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Arrowhead Receives Orphan Drug Designation for ARC-AAT

PASADENA, Calif.--(BUSINESS WIRE)-- Arrowhead Research Corporation (NASDAQ: ARWR), a biopharmaceutical company developing targeted RNAi therapeutics, today announced the United States Food and Drug Administration (FDA) has granted ARC-AAT orphan drug designation. ARC-AAT is Arrowhead's RNAi-based therapeutic candidate being investigated for the treatment of liver disease associated with Alpha-1 Antitrypsin Deficiency (AATD), a rare genetic disease that severely damages the liver and lungs of affected children and adults. Arrowhead is currently conducting part B of a Phase 1 study of ARC-AAT in patients with PiZZ genotype AATD.

"Receiving orphan drug designation is an important milestone in the development of ARC-AAT, which we think is a very promising program aimed at providing a better option for patients with liver disease associated with alpha-1 antitrypsin deficiency," said Bruce D. Given, M.D., Arrowhead's Chief Operating Officer. "The Orphan Drug Act provides important incentives for sponsors to develop drugs that treat rare diseases and we look forward to more engagement with the FDA as the development of ARC-AAT progresses."

The ongoing Phase 1 trial of ARC-AAT is a multi-center, randomized, placebo-controlled, double-blind, single dose-escalation first-in-human study to evaluate the safety, tolerability and pharmacokinetics of ARC-AAT and the effect on circulating AAT levels. The study has been enrolling in dose cohorts of six participants each, with participants randomized at a ratio of 2:1 (active:placebo) to receive a single intravenous injection of either ARC-AAT or placebo (normal saline). The study consists of two parts; Part A in healthy volunteers, which has been completed, and Part B to be conducted in patients with PiZZ genotype AATD. The study evaluates participants for 28 days following dosing, with additional follow-up if needed every 2 weeks until AAT levels return to baseline.

The FDA Office of Orphan Products Development (OOPD) mission is to advance the evaluation and development of products that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions. In fulfilling that task, OOPD evaluates scientific and clinical data submissions from sponsors to identify and designate products as promising for rare diseases and to further advance scientific development of such promising medical products. Orphan drug designation provides incentives for sponsors to develop products for rare diseases. These incentives include increased engagement with FDA on drug development activities, exemption from all future product-specific regulatory fees, the opportunity to apply for R&D funding, tax credits, an increased chance of priority review, and 7 years of orphan exclusivity at time of New Drug Application (NDA) approval.

About Alpha-1 Antitrypsin Deficiency (AATD)

AATD is an autosomal recessive genetic disorder associated with liver disease in children and adults and pulmonary disease in adults. Alpha-1 antitrypsin is a circulating glycoprotein protease inhibitor of the serpin family encoded by the AAT gene and primarily synthesized in the liver. The physiologic function is inhibition of neutrophil proteases to protect healthy tissues during inflammation and prevent tissue damage. The Z mutant is the most common disease variant and has a single amino acid substitution that results in improper protein folding causing severe impairment of secretion from hepatocytes. This lack of secretion leads to accumulation of mutant Z-AAT polymers, which form globules in the hepatocyte endoplasmic reticulum. This triggers continuous hepatocyte injury, leading to fibrosis, cirrhosis, and increased risk of hepatocellular carcinoma.

In clinical practice, approximately 96-98% of AATD-related disease is due to the homozygous PiZZ genotype. PiZZ individuals have severe deficiency of functional AAT leading to pulmonary disease and hepatocyte injury 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 is currently the only available treatment for severe liver manifestations.

The mean estimated prevalence of AATD in the U.S. is 1 per 3000-5000, or approximately 100,000 patients. AATD is also an important cause of pediatric liver disease with an estimated prevalence in children of approximately 20,000 patients, and 50-80% likely to manifest liver disease during childhood. It is an orphan disease that appears to be frequently misdiagnosed or undiagnosed. European prevalence is estimated to be 1 per 2500.

About ARC-AAT

Arrowhead's ARC-AAT is being investigated for the treatment of liver disease associated with Alpha-1 Antitrypsin Deficiency (AATD), a rare genetic disease that severely damages the liver and lungs of affected individuals. ARC-AAT employs a novel unlocked nucleobase analog (UNA) containing RNAi trigger molecule designed for systemic delivery using the Dynamic Polyconjugate delivery system. ARC-AAT is highly effective at knocking down the Alpha-1 antitrypsin (AAT) gene transcript and reducing the hepatic production of the mutant AAT (Z-AAT) protein. Reduction of liver production of the inflammatory Z-AAT protein, which is likely a cause of progressive liver disease in AATD patients, is important as it is expected to halt the progression of liver disease and potentially allow fibrotic tissue repair. The Company is conducting a single dose Phase 1 clinical study, with part A in healthy volunteers and part B in AATD patients.

About Arrowhead Research Corporation

Arrowhead Research Corporation is a biopharmaceutical company developing targeted RNAi therapeutics. The company is leveraging its proprietary Dynamic Polyconjugate delivery platform to develop targeted drugs based on the RNA interference mechanism that efficiently silences disease-causing genes. Arrowhead's pipeline includes ARC-520 for chronic hepatitis B virus and ARC-AAT for liver disease associated with Alpha-1 antitrypsin deficiency.

For more information please visit http://www.arrowheadresearch.com, or follow us on Twitter @ArrowRes. To be added to the Company's email list and receive news directly, please visit http://ir.arrowheadresearch.com/alerts.cfm.

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