{2A} receptors, and serotonin transporters. At a dose of 60 mg, ITI-007 demonstrated relatively low, about 40% mean peak striatal D_2 receptor occupancy in patients with schizophrenia at plasma steady state. Taken into context with data from other clinical trials, ITI-007 60 mg was effective in reducing psychosis in patients with schizophrenia at relatively low striatal D_2 receptor occupancy, lower than the occupancy range required by most other antipsychotic drugs. This mechanism, along with ITI-007's potent interactions at 5-HT_{2A} receptors, serotonin transporters and D_1 receptors, likely contributes to the efficacy of ITI-007 with improved psychosocial function and favorable motoric tolerability representing a potentially novel approach to the treatment of schizophrenia and other neuropsychiatric disorders.

Additional data regarding receptor occupancy within specific brain regions such as the ventral striatum were presented.

Poster #M67 entitled “Positive Phase 3 Clinical Trial of ITI-007 for the Treatment of Schizophrenia: Secondary Endpoints and Subgroup Analyses from a Randomized, Double-Blind, Placebo-Controlled Trial,” was presented on Monday, April 4th. In this trial, once-daily ITI-007 60 mg met the primary endpoint and demonstrated efficacy with statistically significant superiority over placebo at Day 28 as measured by the Positive and Negative Syndrome Scale (PANSS) total score (p=0.022). Moreover, ITI-007 60 mg showed significant efficacy as early as week 1 on both the PANSS total score and PANSS Positive Symptom subscale score, which was maintained at every time point throughout the entire study. ITI-007 60 mg also met the key secondary endpoint of statistically significant improvement on the Clinical Global Impression of Severity of Illness (CGI-S) (p=0.003). Both doses (ITI-007 40 mg and 60 mg) improved global severity of illness, positive symptoms and prosocial behavior.

A high treatment completion rate was observed with ITI-007 (87% of patients completed treatment on ITI-007 60 mg, 82% completed on ITI-007 40 mg, and 75% completed on placebo). Patients randomized to ITI-007 60 mg demonstrated a statistically significant longer time to treatment discontinuation due to any reason compared to placebo (p=0.006) and a statistically significant longer time to treatment discontinuation due to lack of efficacy (p=0.01). Baseline characteristics of the studied patient population indicated a mean of 17 years since first diagnosis and markedly ill at baseline with a mean baseline PANSS total score of 89.8 and a mean baseline CGI-S score of 4.8.

Poster #T66 entitled “Positive Phase 3 Clinical Trial of ITI-007 for the Treatment of Schizophrenia: Safety Results from a Randomized, Double-Blind, Placebo-Controlled Trial,” was presented on Tuesday, April 5th. ITI-007 given once daily in the morning was well-tolerated with no dose titration and demonstrated a safety profile that did not differ from placebo in patients with acutely exacerbated schizophrenia. The number of patients who discontinued treatment in this trial due to an adverse event was low and the time to treatment discontinuation due to an adverse event was not statistically significantly different from placebo for either dose of ITI-007. Patients randomized in this trial included 77.1% males with a mean age of 42.4 years. Administered orally once daily in the morning, the only treatment-emergent adverse event considered at least possibly related to ITI-007 occurring in □5% of patients and at least twice the

rate of placebo were somnolence, sedation and fatigue, all predominantly mild. ITI-007 showed a motoric profile similar to placebo according to adverse event reports or when objectively measured by the Simpson Angus Scale, the Barnes Akathisia Rating Scale, and the Abnormal Involuntary Movement Scale. There was no clinically meaningful increase in prolactin, rather ITI-007 (60 mg) significantly decreased prolactin ($p=0.05$), consistent with its mechanism of action as a dopamine D_2 receptor partial agonist. ITI-007 also showed a metabolic profile similar to placebo.

The oral presentation at SIRS entitled "Positive Phase 3 Clinical Trial of ITI-007 for the Treatment of Schizophrenia: Efficacy Results from a Randomized, Double-Blind, Placebo-Controlled Trial," was presented on Tuesday, April 5th and included an overview of the data presented in the posters.

