Johnson&Johnson

NEWS RELEASE

CAPLYTA® (lumateperone) showed greatest improvement across key efficacy outcomes among adjunctive MDD treatments in new network meta-analysis

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CAPLYTA® ranked highest among FDA-approved adjunctive therapies across four measures of efficacy, based on indirect comparisons from placebo plus antidepressant therapy-controlled trials

Among the secondary endpoints for the adjunctive MDD therapies evaluated, CAPLYTA® demonstrated no weight gain compared to placebo plus antidepressant therapy

Featured in a late-breaking presentation at the 2026 NEI Spring Congress, analysis provides indirect comparisons to help inform treatment decisions in the absence of head-to-head clinical trials

TITUSVILLE, N.J., May 4, 2026 /PRNewswire/ -- Johnson & Johnson (NYSE: JNJ) today announced findings from the first network meta-analysis (NMA) comparing CAPLYTA® (lumateperone) to FDA-approved atypical antipsychotics for add-on treatment of major depressive disorder (aMDD) in adults, drawing on data from 10 registrational randomized clinical trials. The NMA found that CAPLYTA® was favored for the efficacy outcomes across four measures, based on indirect comparisons derived from placebo plus antidepressant therapy (ADT)-controlled trials. The analysis also evaluated safety outcomes, with CAPLYTA® demonstrating no statistically significant weight gain compared to placebo plus ADT and favorable rankings on select tolerability measures.[1] The data were featured in a late-breaking **presentation** at the 2026 Neuroscience Education Institute (NEI) Spring Congress, held from May 1-3, in Kissimmee, Florida.

"The goal of treating patients with MDD should be remission of symptoms, which may mean adding to their current

treatment in order to achieve the best outcomes," said Andrew J. Cutler, M.D., lead author of the analysis and Chief Medical Officer, Neuroscience Education Institute and Clinical Professor of Psychiatry at SUNY Upstate Medical University.* "This analysis is valuable because it gives us indirect comparative insights in a space where we don't have head-to-head trials, which may inform treatment discussions in everyday clinical practice. The findings suggest adjunctive lumateperone has a high likelihood of helping patients achieve meaningful improvement in symptoms. Symptom improvement is an important step toward remission, the ultimate goal of treatment."

Detailed Findings and Methodology

The NMA is a widely used method to indirectly compare treatments evaluated in separate placebo-controlled trials.[2-5] To reflect clinical decision-making at the treatment level, doses were pooled within treatments in this analysis, resulting in a star-shaped network comprising five treatment nodes anchored on placebo plus ADT. Outcomes were selected based on availability of data across the identified clinical trials and comprised four efficacy outcomes – change from baseline in Montgomery-Åsberg Depression Rating Scale (MADRS) score, MADRS response†, MADRS remission‡, and change from baseline in CGI-S score – and four safety outcomes: weight change from baseline, incidence of clinically meaningful weight increase, akathisia, and somnolence. Additional safety and tolerability outcomes were not assessed in this NMA due to inconsistent reporting across trials.[1]

- Efficacy: CAPLYTA® was favored for the efficacy outcomes across four measures, with the largest effect size among all five treatment nodes evaluated: MADRS change from baseline (mean difference [MD] -4.71; 95% credible intervals [CrI] -5.78, -3.63), MADRS response (odds ratio [OR 2.33]; 95% CrI 1.77, 3.05), MADRS remission (OR 2.22; 95% CrI 1.57, 3.07), and CGI-S change from baseline (MD -0.60; 95% CrI -0.74, -0.46).
    - In pairwise treatment comparisons anchored to CAPLYTA®, CAPLYTA® was favored across all comparators for MADRS and CGI-S change from baseline, and versus all but one comparator for MADRS response and MADRS remission.
- Weight: CAPLYTA® demonstrated no statistically significant weight gain compared to placebo plus ADT, ranking most favorably among all treatments evaluated on both weight-related outcomes: mean weight change from baseline (MD -0.08; 95% CrI -0.30, 0.13; 77% probability of superiority) and proportion of patients with a clinically meaningful weight increase of ≥7% (OR 0.41; 95% CrI 0.04, 1.42; 94% probability of lower risk).
    - CAPLYTA® had a 100% probability of superiority versus all comparators on mean weight change.
- Akathisia (inner restlessness): CAPLYTA® was the only treatment comparable to placebo plus ADT for the risk of akathisia (OR 3.78; 95% CrI 0.40, 17.17); the remaining four treatments evaluated showed higher akathisia risk than placebo plus ADT.
- Somnolence: Somnolence risk was higher than placebo plus ADT across all treatments evaluated (CAPLYTA® OR 5.90; 95% CrI 2.86, 11.50). In pairwise comparisons, CAPLYTA® showed comparable risk versus two

treatments and higher risk versus two treatments.

