Arrowhead Pharmaceuticals Presents Initial Top-Line Clinical Data and Preclinical Data on RNAi Candidates ARO-APOC3 and ARO-ANG3

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PASADENA, Calif.--(BUSINESS WIRE)--Sep. 16, 2019-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today presented initial top-line clinical data at The Global Summit on Cardiology and Heart Diseases, being held in Dubai, UAE. The data demonstrate that, in two Phase I single-dose clinical studies in healthy volunteers, ARO-APOC3 reduced plasma Apolipoprotein C-III (apoC-III) and ARO-ANG3 reduced plasma angiopoietin like protein 3 (ANGPTL3), and both candidates reduced triglycerides without drug-related serious or severe adverse events. These initial clinical data also indicate that ARO-APOC3 and ARO-ANG3 administration led to a long duration of effect that potentially enables once every three-month or once every six-month dosing intervals.

Bruce Given, M.D., chief operating officer and head of R&D at Arrowhead, said: “The results presented today at The Global Summit on Cardiology and Heart Diseases suggest that Arrowhead’s RNAi-based cardiometabolic candidates, ARO-APOC3 and ARO-ANG3, hold significant promise for the treatment of patients with hypertriglyceridemia and dyslipidemia. Our clinical and preclinical data clearly show that both ARO-APOC3 and ARO-ANG3 are highly active against their respective targets and lipid parameters. In addition, there is encouraging evidence from genetic studies, preclinical studies, and proof of concept from other drug candidates that inhibiting apoC-III and ANGPTL3 has the potential to help patients with rare diseases, such as familial chylomicronemia syndrome (FCS) and homozygous familial hypercholesterolemia (HoFH), as well as individuals with higher prevalence cardiovascular and metabolic diseases. Achieving deep reductions in plasma triglycerides of 66% and 63% after only a single dose of ARO-ANG3 and ARO-APOC3, respectively, exceeded our expectations. These data compare quite favorably with clinical data from other modalities, including antibodies and antisense, which we include as reference in the backup slides of the presentation available on the Events and Presentations page under the Investors tab on our website. We look forward to sharing a fuller dataset, including a broader set of lipid parameters and full time course from the single ascending dose portions of the ARO-APOC3 and ARO-ANG3 Phase 1 studies in healthy volunteers later this year and the multiple ascending dose portions in various patient populations as data mature.”

Key points discussed include the following:

- Top-line data from a single dose of 100 mg of ARO-APOC3 in healthy volunteers demonstrated mean maximal reductions of plasma triglycerides of 63% and APOC3 protein of 94% without serious or severe adverse events
    - The most common adverse events observed to date, all mild or moderate, have been headache, upper respiratory infection and mild injection site findings
- Top-line data from a single dose of 200 mg of ARO-ANG3 in healthy volunteers demonstrated mean maximal reductions of plasma triglycerides of 66% and ANGPTL3 protein of 79% without drug-related serious or severe adverse events
    - The most common adverse events seen to date, all mild or moderate, have been headache and upper respiratory infection
- ARO-ANG3 reduced triglycerides and LDL-C in LDL receptor knockout mice
- ARO-ANG3 also ameliorates steatosis and improves insulin sensitivity in diet-induced obese mice
- In mouse studies, ANGPTL3 has shown endocrine effects on triglyceride and LDL-C metabolism and apparent autocrine effects on hepatic steatosis and insulin sensitivity
- Published research also indicates that APOC3 and ANGPTL3 are strong potential targets for addressing cardiovascular disease
    - Genetic studies indicate that plasma triglycerides are an independent risk factor for cardiovascular disease
    - Loss of function mutations of APOC3 or ANGPTL3 are associated with markedly reduced triglycerides and other lipid parameters without reported adverse phenotype

AROAPOC31001 (NCT03783377) is a Phase 1 single and multiple dose-escalating study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamic effects of ARO-APOC3 in adult healthy volunteers, hypertriglyceridemic patients, and patients with FCS. The study is designed to enroll up to 63 subjects.

The single-ascending dose (SAD) portion of the study included 4 cohorts of 10 adult healthy volunteers with (6 active: 4 placebo). Each SAD subject received a single-dose administration of either placebo or ARO-APOC3 at dose levels of 10, 25, 50, or 100 mg. The multiple-dose portion is designed to include 3 cohorts of patients with severe hypertriglyceridemia and 1 cohort of patients with FCS. The multiple-dose cohorts will receive two monthly doses of ARO-APOC3.

AROANG1001 (NCT03747224) is a Phase 1 single and multiple dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamic effects of ARO-ANG3 in adult healthy volunteers and patients with dyslipidemia. The study is designed to enroll up to 82 subjects.

The SAD portion of the study included 4 cohorts of 10 adult healthy volunteers per cohort (6 active: 4 placebo). Each SAD subject received a single-dose administration of either placebo or ARO-ANG3 at dose levels of 35, 100, 200, or 300 mg. The multiple-dose portion is designed to include healthy volunteers, patients with non-alcoholic fatty liver disease (NAFLD), patients on a stable statin treatment regimen with elevated low-density lipoprotein cholesterol (LDL-C) and triglycerides, patients with heterozygous or homozygous familial hypercholesterolemia, and patients with severe hypertriglyceridemia.

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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