Arrowhead Presents Interim Data from ARO-ANG3 Phase 2 GATEWAY Study in Patients with HoFH

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- 44-48% Mean Reductions in LDL-C Achieved on Top of Continued Standard of Care

- Phase 3 Planning is Ongoing

PASADENA, Calif.--(BUSINESS WIRE)--May 23, 2023-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today presented interim data from the ongoing Phase 2 GATEWAY clinical study of ARO-ANG3, the company's investigational RNAi therapeutic designed to reduce expression of angiopoietin-like protein 3 (ANGPTL3), in patients with homozygous familial hypercholesterolemia (HoFH). The company is currently planning a Phase 3 study to further investigate ARO-ANG3 and intends to conduct a meeting with regulatory authorities in the second half of 2023 to discuss the proposed study design.

The data were presented at the 91st European Atherosclerosis Society Congress in a poster titled, "ARO-ANG3, an Investigational RNAi Therapeutic, Decreases Serum LDL-Cholesterol, Apolipoprotein B, and Angiopoietin-like Protein 3 in Patients with Homozygous Familial Hypercholesterolaemia," which may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website.

Javier San Martin, M.D., chief medical officer at Arrowhead, said: "Despite advances in the treatment of cardiovascular disease associated with high LDL-cholesterol, patients with HoFH have a particularly high need for additional therapy with a mechanism working outside of the LDL receptor, such as ANGPTL3 inhibition, and with a dose regimen which can help improve adherence and compliance. The data generated in the GATEWAY study of ARO-ANG3 in patients with HoFH and our prior clinical studies in patient populations with different levels and cause of hypercholesterolemia, demonstrate that ANGPTL3 inhibition led to substantial reductions in LDL-cholesterol, Non-HDL-C, triglycerides, ApoB, and other key lipids and atherogenic lipoproteins. These results are very encouraging and support our plan to rapidly advance ARO-ANG3 into a Phase 3 clinical study in patients with HoFH."

Key findings from the GATEWAY study include the following:

- At study week 20, administration of 200 mg or 300 mg ARO-ANG3 on day 1 and day 84 led to the following changes:
  - Mean reductions in LDL-C (Martin-Hopkins) of 48.1% and 44.0%, respectively
    - These reductions were achieved on top of continued standard of care, including statins, ezetimibe, PCSK9 inhibitors, and apheresis
  - Mean reductions in ApoB of 39.2% and 34.5%, respectively
  - Mean reductions in ANGPTL3 of 82.7% and 80.1%, respectively
- ANPTL3 inhibition with ARO-ANG3 also reduced HDL-C, non-HDL-C, and triglycerides, consistent with published human genetic data
- Safety and tolerability
  - Overall, no newly identified patterns of adverse events in HoFH patients
  - No treatment emergent adverse events leading to drug discontinuation, dose interruptions, or study withdrawal
  - One serious adverse event of second degree atrioventricular block reported in a patient with extensive atherosclerotic cardiovascular disease history, considered not related to ARO-ANG3

About Homozygous Familial Hypercholesterolemia

Homozygous familial hypercholesterolemia (HoFH) is the most serious and rare form of familial hypercholesterolemia, which if left untreated leads to early clinical manifestations of coronary artery disease. Most cases of HoFH are due to mutations in the low-density lipoprotein receptor (LDLR) gene coding for the LDL receptor. Thus, patients with HoFH due to dysfunctional or absent LDLR can be resistant to standards of care such as statins and even resistant to alternatives such as PCSK9 inhibitors. Patients with HoFH are therefore a population with a particularly high need for additional therapy with a mechanism working outside of the LDL receptor, such as therapeutic ANGPTL3 inhibition.

About the GATEWAY Phase 2 Study

The AROANG3-2003 GATEWAY study (NCT05217667) is a Phase 2 open-label study to evaluate the efficacy, safety, and tolerability of 200 mg and 300 mg of ARO-ANG3 administered once every 12 weeks in 18 patients with HoFH. The initial treatment period is up to 36 weeks with an optional 24-month extension treatment period. The primary endpoint of the study is the percent change from baseline in LDL-cholesterol.

About ARO-ANG3

ARO-ANG3 is an investigational RNAi therapeutic designed to reduce expression of angiopoietin-like protein 3 (ANGPTL3), a hepatocyte expressed regulator of lipid and lipoprotein metabolism with multiple potential modes of action, including inhibition of lipoprotein lipase and endothelial lipase. Given the inhibitory role of ANGPTL3 in the metabolism of various lipoproteins and triglycerides, reduced expression and reduced circulating levels of ANGPTL3 may increase clearance of LDL-cholesterol, HDL-cholesterol, and triglycerides.

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.

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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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