Arrowhead Pharmaceuticals Initiates Phase 1/2a Study of ARO-MAPT for the Treatment of Alzheimer's Disease and Other Tauopathies

December 8, 2025

- ARO-MAPT utilizes the Targeted RNAi Molecule (TRiM™) platform designed for subcutaneous administration and systemic delivery to the CNS by crossing the blood-brain-barrier

- Study initiation further highlights Arrowhead's innovation and leadership in the delivery of siRNA

PASADENA, Calif.--(BUSINESS WIRE)--Dec. 8, 2025-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced that it has dosed the first subjects in a Phase 1/2a clinical trial of ARO-MAPT, the company's investigational RNA interference (RNAi) therapeutic being developed as a potential treatment for tauopathies including Alzheimer's disease, a progressive neurodegenerative disease characterized by cognitive and functional decline. Alzheimer's disease is the most common cause of dementia, affecting an estimated 32 million people worldwide, and is part of a group of neurodegenerative diseases called tauopathies that are marked by the abnormal accumulation and formation of tau tangles in neurons.

ARO-MAPT is Arrowhead's first investigational RNAi-based therapy to utilize a new proprietary delivery system which, in preclinical studies, has achieved blood-brain-barrier penetration and deep knockdown of target genes across the central nervous system (CNS), including deep brain regions, after subcutaneous injection. This underscores Arrowhead's leadership in the delivery of siRNA to multiple tissues and cell types throughout the body utilizing its proprietary and differentiated Targeted RNAi Molecule (TRiM™) platform.

"Alzheimer's disease is the most common cause of dementia and is debilitating for patients and caregivers. Currently available disease-modifying treatments have focused on amyloid-beta plaque clearance but have shown limited clinical benefit. Tau related pathology may be a critical driver of neurodegeneration, and targeting tau is a promising strategy to potentially slow or stop cognitive and functional decline," said James Hamilton, M.D., Chief Medical Officer and Head of R&D at Arrowhead. "By silencing expression of the gene that encodes the tau protein, ARO-MAPT may prevent or reverse tau protein accumulation in subjects with early Alzheimer's disease, potentially preventing or slowing the progression of the disease. Our ongoing Phase 1/2 study will evaluate single and multiple doses of ARO-MAPT in healthy volunteers and, in parallel, multiple doses of ARO-MAPT in patients with early Alzheimer's disease. We anticipate initial data for the first parts of this study will be available in the second half of 2026."

In preclinical studies in non-human primates presented at the RNA Leaders USA Congress 2025, investigational ARO-MAPT demonstrated potent and long-lasting microtubule associated protein tau (MAPT) mRNA and tau protein suppression, potentially enabling monthly or quarterly subcutaneous dosing with uniform distribution throughout the CNS. Presentation slides from the RNA Leaders USA Congress 2025 may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website.

About ARO-MAPT

ARO-MAPT is designed to silence CNS expression of the microtubule associated protein tau (MAPT) gene, which encodes the tau protein. Aggregation of the toxic tau protein is believed to be a key driver in multiple tauopathies, including Alzheimer's disease. By preventing or potentially reversing tau protein accumulation in subjects with mild cognitive impairment due to Alzheimer's disease and mild Alzheimer's disease dementia, ARO-MAPT has potential to prevent or slow disease progression.

About the AROMAPT-SC-1001 Phase 1/2 Study

AROMAPT-SC-1001 (NCT07221344) a Phase 1/2a placebo-controlled dose-escalating study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of ARO-MAPT in up to 64 healthy subjects (NHV) and up to 48 subjects with early Alzheimer's disease (AD), defined as mild cognitive impairment due to Alzheimer's disease and mild Alzheimer's disease dementia. In Part 1a (in NHV) of the study, subjects will receive one or three weekly doses of ARO-MAPT or placebo by subcutaneous injection, and in Parts 1b (in NHV) and Part 2a (in AD) subjects will receive three weekly doses followed by three monthly doses for a total of six subcutaneous administrations of ARO-MAPT or placebo.

About Arrowhead Pharmaceuticals

Arrowhead Pharmaceuticals develops medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep, and durable knockdown of target genes. RNA interference, or RNAi, is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Arrowhead's RNAi-based therapeutics leverage this natural pathway of gene silencing.

For more information, please visit www.arrowheadpharma.com, or follow us on X (formerly Twitter) at @ArrowheadPharma, LinkedIn, Facebook, and Instagram. To be added to the Company's email list and receive news directly, please visit http://ir.arrowheadpharma.com/email-alerts.

Safe Harbor Statement under the Private Securities Litigation Reform Act:

This news release contains forward-looking statements within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Any statements contained in this release except for historical information may be deemed to be forward-looking statements. Without limiting the generality of the foregoing, words such as "may," "will," "expect," "believe," "anticipate," "hope," "intend," "plan," "project," "could," "estimate," "continue," "target," "forecast" or "continue" or the negative of these words or other variations thereof or comparable terminology are intended to identify such forward-looking statements. In addition, any statements that refer to projections of our future financial performance, trends in our business, expectations for our product pipeline or product candidates, including anticipated regulatory submissions and clinical program results, prospects or benefits of our collaborations with other companies, or other characterizations of future events or circumstances are forward-looking statements. These forward-looking statements include, but are not limited to, statements about the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs; our expectations regarding the potential benefits of the partnership, licensing and/or collaboration arrangements and other strategic arrangements and transactions we have entered into or may enter into in the future; our beliefs and expectations regarding milestone, royalty or other payments that could be due to or from third parties under existing agreements; and our estimates regarding future revenues, research and development expenses, capital requirements and payments to third parties. These statements are based upon our current expectations and speak only as of the date hereof. Our actual results may differ materially and adversely from those

expressed in any forward-looking statements as a result of numerous factors and uncertainties, including the safety and efficacy of our product candidates, decisions of regulatory authorities and the timing thereof, the duration and impact of regulatory delays in our clinical programs, our ability to finance our operations, the likelihood and timing of the receipt of future milestone and licensing fees, the future success of our scientific studies, our ability to successfully develop and commercialize drug candidates, the timing for starting and completing clinical trials, rapid technological change in our markets, the enforcement of our intellectual property rights, and the other risks and uncertainties described in our most recent Annual Report on Form 10-K, subsequent Quarterly Reports on Form 10-Q and other documents filed with the Securities and Exchange Commission from time to time. We assume no obligation to update or revise forward-looking statements to reflect new events or circumstances.

Source: Arrowhead Pharmaceuticals, Inc.

View source version on businesswire.com: https://www.businesswire.com/news/home/20251208566889/en/

Arrowhead Pharmaceuticals, Inc.
Vince Anzalone, CFA
626-304-3400
ir@arrowheadpharma.com

Investors:
LifeSci Advisors, LLC
Brian Ritchie
212-915-2578
britchie@lifesciadvisors.com

Media:
LifeSci Communications, LLC
Kendy Guarinoni, Ph.D.
724-910-9389
kguarinoni@lifescicomms.com

Source: Arrowhead Pharmaceuticals, Inc.