



Arrowhead Pharmaceuticals Receives Breakthrough Therapy Designation from U.S. FDA for ARO-AAT for the Treatment of Alpha-1 Antitrypsin Deficiency Associated Liver Disease

July 29, 2021

- Full enrollment reached in Phase 2 SEQUOIA study of ARO-AAT

PASADENA, Calif.--(BUSINESS WIRE)--Jul. 29, 2021-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced that it was granted Breakthrough Therapy designation (BTD) by the U.S. Food and Drug Administration (FDA) for ARO-AAT, also known as TAK-999, 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). Investigational therapy ARO-AAT was also previously granted Orphan Drug designation and Fast Track designation from the FDA, and Orphan designation from the European Commission.

Javier San Martin, M.D., chief medical officer at Arrowhead, said: "Patients with AATD associated liver disease currently have no available treatment options other than a liver transplant. Being granted Breakthrough Therapy designation from the FDA is an important milestone for the investigational ARO-AAT program. Arrowhead and our collaborators at Takeda share a commitment to patients with AATD. We intend to utilize the benefits that BTD provides, including enhanced access to and guidance from senior management and experienced review staff at the FDA, to expedite the development of ARO-AAT. We hope to get this important investigational medicine to patients rapidly.

Dr. San Martin continued: "I am also pleased to announce that the ARO-AAT Phase 2 SEQUOIA study has recently reached full enrollment of 40 patients. The interim results we recently presented at the 2021 European Association for the Study of the Liver (EASL) International Liver Congress from the AROAAT2002 Phase 2 open label study were highly encouraging. We believe these interim results suggest that investigational ARO-AAT consistently reduced the production of the toxic mutant Z-AAT protein, which has been identified as the cause of progressive liver disease in patients with AATD. Further, these reductions over 6 and 12 months led to multiple important signals associated with healing of liver disease in patients with fibrosis due to AATD."

BTD is a process designed to expedite the development and review of drugs that are intended to treat a serious life-threatening disease or condition and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. A drug that receives BTD is eligible for all Fast Track designation features, intensive FDA guidance on an efficient drug development program, and organizational commitment involving senior managers at the FDA.¹

About Alpha-1 Antitrypsin-Associated Liver Disease

Alpha-1 Antitrypsin-Associated Deficiency (AATD) is a rare genetic disorder associated with liver disease in children and adults and pulmonary disease in adults. AATD is estimated to affect 1 per 3,000-5,000 people in the United States and 1 per 2,500 in Europe. The protein AAT is primarily synthesized and secreted by hepatocytes. Its function is to inhibit enzymes that can break down normal connective tissue. The most common disease variant, the Z mutant, has a single amino acid substitution that results in improper folding of the protein. The mutant protein cannot be effectively secreted and accumulates in globules inside the hepatocytes. This triggers continuous hepatocyte injury, leading to fibrosis, cirrhosis, and increased risk of hepatocellular carcinoma.

Individuals with the homozygous PiZZ genotype have severe deficiency of functional AAT leading to pulmonary disease and liver disease. Lung disease is frequently treated with AAT augmentation therapy. However, augmentation therapy does nothing to treat liver disease, and there is no specific therapy for hepatic manifestations. There is a significant unmet need as liver transplant, with its attendant morbidity and mortality, is currently the only effective therapeutic option.

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](https://twitter.com/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," "hope," "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 or product candidates, including anticipated regulatory submissions and clinical program results, 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, decisions of regulatory authorities and the timing thereof, 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.

¹ <https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/breakthrough-therapy>

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