MapLight Therapeutics Announces Completion of Phase 1 Clinical Trial for Novel M1/M4 Muscarinic Agonist in Development for Schizophrenia and Alzheimer's Disease Psychosis

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- *Extended-release ML-007 was evaluated for safety, tolerability, and pharmacokinetic profile in healthy volunteers across several dosing regimens, alone and when co-administered with an extended-release muscarinic antagonist*
- *Extended-release ML-007 was well tolerated at all doses including doses at and above those planned for use in the company's upcoming Phase 2 trials for the treatment of schizophrenia and Alzheimer's disease psychosis*
- *Pharmacokinetic data demonstrated precise matching of the kinetics of ML-007 with that of the peripheral antimuscarinic, and this close kinetic match correlated with improved tolerability*
- *Treatment-emergent adverse events were uncommon, and all were mild and transient with no serious adverse events observed*
- *MapLight plans to advance ML-007C-MA, a fixed-dose combination tablet formulation of ML-007 and its precision-matched muscarinic antagonist, to Phase 2 clinical trials in 2024*

SAN FRANCISCO AND BOSTON, JANUARY 3, 2024 – MapLight Therapeutics, a clinical-stage biopharmaceutical company working to develop targeted novel therapeutics to improve the lives of people with brain disorders, today announced completion of a Phase 1 clinical trial evaluating the bioavailability, safety, and tolerability of an extended release formulation of ML-007, a novel M_1/M_4 preferring muscarinic agonist, alone and when co-administered with a precision-matched muscarinic antagonist designed to offset peripheral effects. The study included 24 healthy volunteers across three cohorts and assessed the drug's safety, tolerability, and pharmacokinetic profile when dosed using twice-daily and once-daily dosing regimens. This is the company's third Phase 1 study of ML-007, and the first to evaluate the extended-release formulation developed for the treatment of chronic conditions.

Extended-release ML-007 was well tolerated in this trial at all doses, including those planned for use in the company's upcoming Phase 2 clinical trials for the treatment of schizophrenia and Alzheimer's disease psychosis. Plasma exposures at or above anticipated clinically relevant levels were maintained over the duration of the intended dosing interval. The plasma concentration ratios of ML-007 ER and its matched muscarinic antagonist remained within target range at anticipated clinically relevant doses and were associated with excellent tolerability. Treatment-emergent adverse events were uncommon, and all were mild and transient. No serious adverse events nor any unexpected or novel adverse events were observed with ML-007 administration in this study or in prior studies. Findings from this study will enable formulation optimization of ML-007C-MA, the fixed-dose combination of ML-007 and its matched muscarinic antagonist, allowing the company to move ML-007C-MA into Phase 2 clinical trials later this year.

"We believe the new class of muscarinic receptor agents represent a substantial treatment advancement over existing therapies, and we anticipate significant opportunities for new entrants within the class that possess a better overall product profile," stated Christopher Kroeger, M.D., MBA, Chief Executive Officer and Founder. "Achieving our target exposure levels with extended-release ML-007, while also demonstrating a very attractive tolerability profile with the precision pharmacokinetic matching of a muscarinic antagonist, is a tremendous advancement for our program and one that we believe will ultimately yield a best-in-class product with significant benefits for patients."
"There is significant room for improvement when it comes to treatments available today to address schizophrenia and Alzheimer's disease psychosis," said MapLight Chief Medical Officer, Erin Pennock Foff, M.D., Ph.D. "Both conditions afflict large patient populations with a high level of unmet need. This study has generated crucial data that informs the dose and dosing regimen of the combination product, ML-007C-MA, to take into Phase 2 trials. We want to give patients and those who care for them a better treatment option and are now a step closer to that goal."

About ML-007
ML-007 is a muscarinic receptor agonist designed to target M_1 and M_4 muscarinic receptor subtypes with no direct activity on dopamine receptors. Deficits in M_1 receptors are linked to schizophrenia, and M_1 receptors directly regulate neural circuits known to be important in both psychosis and cognition. M_4 receptors regulate a complementary neural circuit known to be important in psychosis.

About ML-007C-MA
ML-007C-MA is a combination muscarinic agent in clinical development for the treatment of neurologic and neuropsychiatric conditions. ML-007C-MA was specifically designed with the goal of delivering the powerful M_1 and M_4 muscarinic agonist activity of ML-007 to the brain, while preventing peripheral side effects by pairing it with a precision matched muscarinic antagonist.

About Schizophrenia
Schizophrenia is a serious, debilitating mental illness characterized by disturbances in perception, thinking, emotional reaction, and behavior. Schizophrenia can cause people to interpret reality abnormally and includes a combination of positive, negative, and cognitive symptoms. Approximately 60% of people with schizophrenia have no response or only a partial response to the available standard of care treatments, leaving a substantial portion of the population with urgent unmet needs.

About Alzheimer's Disease Psychosis
Over 40% of people with Alzheimer's disease (AD) will experience delusions and hallucinations as part of the disease, a condition known as AD psychosis. The condition is often recurrent, severe, and is associated with an increased likelihood of nursing home placement and increased morbidity and mortality. There is no FDA approved medication for the treatment of AD psychosis.

About MapLight Therapeutics
MapLight is working to develop targeted, novel therapeutics to improve the lives of people with difficult-to-treat brain disorders. MapLight's unique discovery platform combines novel, proprietary technologies to uncover the individual circuits that misfire in brain disorders and target those circuits with effective, safe therapeutics. MapLight was founded by a team of renowned neuroscientists who led the discovery of such groundbreaking technologies as optogenetics and STARmap. Learn more at www.maplightrx.com.

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