Arrowhead Presents New Phase 2 Data at AHA 2022 on Cardiometabolic Pipeline

November 7, 2022

- ARO-APOC3 decreased triglycerides by 86%, and non-HDL-C by 45% while increasing HDL-C by 99% in patients with severe hypertriglyceridemia

- ARO-ANG3 decreased triglycerides by 59%, LDL-C by 32%, and was associated with a relative reduction in liver fat fraction in patients with mixed dyslipidemia

- Olpasiran reduced lipoprotein(a) levels by more than 95% in patients with established ASCVD

- Company will host a virtual analyst and investor event on November 9, 2022

PASADENA, Calif.--(BUSINESS WIRE)--Nov. 7, 2022-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today announced the presentation of new clinical data on its pipeline of investigational RNAi-based cardiometabolic medicines, ARO-APOC3, ARO-ANG3, and olpasiran, which is being developed by Amgen, in three late-breaking oral presentations at the American Heart Association (AHA) Scientific Sessions 2022, being held in Chicago. The company will also host a virtual analyst and investor event on November 9, 2022, at 10:00 am ET to discuss these data and Arrowhead's plans for future clinical development of ARO-APOC3 and ARO-ANG3.

"Our team and our partners at Amgen collectively showed promising new clinical data across three late-breaking AHA 2022 presentations on investigational candidates, ARO-APOC3, ARO-ANG3, and olpasiran, which were all developed utilizing Arrowhead's proprietary Targeted RNAi Molecule (TRiM™) technology. The totality of these data demonstrates the significant progress achieved in RNAi drug development and they specifically suggest a potential future treatment paradigm where RNAi may be prominently leveraged in preventive cardiology," said Javier San Martin, M.D, Arrowhead's chief medical officer. "ARO-APOC3, ARO-ANG3, and olpasiran were all highly active at silencing their respective gene targets, which resulted in encouraging changes in multiple relevant lipid and lipoprotein levels. Our confidence in the potential of these investigational medicines continues to grow as we approach the start of multiple potentially pivotal Phase 3 studies with the goal to get these important medicines to the patients that need them."

In the SHASTA-2 study in subjects with severe hypertriglyceridemia who had baseline triglycerides (TGs) of greater than 500 mg/dL, treatment with ARO-APOC3 at doses of 10 mg, 25 mg, and 50 mg all durably decreased APOC3 up to 87%, TGs up to 86%, non-HDL-C up to 45%, and increased HDL-C up to 99% through the week 16 timepoint. ARO-APOC3 has been well tolerated with treatment emergent adverse events reported to date that reflect the underlying comorbidities and conditions of the population under study.

In the ARCHES-2 study in subjects with mixed dyslipidemia who had baseline median TGs of 226 mg/dL, treatment with ARO-ANG3 at doses of 50 mg, 100 mg, or 200 mg resulted in substantial reductions of ANGPTL3 up to 71% at week 8, TGs up to 59% at week 16, and LDL-C up to 32% at week 16. ARO-ANG3 was also associated with relative reduction in liver fat fraction at week 24, with no adverse events related to liver function test changes reported to date. ARO-ANG3 has been well tolerated with treatment emergent adverse events reported to date consistent with those expected in this patient population and with associated underlying comorbidities.

Amgen also presented end-of-treatment data from its Phase 2 OCEAN(a)-DOSE study of TRiM-enabled investigational olpasiran in adults with elevated lipoprotein(a) [Lp(a)] levels (greater than 150 nmol/L) and a history of atherosclerotic cardiovascular disease (ASCVD). These data were presented during the Nov. 6 Late-Breaking Science Session and simultaneously published in the New England Journal of Medicine. At week 36, Lp(a) increased by a mean of 3.6% in the placebo arm, whereas there were substantial reductions of Lp(a) levels in all olpasiran arms. Placebo-adjusted mean percent reductions were 70.5% for patients receiving 10 mg every 12 weeks, 97.4% for patients receiving 75 mg every 12 weeks, 101.1% for patients receiving 225 mg every 12 weeks and 100.5% for patients receiving 225 mg every 24 weeks.

The November 9, 2022 analyst and investor event will feature presentations from key opinion leaders, Christie M. Ballantyne, M.D. (Baylor College of Medicine) and Robert S. Rosenson, M.D. (Icahn School of Medicine at Mount Sinai), who will discuss the data presented at AHA, the current treatment landscape for various lipid disorders with unmet medical needs, and the potential of ARO-APOC3 and ARO-ANG3 to address dysregulated lipids and lipoproteins that may contribute to the substantial residual risk of cardiovascular disease that persists despite existing therapies.

A copy of the presentation materials and a webcast link for the analyst and investor event will be available on the Events and Presentations page under the Investors section of the Arrowhead website.

ARO-ANG3 is the company's investigational RNA interference (RNAi) therapeutic designed to silence the hepatic expression of angiopoietin-like protein 3 (ANGPTL3), a liver synthesized inhibitor of lipoprotein lipase and endothelial lipase, being developed as a treatment for patients with mixed dyslipidemia. In the Phase 2 ARCHES-2 clinical study (NCT04832971), eligible subjects (n=203) were randomized 3:1 to receive subcutaneous injections of 50, 100, or 200 mg ARO-ANG3 or placebo on day 1 and at week 12. Subjects were on a stable diet and optimal statin/lipid-lowering therapies. In subjects with hepatic steatosis, liver fat was assessed at baseline and week 24 by magnetic resonance imaging-derived proton density fat fraction (MRI-PDFF). The primary endpoint is the percent change from baseline in fasting triglycerides (TGs) at week 24. This interim analysis (data cutoff July 6, 2022) evaluated data when all subjects reached week 12. Serum lipid and lipoprotein levels, including LDL-C, were determined at week 16 after all most subjects had received both doses.

ARO-APOC3 is the company's investigational RNAi therapeutic targeting apolipoprotein C-III (APOC3) being developed as a treatment for patients with hypertriglyceridemia (HTG), severe hypertriglyceridemia (SHTG), and familial chylomicronemia syndrome (FCS). In the Phase 2 SHASTA-2 clinical study (NCT04720534), eligible subjects (n=177/216 planned subjects) were randomized 3:1 to receive subcutaneous injections of 10, 25, or 50 mg ARO-APOC3 or placebo on day 1 and at week 12. Patients with FCS were excluded. The primary endpoint is percent change from baseline in fasting TGs at week 24. This interim analysis (data cutoff July 25, 2022) evaluated data when greater than 50% of subjects had reached week 12 and received both doses. Serum lipid, lipoprotein, and apolipoprotein levels were reported at week 16, four weeks after the second dose of ARO-APOC3 or placebo.

OCEAN(a)-DOSE is Amgen's multicenter, randomized, double-blind, placebo-controlled dose-finding study of olpasiran in 281 patients with established ASCVD and Lp(a) levels >150 nmol/L. Patients were randomized to one of four doses of olpasiran (10 mg Q12 weeks, 75 mg Q12 weeks, 225 mg Q12 weeks or 225 mg Q24 weeks) or placebo, given subcutaneously. Across cohorts, the median baseline Lp(a) concentration was 260.3

nmol/L. Patients who received 75 mg or higher every 12 weeks had a 95% or greater reduction in Lp(a) compared to placebo at week 36. At these doses (75 mg or higher), more than 98% of patients achieved an Lp(a) level of 125 nmol/L or less at week 36. Overall, the rates of adverse events were similar in the olpasiran and placebo arms. The most common treatment-related adverse events were injection site reactions, primarily pain.

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 Twitter @ArrowheadPharma. 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," or "continue" 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 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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