"These data provide additional insights into the positive efficacy, safety and tolerability results seen in our ITI-007 studies in patients with schizophrenia, suggesting there is a broad beneficial effect with ITI-007 in schizophrenia and potentially across multiple indications," said Dr. Sharon Mates, Chairman and CEO of Intra-Cellular Therapies. "We believe, if approved, ITI-007 may provide an advancement in the treatment of schizophrenia by offering patients an effective therapy and the possibility of achieving long-term benefits by staying on treatment."

About ITI-007

ITI-007 is our lead drug development candidate with mechanisms of action that, we believe, have the potential to yield a first-in-class therapy for multiple therapeutic indications. In our pre-clinical and clinical trials to date, ITI-007 combines potent serotonin 5-HT_{2A} receptor antagonism, dopamine receptor phosphoprotein modulation (DPPM), glutamatergic modulation, and serotonin reuptake inhibition into a single drug candidate for the treatment of acute and residual schizophrenia, as well as for the treatment of bipolar disorder, including bipolar depression. At dopamine D_2 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 $GluN_{2B}$ receptors in a mesolimbic specific manner. We believe that this regional selectivity in brain areas thought to mediate the efficacy of antipsychotic drugs, together with serotonergic, glutamatergic, and dopaminergic interactions, may result in efficacy for a broad array of symptoms associated with schizophrenia and bipolar disorder with improved psychosocial function. The serotonin reuptake

inhibition potentially allows for antidepressant activity in the treatment of schizoaffective disorder, co-morbid depression, and/or as a stand-alone treatment for major depressive disorder. We believe ITI-007 may also be useful for the treatment of other psychiatric and neurodegenerative disorders, particularly behavioral disturbances associated with dementia, autism, and other CNS diseases.

About Schizophrenia

Schizophrenia is a disabling and chronic mental illness affecting over 1% of the world's population. Schizophrenia is characterized by multiple symptoms during an acute phase of the disorder that can include so-called "positive" symptoms, such as hearing voices, disorganized thinking, grandiose beliefs and suspiciousness or paranoia. These symptoms can be accompanied by additional, harder-to-treat symptoms, such as social withdrawal and blunted emotional response and expression, collectively referred to as "negative" symptoms, difficulty concentrating or cognitive impairment, depression, and insomnia. Such residual symptoms often persist even after the acute positive symptoms subside, and contribute substantially to the social and employment disability associated with schizophrenia. Current antipsychotic medications provide some relief for the symptoms associated with the acute phase of the disorder, but they do not effectively treat the residual phase symptoms and psychosocial impairment associated with chronic schizophrenia. Currently available medications used to treat acute schizophrenia are limited in their use due to side effects that can include movement disorders, weight gain, metabolic disturbances, and cardiovascular disorders. There is an unmet medical need for new therapies that have improved side effect and efficacy profiles.

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, ITI-007, for the treatment of schizophrenia, bipolar disorder, behavioral disturbances in dementia, depression and other neuropsychiatric and neurological disorders. ITI-007, a first-in-class molecule, is in Phase 3 clinical development for the treatment of schizophrenia and bipolar depression. The Company is also utilizing its phosphodiesterase platform and other proprietary chemistry platforms to develop drugs for the treatment of CNS and other disorders.

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, our clinical and non-clinical development plans; the progress, timing and results of our clinical trials; the safety and efficacy of our product development candidates; our beliefs about the potential uses and benefits of ITI-007; and our research 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 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 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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ITI-007 Exhibits Unique Pharmacology: Combined Results from Positron Emission Tomography (PET) Studies in Healthy Volunteers and Patients with Schizophrenia

Kimberly E Vanover[1], Robert E. Davis[1], Cedric O'Gorman[1], Jelena Saillard[1], Michal Weingart[1], Sharon Mates[1]
Yun Zhou[2], Weiguo Ye[2], Dean F. Wong[2]
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#S66

