Arrowhead Preclinical Data Demonstrates RNAi Therapy Prevents and Reverses Alpha-1 Liver Disease at The International Liver Congress™

April 12, 2019

PASADENA, Calif.--(BUSINESS WIRE)--Apr. 12, 2019-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today presented preclinical data at The International Liver Congress™ 2019 (ILC), the annual meeting of the European Association for the Study of the Liver (EASL), demonstrating that sustained reduction of mutant Z-AAT protein by RNA interference (RNAi) substantially reversed the alpha-1 antitrypsin deficiency (AATD) disease phenotype in the PiZ mouse model. Arrowhead has completed a Phase 1 clinical trial of ARO-AAT, the company's second generation subcutaneously administered RNAi therapeutic being developed as a treatment for AATD-related liver disease. Pending regulatory clearance, Arrowhead intends to initiate an adaptive Phase 2/3 trial with the potential to serve as a pivotal registrational study.

Bruce Given, M.D., chief operating officer and head of R&D at Arrowhead, said: "The results presented today at EASL from a long-term term preclinical study of our prior generation compound, ARC-AAT, suggest that RNAi holds great promise for the treatment of patients with AATD-associated liver disease. It is particularly encouraging that we were able to prevent liver damage and reverse existing damage in the PiZ mouse model that harbors the human Z-AAT gene and recapitulates many features of AATD liver disease. This gives us added confidence in the ARO-AAT clinical candidate as we embark on a Phase 2/3 clinical study, which has the potential to be registrational."

In the study presented at ILC, PiZ mice were treated with ARC-AAT for 33 weeks. Measurements of plasma Z-AAT levels, Z-AAT protein accumulation in the liver, and expression of genes previously implicated in liver injury and development of fibrosis were taken. In addition, histological evaluations of globules and inflammation and an ultrastructural evaluation of the liver by electron microscopy were performed.

Key results include the following:

- Sustained RNAi reduction of Z-AAT substantially reversed the AATD disease phenotype:
  - Deeply reduced monomeric Z-AAT protein in the liver
  - Reduced polymeric Z-AAT in the liver
  - Prevented the dramatic increase in globule size seen in age-matched control PiZ mice
  - Improved abnormal endoplasmic reticulum morphology
  - Prevented inflammation
  - Prevented/reduced expression of fibrosis, redox-regulation, stress, apoptosis and autophagosome-associated genes
  - Resulted in abundance of healthy mitochondria

Poster Presentation Details:

Reduction of hepatic Z-alpha1 antitrypsin by RNA interference (RNAi) prevents and reverses liver disease including hepatic mitochondrial injury in the PiZ mouse

- Presentation Reference: FRI-446
- Session: Poster: Rare liver diseases (including pediatric and genetic)
- Session Date and Time: April 12, 2019 at 9:00 a.m. to 5:00 p.m. CET
- Authors: Christine Wooddell, *et al.*

Additional details, including the presentation abstract, can be found on the ILC website at https://ilc-congress.eu/. A copy of presentation materials can be accessed by visiting the Events section under the Investors tab 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.

Source: Arrowhead Pharmaceuticals, Inc.

View source version on businesswire.com: https://www.businesswire.com/news/home/20190412005066/en/

Source: Arrowhead Pharmaceuticals Inc.

Contacts:
Arrowhead Pharmaceuticals, Inc.
Vince Anzalone, CFA
626-304-3400
ir@arrowheadpharma.com

Investors and Media:
LifeSci Advisors, LLC
Brian Ritchie
212-915-2578
britchie@lifesciadvisors.com
www.lifesciadvisors.com