Arrowhead Pharmaceuticals Completes Enrollment in SHASTA-3, SHASTA-4, and MUIR-3 Phase 3 Studies of Plozasiran

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- Study completion anticipated in mid-2026 with subsequent data readout and regulatory submissions for treatment of severe hypertriglyceridemia

PASADENA, Calif.--(BUSINESS WIRE)--Jun. 23, 2025-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced that it has completed enrollment in SHASTA-3, SHASTA-4, and MUIR-3, the company's global Phase 3 clinical studies designed to support regulatory submissions for marketing approval of investigational plozasiran in the treatment of severe hypertriglyceridemia. Arrowhead anticipates completing the primary portion of these studies in mid-2026 with topline data expected shortly thereafter and planned submissions for regulatory review and potential approval to follow. The company previously submitted a New Drug Application (NDA) for plozasiran based on positive Phase 3 PALISADE study results in patients with familial chylomicronemia syndrome, which the U.S. FDA has accepted with a Prescription Drug User Fee Act (PDUFA) action date set for November 18, 2025.

"Completion of enrollment for the SHASTA-3, SHASTA-4, and MUIR-3 studies represent important milestones for plozasiran," said Bruce Given, M.D., Chief Medical Scientist at Arrowhead. "These studies bring us closer to generating the datasets needed to support potential global regulatory submissions for plozasiran as a treatment for severe hypertriglyceridemia, pending positive results. With a primary endpoint focused on triglyceride reduction at 12 months, we remain on track for study completion by mid-2026. Arrowhead's clinical development, clinical operations, and regulatory teams continue to execute complex global clinical studies with speed and precision. We owe the entire team involved a debt of gratitude for efficiently initiating these studies in 24 countries and enrolling approximately 2,200 patients. We're grateful to the investigators, caregivers, and patients for participating in these clinical studies, and we thank them for their trust in Arrowhead and in plozasiran."

About Severe Hypertriglyceridemia

Severe hypertriglyceridemia (SHTG) is characterized by triglyceride (TG) levels greater than 500 mg/dL, with the most severe form being familial chylomicronemia syndrome (FCS) where TGs typically exceed 880 mg/dL. SHTG significantly increases the risk of acute pancreatitis (AP), which can often include recurrent attacks requiring repeat hospital admissions and worsening outcomes. AP risk is proportional to the number, characteristics, and concentration of triglyceride rich lipoproteins (TRLs), particularly chylomicrons, and increases as TGs rise. Elevated TGs can also increase the risk of atherosclerotic cardiovascular disease (ASCVD). Limited treatment options exist to sustainably reduce TGs below guideline directed risk thresholds.

About SHASTA-3 and SHASTA-4 Phase 3 Studies

SHASTA-3 (NCT06347003) and SHASTA-4 (NCT06347016) are double-blind, placebo-controlled, Phase 3 studies to evaluate the efficacy and safety of plozasiran in adults with severe hypertriglyceridemia. Between the two studies, approximately 750 participants were randomized to receive 4 doses (once every 3 months) of 25 mg plozasiran or placebo. The primary endpoint is percent change in fasting serum triglyceride levels from baseline to month 12 compared to placebo. After month 12, eligible participants will be offered an opportunity to continue in an optional open-label extension.

About MUIR-3 Phase 3 Study

MUIR-3 (NCT06347133) is a double-blind, placebo-controlled, Phase 3 study to evaluate the efficacy and safety of plozasiran in adults with hypertriglyceridemia (TGs greater than 150 mg/dL and less than 500 mg/dL). Approximately 1,450 participants were randomized to receive 4 doses (once every 3 months) of 25 mg plozasiran or placebo. The primary endpoint is percent change in fasting serum triglyceride levels from baseline to month 12 compared to placebo.

About Plozasiran

Plozasiran, previously called ARO-APOC3, is a first-in-class investigational RNA interference (RNAi) therapeutic designed to reduce production of apolipoprotein C-III (APOC3) which is a component of triglyceride rich lipoproteins (TRLs) and a key regulator of triglyceride metabolism. APOC3 increases triglyceride levels in the blood by inhibiting breakdown of TRLs by lipoprotein lipase and uptake of TRL remnants by receptors in the liver. The goal of treatment with plozasiran is to reduce the level of APOC3, thereby reducing triglycerides and restoring lipids to more normal levels.

In multiple clinical studies, investigational plozasiran has demonstrated reductions in triglycerides and multiple atherogenic lipoproteins in patients with familial chylomicronemia syndrome (FCS), severe hypertriglyceridemia (SHTG), and mixed hyperlipidemia. Plozasiran has been generally well tolerated to date with treatment emergent adverse events reported that generally reflect the comorbidities and underlying conditions of the study populations. Across clinical studies and study populations, the most frequently reported treatment emergent adverse events for the 25 mg dose that is proposed for marketing approval were COVID-19, upper respiratory tract infection, headache, Type 2 diabetes mellitus, and abdominal pain.

Plozasiran is being investigated in the SUMMIT program of clinical studies, including the PALISADE Phase 3 study in patients with FCS, the SHASTA studies in patients with SHTG, and the MUIR studies in patients with mixed hyperlipidemia.

Plozasiran in the treatment of patients with FCS has been granted Breakthrough Therapy Designation, Orphan Drug Designation, and Fast Track Designation by the U.S. Food and Drug Administration and Orphan Medicinal Product Designation by the European Medicines Agency. Investigational plozasiran has been submitted for marketing authorization in treatment of FCS to multiple global regulatory authorities but has not been reviewed or approved to treat any disease.

About Arrowhead Pharmaceuticals, Inc.

Arrowhead Pharmaceuticals, Inc. 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," "might," "will," "expect," "believe," "anticipate," "goal," "endeavor," "strive," "hope," "intend," "plan," "project," "could," "estimate," "potential," "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 regulatory approval for and commercial launch of plozasiran; 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.

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