"The adjunctive treatments approved for MDD share a common indication but differ in their pharmacologic profiles, efficacy, and tolerability," said Leonardo Diaz, M.D., Vice President, U.S. Medical Affairs, CAPLYTA®, Johnson & Johnson. "This NMA provides indirect comparative evidence derived from placebo-controlled studies that may help inform treatment decisions, reinforcing the role of CAPLYTA as an important treatment option for the many adults with MDD who do not achieve adequate symptom control with an antidepressant alone."

NMA is a structured, protocol-driven analytical process widely accepted and utilized by regulatory agencies, health technology assessment agencies, and medical guideline committees to compare treatment options when head-to-head trials are limited or unavailable. As NMAs rely on indirect comparisons across studies that can differ in design and patient populations, findings should be interpreted cautiously alongside the totality of evidence, including individual trial results and clinical considerations.[2-5]

Editor's note:

* Andrew J. Cutler, M.D., has provided consulting, advisory, and speaking services to Johnson & Johnson. He has not been paid for any media work.

† Clinical response was defined as ≥50% reduction in MADRS score from baseline.

‡ Remission was defined as MADRS score ≤10, or MADRS score ≤10 with ≥50% reduction from baseline, depending on the trial.

About Major Depressive Disorder (MDD)

MDD is one of the most common psychiatric disorders and a leading cause of disability worldwide, impacting an estimated 332 million people – or about 4 percent of the population.[6] In the U.S. alone, about 22 million adults are living with the disease.[7] While depression is typically treated with a "one-size-fits-all" approach, no two cases are the same. MDD is a complex, heterogeneous disorder involving multiple regions of the brain and presenting with as many as 256 unique symptom combinations. As a result, responses to treatment vary widely.[8-9] Only 1 in 3 patients reach remission with their first antidepressant, and rates continue to decline further with each subsequent treatment – leaving many to spend years cycling through multiple treatments trying to find complete, sustained symptom relief.[10-11] Moreover, MDD is a risk factor for the development and worsening of a range of comorbidities, illustrating the importance of integrating mental and general health care.[12]

About the Network Meta-Analysis

The NMA evaluated the comparative efficacy and safety of five atypical antipsychotics approved by the FDA as adjunctive therapy for adults with MDD, including aripiprazole (Abilify®), brexpiprazole (Rexulti®), cariprazine (Vraylar®), lumateperone (CAPLYTA®) and quetiapine XR (Seroquel XR®). The analysis included 10 randomized, double-blind, parallel-group, placebo-controlled trials identified through a systematic literature review using Section

14: Clinical Studies in the U.S. Prescribing Information of each of the five products. A Bayesian statistical framework with a star-shaped network design was used, with ADT plus placebo as the common comparator, enabling indirect comparative estimates for efficacy outcomes (MADRS change from baseline, MADRS response, MADRS remission, and CGI-S change from baseline) and safety outcomes (weight change from baseline, weight increase of 7% or more, akathisia, and somnolence).[1]

This NMA adheres to all governing standards and requirements as demanded by global health technology assessment agencies, journal review committees and regulatory authorities. The NMA was funded by Janssen Research & Development, LLC.

About CAPLYTA® (lumateperone)

CAPLYTA® 42 mg is an oral, once daily atypical antipsychotic approved in adults as an adjunctive therapy with antidepressants for major depressive disorder (MDD), 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 partial agonist activity at central dopamine D_2 receptors.

A supplemental New Drug Application (sNDA) for CAPLYTA® with long-term data evaluating the safety and efficacy of the medication for delayed time to relapse in schizophrenia was recently **approved** by the U.S. Food and Drug Administration. The medication is also being studied for other neuropsychiatric disorders. CAPLYTA® is not FDA-approved for these disorders.

INDICATIONS

CAPLYTA® (lumateperone) is a prescription medicine used in adults along with an antidepressant to treat major depressive disorder (MDD); to treat depressive episodes associated with bipolar I or bipolar II disorder (bipolar depression) alone or with lithium or valproate; or to treat schizophrenia. It is not known if CAPLYTA is safe and effective in children.

IMPORTANT SAFETY INFORMATION

Medicines like CAPLYTA can raise the risk of death in elderly people who have lost touch with reality (psychosis) due to confusion and memory loss (dementia). CAPLYTA is not approved for treating people with dementia-related psychosis.

