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NEWS RELEASE

Supplemental new drug application submitted to U.S. FDA for CAPLYTA® (lumateperone) with data demonstrating significant schizophrenia relapse prevention compared to placebo

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Submission is based on long-term Phase 3 data demonstrating 63 percent reduction in risk of relapse in adults with schizophrenia compared to placebo

CAPLYTA® is FDA approved to treat schizophrenia and is the first and only approved treatment for bipolar I and II depression as an adjunctive and monotherapy

With the addition of CAPLYTA® to Johnson & Johnson's robust portfolio of therapies, the Company now offers the broadest range of treatment options for adults with schizophrenia

TITUSVILLE, N.J., July 8, 2025 /PRNewswire/ -- Johnson & Johnson (NYSE:JNJ) announced today the submission of a supplemental New Drug Application (sNDA) to the U.S. Food and Drug Administration (FDA) based upon long-term data evaluating the safety and efficacy of CAPLYTA® (lumateperone) for the prevention of relapse in schizophrenia. CAPLYTA® is the newest addition to Johnson & Johnson's portfolio of schizophrenia therapies, which now offers the broadest range of oral and long-acting injectable treatment options to support each patient's individual treatment journey.

"For people living with schizophrenia, relapses can be devastating as they disrupt lives, undo hard-earned treatment progress toward patients' goals, and increase the risk of hospitalization with each episode," said Christoph U. Correll, M.D., Clinical Professor of Psychiatry at the Zucker School of Medicine at Hofstra/Northwell, New York.[a] "CAPLYTA® substantially lowers the chance of relapse for patients

compared to placebo, which is often a major source of anxiety and suffering for them and their families."

The submission is supported by positive results from a Phase 3, double-blind, multicenter, placebo-controlled, randomized withdrawal trial, which on the primary endpoint found time to relapse during the 26-week double-blind treatment phase was significantly longer in patients receiving CAPLYTA® compared to those receiving placebo (p=0.0002). Treatment with CAPLYTA® was also associated with a 63 percent reduction in risk of relapse versus placebo (hazard ratio [95% CI] = 0.37, [0.22, 0.65]). The key secondary endpoint showed a significantly delayed time to all-cause discontinuation, including relapse, compared with placebo during the double-blind phase (p=0.0007). The safety profile of CAPLYTA® was consistent with the existing body of clinical data, and no new safety concerns were identified. The most commonly reported adverse event that was observed at a rate greater than or equal to 5% and twice the rate of placebo was headache.[i]

Schizophrenia affects up to an estimated 2.8 million adults in the United States, yet it remains insufficiently treated, with approximately 40 percent of people not receiving care.[ii] When left untreated, this complex mental health disorder can lead to episodes of psychosis, hallucinations, or other disruptive behaviors, which can damage and interrupt the lives of those living with schizophrenia as well as their loved ones.[iii] Relapses, or a recurrence of symptoms, are associated with significant functional decline, increased caregiver burden, and a greater likelihood of hospitalization.[iii] On average, an adult with schizophrenia experiences nine relapses in less than six years.[iv]

"Relapse prevention is a critical goal for the long-term care and management of this debilitating disorder," said Bill Martin, Ph.D., Global Therapeutic Area Head, Neuroscience, Johnson & Johnson Innovative Medicine. "These Phase 3 results provide compelling evidence of meaningful relapse prevention, which is critical in preserving long-term patient stability, breaking the cycle of hospitalization, and helping to control symptom progression. We're committed to building on the decade of research reinforcing the robust efficacy, proven safety, and favorable tolerability of CAPLYTA® and providing additional data to support the long-term use of this medicine in neuropsychiatric disorders."

While its exact mechanism of action is unknown, CAPLYTA® is characterized by high serotonin 5-HT_{2A} receptor occupancy and lower amounts of dopamine D_2 receptor occupancy at therapeutic doses. In short-term clinical studies, CAPLYTA® was similar to placebo in weight change, metabolic effects, and extrapyramidal symptoms, which are often cited as reasons for treatment discontinuation. The most commonly reported adverse events were somnolence/sedation, dizziness, nausea, and dry mouth. CAPLYTA® can be taken at any time of day with or without food and does not require titration, allowing adult patients to start treatment at the effective dose.

CAPLYTA® is FDA approved for the treatment of schizophrenia, as well as depressive episodes associated with bipolar I or II disorder in adults, as monotherapy, and as adjunctive therapy with lithium or valproate. An **sNDA for CAPLYTA®** as an adjunctive treatment for adults with major depressive disorder (MDD) is currently under FDA

review. If approved, CAPLYTA® has the potential to become a new standard of care to treat some of today's most prevalent and debilitating mental health disorders.

Editor's note:

a. Christoph U. Correll, M.D., has provided consulting, advisory, and speaking services to Johnson & Johnson. He has not been paid for any media work.

