Arrowhead Pharmaceuticals Reports Successful Topline Results for Plozasiran from the Pivotal Phase 3 PALISADE Study in Patients with Familial Chylomicronemia Syndrome

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- Plozasiran achieved statistically significant median reductions in triglycerides up to 80% and mean reductions in APOC3 up to 94% at month 10

- Plozasiran achieved a statistically significant reduction in incidence of acute pancreatitis versus placebo

- Plozasiran is the company's first investigational RNAi-based therapy to show clinical efficacy in a Phase 3 study

- Arrowhead plans to highlight recent data for its cardiometabolic pipeline at its June 25, 2024, Cardiometabolic event as part of the 2024 Summer Series of R&D Webinars

PASADENA, Calif.--(BUSINESS WIRE)--Jun. 3, 2024-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced topline results from the pivotal Phase 3 PALISADE study of investigational plozasiran in patients with genetically confirmed or clinically diagnosed familial chylomicronemia syndrome (FCS), a severe genetic disease with significant unmet need and no FDA approved therapies. PALISADE successfully met the primary endpoint of lowering triglycerides and met all key secondary endpoints, including reducing the incidence of acute pancreatitis compared to placebo.

"The strong results from the Phase 3 PALISADE study, evaluating plozasiran in patients with FCS, significantly build upon the promising results from the Phase 2 SHASTA-2 and MUIR studies in patients with severe hypertriglyceridemia and mixed hyperlipidemia, recently published in JAMA Cardiology and the New England Journal of Medicine. These findings highlight the potential of plozasiran as a promising therapy for patients with various cardiometabolic disorders," said Bruce Given, M.D., chief medical scientist at Arrowhead. "We look forward to discussing results at our June 25th Cardiometabolic event as part of our 2024 Summer Series of R&D Webinars and presenting the full PALISADE data at upcoming medical conferences."

The primary endpoint for the PALISADE study was placebo adjusted median change in triglycerides at Month 10. At that timepoint, patients treated with quarterly doses of 25 and 50 mg plozasiran achieved median triglyceride reductions of -80% and -78%, respectively, with a maximal reduction of -98%. At month 12, patients treated with 25 and 50 mg plozasiran achieved median triglyceride reductions of -78% and -73%, respectively, with a maximal reduction of -99%. These compared with median triglyceride reductions in placebo-treated patients of -17% at month 10 (primary endpoint, $p<0.001$) and -7% at month 12. Mean reductions in Apolipoprotein C-III (APOC3) at month 10 were -88% and -94% at 25 and 50 mg plozasiran, respectively.

In addition to meeting the primary endpoint, plozasiran met all key secondary endpoints and demonstrated statistical significance versus placebo.

There were 4 multiplicity-controlled key secondary endpoints: 1) percent change from baseline at Months 10 and 12 (averaged) in fasting triglycerides; 2) percent change from baseline at Month 10 in fasting APOC3; 3) percent change from baseline at Month 12 in fasting APOC3; 4) incidence of positively adjudicated events of acute pancreatitis during the randomized period.

Plozasiran demonstrated a favorable safety profile in the PALISADE study. The number of subjects reporting treatment emergent adverse events (AEs) were similar in plozasiran and placebo groups. Severe and serious AEs were less common with plozasiran than with placebo. The most common AEs reported were abdominal pain, COVID-19, nasopharyngitis, headache and nausea.

Christopher Anzalone, Ph.D., president and CEO at Arrowhead, added, "We see plozasiran data as best in class and with the potential to address multiple cardiometabolic diseases with substantial unmet need. We will now communicate the results to the FDA and discuss filing a New Drug Application for FCS. We will also continue to advance multiple additional Phase 3 studies for other patient populations. It is gratifying to see one of our investigational RNAi-based medicines get potentially closer to the patients who need it most. This moment represents validation of all the hard work from so many talented Arrowhead employees, our collaborators, and the FCS community over the years. We would like to express our sincere gratitude to the patients, caregivers, investigators, and study teams involved in the PALISADE study."

Arrowhead plans to highlight recent data for its cardiometabolic pipeline at its June 25, 2024, Cardiometabolic event as part of the 2024 Summer Series of R&D Webinars. The company also plans to present full results from the Phase 3 PALISADE study at upcoming medical congresses and will begin to engage with global regulatory authorities about these data.

About PALISADE Phase 3 Study

The PALISADE study (NCT05089084) is a Phase 3 placebo controlled study to evaluate the efficacy and safety of plozasiran in adults with genetically confirmed or clinically diagnosed FCS. The primary endpoint of the study is percent change from baseline in fasting TG versus placebo at Month 10. A total of 75 subjects distributed across 39 different sites in 18 countries were randomized to receive 25 mg plozasiran, 50 mg plozasiran, or matching placebo once every three months. Participants who completed the randomized period were eligible to continue in a 2-part extension period, where all participants receive plozasiran.

About Familial Chylomicronemia Syndrome

Familial chylomicronemia syndrome (FCS) is a severe and ultrarare genetic disease often caused by various monogenic mutations. FCS leads to extremely high triglyceride (TG) levels, typically over 880 mg/dL. Such severe elevations can lead to various serious signs and symptoms including acute and potentially fatal pancreatitis, chronic abdominal pain, diabetes, hepatic steatosis, and cognitive issues. Currently, the therapeutic options that can adequately treat FCS are limited.

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 hepatic 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 demonstrated reductions in triglycerides and multiple atherogenic lipoproteins in patients with familial chylomicronemia syndrome (FCS), severe hypertriglyceridemia (SHTG), and mixed hyperlipidemia. Plozasiran has demonstrated a favorable safety profile to date with treatment emergent adverse events reported that reflect the comorbidities and underlying conditions of the study populations. Plozasiran is currently being investigated in the PALISADE Phase 3 clinical study in patients with FCS, which recently completed, and the Phase 3 SHASTA-3 and SHASTA-4 studies in patients with SHTG.

Plozasiran has been granted Orphan Drug Designation and Fast Track Designation by the U.S. Food and Drug Administration and Orphan Drug Designation by the European Medicines Agency.

About Plozasiran EAP

Arrowhead is committed to bringing new investigational medicines to patients with serious diseases as quickly and efficiently as possible. The company has established an early access program (EAP) for some individuals living with FCS. As with any investigational medicine that has not been approved by regulatory authorities, investigational plozasiran may or may not be effective in treating your diagnosis or condition, and there may be risks associated with its use. If you are a patient or caregiver wishing to know more about this plozasiran EAP for FCS, please discuss this EAP and all treatment options with your treating physician. If you are a treating physician and are seeking information about the plozasiran EAP or would like to request access for a patient, please contact EAP@arrowheadpharma.com.

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 or on LinkedIn. To be added to the Company's email list and receive news directly, please visit http://ir.arrowheadpharma.com/email-alerts.

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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 impact of the ongoing COVID-19 pandemic on our business, 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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