Arrowhead Pharmaceuticals Presents Late-Breaking Clinical Data on ARO-AAT at Liver Meeting® 2018

November 9, 2018

- Three monthly doses of 300 mg ARO-AAT led to reductions in serum alpha-1 antitrypsin to below the level of quantitation in 100% of subjects
- Reductions were sustained for greater than 14 weeks indicating that quarterly or less frequent dosing appears feasible
- Single and multiple doses of ARO-AAT appear to be well-tolerated at all doses tested

PASADENA, Calif.--(BUSINESS WIRE)--Nov. 9, 2018-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today announced clinical data from a Phase 1 study of ARO-AAT, the company's second generation subcutaneously administered RNA interference (RNAi) therapeutic being developed as a treatment for a rare genetic liver disease associated with alpha-1 antitrypsin (AAT) deficiency, will be presented in a late-breaking poster at The Liver Meeting®, the Annual Meeting of the American Association for the Study of Liver Disease (AASLD), being held in San Francisco.

In the AROAAT1001 study, 45 normal healthy volunteers (NHV) received a single dose of ARO-AAT (n=16), three monthly doses of ARO-AAT (n=12), or placebo (n=17). Key data presented include the following:

- ARO-AAT at single- and multiple-doses produced robust and consistent reductions in serum AAT levels
  - Single-doses of 200 and 300 mg resulted in greater than 91% serum AAT reduction, with 3 of 4 subjects having concentrations below the level of quantitation (BLQ)
  - In 200 and 300 mg single-dose cohorts, an average serum AAT reduction of greater than 90% was sustained for 6 weeks
  - In the multiple-dose cohorts of 200 and 300 mg, for subjects receiving all 3 doses, an average of greater than 90% reduction in serum AAT was sustained for longer than 14 weeks
  - The maximum NADIR reduction is 94%
- Monthly serum AAT follow up is ongoing with 9 of 10 subjects at BLQ in the multiple-dose cohorts, including 100% of subjects from the 300 mg cohort
- Duration of response indicates that quarterly or less frequent dosing appears feasible
- ARO-AAT has been well tolerated at all doses tested (up to 300 mg) given three times every 28 days
  - The most common adverse events (AE) were upper respiratory tract infection (39%) and headache (32%)

"The ARO-AAT data being presented at The Liver Meeting demonstrate the power of our Targeted RNAi Molecule (TRiM™) platform, which is the basis of our growing pipeline of RNAi therapeutics targeting a diverse range of diseases," said Bruce Given, M.D., Arrowhead's chief operating officer and head of R&D. "These data indicate that ARO-AAT can produce robust and consistent reductions in the liver production of the AAT protein. In addition, the duration of response indicates that a dosing interval of once a quarter or even less frequent is feasible. Our next step is to initiate a Phase 2 study to evaluate whether this reduction can, over time, have an impact on the progressive liver disease in alpha-1 patients, whose only treatment option currently is liver transplant."

Poster Details:

A Phase 1 Single and Multiple Dose-Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Effect of ARO-AAT on Serum Alpha-1 Antitrypsin levels in Normal Adult Volunteers

- Publication Number: LB-9
- Session: Late-Breaking Poster Session
- Session Date and Time: November 12, 2018 from 8:00 a.m. to 5:30 p.m. PT
- Location: Moscone Center North/South Building, Hall C
- Authors: Dr. Christian Schwabe, *et al.*

A copy of the poster may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website.

ARO-AAT is designed to silence the production of the misfolded Z-AAT protein with the intent to:

- Prevent accumulation of the disease-causing protein in the liver
- Allow for clearance of the accumulated protein

- Prevent repeated cycles of cellular damage
- Reverse fibrosis associated with prior damage

About AROAAT1001

AROAAT1001 (NCT03362242) is a Phase 1 randomized, double-blind, placebo controlled single-ascending dose (SAD) and multiple-ascending dose (MAD) study to evaluate the safety, tolerability, pharmacokinetics, and effect of subcutaneous doses of ARO-AAT on serum alpha-1 antitrypsin levels in healthy adult volunteers. The SAD portion of the study included four cohorts at dose levels of 35, 100, 200, and 300 mg and the MAD portion of the study included three cohorts at dose levels of 100, 200, and 300 mg. Additional cohorts were planned at a dose of 400 mg, but were deemed unnecessary based on observed activity at lower doses. AROAAT1001 enrolled 45 healthy volunteers.

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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