Arrowhead Announces Improvement in Fibrosis after ARO-AAT Treatment in Patients with Alpha-1 Liver Disease

April 28, 2021

PASADENA, Calif.--(BUSINESS WIRE)--Apr. 28, 2021-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today announced positive interim 48-week liver biopsy results from the AROAAT2002 study, an open-label Phase 2 clinical study of ARO-AAT, the company's second generation investigational RNA interference (RNAi) therapeutic being co-developed with Takeda Pharmaceutical Company Limited ("Takeda") as a treatment for the rare genetic liver disease associated with alpha-1 antitrypsin deficiency (AATD). The results demonstrate that ARO-AAT treatment led to a consistent and substantial reduction in intra-hepatic mutant AAT protein (Z-AAT), both Z-AAT monomer and Z-AAT polymer; a consistent decrease in histological globule burden; improvements in fibrosis; and, improvements in other relevant biomarkers of liver health. Arrowhead intends to present additional interim AROAAT2002 data at an upcoming medical congress, pending abstract acceptance.

After 48 weeks of treatment with investigational ARO-AAT in cohort 2 (n=5) of the AROAAT2002 study, the following results were observed:

- Four of the five patients achieved a 1 or greater stage improvement in Metavir fibrosis stage, with no worsening of fibrosis in the fifth patient
- All five patients demonstrated reductions in histological globule assessment scores
- Total intra-hepatic Z-AAT decreased by 77-97%

After only 24 weeks of treatment with investigational ARO-AAT in cohort 1 (n=4) of the AROAAT2002 study, the following results were observed:

- Two of the four patients achieved a 1 or greater stage improvement in Metavir fibrosis stage, with no worsening of fibrosis in the other two patients
    - The two patients who improved fibrosis stages during treatment were both deemed cirrhotic (F4) when the study began
- All four patients demonstrated reductions in histological globule assessment scores
- As previously reported, total intra-hepatic Z-AAT decreased by 72-95%

Javier San Martin, M.D., chief medical officer at Arrowhead, said: "The results from treatment with investigational ARO-AAT in the Phase 2 AROAAT2002 open-label study continue to impress us. We believe the pharmacodynamic effect in alpha-1 patients is clear and consistent. The results from 24 and 48 weeks of treatment also indicate that when production of the Z-AAT protein is inhibited, the liver has the ability to clear the accumulated mutant protein and begin the fibrosis regression process earlier and more efficiently than we anticipated, even in patients with severe liver disease. We look forward to sharing more details about these exciting results at an upcoming medical congress. We also intend to use these and other results to inform further interactions with regulatory authorities to pursue opportunities for potential accelerated approval pathways, if appropriate. Our collaboration with Takeda on the ARO-AAT program has been highly productive, and we continue to see them as the ideal partner as the program advances towards patients in need of new therapies for alpha-1 liver disease."

In October 2020, Arrowhead and Takeda 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 United States 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 received an upfront payment of $300 million and is eligible to receive potential development, regulatory and commercial milestones of up to $740 million.

AROAAT2002 (NCT03946449) is a pilot open-label, multi-dose, Phase 2 study to assess the response to ARO-AAT in 16 patients with AATD associated liver disease and baseline liver fibrosis. All eligible participants receive 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, 12 months, 18 months, and 24 months of treatment with ARO-AAT.

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 businesses, 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 continuing impact of the COVID-19 pandemic, 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.

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