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): March 28, 2023

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, NY 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))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock	ITCI	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

ITEM 8.01 Other Events.

On March 28, 2023, Intra-Cellular Therapies, Inc. (the "Company") announced positive topline results from Study 403 evaluating lumateperone as monotherapy in patients with major depressive disorder with mixed features and bipolar depression with mixed features.

The Company's press release announcing the results is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

ITEM 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Description
99.1	Press release dated March 28, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

The press release may contain hypertext links to information on our website. The information on our website is not incorporated by reference into this Current Report on Form 8-K and does not constitute a part of this Form 8-K.

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
Senior Vice President of Finance, Chief Financial Officer, Treasurer and Assistant Secretary

Date: March 28, 2023

Exhibit 99.1

Intra-Cellular Therapies Announces Positive Topline Results from Study 403 Evaluating Lumateperone as Monotherapy in Patients with Major Depressive Disorder with Mixed Features and Bipolar Depression with Mixed Features

Lumateperone 42mg was statistically significant on the primary endpoint of symptom reduction on the Montgomery Asberg Depression Rating Scale (MADRS) for each patient population including:

- *combined major depressive disorder (MDD) with mixed features and bipolar depression with mixed features (5.7 point reduction v. placebo; p<0.0001; Cohen's d effect size (ES) = 0.64)*
- *MDD with mixed features (5.9 point reduction v. placebo; p<0.0001; ES= 0.67)*
- *bipolar depression with mixed features (5.7 point reduction v. placebo; p<0.0001; ES= 0.64)*

Lumateperone 42mg was statistically significant on the key secondary endpoint of the clinician's assessment of improvement in the overall severity on the Global Impression of Severity Scale (CGI-S) for each patient population including:

- *combined MDD with mixed features and bipolar depression with mixed features (p<0.0001; ES= 0.59)*
- *MDD with mixed features (p=0.0003; ES= 0.57)*
- *bipolar depression with mixed features (p<0.0001; ES= 0.61)*

Favorable safety and tolerability profile observed, consistent with prior lumateperone trials

Conference call scheduled today at 8:30 a.m. ET

NEW YORK, March 28, 2022 (GLOBE NEWSWIRE) — Intra-Cellular Therapies, Inc. (Nasdaq:ITCI), a biopharmaceutical company focused on the development and commercialization of therapeutics for central nervous system (CNS) disorders, today announced positive topline results from Study 403 evaluating lumateperone 42mg as monotherapy in the treatment of major depressive episodes in patients with major depressive disorder with mixed features and in patients with bipolar depression with mixed features.

Lumateperone 42mg given once daily met the primary endpoint in the study by demonstrating a statistically significant and clinically meaningful reduction in the MADRS total score compared to placebo at Week 6, as follows:

Primary Endpoint: Change from baseline vs. placebo on the MADRS Total Score at Week 6 (ITT study population)

	Least Squares (LS) Mean Reduction vs. Baseline[1]				
	Lumateperone 42mg	Placebo	LS Mean Difference[1]	p value	Cohen's d effect size
Combined patient population of MDD with mixed features and bipolar depression with mixed features	18.1	12.4	-5.7	p<0.0001	0.64
Population of patients with MDD with mixed features	18.2	12.2	-5.9	p<0.0001	0.67
Population of patients with bipolar depression with mixed features	17.7	12.0	-5.7	p<0.0001	0.64

[1] Rounded to nearest tenth.

Lumateperone 42mg also met the key secondary endpoint in the study by demonstrating a statistically significant and clinically meaningful reduction in the CGI-S score compared to placebo at Week 6 in the combined patient population of MDD with mixed features and bipolar depression with mixed features ($p<0.0001$; ES= 0.59), patients with MDD with mixed features ($p=0.0003$; ES= 0.57), and patients with bipolar depression with mixed features ($p<0.0001$; ES=0.61).

In this study, lumateperone was generally safe and well tolerated, with a side effect profile consistent with prior lumateperone trials. The most commonly reported adverse events that were observed at a rate greater than or equal to 5% and at least twice the rate of placebo in the total population were somnolence, dizziness, and nausea.

"We are very pleased with the results of this highly successful trial in these difficult to treat patient populations with mixed features in MDD and mixed features in bipolar depression," said Dr. Sharon Mates, Chairman and CEO of Intra-Cellular Therapies. "This study provides proof of concept in these patient populations and further validates lumateperone's broad potential in mood disorders. We look forward to discussing these results with the FDA and determining next steps for the program."

“In this study, lumateperone demonstrated a robust effect in both patients with MDD with mixed features and patients with bipolar depression with mixed features. This is particularly significant considering these patients suffer from greater symptom severity, increased recurrence of mood episodes, higher comorbidity and increased risk of suicide,” said Stephen Stahl MD, PhD, DSc (Hon.), Adjunct Professor, Department of Psychiatry, University of California, San Diego School of Medicine, La Jolla, California and Clinical Professor of Psychiatry and Neuroscience, University of California Riverside. “Given the lack of available therapies for these patient populations, there is a tremendous need for treatment options.”

