**ARROWHEAD PRESENTS NEW PHASE 2 DATA ON PLOZASIRAN AND ZODASIRAN AT AHA 2023**

**November 13, 2023**

- Plozasiran achieved mean max reductions of up to 90% in APOC3 and 87% in triglycerides in patients with severe hypertriglyceridemia.

- In patients with mixed dyslipidemia, mean max reduction in APOC3 was up to 90% leading to robust and durable reductions in multiple atherogenic lipoproteins.

- Company will host a virtual analyst and investor event today, November 13, 2023, at 4:30 pm ET.

**PASADENA, Calif.--(BUSINESS WIRE)--Nov. 13, 2023--** Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today presented new Phase 2 clinical data from the ongoing SHASTA-2 and MUIR studies of plozasiran (ARO-APOC3) and the ARCHES-2 study of zodasiran (ARO-ANG3) at the American Heart Association (AHA) Scientific Sessions 2023, being held in Philadelphia, PA, on November 11-13, 2023.

"The compelling data presented today at AHA support the further development of plozasiran in Phase 3 studies, including in patients with severe hypertriglyceridemia (SHTG), and potentially in a clinical outcomes trial for patients with increased risk for atherosclerotic cardiovascular disease (ASCVD) due to elevated triglyceride rich lipoproteins (TRLs)," said Christie M. Ballantyne, M.D., Baylor College of Medicine. "Numerous epidemiologic studies have shown an association between higher TRLs and an increased risk of ASCVD. Despite potent LDL-C lowering therapies, residual ASCVD risk persists due in part to high levels of atherogenic TRLs. Importantly, plozasiran is the first investigational RNAi-based molecule to demonstrate substantial reductions in TRLs in a mixed dyslipidemia population."

**Plozasiran Data**

In the Phase 2 SHASTA-2 study of plozasiran in 226 subjects with SHTG who had baseline triglycerides (TGs) of greater than 500 mg/dL, two doses of 10 mg, 25 mg, or 50 mg of plozasiran once every 12 weeks reduced TGs to near normal levels and achieved TG levels below the risk threshold for acute pancreatitis (less than 500 mg/dL) in over 90% of patients. At 24 weeks, plozasiran durably decreased serum APOC3 to -79%, TGs to -74%, and remnant cholesterol to -63%, while increasing HDL-cholesterol to +68%.

Plozasiran continues to show a favorable safety profile to date. Treatment emergent adverse events (TEAEs) reported to date reflect the comorbidities and underlying conditions of the study population. Serious TEAEs were not related to plozasiran and were resolved without sequelae, except two subjects with malignancies.

In the Phase 2 MUIR study of plozasiran in 353 subjects with mixed dyslipidemia who had fasting TGs between 150-499 mg/dL and either LDL-cholesterol greater than 70 mg/dL or non-HDL-cholesterol greater 100 mg/dL, two doses of 10 mg, 25 mg, or 50 mg of plozasiran once every 12 weeks or once every 24 weeks silenced APOC3 and demonstrated robust reductions in atherogenic lipoproteins. At 24 weeks, plozasiran reduced TGs to -64%, remnant cholesterol to -54%, apolipoprotein B (ApoB) to -19%, and Non-HDL-cholesterol to -27%, while increasing HDL-cholesterol to +51%.

TEAEs reported to date reflect the comorbidities and underlying conditions of the study population. Most serious TEAEs recovered with no sequelae.

Details about the AHA presentations are listed below.

- **Title:** ARO-APOC3, an Investigational RNAi Therapeutic, Silences APOC3 and Reduces Triglycerides to Near Normal Levels in Patients With Severe Hypertriglyceridemia: SHASTA-2 Study Results
  - Date/Time: November 13, 2023, 9:45 a.m. EST
  - Presenter: Daniel Gaudet
  - Session: Lipid Lowering via Novel Pathways

- **Title:** ARO-APOC3, an Investigational RNAi Therapeutic, Silences APOC3 and Reduces Atherosclerosis-Associated Lipoproteins in Patients With Mixed Dyslipidemia: MUIR Study Results
  - Date/Time: November 13, 2023, 1:30 p.m. EST
  - Presenter: Christie M Ballantyne
  - Session: Emerging Approaches to Lipid Lowering

**Zodasiran Data**

In the Phase 2 ARCHES-2 study of zodasiran in 204 subjects with mixed dyslipidemia who had fasting TGs between 150-499 mg/dL and either LDL-cholesterol greater than 70 mg/dL or non-HDL-cholesterol greater 100 mg/dL, two doses of 50 mg, 100 mg, or 200 mg of zodasiran once every 12 weeks silenced the expression of angioptotin-like protein 3 (ANGPTL3) and decreased atherogenic lipoproteins. Treatment with zodasiran 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 a relative reduction in liver fat fraction at week 24, with no adverse events related to liver function test changes reported to date. ARO-ANG3 TEAEs reported to date are consistent with those expected in this patient population and with associated underlying comorbidities.

Details about the AHA presentation are listed below.

- **Title:** ARO-ANG3, an Investigational RNAi Therapeutic, Silences the Expression of ANGPTL3 and Decreases Atherogenic Lipoproteins in Patients With Mixed Dyslipidemia: ARCHES-2 Study Results
  - Date/Time: November 13, 2023, 1:30 p.m. EST
  - Presenter: Robert S Rosenson
  - Session: Emerging Approaches to Lipid Lowering

**Virtual Analyst and Investor Event**
The company is hosting a virtual analyst and investor event today, November 13, 2023, at 4:30 pm ET featuring key opinion leaders who will discuss the plozasiran data and its potential as a treatment for SHTG and mixed dyslipidemia in patients with ASCVD. To register for the event, please visit: https://lifescievents.com/event/arrowhead/.

The analyst and investor event will feature presentations from Arrowhead management and three experts in the treatment and management of lipid and lipoprotein disorders:

- Daniel Gaudet, MD, PhD, Professor of Medicine at Université de Montréal, who will discuss plozasiran in the context of the current treatment landscape for severe hypertriglyceridemia
- Børge Nordestgaard, MD, Professor & Chief Physician, Copenhagen University Hospital, University of Copenhagen, Denmark, who will discuss remnant cholesterol and its role in cardiovascular disease
- Steven Nissen, MD, Chief Academic Officer for the Heart and Vascular Institute at the Cleveland Clinic, who will discuss the potential of a cardiovascular outcomes study of plozasiran

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.

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," "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.

Source: Arrowhead Pharmaceuticals, Inc.