ABSTRACT

Background
ITI-007 is a first-in-class investigational new drug in clinical development for the treatment of schizophrenia. Through synergistic actions via serotonergic, dopaminergic and glutamatergic systems, ITI-007 represents a novel approach to the treatment of schizophrenia and other neuropsychiatric disorders. ITI-007 is a potent antagonist at 5-HT2A receptors, a mesolimbic/mesocortical dopamine phosphoprotein modulator (DPPM) with activity as a pre-synaptic partial agonist and post-synaptic antagonist at dopamine D2 receptors, a mesolimbic D1 receptor/glutamate-GluN2B-receptor phosphoprotein modulator and a serotonin reuptake inhibitor. Phase 2 clinical trial (ITI-007-005) data indicated that 60 mg ITI-007 was effective in reducing symptoms of schizophrenia with a safety and side effect profile similar to placebo (Lieberman et al., Biological Psychiatry, 2015 online ahead of print). The purpose of the present studies was to determine brain occupancy of ITI-007 at key pharmacological targets thought to mediate its efficacy, including dopamine D2 receptor occupancy (D2RO).

Methods
Healthy volunteers (Clinical Study ITI-007-003; Davis et al. Psychopharmacology, 2015, 232:2863) or patients with stable schizophrenia who were washed off their antipsychotic medications at least two weeks (inpatient ITI-007-008) received a baseline scan and up to 3 post-treatment scan(s). Healthy volunteers were evaluated after a single dose of ITI-007 (10, 20, 30, or 40 mg) and patients with schizophrenia received ITI-007 (60 mg) once daily for approximately two weeks, to plasma steady state. Carbon-11-Raclopride, carbon-11-ar100907, and carbon-11-DASB were used as the radiopharmaceuticals for imaging striatal D2 receptors, cortical 5-HT2A receptors, and striatal serotonin transporters, respectively. Brain regions of interest were outlined using magnetic resonance tomography (MRT) with cerebellum as the reference region. Binding potentials were estimated using a simplified reference tissue model. D2RO was expressed as percent change in the binding potentials before and after ITI-007 administration.

Results
In healthy volunteers, ITI-007 (10 mg) demonstrated high occupancy (~80 %) of cortical 5-HT$_{2A}$ receptors and low occupancy of striatal D2 receptors (~12%). D2RO increased with dose. ITI-007 (40 mg) resulted in peak occupancy up to 39% of striatal D2 receptors and 33% of striatal serotonin transporters. In patients with schizophrenia, 60 mg ITI-007 demonstrated ~40% D2RO.

Discussion
Taken into context with data from other clinical trials (ITI-007-005 and ITI-007-301) in which ITI-007 60 mg was effective in reducing psychosis in patients with schizophrenia, ITI-007 was effective at relatively low striatal D2 receptor occupancy, lower than the occupancy range required by most other antipsychotic drugs. Unlike any existing schizophrenia treatment, this dopamine receptor phosphoprotein modulator, or DPPM, acts as a pre-synaptic partial agonist and post-synaptic antagonist at D2 receptors. This mechanism along with potent interactions at 5-HT2A receptors, serotonin transporters and D1 receptors with indirect glutamatergic modulation likely contributes to the efficacy of ITI-007 with improved psychosocial function and favorable motoric tolerability. As such, ITI-007 represents a novel approach to the treatment of schizophrenia.

RESULTS

Table 1. Pharmacological Profile

In Vitro Receptor Binding Affinities		
Target	ITI-007 Ki (nM)	IC200131 Ki (nM)
5-HT2A	0.5	61
D2	32	574
D1	52	>1000
SERT	62	~70

- 5-HT2A receptor antagonist
- Dopamine phosphoprotein modulator (DPPM)
- Glutamatergic phosphoprotein modulator
- Serotonin reuptake inhibitor

Table 2. Peak Striatal D2 Receptor Occupancy in Healthy Volunteers[a]

		Baseline BP_{ND}		%D_2RO			
Subject	Start Time of Scan 0.5 – 1 h Post-dose	Caudate	Putamen	Caudate	Putamen	Mean for Dorsal Striatum	Group Mean
003-N001	10 mg	2.16	2.87	7.3	5.4	6	12%
003-N002		2.61	3.21	17.1	16.4	17	
003-N003	20 mg	2.55	3.26	18.1	21.1	19	19%
003-N004		2.37	2.83	16.3	20.6	20	
003-N008	30 mg	2.51	3.08	30.3	30.0	30	27%
003-N009		2.77	3.12	19.7	15.9	18	
003-N010		2.87	4.02	31.8	31.4	32	
003-N012	40 mg	2.79	3.05	42.8	34.9	39	29%
003-N013		3.50	3.79	18.9	18.5	19	

[a]Study ITI-007-008 in patients with schizophrenia was conducted using a high resolution research tomograph (HRRT) with higher resolution than the GE Advance PET scanner used in Study ITI-007-003 in healthy volunteers, resulting in higher baseline binding potentials and allowing for the collection of D2RO in ventral striatum in patients with schizophrenia.