About Schizophrenia

Schizophrenia is a complex, chronic brain disorder that affects how people think, feel, speak, and act. It affects up to an estimated 2.8 million adults in the United States yet remains widely misunderstood and insufficiently treated.[ii] Symptoms vary by person, but confusion and distortions in perceptions, emotions, and behavior are common. Evidence shows that the first three to five years after diagnosis – "the critical period" – from symptom onset are key for a patient's treatment, as this is when the condition progresses most rapidly.[v,vi] A comprehensive treatment plan, which may include medication, therapy, and psychosocial services, can be critical in delaying the time to relapse for adults with schizophrenia.[iii]

About Study 304

This study was a multicenter, multi-national, double-blind, placebo-controlled, randomized withdrawal study of lumateperone for the prevention of symptomatic relapse in adult patients with schizophrenia. The approximately 47-week study included an 18-week open-label phase where patients with schizophrenia were treated with lumateperone 42 mg per day. Patients who met the stabilization criteria during the open-label period progressed to the double-blind treatment phase. These patients were randomized to continue on lumateperone 42 mg (N=114) or switched to placebo (N=114) for up to 26 weeks or until the time to relapse occurred. The primary endpoint was time to first symptom relapse and the key secondary endpoint was time to all cause discontinuation during the double-blind phase.

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-HT_{2A} receptors and postsynaptic antagonist activity at central dopamine D_2 receptors.

CAPLYTA® is under FDA review for potential approval as an adjunctive treatment for adults with major depressive

disorder and is being studied for other neuropsychiatric and neurological disorders. CAPLYTA® is not FDA-approved for these disorders.

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. 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 Warnings.

About Johnson & Johnson

At Johnson & Johnson, we believe health is everything. Our strength in healthcare innovation empowers us to build

a world where complex diseases are prevented, treated, and cured, where treatments are smarter and less invasive, and solutions are personal. Through our expertise in Innovative Medicine and MedTech, we are uniquely positioned to innovate across the full spectrum of healthcare solutions today to deliver the breakthroughs of tomorrow and profoundly impact health for humanity.

Learn more at **https://www.jnj.com/** or at **www.innovativemedicine.jnj.com.** Follow us at @JNJInnovMed.

Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 regarding product development and the potential benefits and treatment impact of CAPLYTA®. The reader is cautioned not to rely on these forward-looking statements. These statements are based on current expectations of future events. If underlying assumptions prove inaccurate or known or unknown risks or uncertainties materialize, actual results could vary materially from the expectations and projections of Johnson & Johnson. Risks and uncertainties include, but are not limited to: challenges and uncertainties inherent in product research and development, including the uncertainty of clinical success and of obtaining regulatory approvals; uncertainty of commercial success; manufacturing difficulties and delays; competition, including technological advances, new products and patents attained by competitors; challenges to patents; product efficacy or safety concerns resulting in product recalls or regulatory action; changes in behavior and spending patterns of purchasers of health care products and services; changes to applicable laws and regulations, including global health care reforms; and trends toward health care cost containment. A further list and descriptions of these risks, uncertainties and other factors can be found in Johnson & Johnson's most recent Annual Report on Form 10-K, including in the sections captioned "Cautionary Note Regarding Forward-Looking Statements" and "Item 1A. Risk Factors," and in Johnson & Johnson's subsequent Quarterly Reports on Form 10-Q and other filings with the Securities and Exchange Commission. Copies of these filings are available online at **www.sec.gov**, **www.jnj.com** or on request from Johnson & Johnson. Johnson & Johnson does not undertake to update any forward-looking statement as a result of new information or future events or developments.

Footnotes

[i] Intra-Cellular Therapies Announces Positive Topline Results in Phase 3 Trial Evaluating CAPLYTA for the Prevention of Relapse in Patients with Schizophrenia. GlobeNewswire, 05 Nov. 2024, **https://www.globenewswire.com/news-release/2024/11/05/2974784/30597/en/Intra-Cellular-Therapies-Announces-Positive-Topline-Results-in-Phase-3-Trial-Evaluating-CAPLYTA-for-the-Prevention-of-Relapse-in-Patients-with-Schizophrenia.html**.

[ii] "Schizophrenia Fact Sheet." Treatment Advocacy Center, 10 Mar. 2025, **www.tac.org/reports_publications/schizophrenia-fact-sheet/**.

iii Alphs L, et al. Factors associated with relapse in schizophrenia despite adherence to long-acting injectable therapy. Int Clin Psychopharmacol. 2016;31(4)202-209. doi:10.1097/YIC.0000000000000125

[iv] Lafeuille MH, Gravel J, Lefebvre P, et al. Patterns of relapse and associated cost burden in schizophrenia patients receiving atypical antipsychotics. J Med Econ. 2013;16(11):1290-1299. doi: 10.3111/13696998.2013.841705

[v] Birchwood, M. "Early intervention and sustaining the management of vulnerability." The Australian and New Zealand journal of psychiatry vol. 34 Suppl (2000): S181-4. doi:10.1080/000486700241

[vi] Tandon, Rajiv et al. "The schizophrenia syndrome, circa 2024: What we know and how that informs its nature." Schizophrenia research vol. 264 (2024): 1-28. doi:10.1016/j.schres.2023.11.015

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