Arrowhead Interim Clinical Data Demonstrate ARO-AAT Treatment Improved Multiple Biomarkers of Alpha-1 Liver Disease

November 13, 2020

- Serum Z-AAT reductions of 86-93%

- All patients demonstrated greater than 80% reduction in liver Z-AAT monomer

- 3 of 4 patients had a decrease in liver globule involvement

- 3 of 4 patients demonstrated reductions in Z-AAT polymer with a range of 68-97%

- All patients showed ALT reductions ranging from 36-66%

PASADENA, Calif.--(BUSINESS WIRE)--Nov. 13, 2020-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced positive interim clinical data from AROAAT2002, an open-label Phase 2 clinical study of ARO-AAT, the company's second-generation investigational RNA interference (RNAi) therapeutic being developed as a treatment for the rare genetic liver disease associated with alpha-1 antitrypsin deficiency (AATD). The data demonstrate that three doses of ARO-AAT over 24-weeks resulted in consistent reductions of the disease-causing mutant Z protein (Z-AAT) and improvements in clinically relevant biomarkers of liver disease. The results were presented in a late-breaking poster at The Liver Meeting Digital Experience, the Annual Meeting of the American Association for the Study of Liver Disease (AASLD).

A copy of the poster 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: "These data presented at AASLD strongly suggest that ARO-AAT is doing what it's designed to do, which is reduce the production of the misfolded mutant Z-AAT protein. Moreover, these compelling results indicate that the liver may have the ability to clear out accumulated Z-AAT and begin to heal itself faster than anticipated. Importantly, we saw reductions in serum Z-AAT and liver Z-AAT which led to improvements in multiple markers, such as liver globules, ALT/GGT and Pro-C3. These are all positive indications of a strong pharmacodynamic response and improvement in liver health, following just three doses of ARO-AAT. We anticipate data from additional patient cohorts will be available in the coming months, which will be included in our planned discussions with the U.S. Food and Drug Administration and other regulatory agencies, aimed at exploring areas where the ARO-AAT program could potentially be streamlined and accelerated."

In the AROAAT2002 study, four patients with homozygous PiZZ alpha-1 antitrypsin deficiency and evidence of fibrosis at screening, each received three doses of ARO-AAT on week 0, 4, and 16. Liver biopsies were performed at screening and at week 24. Assessments included safety (including pulmonary function tests), changes in serum Z-AAT, liver Z-AAT, ALT, GGT, Pro-C3, liver elastography (FibroScan®), and liver globule assessment. Additional histologic adjudication is ongoing.

Key data presented include the following:

Pharmacodynamic Response at 24 weeks

- Serum Z-AAT reductions were 86-93%
- Total intra-hepatic Z-AAT reductions were 72-95%
- All patients demonstrated greater than 80% reduction in liver Z-AAT monomer (soluble)
- 3 of 4 patients demonstrated reductions in Z-AAT polymer (insoluble) with a range of 68-97%
- 3 of 4 patients had a decrease in liver globule involvement and 1 subject remained unchanged
- All patients showed reductions in ALT (range 36-66%) and in GGT (range 43-58%)
- 3 of 4 patients demonstrated a substantial reduction of greater than 20% in FibroScan® values
- 3 of 4 patients showed greater than 30% reduction in serum Pro-C3, a marker of fibrogenesis

Safety

- Overall, ARO-AAT 200 mg as a subcutaneous injection was well tolerated in PiZZ AATD subjects
- One treatment emergent SAE of Epstein bar virus related myocarditis was reported
- No treatment emergent AEs related to change in pulmonary status or pulmonary function were reported
- No clinically meaningful changes in ppFEV1 from baseline to Week 24 were observed

In October 2020, Arrowhead and Takeda Pharmaceutical Company Limited announced a collaboration and licensing agreement to develop ARO-AAT. Under the terms of the agreement, Arrowhead and Takeda will co-develop ARO-AAT which, if approved, will be co-commercialized in the U.S. under a 50/50 profit-sharing structure. Outside the U.S., Takeda will lead the global commercialization strategy and receive an exclusive license to commercialize ARO-AAT with Arrowhead eligible to receive tiered royalties of 20-25% on net sales. Arrowhead will receive an upfront payment of $300 million and is eligible to receive potential development, regulatory and commercial milestones up to $740 million. Closing of the transaction is contingent on completion of review under antitrust laws, including the Hart-Scott-Rodino Antitrust Improvements Act of 1976 in the U.S.

AROAAT2002 (NCT03946449) is a pilot open-label, multi-dose, Phase 2 study to assess the response to ARO-AAT in approximately 16 patients with AATD associated liver disease and baseline liver fibrosis who will be enrolled in three cohorts. All eligible participants will require a pre-dose biopsy and an end of study biopsy. Treated participants will also be offered the opportunity to continue treatment in an open-label extension (OLE). Including the OLE, interim assessments will be made after 6 months and 18 months (cohorts 1, 1b), and 12 months and 24 months (cohort 2) of treatment with ARO-AAT. Arrowhead is also evaluating ARO-AAT in the ongoing SEQUOIA Phase 2/3 trial, which began in August 2019.

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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