Table 3. Peak 5-HT2A Receptor & SERT Occupancy in Healthy Volunteers

		Baseline BP_{ND}		%5-HT2ARO			
Subject	Start Time of Scan 0.5 – 1 h Post-dose	Prefrontal Cortex	Orbital Cortex	Prefrontal Cortex	Orbital Cortex	Mean for Cortical	Group Mean
003-N015	10 mg	2.50	2.51	83.8	85.5	85	88%
003-N016		1.62	1.74	91.6	89.2	90	
		Baseline BP_{ND}		%SERTRO			
Subject	Start Time of Scan 0.5 – 1 h Post-dose	Caudate	Putamen	Caudate	Putamen	Mean for Dorsal Striatum	Group Mean
003-N011	40 mg	1.76	1.88	8.3	19.0	14	23%
003-N014		2.48	2.72	33.1	29.2	31	

Table 4. Peak Striatal D2 Receptor Occupancy in Patients with Schizophrenia[a]

		Baseline BP_{ND}			%D_2RO				
Subject	Start Time of Scan 1 h Post-Dose	Caudate	Putamen	Ventral Striatum	Caudate	Putamen	Ventral Striatum	Mean ± SD Dorsal Striatum	Mean ± SD Ventral Striatum
B-N001*	60 mg	3.040	3.149	2.440[b]	17.9	18	18.9	39% ± 12%	31% ± 12%
B-N002		4.033	5.234	3.346	43.1	39.2	42.8		
B-N003		4.216	5.529	3.534	35.5	34	37.8		
B-N004		3.399	4.556	2.190[b]	49.8	47.5	25		
B-N005		3.641	4.629	3.026	52.3	50	42.1		
B-N006		3.684	4.074	2.714[b]	41	34.1	17.3		

*B-N001 showed low plasma levels at the start of the scan, indicating the dose may have been missed; a reanalysis without this low outlier confirmed the initial analysis result with mean striatal D2RO approximately 40% with 60 mg ITI-007, but, as would be expected, with less variability (43% ± 7%; range 35% to 51%; 41% median).
[b]BP_{ND} values at baseline <=3 on the higher resolution HRRT may not be sufficiently high to measure displacement; excluding these values, mean ventral striatal D2RO was 40.9%.

RESULTS (cont'd)

Figure 1.

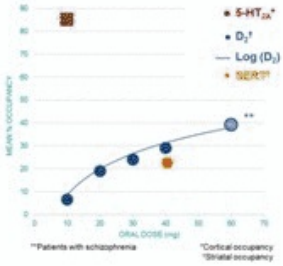
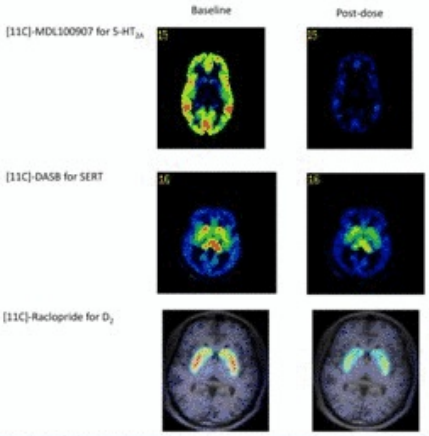


Figure 2.



CONCLUSIONS

- ITI-007 demonstrated dose-related occupancy of human brain dopamine D2 receptors, 5-HT2A receptors, and serotonin transporters.
- Taken into context with data from other clinical trials (ITI-007-005 and ITI-007-301), ITI-007 60 mg was effective in reducing psychosis in patients with schizophrenia at relatively low (~40%) dorsal striatal D2 receptor occupancy, lower than the occupancy range required by most other antipsychotic drugs.
- This profile likely contributes to the efficacy of ITI-007 with improved psychosocial function and favorable motoric tolerability.
- ITI-007 is currently in Phase 3 clinical development for the treatment of schizophrenia and bipolar depression.

