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Journal of the American Medical Association (JAMA) Publishes Results from First-Ever Randomized, Placebo-Controlled Clinical Trial Assessing the Dose-Dependent Efficacy of MM120 (Lysergide D-Tartrate, LSD) in Generalized Anxiety Disorder (GAD)

The Phase 2b study demonstrated a statistically significant dose-response relationship at the primary endpoint following a single administration of MM120 across four dose levels, with improvements sustained throughout the 12-week observation period

MM120 100 µg was determined to be the optimal dose, meeting its primary and key secondary endpoints, demonstrating a clinically and statistically significant improvement vs. placebo, and a 65% clinical response rate and 48% clinical remission rate at Week 12

MM120 was well-tolerated, with treatment-related adverse events occurring on dosing day and being consistent with the expected perceptual effects of LSD

NEW YORK--(BUSINESS WIRE)-- Mind Medicine (MindMed) Inc. (NASDAQ: MNMD), (the "Company" or "MindMed"), a late-stage clinical biopharmaceutical company developing novel product candidates to treat brain health disorders, today announced that JAMA has published full results from the Company's positive Phase 2b study of MM120 (lysergide D-tartrate, LSD) in 198 adults with moderate-to-severe GAD. This is the first randomized, placebo-controlled trial to evaluate a single treatment across four dose levels (25, 50, 100, or 200 µg) as a monotherapy and did not include any form of study-related psychotherapeutic intervention. The study met its primary and key secondary endpoints, with MM120 demonstrating a dose-response relationship and significant symptom improvement versus placebo on the Hamilton Anxiety Rating Scale (HAM-A), a validated clinical tool used to assess the severity of anxiety.

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Representative Image of MM120 ODT/Courtesy of Catalent

The 100 µg dose of MM120, now being evaluated in three pivotal Phase 3 trials, showed the optimal level of clinical activity in the study. At Week 4, it achieved a 7.6-point greater reduction in HAM-A scores compared to placebo (-21.3 vs. -13.7; $p<0.0004$; Cohen's $d=0.88$) with a 65% clinical response rate and 48% clinical remission rate sustained to Week 12. MM120 was generally well-tolerated in this study, with

most adverse events rated as mild-to-moderate, transient, occurring on the dosing day, and being consistent with the expected acute effects of the trial drug. Based on these Phase 2b study results and the significant unmet medical need in the treatment of GAD, the U.S. Food & Drug Administration (FDA) has provided Breakthrough Therapy Designation to MM120 for GAD.

“This study is a true turning point in the field of psychiatry,” said study author Maurizio Fava, M.D., member of the MindMed Scientific Advisory Board and Chair of Mass General Brigham Department of Psychiatry.* “For the first time, LSD has been studied with modern scientific rigor, and the results are both clinically meaningful and potentially paradigm-shifting for the treatment of GAD. GAD affects 26 million adults in the U.S., yet no new medications have been approved since 2007—and first-line treatments fail 50% of patients. I have seen firsthand the devastating toll GAD takes on patients and their families, which is why it is so significant that a single dose of MM120 delivered rapid, robust, and lasting effects. These results highlight the promise of psychedelics in psychiatric medicine and represent a critical step toward expanding effective options for those who are suffering.”

Pre-specified secondary outcomes in the study included changes from baseline in HAM-A; clinician-rated disease severity measured by Clinical Global Impression-Severity (CGI-S) scale and changes from baseline in depressive symptoms as measured by Montgomery-Åsberg Depression Rating Scale (MADRS), in addition to measures of functional disability and quality of life.

- CGI-S scores on average improved from 4.8 to 2.2 in the 100 µg dose group, representing a two-category shift from ‘markedly ill’ to ‘borderline ill’ at Week 12, compared with 4.9 to 3.5 in the placebo group (p=0.003).
- Clinical activity was rapid, observed as early as study day 2, and durable, with further improvements observed in mean HAM-A or CGI-S scores between Weeks 4 and 12.
- MADRS score improvements in the 100 µg arm of the study were clinically and statistically significant compared to the placebo group, with a difference of 5.7 points ($p \leq 0.05$) at Week 4 and a difference of 6.4 points ($p \leq 0.05$) at Week 12.