About Study 403

Study 403 was a randomized, double-blind, placebo-controlled, global study to evaluate the efficacy and safety of lumateperone as monotherapy treatment for patients with major depressive episodes associated with MDD or Bipolar I or Bipolar II Disorder who also met the Diagnostic and Statistical Manual of Mental Disorder, 5th Edition (DSM-5) criteria for mixed-features. Additionally, patients were required to have a MADRS total score of ≥24, CGI-S of ≥4, and a Young Mania Rating scale (YMRS) score between 4 and 16.

Patients were randomized 1:1 to lumateperone 42mg (N=192) or placebo (N=191) with similar distribution between the two conditions. The primary endpoint of the study was the change from baseline versus placebo on the MADRS total score at Week 6 and the key secondary endpoint was the CGI-S which assessed the global severity of illness.

As initially designed, Study 403 evaluated lumateperone as a monotherapy treatment for patients with bipolar depression. Following the successful completion of our bipolar depression monotherapy and adjunctive program, Study 403 was amended to evaluate lumateperone as a treatment for patients with MDD with mixed features and bipolar depression with mixed features. The results presented above with respect to mixed features exclude the patients initially enrolled in Study 403 with bipolar depression. While these patients were diagnostically confirmed for bipolar depression, they were not diagnostically confirmed for bipolar depression with mixed features. A sensitivity analysis was conducted for the total population (ITT N=477) including these initially enrolled patients and the patients with bipolar depression with mixed features and patients with MDD with mixed features. In this pre-specified sensitivity analysis, lumateperone 42mg was statistically significant on the MADRS total score (5.6 point reduction v. placebo; $p<0.0001$; ES= 0.62) and CGI-S ($p<0.0001$; ES= 0.61).

In this study, lumateperone was generally safe and well tolerated in all patients who received at least one dose of drug, with a side effect profile consistent with prior lumateperone trials. Adverse events were mostly mild to moderate and similar to those seen in prior lumateperone studies in bipolar depression and schizophrenia.

About Mixed Features in Bipolar Depression and Major Depressive Disorder

Bipolar disorders and major depressive disorder are highly prevalent serious mental illnesses.

Bipolar disorders affect approximately 11 million adults in the U.S. and bipolar depression is the most common clinical presentation of the disorder. Patients with bipolar disorder generally spend more time in the depressive phase compared to the manic phase.

MDD affects approximately 21 million adults in the U.S. each year.

During a current major depressive episode, about one-third of patients with either bipolar disorder or MDD present with mixed features. Mixed features is defined by a patient having co-occurring subthreshold manic symptoms during their depressive episode or a patient having co-occurring subthreshold depressive symptoms during their manic episode.

Depressed patients with the presence of mixed features have greater severity of illness, higher rates of suicidal ideation and suicide, higher recurrence rates, and higher comorbidities. These patients are more difficult to treat than patients exhibiting depressive episodes without mixed features. The inclusion of the mixed features specifier in DSM-5 underscores the recently recognized importance of this clinical presentation.

Conference Call and Webcast Details

The Company will host a live conference call and webcast today at 8:30 AM Eastern Time to discuss the results of Study 403. To attend the live conference call by phone please use this registration link [https://register.vevent.com/register/BI1f632b04f9b948ef9255ce3e5108d7d6]. All participants must use the link to complete the online registration process in advance of the conference call.

The live and archived webcast can be accessed under “Events & Presentations” in the Investors section of the Company’s website at www.intracellulartherapies.com. Please log in approximately 5-10 minutes prior to the event to register and to download and install any necessary software.

CAPLYTA® (lumateperone) is indicated in adults for the treatment of schizophrenia and depressive episodes associated with bipolar I or II disorder (bipolar depression) as monotherapy and as adjunctive therapy with lithium or valproate.

Important Safety Information

Boxed Warnings:

- **Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. CAPLYTA is not approved for the treatment of patients with dementia-related psychosis.**
- **Antidepressants increased the risk of suicidal thoughts and behaviors in pediatric and young adults in short-term studies. All antidepressant-treated patients should be closely monitored for clinical worsening, and for emergence of suicidal thoughts and behaviors. The safety and effectiveness of CAPLYTA have not been established in pediatric patients.**

Contraindications: CAPLYTA is contraindicated in patients with known hypersensitivity to lumateperone or any components of CAPLYTA. Reactions have included pruritus, rash (e.g., allergic dermatitis, papular rash, and generalized rash), and urticaria.

Warnings & Precautions: Antipsychotic drugs have been reported to cause:

- **Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis**, including stroke and transient ischemic attack. See Boxed Warning above.
- **Neuroleptic Malignant Syndrome (NMS)**, which is a potentially fatal reaction. Signs and symptoms include: high fever, stiff muscles, confusion, changes in breathing, heart rate, and blood pressure, elevated creatinine phosphokinase, myoglobinuria (and/or rhabdomyolysis), and acute renal failure. Patients who experience signs and symptoms of NMS should immediately contact their doctor or go to the emergency room.
- **Tardive Dyskinesia**, a syndrome of uncontrolled body movements in the face, tongue, or other body parts, which may increase with duration of treatment and total cumulative dose. TD may not go away, even if CAPLYTA is discontinued. It can also occur after CAPLYTA is discontinued.