ACKNOWLEDGEMENTS AND CONTACT

KEV, RED, CO'G, JS, MW and SM are full time employees of Intra-Cellular Therapies, Inc. (ITCI).
The data in patients with schizophrenia were collected in collaboration with Dr. Dean Wong and colleagues at The Johns Hopkins University and with Dr. Robert Litman and colleagues at CBH Health in a clinical trial paid for by ITCI.
Contact: cogorman@intracellulartherapies.com

Positive Phase 3 Clinical Trial of ITI-007 for the Treatment of Schizophrenia: Secondary Endpoints & Subgroup Analyses from a Randomized, Double-Blind, Placebo-Controlled Trial

Kimberly E Vanover[1], Robert E. Davis[1], Cedric O'Gorman[1], Jelena Saillard[1], Michal Weingart[1], Sharon Mates[1], Christoph U. Correll[2]

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#M67

ABSTRACT

Background

ITI-007 is a first-in-class investigational new drug in clinical development for the treatment of schizophrenia. Through synergistic actions via serotonergic, dopaminergic and glutamatergic systems, ITI-007 represents a novel approach to the treatment of schizophrenia and other neuropsychiatric disorders. ITI-007 is a potent antagonist at 5-HT2A receptors, a mesolimbic/mesocortical dopamine phosphoprotein modulator (DPPM) with activity as a pre-synaptic partial agonist and post-synaptic antagonist at dopamine D2 receptors, a mesolimbic D1-receptor-glutamate GluN2B receptor phosphoprotein modulator and a serotonin reuptake inhibitor. Phase 2 clinical trial (ITI-007-005) data indicated that 60 mg ITI-007 was effective in reducing symptoms of schizophrenia with a safety and side effect profile similar to placebo (Lebenstein et al., Biological Psychiatry, 2015 online ahead of print). A Phase 3 clinical trial (ITI-007-301) was conducted to evaluate the efficacy and safety of ITI-007 for the treatment of schizophrenia.

Methods

In the Phase 3 trial (ITI-007-301) patients with an acutely exacerbated episode of schizophrenia were randomized to receive one of three oral treatments once daily for 4 weeks: 60 mg ITI-007, 40 mg ITI-007, or placebo in a 1:1:1 ratio. The primary endpoint was change from baseline on the Positive and Negative Syndrome Scale (PANSS) total score at Day 28 compared to placebo. The key secondary endpoint was the Clinical Global Impression scale for Severity of Illness (CGI-S). Additional analyses on secondary endpoints and patient subgroups were conducted.

Results

In this trial, once-daily ITI-007 60 mg met the primary endpoint and demonstrated efficacy with statistically significant superiority over placebo at Day 28 as measured by the PANSS total score ($p<0.022$). Moreover, ITI-007 60 mg showed significant efficacy as early as week 1 on both the PANSS total score and PANSS Positive Symptom subscale score, which was maintained at every time point throughout the entire study. ITI-007 60 mg also met the key secondary endpoint of statistically significant improvement on the CGI-S ($p<0.005$). Consistent with previous studies, ITI-007 was safe and well-tolerated. [Please see companion abstract/poster TBA for more details on safety.] Additional analyses on secondary endpoints and patient subgroups will be presented.

Discussion

These findings confirm and extend the positive results demonstrated at 60 mg in the Phase 2 study. Taken into context with data from another clinical trial (ITI-007-008, see abstract/poster TBA) in which ITI-007 60 mg was associated with a mean of approximately 40% striatal dopamine D2 receptor occupancy using positron emission tomography (PET), ITI-007 demonstrated efficacy at relatively low striatal D2 receptor occupancy, lower than the occupancy range required by most other antipsychotic drugs. Unlike any existing schizophrenia treatment, this dopamine receptor phosphoprotein modulator, or DPPM, acts as a pre-synaptic partial agonist and post-synaptic antagonist at D2 receptors. This mechanism along with potent interactions at 5-HT2A receptors, serotonin reuptake inhibition and indirect glutamatergic modulation likely contributes to the efficacy with improved psychosocial function. ITI-007 further exhibits improvements with a differentiated profile on important secondary endpoints and in patient subgroups who represent particularly vulnerable populations in need of improved treatment. As such, ITI-007 represents a novel approach to the treatment of schizophrenia.