The dose-response results support the selection of MM120 100 µg for the Company’s ongoing Phase 3 development program for MM120 Orally Disintegrating Tablet (ODT). MindMed is currently enrolling participants in its Voyage and Panorama Phase 3 studies to assess the efficacy, durability, and safety of MM120 ODT in the treatment of GAD, and in its Emerge study to assess MM120 ODT for the treatment of major depressive disorder (MDD). Topline data for Voyage is expected in the first half of 2026 and for Panorama and Emerge in the second half of 2026.

“Our Phase 2b results—marking the first well-controlled clinical study to evaluate dose-response relationships of LSD in a psychiatric population—demonstrate the meaningful impact of a single 100 µg dose of MM120 in significantly reducing anxiety symptoms,” said Daniel R. Karlin, M.D., M.A., Chief Medical Officer of MindMed. “These findings confirm that LSD can be rigorously studied and help catalyze a long-overdue transformation in the field of psychiatry. With enrollment underway in our Phase 3 Voyage, Panorama, and Emerge trials, we’re eager to further evaluate MM120 ODT’s potential to treat the two most common psychiatric disorders—GAD and MDD—affecting over 60 million people in the U.S.”

About the MMED008 Phase 2b Study

MMED008 was a multi-center, parallel, randomized, placebo-controlled, double-blind, Phase 2b study designed to assess the dose-response, efficacy, safety, and tolerability of a single dose of MM120. Participants were randomized equally to receive a single treatment with MM120 25, 50, 100, or 200 µg or placebo. Primary and key secondary outcomes were dose-response relationships assessed by change from baseline to Weeks 4 and 8 on the Hamilton Anxiety Rating Scale (HAM-A), respectively.

The study was conducted at 22 outpatient psychiatric research sites in the United States in 198 adults with a primary GAD diagnosis presenting with moderate-to-severe symptoms as defined by HAM-A.

For the primary and key secondary endpoint, MM120 demonstrated a statistically significant dose-response relationship as assessed by the multiple comparison procedure-modeling (MCP-Mod) approach using changes from baseline in HAM-A. MM120 100 and 200 µg significantly reduced HAM-A from baseline to Week 4 with placebo-adjusted improvement in HAM-A of -7.6 (95% CI, -11.8 to -3.4; $p<0.001$, and -5.50 (95% CI, -9.7 to -1.3; $p=0.01$) points, while 25 and 50 µg did not reach statistical significance, demonstrating placebo-adjusted improvements of -3.4 (95% CI, -7.7 to 0.9; $p=0.12$) and -0.9 (95% CI, -5.2 to 3.3; $p=0.66$). MM120 had adverse events consistent with the expected effects of LSD including visual perceptual changes (illusion, pseudo-hallucination, and visual hallucination) occurring in 51.4%, 77.5%, 92.5%, 100%, and 10.3%; nausea in 7.7%, 27.5%, 42.5%, 65.0%, and 7.7%; and headache in 15.4%, 27.5%, 35.0%, 27.5%, and 23.1%, in the 25, 50, 100, 200 µg, and placebo groups, respectively.

The study included 3 phases: screening, baseline and randomization (dosing day), and follow-up, approximately at 12 weeks. Participants taking medications for mood or anxiety at screening discontinued them under the supervision of site physicians. Before the baseline visit, a medication washout was required and during the baseline visit, dosing session monitors (DSMs) educated participants on session logistics, staff interactions, and MM120.

On dosing day, participants received a single oral dose of MM120 or placebo. Each participant was continuously monitored on-site by the same DSMs who conducted their education at the baseline visit. Participants were offered standardized music and eyeshades and could lie down, move freely around the room, read, write, or draw. DSMs assisted participants with functional needs, such as eating and toileting, upon participant request. Engaging in psychotherapy with the participant was explicitly prohibited by the study protocol.

