MapLight Therapeutics Announces Positive Topline Results from Phase 2 ZEPHYR Trial of ML-007C-MA in Schizophrenia

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The trial, designed and sized to support registration, met its primary endpoint, with the 210/3 mg BID dose demonstrating a statistically significant improvement in PANSS total score compared to placebo at Week 5 with an effect size of 0.37 (LS mean difference vs PBO -4.5, p=0.015)

Cognitive performance was improved (ES=0.51, p=0.041) in those with baseline cognitive impairment on a prespecified secondary endpoint

210/3 mg BID dose also achieved significant separation on key secondary endpoints, including CGI-S (ES=0.48, p=0.002) and PANSS Positive Marder Factor (ES=0.39, p=0.012)

ML-007C-MA was generally well tolerated at both doses studied, with no serious or drug-related severe adverse events and low rates of GI-related discontinuations

No fasting requirement and a one-dose titration support a tolerability profile expected to translate into real-world adherence

Data support proceeding with an additional trial, also designed to be registrational, to replicate this result; Company to engage with FDA at End-of-Phase 2 Meeting

Company to host live webcast today at 8:00 AM ET

SAN FRANCISCO and BOSTON, July 27, 2026 (GLOBE NEWSWIRE) -- MapLight Therapeutics, Inc. (Nasdaq: MPLT), a clinical-stage biopharmaceutical company focused on improving the lives of patients suffering from debilitating central nervous system disorders, today announced positive topline results from its Phase 2 ZEPHYR trial evaluating ML-007C-MA, an oral M1/M4 muscarinic agonist (betovumeline) co-formulated with a peripherally acting anticholinergic (fesoterodine), in adults with an acute exacerbation of schizophrenia. The trial met its primary endpoint, with the 210/3 mg twice-daily (BID) dose demonstrating a statistically significant and clinically meaningful reduction in Positive and Negative Syndrome Scale (PANSS) total score compared to placebo at Week 5.

In the modified intent-to-treat (mITT) population, the BID arm achieved an effect size of 0.37 (*Cohen's d*) and these participants experienced a mean 4.5-point improvement in PANSS total score versus placebo (p=0.015). In a prespecified analysis of participants who completed five weeks of treatment, in which there are no modelled assumptions for missing data, the effect size was 0.50 (LS mean difference from placebo -6.0, p=0.002), driven by greater improvement in the treatment arm rather than the placebo arm. ML-007C-MA also achieved significance on key secondary endpoints in the BID arm, including Clinical Global Impression of Severity (CGI-S) (effect size=0.48; p=0.002), PANSS positive Marder factor (effect size=0.39; p=0.012), and multiple other secondary and exploratory outcomes.

Notably, ML-007C-MA demonstrated a robust and clinically meaningful improvement in cognitive performance in the BID arm, based on the pre-specified secondary endpoint assessed via the Cogstate battery in participants with baseline cognitive impairment (effect size=0.51; 0.44 points versus placebo; p=0.041). This cognitive benefit did not demonstrate correlation with the change in PANSS score, suggesting the effect was independent of, and not secondary to, improvement in psychotic symptoms.

“We are very encouraged by these results, which show that ML-007C-MA delivered clinically meaningful antipsychotic efficacy alongside a favorable tolerability profile designed to translate into real-world use," said Chris Kroeger, M.D., Co-Founder and Chief Executive Officer of MapLight. "Just as importantly, we observed a robust signal on a pre-specified secondary cognition endpoint that appears independent of antipsychotic effect. Cognitive impairment affects the majority of people living with schizophrenia and remains an area where no therapy has yet been approved. We believe the combination of a significant effect on PANSS and other concordant endpoints, along with a meaningful effect on cognitive performance, represents a powerful, comprehensive overall efficacy profile in schizophrenia, and strengthens the rationale for our ongoing VISTA trial in Alzheimer's disease psychosis and the broader indication expansion for ML-007C-MA."

The 330/6 mg once-daily (QD) dose, which results in lower daily exposure than BID dosing, demonstrated numerical improvement over placebo, but did not achieve statistical significance on the primary endpoint. However, it did demonstrate separation on CGI-S (p=0.036), PANSS positive Marder factor (p=0.045), and Readiness for Discharge Questionnaire (p=0.027) and numerical separation on several other endpoints. The Company is conducting further analyses to inform the potential path forward for a once-daily regimen.

Safety and Tolerability

ML-007C-MA was generally well tolerated across all doses studied. Treatment-emergent adverse events (TEAEs) were mostly mild and primarily cholinergic in nature, and there were no serious adverse events or drug-related severe TEAEs with either dose. The only severe TEAE in an active arm was a case of pneumonia, which was assessed as unrelated to study treatment. One serious TEAE of worsening schizophrenia occurred in the placebo arm. All-cause discontinuation across both active arms was low, at 19.9%.

At the 210/3 mg BID dose, TEAEs were reported in 74.7% of participants compared with 48.1% receiving placebo, with most events mild in severity. Gastrointestinal events were mostly mild and rarely associated with discontinuation (two participants, 2.0%), and there were low rates of moderate GI events. No participant failed to reach target dose due to tolerability, and dose reductions due to TEAEs were infrequent (four participants, or 4.0%, three of whom completed treatment).