RESULTS

Figure 1. Subject Disposition

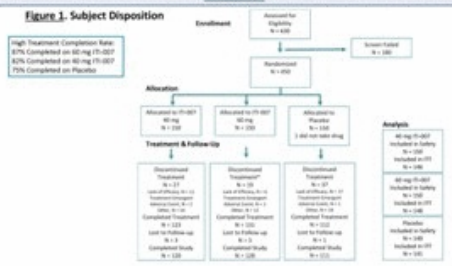


Figure 2. Time to Discontinue Treatment due to Any Reason

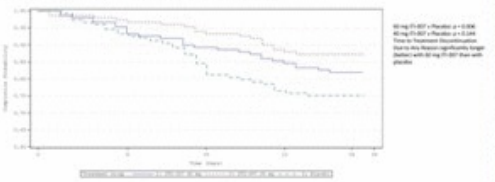


Figure 3. Time to Discontinue Treatment due to Lack of Efficacy

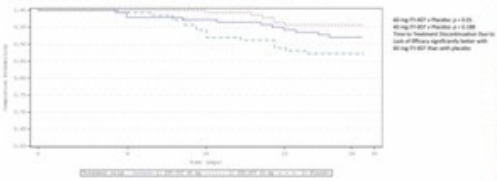


Table 1. Baseline Characteristics (ITT Population)

	Placebo N = 141	ITI-007 40 mg N = 146	ITI-007 60 mg N = 148	Total N = 435
Years since 1st Diagnosis (mean±SD)	17.4 ± 10.62	17.0 ± 10.59	16.5 ± 10.35	17.0 ± 10.5
BL PANSS (mean ± SD)	90.1 ± 11.12	89.3 ± 10.18	90.1 ± 9.53	89.8 ± 10.27
BL CGI-S (mean ± SD)	4.8 ± 0.63	4.7 ± 0.58	4.8 ± 0.54	4.8 ± 0.58

RESULTS (cont'd)

ITI-007 Demonstrates Antipsychotic Efficacy

Figure 4. ITI-007 (60 mg) met the primary objective of this Phase 3 clinical trial, separated from placebo as early as week 1 and maintained efficacy at every time point on the PANSS total score.

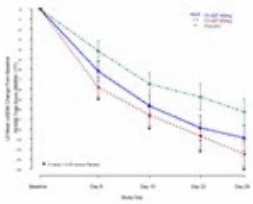


Figure 5. Both 40 mg and 60 mg were statistically significantly superior to placebo on CGI-S at study day 22 and 28.

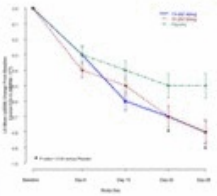


Figure 6. Both 40 mg and 60 mg were statistically superior to placebo on the PANSS Positive Symptom Subscale.

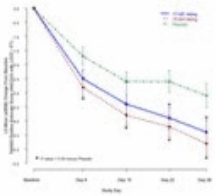


Figure 7. Both 40 mg and 60 mg were statistically superior to placebo on the PANSS-derived Prosocial Factor.

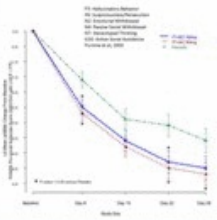
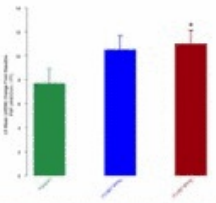


Figure 8. ITI-007 60 mg was statistically superior to placebo on the Personal and Social Performance Scale (PSP).



CONCLUSIONS

- ITI-007 demonstrated antipsychotic efficacy as measured by the PANSS total score at a dose (60 mg) that was well-tolerated in patients with acutely exacerbated schizophrenia with a safety profile that did not differ from placebo.
- Both doses of ITI-007 improved global illness severity, positive symptoms and prosocial behavior.
- ITI-007 represents a novel approach to the treatment of schizophrenia.