Trained, certified raters assessed all outcome measures. To mitigate bias, DSMs were prohibited from conducting efficacy assessments and outcomes were evaluated by independent central raters blinded to protocol, treatment assignment and study visit. Anxiety and depression endpoint assessments were evaluated by independent central raters blinded to protocol, treatment allocation, and study visit. Participant- and rater-blinding were assessed using a 5-point blinding questionnaire, which assessed whether participants and raters believed that allocation had been to active drug, placebo, or was indiscernible.

About Generalized Anxiety Disorder (GAD)

GAD is one of the most common psychiatric disorders, affecting approximately 26 million U.S. adults.[1] People with GAD experience constant, overwhelming worry that is hard to control. Common symptoms include fatigue, muscle tension, trouble concentrating, and difficulty sleeping.[2] GAD involves disrupted activity, connectivity, or neuroplasticity in key

regions of the brain such as the prefrontal cortex, amygdala, and thalamus, leading to impaired emotional regulation and clinical symptoms.[3,4] GAD often occurs alongside other health problems like chronic physical symptoms, depression, other anxiety disorders, and trauma-related conditions. Together, these issues can seriously impact a person's daily life, including substantial functional, economic, and quality-of-life burdens and are associated with increased healthcare utilization and costs.[5-7]

Mental health conditions like GAD, major depressive disorder (MDD) and post-traumatic stress disorder (PTSD) often overlap. More than 50% of patients with GAD also have MDD. Co-occurring MDD and GAD is associated with increases in mean annual per patient inpatient visits, office visits, emergency department visits, annual drug costs, and total medical costs.[6,8] Approximately 80% of individuals with PTSD meet the criteria for another psychiatric diagnosis, underscoring the interconnection across these disorders and the urgent need for more effective treatment options.[9]

While several GAD pharmacotherapies are approved, many patients do not experience sustained relief, and approximately 50% inadequately respond to first-line treatments.[10] Serotonin reuptake inhibitors (SRIs) are commonly used first-line, but lack of efficacy and side effects can contribute to disease burden, treatment nonadherence, and discontinuation.[11] Benzodiazepines have shown acute efficacy in GAD, but their use is limited by side effects and risks of misuse and dependence.[12,13] Despite the significant personal and societal burden of GAD, there has been little innovation in the treatment of GAD in the past several decades, with the last new drug approval occurring in 2007.[14]

About Lysergide D-tartrate (LSD)

Lysergide D-tartrate (LSD) is one of the most extensively studied psychopharmaceuticals in history, with over 1,000 published reports.[15] First synthesized in the 1930s by Swiss chemist Albert Hofmann in his search for antifungal agents from ergot fungus, its profound psychological effects were discovered accidentally—an event that transformed psychiatric research. As a classic psychedelic, LSD temporarily alters perception, cognition, and emotions, while remaining physiologically safe, non-addictive, and free from withdrawal symptoms.[15] While its precise mechanism of action in the treatment of psychiatric illness is unknown, mechanistic hypotheses suggest its acute perceptual, cognitive, and affective effects are mediated by agonism of the serotonin 5-hydroxytryptamine 2A (5-HT2A) receptor, and sustained increases in neuroplasticity in a variety of brain regions.[16,17]

About MM120 Orally Disintegrating Tablet (ODT)

MM120 ODT (lysergide D-tartrate or LSD) is a synthetic ergotamine belonging to the group of classic, or serotonergic, psychedelics which acts as a partial agonist at human serotonin-2A (5-HT2A) receptors. MM120 ODT is MindMed's proprietary and pharmaceutically optimized form of LSD. MM120 ODT is an advanced formulation incorporating Catalent's Zydis® ODT fast-dissolve technology which has a unique clinical profile with more rapid absorption, improved bioavailability and reduced gastrointestinal side effects. MindMed is developing MM120, the tartrate salt form of lysergide, for generalized anxiety disorder (GAD), major depressive disorder (MDD), and is exploring its potential applications in other serious brain health disorders.

