November 14, 2016

Arrowhead Pharmaceuticals Presents New Data on ARC-AAT

PASADENA, Calif.--(BUSINESS WIRE)-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) delivered a poster presentation with Phase 1 clinical data and an oral presentation with preclinical data on ARC-AAT, its investigational medicine for the treatment of liver disease associated with alpha-1 antitrypsin deficiency (AATD), at The Liver Meeting® 2016, the Annual Meeting of the American Association for the Study of Liver Disease (AASLD), in Boston. The data indicate that in a first-in-human clinical study, ARC-AAT was well tolerated and induced deep and durable reduction of the target AAT protein. The preclinical data suggest that treatment with ARC-AAT over time may improve liver health and prevent further damage.

Bruce Given, M.D., chief operating officer of Arrowhead Pharmaceuticals, said: "We showed some exciting data today indicating that ARC-AAT, both clinically and in a preclinical model, is doing precisely what it is designed to do. In these studies, ARC-AAT led to deep, durable, and dose-dependent silencing of the liver production of the AAT protein. Accumulation of the mutant Z-AAT is believed to be the cause of progressive liver disease in patients with AATD, and reducing the production is important as it is expected to halt the progression of liver disease. Specifically, in the clinical study ARC-AAT led to a maximum reduction of up to 90% in the highest dose group, which we believe to be near full suppression of the liver production of the protein, and a mean maximum reduction of 88%. We are also pleased that in the clinical study ARC-AAT was well tolerated at all dose levels studied (0.3 - 8 mg/kg), which is consistent with the tolerability profile of our other clinical programs that use the same DPC_{iv}^{TM} (EX1) delivery vehicle."

The poster titled, "**RNA interference (RNAi) with ARC-AAT provides deep and prolonged knockdown of alpha-1 antitrypsin levels in healthy volunteers**," publication LB-24 in the late-breaking poster session, describes data from a Phase 1, multi-center, randomized, placebo-controlled, double-blind, single dose-escalation first-in-human study to evaluate the safety, tolerability, pharmacokinetics of ARC-AAT and the effect on circulating alpha-1 antitrypsin (AAT) levels. Key findings from the study include the following:

- Dose-dependent reductions in serum AAT of up to 90% were observed
- Duration of effect indicates that monthly, or less frequent, dosing is likely
- Pharmacokinetic (PK) parameters were linear across dose levels with a constant half-life
- There have been no drop outs due to adverse events (AE), no clinically significant changes in ECGs, DLCO or FEV1, and one serious adverse event (SAE) in a placebo subject
- No clinically significant transaminase (ALT, AST) elevations were reported
- The most frequently reported ARC-AAT related AEs were headache, nausea and rigor (each, 3 events in 36 [8%] subjects)

The oral presentation titled, "**RNA interference therapeutic ARC-AAT prevents production of Z-alpha1 antitrypsin polymers and reverses liver disease phenotype in PiZ mouse model**," publication 124 in the session Parallel 19: Pediatric and Metabolic Liver Diseases: Basic and Translational, describes data from a 33-week study of ARC-AAT in the PiZ mouse model. Key findings from the study include the following:

- Cleared Z-hAAT protein from the cytoplasm and reduced by > 90% in serum
- Prevented and reversed polymer accumulation, with Z-hAAT monomer reduced by 87% and polymer by 42% at week 33
- Halted accumulation of Z-hAAT globules in the liver, with 61% less in ARC-AAT treated compared to saline controls and 24% less than at baseline
- Improved liver health and prevented further damage based on histopathology improvements compared to baseline and saline controls
- Prevented liver inflammation with fewer inflammatory foci and reduced total area of inflammation
- Prevented liver tumors
- Normalized gene expression associated with liver disease

A copy of presentation materials will be made available on the Events and Presentations page under the Investors section of the Arrowhead website.

About ARC-AAT

Arrowhead's ARC-AAT is being investigated for the treatment of liver disease associated with alpha-1 antitrypsin deficiency (AATD), a rare genetic disease that severely damages the liver and lungs of affected individuals. The mean estimated prevalence of AATD in the U.S. is 1 per 3000-5000, or approximately 100,000 patients. AATD is also an important cause of pediatric liver disease with an estimated prevalence in children of approximately 20,000 patients, and 50-80% likely to manifest liver disease during childhood. It is a rare disease that is frequently misdiagnosed or undiagnosed. ARC-AAT employs a novel unlocked nucleobase analog (UNA) containing RNAi trigger molecule designed for systemic delivery using the Dynamic Polyconjugate™ delivery system. ARC-AAT is highly effective at knocking down the alpha-1 antitrypsin (AAT) gene transcript and reducing the hepatic production of the mutant AAT (Z-AAT) protein in animal studies. Reduction of liver production of the inflammatory Z-AAT protein, which is believed to be the cause of progressive liver disease in AATD patients, is important as it is expected to halt the progression of liver disease. ARC-AAT was granted orphan drug designation in both the United States and in Europe, the latter being held on Arrowhead's behalf by a local EU representative Pharma Gateway AB. Arrowhead is conducting a Phase 1 clinical study of ARC-AAT, with part A in healthy volunteers (now complete) and part B in AATD patients, and a Phase 2 multiple dose study in AATD patients.

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. The company's pipeline includes ARC-520 and ARC-521 for chronic hepatitis B virus infection, ARC-AAT for liver disease associated with alpha-1 antitrypsin deficiency, ARC-F12 for hereditary angioedema and thromboembolic disorders, ARC-LPA for cardiovascular disease, and ARC-HIF2 for renal cell carcinoma.

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/alerts.cfm.

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 future success of our scientific studies, our ability to successfully develop 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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