Arrowhead Presents Positive New Phase 1/2 Clinical Data on Cardiometabolic Candidates ARO-APOC3 and ARO-ANG3 at European Society of Cardiology Congress 2020

August 31, 2020

PASADENA, Calif.--(BUSINESS WIRE)--Aug. 31, 2020-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today announced the presentation of positive new Phase 1/2 clinical data on two RNAi-based cardiometabolic candidates, ARO-APOC3 targeting apolipoprotein C-III (APOC3) being developed as a treatment for patients with hypertriglyceridemia, and ARO-ANG3 targeting angiopoietin like protein 3 (ANGPTL3) being developed as a treatment for mixed dyslipidemias. The data were presented in back-to-back oral presentations at the European Society of Cardiology (ESC) Congress 2020.

Javier San Martin, M.D., chief medical officer at Arrowhead, said: “These positive results from the healthy volunteer, repeat-dose portion of the Phase 1/2 clinical studies of our cardiometabolic candidates, ARO-APOC3 and ARO-ANG3, strongly support our plans to rapidly advance both drug candidates into later stage development. Both RNAi-based investigational therapies demonstrated three important characteristics: First, they had favorable safety and tolerability profiles, consistent with our other TRiM™-enabled candidates; second, they achieved high levels of pharmacologic activity against their respective targets, with a long duration of effect that may enable an attractive and convenient dosing interval of once every 4 or 6 months; and third, inhibition of the targets led to favorable improvements in multiple lipid parameters. These are precisely the traits we were looking for and further support our belief that RNAi is the optimal mechanism to inhibit APOC3 and ANGPTL3. We are excited about the promise of ARO-APOC3 and ARO-ANG3 as potential new treatment options for large populations of currently underserved patients with cardiovascular disease risk from hypertriglyceridemia and mixed dyslipidemias. We also look forward to presenting additional data from studies in various patient populations at the National Lipid Association and American Heart Association meetings later this year.”

ARO-APOC3 Presentation Details:

- Title: **RNA Interference Targeting Apolipoprotein C-3 with ARO-APOC3 in Healthy Volunteers Mimics Lipid and Lipoprotein Findings Seen in Subjects with Inherited Apolipoprotein C-3 Deficiency**
- Authors: Christian Schwabe, *et al.*
- Presenter: Christie M. Ballantyne
- Type: Oral Presentation
- Date and Time: August 31, 2020, at 10:50 CEST

Key points presented include the following:

- In normal volunteers, repeat doses of ARO-APOC3, an investigational RNAi therapeutic that silences APOC3 mRNA, resulted in:
    - Reduction in APOC3
    - Maximal mean fasting lipid, lipoprotein, and apolipoprotein changes of:
        - -75% for triglycerides (TG)
        - -25% for low-density lipoprotein cholesterol (LDL-C)
        - -33% for apolipoprotein B (ApoB)
        - +75% for high-density lipoprotein cholesterol (HDL-C)
- ARO-APOC3 had a favorable safety and tolerability profile
- APOC3 inhibition produced expected favorable lipid changes, with reduced TG and LDL-C and increased HDL-C

ARO-ANG3 Presentation Details:

- Title: **RNAi Inhibition of Angiopoietin-like Protein 3 (ANGPTL3) with ARO-ANG3 Mimics the Lipid and Lipoprotein Profile of Familial Combined Hypolipidemia**
- Authors: Gerald F. Watts, *et al.*
- Presenter: Gerald F. Watts
- Type: Oral Presentation
- Date and Time: August 31, 2020, at 11:00 CEST

Key points presented include the following:

- In normal volunteers, repeat doses of ARO-ANG3, an investigational RNAi therapeutic that silences ANGPTL3 mRNA, demonstrated:
    - Dose-dependent reduction in fasting ANGPTL3
    - Maximal mean reductions in fasting lipid, lipoprotein, and apolipoprotein concentrations of:
        - -71% in TG
        - -50% in LDL-C
        - -42% in ApoB
        - -34% in non-HDL-C
        - -47% in HDL-C
    - Lipid, lipoprotein, and apolipoprotein reductions sustained to week 16

- ARO-ANG3 had a favorable safety and tolerability profile
- ANGPTL3 inhibition has the potential to treat mixed dyslipidemia and decrease residual risk in patients with cardiovascular disease on guideline-recommended standard of care

A copy of the presentation materials may be accessed 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. 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 various factors and uncertainties, including the safety and efficacy of our product candidates, 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, and the enforcement of our intellectual property rights. Our most recent Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q discuss some of the important risk factors that may affect our business, results of operations and financial condition. We assume no obligation to update or revise forward-looking statements to reflect new events or circumstances.

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