ACKNOWLEDGEMENTS AND CONTACT

KEV, RED, CO'G, JS, MW and SM are full time employees of Intra-Cellular Therapies, Inc. (ITCI).
CUC has been a consultant and/or advisor to or has received honoraria from: Alkermes, Forum, Gerson Lehrman Group, IntraCellular Therapies, Janssen/ J&J, Lundbeck, Medavante, Medscape, Otsuka, Pfizer, ProPhase, Sunovion, Supernus, Takeda, and Teva. He received grant support from Takeda.
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Positive Phase 3 Clinical Trial of ITI-007 for the Treatment of Schizophrenia: Safety Results from a Randomized, Double-Blind, Placebo-Controlled Trial

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#T66

ABSTRACT

Background

ITI-007 is a first-in-class investigational new drug in clinical development for the treatment of schizophrenia. Through synergistic actions via serotonergic, dopaminergic and glutamatergic systems, ITI-007 represents a novel approach to the treatment of schizophrenia and other neuropsychiatric disorders. ITI-007 is a potent antagonist at 5-HT2A receptors, a mesolimbic/mesocortical dopamine phosphoprotein modulator (DPPM) with activity as a pre-synaptic partial agonist and post-synaptic antagonist at dopamine D2 receptors, a mesolimbic D1 receptor/glutamate GluR2B receptor phosphoprotein modulator and a serotonin reuptake inhibitor. Phase 2 clinical trial (ITI-007-005) data indicated that 60 mg ITI-007 was effective in reducing symptoms of schizophrenia with a safety and side effect profile similar to placebo (Lieberman et al., Biological Psychiatry, 2015 online ahead of print). A Phase 3 clinical trial (ITI-007-301) was conducted to evaluate the efficacy and safety of ITI-007 for the treatment of schizophrenia.

Methods

In the Phase 3 trial (ITI-007-301) patients with an acutely-exacerbated episode of schizophrenia were randomized to receive one of three oral treatments once daily for 4 weeks: 60 mg ITI-007, 40 mg ITI-007, or placebo in a 1:1:1 ratio. The primary endpoint was change from baseline on the Positive and Negative Syndrome Scale (PANSS) total score at Day 28 compared to placebo. Vital signs, 12 lead ECGs, clinical laboratory values, and adverse events were reported.

Results

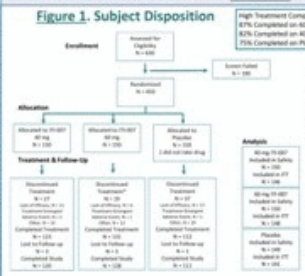
In this trial, once-daily ITI-007 60 mg met the primary endpoint and demonstrated efficacy with statistically significant superiority over placebo at Day 28 as measured by the PANSS total score (p=0.022). [Please see companion abstract/poster #67 for more details on efficacy]. Consistent with previous studies, ITI-007 was safe and well-tolerated as evidenced by a motoric, metabolic, and cardiovascular profile similar to placebo, and no clinically significant changes in akathisia, extrapyramidal symptoms, prolactin, body weight, glucose, insulin, and lipids.

Discussion

These findings confirm and extend the positive results demonstrated at 60 mg in the Phase 2 study. Taken into context with data from another clinical trial (ITI-007-008; see abstract/poster 066 in which ITI-007 60 mg was associated with a mean of approximately 40% striatal dopamine D2 receptor occupancy using positron emission tomography (PET), ITI-007 demonstrated efficacy at relatively low striatal D2 receptor occupancy, lower than the occupancy range required by most other antipsychotic drugs. Unlike any existing schizophrenia treatment, this dopamine receptor-phosphoprotein modulator, or DPPM, acts as a pre-synaptic partial agonist and post-synaptic antagonist at D2 receptors. This mechanism likely contributes to the favorable safety profile of ITI-007, with reduced risk for hyperprolactinemia, akathisia, extrapyramidal symptoms, and other motoric side effects. ITI-007 also lacks off-target pharmacological interactions that may contribute to cardiovascular and metabolic liability of other treatment options. As such, ITI-007 represents a novel approach to the treatment of schizophrenia.

