MAPLIGHT THERAPEUTICS ANNOUNCES SUCCESSFUL COMPLETION OF SECOND PHASE 1 CLINICAL TRIAL OF THE NOVEL MUSCARINIC RECEPTOR AGONIST ML-007

- *Study assessed safety, tolerability, and pharmacokinetics (PK) in 106 subjects across ten healthy adult cohorts and three healthy elderly cohorts*
- *ML-007 was found to be safe and well tolerated across all cohorts when dosed alone or in combination with a muscarinic antagonist with a PK profile optimally aligned to the PK profile of ML-007*
- *Safety, tolerability, and PK results were comparable in healthy elderly and healthy adult subjects at all doses*
- *Study findings provide support for twice daily dosing of ML-007 across age groups*
- *MapLight plans to advance a combination tablet formulation of ML-007 and muscarinic antagonist to Phase 2 in 2024*

SAN FRANCISCO, August 24, 2023 - 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 second Phase 1 clinical trial evaluating ML-007, a novel M_1/M_4 muscarinic receptor agonist targeting brain circuits shown to be dysfunctional in neurodegenerative and neurocognitive disorders such as schizophrenia, Alzheimer's disease psychosis, and dyskinesias. The study explored dosing of ML-007 alone and when paired with a muscarinic antagonist chosen for its peripheral selectivity and PK properties. The precision of the PK match between the muscarinic agonist and antagonist was designed to facilitate dose escalation of ML-007, enhance the tolerability profile by effectively neutralizing peripheral muscarinic activity, and to support MapLight's strategy to co-formulate ML-007 and the antagonist as a single, twice-daily combination tablet for both adult and elderly patients.

This randomized, three-part study included 106 subjects across ten healthy adult cohorts and three healthy elderly cohorts. Single and multiple oral doses of ML-007 with and without the muscarinic antagonist were explored. A consistently favorable safety and tolerability profile was achieved across all cohorts. At clinically relevant doses, adverse events were generally mild, transient, and correlated with dose escalated C_{max} effects.

ML-007 was safe and well tolerated alone at all doses, including those that resulted in and exceeded anticipated clinically relevant exposures. When paired with the muscarinic antagonist, plasma ML-007 concentrations twelve times the minimum plasma target concentration were well tolerated, and an intolerable dose was not identified. No severe or serious adverse events were observed in the study. Importantly, multi-dose tolerability was comparable in elderly and healthy adult cohorts across all explored doses, as assessed by spectrum, severity, and duration of adverse events.

Pharmacokinetic data obtained in this study support twice daily dosing across age groups. The study results also confirmed that ML-007 is highly permeable, bioavailable, and that exposures of ML-007 increase proportionally with increases in dose. MapLight plans to advance a fixed-

dose, extended-release combination of ML-007 and muscarinic antagonist into Phase 2 studies next year, with twice-daily dosing across age groups in those studies.

“Currently available treatments do not adequately address the needs of people experiencing psychosis or dyskinesias related to drug treatment. These medications can have intolerable side effects and lead to significant safety concerns for some patient populations, particularly older patients," said MapLight’s Chief Medical Officer, Erin Foff, M.D., Ph.D. "This study generated crucial data to help inform further development of ML-007 as a novel option for patients with these conditions. We are extremely encouraged by the safety profile observed in both younger and older subjects.”

“These results indicate ML-007 can target M_1 and M_4 receptors with an attractive safety, tolerability, and PK profile. We believe ML-007 has the potential to demonstrate efficacy across multiple indications, and we are considering the broad utility of ML-007 as we build out our Phase 2 development plan,” stated Christopher Kroeger, M.D., MBA, Chief Executive Officer, and Founder.

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 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 need.

About Dyskinesias
Dyskinesias are a category of movement disorders that are characterized by uncontrollable, abnormal, and repetitive muscle movements that can be disruptive to function and quality of life. Dyskinesia can be the result of an underlying condition or develop as a side effect of dopaminergic medications (drug-induced dyskinesia), commonly used to treat Parkinson’s disease, depression, bipolar disorder, schizophrenia, and irritability in autism.

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 Therapeutics is working to develop targeted, novel therapeutics to improve the lives of people with difficult-to-treat brain disorders. The company’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 in 2019 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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Media Contact for MapLight Therapeutics
Charmaine Lykins, Chief Commercial Officer, clykins@maplightrx.com