Arrowhead Presents Positive Interim Clinical Data on ARO-HSD Treatment in Patients with Suspected NASH at EASL International Liver Congress

June 23, 2021

PASADENA, Calif.--(BUSINESS WIRE)--Jun. 23, 2021-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today presented positive interim results from AROHSD1001, an ongoing Phase 1/2 clinical study of ARO-HSD, the company's investigational RNA interference (RNAi) therapeutic being developed as a treatment for patients with alcohol-related and nonalcohol related liver diseases, such as nonalcoholic steatohepatitis (NASH), at The International Liver Congress - The Annual Meeting of the European Association for the Study of the Liver (EASL). The data demonstrate that ARO-HSD is the first investigational therapeutic to achieve robust reductions in messenger RNA (mRNA) and protein levels of hepatic HSD17B13, leading to reductions in alanine aminotransferase (ALT), a liver enzyme typically elevated in liver diseases including NASH.

Javier San Martin, M.D., chief medical officer at Arrowhead, said: "Genetic studies have recently shown that HSD17B13 is a compelling target for multiple forms of liver disease. It is exciting to present clinical data at EASL demonstrating that ARO-HSD is the first investigational medicine using any therapeutic modality to achieve inhibition of HSD17B13 in patients. It is also highly encouraging to see ALT levels drop significantly following just two doses of ARO-HSD. These data and the strong genetic evidence of HSD17B13 as a potential therapeutic target provide us with increased confidence as we consider the design of potential late-stage clinical studies for ARO-HSD."

Pharmacodynamics and Efficacy

All five patients with suspected NASH showed a strong pharmacodynamic effect as measured by liver biopsy at Day 71. HSD17B13 mRNA was reduced by a mean of 84%, with a range of 62-96%. HSD17B13 protein was reduced by 83% or greater. Two patients had a protein decrease of 92% and 97%, while the other three patients' Day 71 measurements were reduced to below the lower limit of quantitation.

Mean ALT reduction from baseline was 46%, with all patients showing reductions ranging from 26-53%. ARO-HSD is the first investigational RNAi therapeutic to demonstrate robust inhibition of hepatic HSD17B13 mRNA and protein expression with associated reductions in ALT.

Safety and Tolerability

ARO-HSD was well tolerated without any identified safety signals in healthy volunteers given a single dose of ARO-HSD at 25mg, 50mg, 100mg or 200 mg and in the 5 patients with suspected NASH given a single 100 mg dose of ARO-HSD on Days 1 and 29. Adverse events were similar between subjects receiving ARO-HSD or placebo. Two instances of mild injection site bruising and mild injection site erythema were observed in ARO-HSD treated subjects. There were no ARO-HSD associated grade 3 or 4 laboratory abnormalities (NCI-CTCAE v5.0), no drug related serious or severe adverse events, and there were no drug discontinuations.

AROHSD1001 (NCT04202354) is a Phase 1/2 single and multiple dose-escalating study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamic effects of ARO-HSD in up to 74 normal healthy volunteers and patients with NASH or suspected NASH. Additional exploratory objectives include the assessment of various measures of drug activity using liver biopsy.

Presentation Details

Title: **ARO-HSD reduces hepatic HSD17B13 mRNA expression and protein levels in patients with suspected NASH**
Authors: Edward Gane, *et al.*
Type: Late-Breaking Poster
Date and Time: June 23, 2021 at 8:00 CEST

A copy of the presentation materials may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website. The abstract was also selected for inclusion in The International Liver Congress 2021 Official Scientific Press Conference: NAFLD/NASH on June 25, 2021.

HSD17B13 is a member of the hydroxysteroid dehydrogenase family involved in the metabolism of hormones, fatty acids, and bile acids. Published human genetic data indicate that a loss of function mutation in HSD17B13 provides strong protection against alcoholic hepatitis, cirrhosis, and NASH, with approximately 30-50% risk reduction compared to non-carriers.[1]

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. Any statements contained in this release except for historical information may be deemed to be forward-looking statements. Without limiting the generality of the foregoing, words such as "may," "will," "expect," "believe," "anticipate," "intend," "plan," "project," "could," "estimate," or

“continue” are intended to identify such forward-looking statements. In addition, any statements that refer to projections of our future financial performance, trends in our business, expectations for our product pipeline, prospects or benefits of our collaborations with other companies, or other characterizations of future events or circumstances are forward-looking statements. 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 numerous factors and uncertainties, including the impact of the ongoing COVID-19 pandemic on our business, 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, the enforcement of our intellectual property rights, and the other risks and uncertainties described in our most recent Annual Report on Form 10-K, subsequent Quarterly Reports on Form 10-Q and other documents filed with the Securities and Exchange Commission from time to time. We assume no obligation to update or revise forward-looking statements to reflect new events or circumstances.

Source: Arrowhead Pharmaceuticals, Inc.

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[1] The New England Journal of Medicine. 2018, 1096-1106

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