RESULTS

Figure 1. Subject Disposition



In this trial, once-daily ITI-007 60 mg met the primary endpoint and demonstrated efficacy with statistically significant superiority over placebo at Day 28 as measured by the PANSS total score (p=0.022). ITI-007 (60 mg) met the primary objective of this Phase 3 clinical trial, separated from placebo as early as week 1 and maintained efficacy at every time point on the PANSS total score.

[Please see companion abstract/poster M67 for more details on efficacy].

Figure 2. Time to Discontinue Treatment due to Any Reason

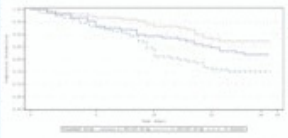


Figure 3. Time to Discontinue Treatment due to Adverse Event

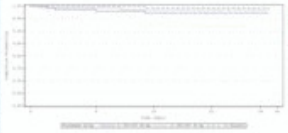


Table 1. Demographics (Safety Population)

	Placebo N = 149	ITI-007 40 mg N = 150	ITI-007 60 mg N = 150	Total N = 449
Male [n (%)]	123 (82.6%)	113 (75.3%)	110 (73.7%)	346 (77.1%)
Age (mean±SD)	41.4 ± 10.29	43.5 ± 10.08	42.4 ± 10.30	42.4± 10.23
Years since 1st Diagnosis (mean±SD)	17.2 ± 10.58	16.8 ± 10.53	16.6 ± 10.30	16.9 ± 10.45

Table 2. Most Frequent Adverse Events with Once Daily Administration in the Morning (Safety Population)

Most Frequent (>5% and twice the rate of placebo) Treatment-emergent adverse events (TEAEs) considered at least possibly related to study treatment n (%)	Placebo (N=149)	40 mg ITI-007 (N=150)	60 mg ITI-007 (N=150)
Mild to Moderate Somnolence	6 (4.0%)	16 (10.7%)	26 (17.3%)
Mild Sedation	8 (5.4%)	14 (9.3%)	18 (12.0%)
Mild to Moderate Fatigue	2 (1.3%)	6 (4.0%)	8 (5.3%)

RESULTS (cont'd)

ITI-007 Demonstrated a Motoric and Metabolic Profile Similar to Placebo

Figure 4. ITI-007 Did Not Induce Extrapyramidal Side Effects or Akathisia

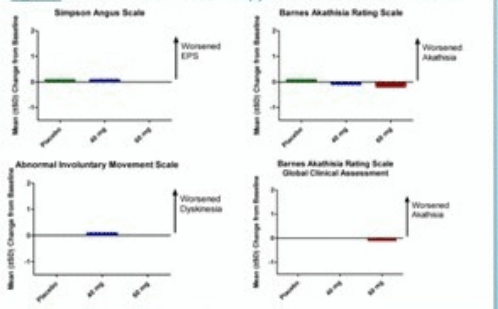


Figure 5. No Clinically Meaningful Increase in Any Metabolic Parameter

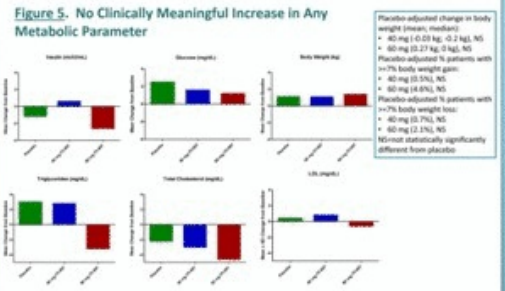
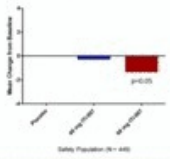


Figure 6. No Clinically Meaningful Increase in Prolactin, Rather ITI-007 (60 mg) Significantly Decreased Prolactin, Consistent with Its Mechanism of Action as a Dopamine D2 Receptor Partial Agonist



CONCLUSIONS

- ITI-007 given once daily in the morning was well-tolerated with no dose titration and demonstrated a safety profile that did not differ from placebo in patients with acutely exacerbated schizophrenia.
- Patients randomized to both doses of ITI-007 showed high treatment completion rates.
- ITI-007 showed a motoric profile similar to placebo according to adverse event reports or when objectively measured.
- ITI-007 showed a metabolic profile similar to placebo.
- ITI-007 represents a novel approach to the treatment of schizophrenia.

ACKNOWLEDGEMENTS AND CONTACT

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