Based on the significant unmet medical need in the treatment of GAD, along with the initial clinical data from the Phase 2b study and other research conducted by MindMed, the U.S. Food and Drug Administration (FDA) has granted Breakthrough Therapy Designation for the MM120 program in GAD. MindMed has also been granted an Innovation Passport for the potential treatment of GAD under the United Kingdom Innovative Licensing and Access Pathway (ILAP) by the U.K. Medicines and Healthcare products Regulatory Agency. The Innovation Passport is the entry point to the ILAP, which aims to accelerate time to market and facilitate patient access to medicines in the U.K.

About MindMed

MindMed is a late-stage clinical biopharmaceutical company developing novel product candidates to treat brain health disorders. Our mission is to be the global leader in the development and delivery of treatments that unlock new opportunities to improve patient outcomes. We are developing a pipeline of innovative product candidates, with and without acute perceptual effects, targeting neurotransmitter pathways that play key roles in brain health. MindMed trades on NASDAQ under the symbol MNMD.

Forward-Looking Statements

Certain statements in this news release related to the Company constitute "forward-looking information" within the meaning of applicable securities laws and are prospective in nature. Forward-looking information is not based on historical facts, but rather on current expectations and projections about future events and are therefore subject to risks and uncertainties which could cause actual results to differ materially from the future results expressed or implied by the forward-looking statements. These statements generally can be identified by the use of forward-looking words such as "will", "may", "should", "could", "intend", "estimate", "plan", "anticipate", "expect", "believe", "potential" or "continue", or the negative thereof or similar variations. Forward-looking information in this news release includes, but is not limited to, statements regarding the Company’s anticipated topline readout (Part A results) for the Phase 3 Voyage study of MM120 ODT in GAD in the first half of 2026; the Company’s anticipated topline readout (Part A results) for the Phase 3 Panorama study for MM120 ODT in GAD in the second half of 2026; the Company’s anticipated topline readout (Part A results) for the Phase 3 Emerge study for MM120 ODT in MDD in the second half of 2026; the Company’s beliefs regarding potential benefits of its product candidates; and potential additional indications for MM120 ODT. There are numerous risks and uncertainties that could cause actual results and the Company's plans and objectives to differ materially from those expressed in the forward-looking information, including history of negative cash flows; limited operating history; incurrence of future losses; availability of additional capital; compliance with laws and regulations; legislative and regulatory developments, including decisions by the Drug Enforcement Administration and states to reschedule any of the Company’s product candidates, if approved, containing Schedule I controlled substances, before they may be legally marketed in the U.S.; difficulty associated with research and development; risks associated with clinical studies or studies; heightened regulatory scrutiny; early stage product development; clinical study risks; regulatory approval processes; novelty of the psychedelic inspired medicines industry; ability to maintain effective patent rights and other intellectual property protection; as well as those risk factors discussed or referred to herein and the risks, uncertainties and other factors described in the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2024, the Company’s Quarterly Report on Form 10-Q for the fiscal quarter ended March 31, 2025 and the Company’s Quarterly Report on Form 10-Q for the fiscal quarter ended June 30, 2025 under headings such as "Special Note Regarding Forward-

Looking Statements," and "Risk Factors" and "Management's Discussion and Analysis of Financial Condition and Results of Operations" and other filings and furnishings made by the Company with the securities regulatory authorities in all provinces and territories of Canada which are available under the Company's profile on SEDAR+ at www.sedarplus.ca and with the U.S. Securities and Exchange Commission on EDGAR at www.sec.gov. Except as required by law, the Company undertakes no duty or obligation to update any forward-looking statements contained in this release as a result of new information, future events, changes in expectations or otherwise.

*Massachusetts General Brigham was not involved in the conduct of this study.

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