CAPLYTA and antidepressant medicines increase the risk of suicidal thoughts and actions in

people 24 years of age and younger, especially within the first few months of treatment or when the dose is changed. Depression and other serious mental illnesses are the most important causes of suicidal thoughts and actions. Patients and their families or caregivers should watch for new or worsening depression symptoms, especially sudden changes in mood, behaviors, thoughts, or feelings. This is very important when CAPLYTA or an antidepressant medicine is started or when the dose is changed. Report any changes in these symptoms to your healthcare provider immediately.

Do not take CAPLYTA if you are allergic to any of its ingredients. Get emergency medical help if you are having an allergic reaction (e.g., rash, itching, hives, swelling of the tongue, lip, face, or throat).

CAPLYTA may cause serious side effects, including:

- Stroke (cerebrovascular problems) in elderly people with dementia-related psychosis that can lead to death.
- Neuroleptic malignant syndrome (NMS): high fever, confusion, changes in your breathing, heart rate, and blood pressure, stiff muscles, and increased sweating; these may be symptoms of a rare but potentially fatal condition. Contact your healthcare provider or go to the emergency room if you experience signs and symptoms of NMS.
- Uncontrolled body movements (tardive dyskinesia, TD) in your face, tongue, or other body parts. TD may not go away, even if you stop taking CAPLYTA. It may also occur after you stop taking CAPLYTA.
- Problems with your metabolism including high blood sugar, diabetes, increased fat (cholesterol and triglyceride) levels in your blood and weight gain. Your healthcare provider should check your blood sugar, fat levels, and weight before you start and during your treatment with CAPLYTA. Extremely high blood sugar levels can lead to coma or death. Call your healthcare provider if you have any of the following symptoms of high blood sugar: feeling very thirsty, hungry, sick to your stomach, needing to urinate more than usual, weak/tired, or confused, or your breath smells fruity.
- Low white blood cell count. Your healthcare provider may do blood tests during the first few months of treatment with CAPLYTA.
- Decreased blood pressure (orthostatic hypotension). You may feel lightheaded, dizzy, or faint when you rise too quickly from a sitting or lying position.
- Falls. CAPLYTA may make you sleepy or dizzy, may cause a decrease in your blood pressure when changing position (orthostatic hypotension), and can slow your thinking and motor skills which may lead to falls that can cause broken bones or other injuries.
- Seizures (convulsions).
- Sleepiness, drowsiness, feeling tired, difficulty thinking and doing normal activities. Until you know how CAPLYTA affects you, do not drive, operate heavy machinery, or do other dangerous activities.

- Problems controlling your body temperature so that you feel too warm. Avoid getting overheated or dehydrated while taking CAPLYTA.
- Difficulty swallowing that can cause food or liquid to get into the lungs.

The most common side effects of CAPLYTA include sleepiness, dizziness, nausea, dry mouth, feeling tired, and diarrhea.

These are not all the possible side effects of CAPLYTA. Tell your healthcare provider if you have or have had heart problems or a stroke, high or low blood pressure, diabetes, or high blood sugar, problems with cholesterol, have or have had a low white blood cell count, seizures (convulsions), or kidney or liver problems.

CAPLYTA may cause fertility problems in females and males. You should notify your healthcare provider if you become pregnant or intend to become pregnant while taking CAPLYTA. There is a pregnancy registry for females who are exposed to CAPLYTA during pregnancy. CAPLYTA may cause abnormal involuntary movements and/or withdrawal symptoms in newborn babies exposed to CAPLYTA during the third trimester. Talk to your healthcare provider if you breastfeed or are planning to breastfeed as CAPLYTA passes into breast milk.

Tell your healthcare provider about all the medicines you're taking. CAPLYTA may affect the way other medicines work, and other medicines may affect how CAPLYTA works, causing possible serious side effects. Do not start or stop any medicines while taking CAPLYTA without talking to your healthcare provider. You are encouraged to report negative side effects of prescription drugs. Contact Intra-Cellular Therapies, Inc. at 1-800-526-7736 or FDA at 1-800-FDA-1088 or **www.fda.gov/medwatch**.

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

US-CAP-2500827

Please see full **Prescribing Information**, including Boxed WARNINGS, and **Medication Guide** for CAPLYTA.

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.

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Cautions Concerning Forward-Looking Statements

This press release contains "forward-looking statements" as defined in the Private Securities Litigation Reform Act of 1995 related to product development and the potential benefits and treatment impact of CAPLYTA® (lumateperone). 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**, **www.investor.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

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