- **Metabolic Changes**, including hyperglycemia, diabetes mellitus, dyslipidemia, and weight gain. Hyperglycemia, in some cases extreme and associated with ketoacidosis, hyperosmolar coma or death, has been reported in patients treated with antipsychotics. Measure weight and assess fasting plasma glucose and lipids when initiating CAPLYTA and monitor periodically during long-term treatment.
- **Leukopenia, Neutropenia, and Agranulocytosis (including fatal cases)**. Complete blood counts should be performed in patients with pre-existing low white blood cell count (WBC) or history of leukopenia or neutropenia. CAPLYTA should be discontinued if clinically significant decline in WBC occurs in absence of other causative factors.
- **Decreased Blood Pressure & Dizziness**. Patients may feel lightheaded, dizzy or faint when they rise too quickly from a sitting or lying position (orthostatic hypotension). Heart rate and blood pressure should be monitored and patients should be warned with known cardiovascular or cerebrovascular disease. Orthostatic vital signs should be monitored in patients who are vulnerable to hypotension.
- **Falls**. CAPLYTA may cause sleepiness or dizziness and can slow thinking and motor skills, which may lead to falls and, consequently, fractures and other injuries. Patients should be assessed for risk when using CAPLYTA.
- **Seizures**. CAPLYTA should be used cautiously in patients with a history of seizures or with conditions that lower seizure threshold.
- **Potential for Cognitive and Motor Impairment**. Patients should use caution when operating machinery or motor vehicles until they know how CAPLYTA affects them.
- **Body Temperature Dysregulation**. CAPLYTA should be used with caution in patients who may experience conditions that may increase core body temperature such as strenuous exercise, extreme heat, dehydration, or concomitant anticholinergics.
- **Dysphagia**. CAPLYTA should be used with caution in patients at risk for aspiration.

Drug Interactions: CAPLYTA should not be used with CYP3A4 inducers. Dose reduction is recommended for concomitant use with strong CYP3A4 inhibitors or moderate CYP3A4 inhibitors.

Special Populations: Newborn infants exposed to antipsychotic drugs during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms following delivery. Breastfeeding is not recommended. Dose reduction is recommended for patients with moderate or severe hepatic impairment.

Adverse Reactions: The most common adverse reactions in clinical trials with CAPLYTA vs. placebo were somnolence/sedation, dizziness, nausea, and dry mouth.

CAPLYTA is available in 10.5 mg, 21 mg, and 42 mg capsules.

Please click here to see full Prescribing Information including **Boxed Warning**.

About CAPLYTA (lumateperone)

CAPLYTA 42 mg is an oral, once daily atypical antipsychotic approved in adults for the treatment of schizophrenia and depressive episodes associated with bipolar I or II disorder (bipolar depression) as monotherapy and as adjunctive therapy with lithium or valproate. While the mechanism of action of CAPLYTA is unknown, the efficacy of CAPLYTA could be mediated through a combination of antagonist activity at central serotonin 5-HT2A receptors and postsynaptic antagonist activity at central dopamine D2 receptors.

Lumateperone is being studied for the treatment of major depressive disorder, and other neuropsychiatric and neurological disorders. Lumateperone is not FDA-approved for these disorders.

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. For more information, please visit www.intracellulartherapies.com.

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 plans to discuss the results of Study 403 with the FDA; whether clinical trial results will be predictive of future real-world results; whether CAPLYTA will serve an unmet need; the goals of our development programs; our beliefs about the potential utility of our 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: there are no guarantees that CAPLYTA will be

commercially successful; we may encounter issues, delays or other challenges in commercializing CAPLYTA; the COVID-19 pandemic may negatively impact our commercial plans and sales for CAPLYTA; the COVID-19 pandemic may negatively impact the conduct of, and the timing of enrollment, completion and reporting with respect to, our clinical trials; whether CAPLYTA receives adequate reimbursement from third-party payors; the degree to which CAPLYTA receives acceptance from patients and physicians for its approved indications; challenges associated with execution of our sales activities, which in each case could limit the potential of our product; results achieved in CAPLYTA in the treatment of schizophrenia and bipolar depression following commercial launch of the product may be different than observed in clinical trials, and may vary among patients; any other impacts on our business as a result of or related to the COVID-19 pandemic; challenges associated with supply and manufacturing activities, which in each case could limit our sales and the availability of our product; impacts on our business, including on the commercialization of CAPLYTA and our clinical trials, as a result of the conflict in Ukraine; risks associated with our current and planned clinical trials; we may encounter unexpected safety or tolerability issues with CAPLYTA following commercial launch for the treatment of schizophrenia or bipolar depression or in ongoing or future trials and other development activities; 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 or in clinical trials for other indications; 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:

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