The rates of anticholinergic events were low, and no clinically meaningful signals were observed with ML-007C-MA for urinary retention, metabolic or hepatic parameters, extrapyramidal symptoms, or blood pressure. Small increases in heart rate were observed, consistent with the known profile of fesoterodine. With no fasting requirement and a short, one-dose titration, these clinical trial results are expected to translate into real-world use, supporting patient adherence and compliance. "Despite recent advances in schizophrenia treatment, patients and clinicians continue to need therapies that pair meaningful symptom control with a tolerability profile patients can sustain over time," said John M. Kane, M.D., Professor of Psychiatry and Molecular Medicine at the Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Co-Director of the Institute for

Behavioral Science at the Feinstein Institutes for Medical Research, and member of MapLight Therapeutics' Clinical Advisory Board. "The ZEPHYR results are notable on both fronts: a statistically significant improvement on the primary endpoint and cognitive performance, alongside a meaningfully differentiated safety profile that matters most for the management of patients over time. If confirmed in a further study and approved, ML-007C-MA could offer physicians a valuable additional tool in the treatment arsenal for people living with schizophrenia."

Future Development

The Company plans to engage with the FDA at an End-of-Phase 2 (EOP2) meeting to discuss the path forward for ML-007C-MA in schizophrenia, including the design of a Phase 3 trial which, together with ZEPHYR, would support an initial New Drug Application (NDA) submission. Planning and site identification for this additional, confirmatory trial are already underway ahead of the MapLight's EOP2 FDA interactions. The Company is also planning a separate confirmatory trial to evaluate the BID dose used in ZEPHYR along with other dosing regimens, including a possible QD option. VISTA, MapLight's ongoing trial designed to support registration for the treatment of hallucinations and delusions associated with Alzheimer's disease psychosis, is also evaluating ML-007C-MA 210/3 mg BID (the same dose associated with the cognitive effect in ZEPHYR), with topline results expected in the second half of 2027.

Additionally, the Company recently reported results for IRIS, a Phase 2 trial evaluating ML-004, an 5-$HT_{1B/1D}$ agonist in autism spectrum disorder (ASD), where a prespecified subgroup analysis in adolescents with significant baseline irritability demonstrated meaningful improvement over placebo on both caregiver- and clinician-rated scales alongside a favorable safety and tolerability profile. Based on these results, the Company intends to engage with the FDA in an EOP2 meeting to determine the next steps for development of ML-004 in irritability associated with ASD.

Live Webcast

The Company will host a live webcast to discuss the Phase 2 ZEPHYR trial results today, Monday, July 27, 2026, at 8:00 a.m. ET. Those who would like to participate may access the live webcast here, or register in advance for the teleconference here.

The event will also be accessible through the "Events and Presentations" page within the Investors section of the Maplight website at https://ir.maplightrx.com/news-events/events-presentations. An archived replay will also be available on the website for at least 90 days following the event.

About ZEPHYR

ZEPHYR is a randomized, double-blind, placebo-controlled trial at 25 US sites that evaluated the efficacy, safety, and tolerability of ML-007C-MA in inpatient adult participants with schizophrenia experiencing an acute exacerbation of psychosis. A total of 307 participants were randomized 1:1:1 to receive either placebo, ML-007C-MA 210/3 mg twice daily, or ML-007C-MA 330/6 mg once daily. The primary endpoint for the trial was the change in PANSS total score from baseline to Week 5. Key secondary endpoints included change in CGI-S score and PANSS-Marder positive and negative factor scores from baseline to Week 5. Change in cognitive function in participants with baseline cognitive impairment from baseline to Week 5 was assessed as a prespecified secondary endpoint.

About ML-007C-MA

ML-007C-MA is an oral, extended-release, fixed-dose combination of the investigational M1/M4 muscarinic agonist ML-007 (betovumeline), co-formulated with a peripherally acting anticholinergic (fesoterodine). ML-007C-MA is designed to activate both M1 and M4 muscarinic receptors in the central nervous system to drive efficacy, while synchronizing the pharmacokinetics of the agonist and antagonist components to mitigate peripheral cholinergic side effects.

About MapLight Therapeutics

MapLight Therapeutics is a clinical-stage biopharmaceutical company focused on improving the lives of patients suffering from debilitating central nervous system disorders. The Company was founded by globally recognized leaders in psychiatry and neuroscience research to address the lack of circuit-specific pharmacotherapies available for patients. The Company's discovery platform holds the potential to fill this void by identifying neural circuits causally linked to disease and targeting those circuits for therapeutic modulation.

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

Forward-Looking Statements

Certain statements in this press release may constitute "forward-looking statements" within the meaning of the federal securities laws, including, but not limited to, the clinical development and potential benefits of ML-007C-MA and ML-004, the design, timing and conducting of future clinical trials, the registrational pathway for the Company's product candidates, including holding EOP2 meetings with the FDA for ML-007C-MA and ML-004 and planned regulatory submissions, the availability and timing of results from the Company's Phase 2 VISTA trial, and the potential benefits of the Company's discovery platform. Words such as "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "design," "estimate," "predict," "potential," "develop," "plan" or the negative of these terms, and similar expressions, are intended to identify forward-looking statements. While the Company believes these forward-looking statements are reasonable, undue reliance should not be placed on any such forward-looking statements, which are based on information available to the Company on the date of this release. These forward-looking statements are based upon current estimates and assumptions and are subject to various risks and uncertainties (including, without limitation, those set forth in the Company's filings with the U.S. Securities and Exchange Commission (SEC)), many of which are beyond the Company's control and subject to change. Actual results could be materially different. Risks and uncertainties include: the unpredictable relationship between preclinical study results and clinical study results; the risk that results obtained in any clinical trials to date may not be indicative of results obtained in ongoing or future trials; the timing or likelihood of regulatory filings and approvals; expectations regarding the Company's ability to fund its current operations; and other risks and uncertainties identified in the Company's Quarterly Report on Form 10-Q for the quarter ended March 31, 2026, and subsequent disclosure documents the Company may file with the SEC. The Company claims the protection of the safe harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. The Company expressly disclaims any obligation to update or alter any statements whether as a result of new information, future events or otherwise, except as required by law.

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