Arrowhead Presents New Clinical Data on Cardiometabolic Candidates ARO-APOC3 and ARO-ANG3 at AHA Scientific Sessions 2019

November 18, 2019

- Company Expects to Initiate Phase 3 Clinical Trials Next Year

PASADENA, Calif.--(BUSINESS WIRE)--Nov. 18, 2019-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today presented updated Phase 1 clinical data on its two RNAi-based cardiometabolic candidates, ARO-APOC3 targeting apolipoprotein C-III (APOC3) being developed as a potential treatment for patients with severe hypertriglyceridemia and familial chylomicronemia syndrome (FCS), and ARO-ANG3 targeting angiopoietin like protein 3 (ANGPTL3) being developed for the treatment of dyslipidemias, such as homozygous familial hypercholesterolemia (HoFH), and metabolic diseases. The data were presented in two late-breaking oral presentations at the American Heart Association (AHA) Scientific Sessions 2019, in Philadelphia.

Bruce Given, M.D., chief operating officer and head of R&D at Arrowhead, said: “The data presented at AHA on cardiometabolic candidates ARO-APOC3 and ARO-ANG3 are further validation of the TRiM™ platform and Arrowhead’s ability to consistently develop RNAi therapeutics that achieve deep and durable levels of gene knockdown across a broad range of targets. In particular, the knockdown in APOC3 and ANGPTL3 proteins and the resulting reductions in triglycerides and various lipid parameters strongly support our plan to initiate Phase 3 studies in 2020.”

Presentation Details:

RNA Interference Targeting Apolipoprotein C-III Results in Deep and Prolonged Reductions in Plasma Triglycerides

- Session: Late Breaking Science VI: New Frontiers in Lipid Therapy
- Date and Time: November 18, 2019 from 9:32 AM EST
- Authors: Dr. Christie Ballantyne, presenting on behalf of Dr. Christian Schwabe, *et al.*

Key points presented on the AROAPOC31001 Phase 1/2a clinical study included the following:

- Safety and tolerability
  - 40 subjects enrolled to receive a single dose (24 active, 16 placebo)
  - No serious or severe adverse events (AEs) reported
  - One AE of moderate transient ALT elevation (peak of 210 U/L on Day 22) in a subject receiving ARO-APOC3 who had elevated ALT at baseline (65 U/L), with return to baseline by Day 85 (61 U/L).
  - 8 Local Injection Site Reactions (LISRs) – all rated mild, more common at higher doses
- Activity
  - Dose dependent reductions in serum APOC3 were observed
    - Mean maximum reduction from baseline in serum APOC3 levels ranged from 72% [10 mg dose] to 94% [100 mg dose]
    - Reduction in serum APOC3 levels was maintained through the end of study with week 16 mean reductions of 70% [25 mg dose] to 91% [100 mg dose]
  - Reductions in triglycerides (TGs) and VLDL-C were observed
    - Mean maximum reduction from baseline in serum TGs ranged from 53% (77 mg/dL) [10 mg dose] to 64% (92 mg/dL) [100 mg dose]
    - Mean maximum reduction from baseline in serum VLDL-C ranged from 53% (16 mg/dL) [10 mg dose] to 68% (19 mg/dL) [50 mg dose]
    - Reduction in serum TG and VLDL-C was maintained through the end of study, with week 16 mean reductions of 41%-55% for TG and 42-53% for VLDL-C
  - Changes in LDL- and HDL- cholesterol were observed
    - Mean maximum reduction from baseline in serum LDL-C of 12% (19 mg/dL) [25 mg dose] to 25% (35 mg/dL) [10 mg dose]
    - Dose dependent increase in serum HDL-C with mean maximum increase from baseline in serum HDL-C from 30% (13 mg/dL) [10 mg dose] to 69% (32 mg/dL) [100 mg dose]
    - Serum HDL-C increases were maintained through the end of study, with week 16 mean increases of 28% (12 mg/dL) [10 mg dose] to 52% (22 mg/dL) [100 mg dose]
- Multiple dose evaluations in patients with severe hypertriglyceridemia and/or familial chylomicronemia syndrome are underway

RNA Interference Targeting Hepatic Angiopoietin-Like Protein 3 Results in Prolonged Reductions in Plasma Triglycerides and LDL-C in Human Subjects

- Session: Late Breaking Science VI: New Frontiers in Lipid Therapy
- Date and Time: November 18, 2019 from 9:38 AM EST
- Authors: Dr. Gerald Watts, *et al.*

Key points presented on the AROANG1001 Phase 1/2a clinical study included the following:

- Safety and tolerability
    - 40 subjects enrolled to receive a single dose (24 active, 16 placebo)
    - No drug related severe or serious AEs
    - Two AEs of mild transient elevations in ALT (one active, one placebo)
        - ALT elevation in one subject on ARO-ANG3 confounded by concomitant ingestion of herbal supplement with known liver toxic profile (Peak ALT 192 U/L Day 99, normal by Day 113)
    - 1 mild drug related LISR
- Activity
    - Dose dependent reductions in serum ANGPTL3 were observed
        - Mean maximum reduction from baseline in ANGPTL3 ranged from 55% (50 ng/mL) [35 mg] to 83% (63 ng/mL) [300 mg]
        - Reductions in ANGPTL3 were maintained through end of study, with week 16 mean reductions of 43% (42 ng/mL) [35 mg] to 75% (57 ng/mL) [300 mg]
    - Dose dependent reductions in TGs and VLDL-C were observed
        - Mean maximum TG reduction from baseline of 31% (38 mg/dL) [35 mg] to 66% (167 mg/dL) [200 mg]
        - Mean maximum VLDL-C reduction from baseline of 30% (8 mg/dL)[35 mg] to 65% (33 mg/dL) [200 mg]
        - Reduction in TG and VLDL-C maintained through end of study in 200 mg and 300 mg cohorts, with week 16 mean reductions of 47% to 53% for TG, and 49% to 51% for VLDL-C
    - Changes in LDL- and HDL- cholesterol were observed
        - Mean maximum HDL-C reduced by 8% (4 mg/dL) [35 mg] to 26% (12 mg/dL) [300 mg]
        - HDL-C mean reductions at week 16 of up to 16% (7 mg/dL) [200 mg]
        - Mean maximum LDL-C reduced by 9% (16 mg/dL) [200 mg] to 30% (48 mg/dL) [300 mg]
        - LDL-C mean reductions at week 16 of up to 28% (46 mg/dL) [100 mg] after single dose
            - Mean maximum reduction in LDL-C with 200 mg single dose was blunted by two subjects in this cohort with increasing LDL-C post-dose
        - Multiple dose healthy volunteer data at 200 mg dose demonstrates similar reductions to 100 mg and 300 mg doses of 33%-46% reduction in LDL-C from baseline two weeks after a second dose
    - Multiple dose evaluations in patients with non-alcoholic fatty liver disease (NAFLD) (cohort 5), hyperlipidemia while on statins (cohort 6), familial hypercholesterolemia (cohort 7), severe hypertriglyceridemia (cohort 8) are underway

Copies of the presentations can 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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