Arrowhead Pharmaceuticals Receives Fast Track Designation for ARO-AAT for Treatment of Alpha-1 Liver Disease

June 27, 2019

PASADENA, Calif.--(BUSINESS WIRE)--Jun. 27, 2019-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today announced that the U.S. Food and Drug Administration (FDA) has granted Fast Track designation to 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 deficiency (AATD). Arrowhead is in final preparations to initiate SEQUOIA (AROAAT2001), a potentially pivotal Phase 2/3 clinical study in the U.S. and Europe, and AROAAT2002, a Phase 2 open-label clinical study in Europe.

"With no currently approved agents to treat AATD-associated liver disease, alpha-1 patients and their physicians have an urgent need for new therapeutic options," said Bruce Given, M.D., Arrowhead's chief operating officer and head of R&D. "We view this FDA Fast Track designation as continued support that ARO-AAT has the potential to address this unmet need. Importantly, Fast Track designation provides a number of important advantages that could expedite the development and review of ARO-AAT."

Fast Track is a process designed to facilitate the development and expedite the review of drugs to treat serious conditions and fill an unmet medical need. The purpose is to get important new drugs to the patient earlier.

A drug that receives fast track designation is eligible for some or all of the following:

- More frequent meetings with FDA to discuss the drug's development plan and ensure collection of appropriate data needed to support drug approval
- More frequent written communication from FDA about such things as the design of the proposed clinical trials and use of biomarkers
- Eligibility for accelerated approval and priority review, if relevant criteria are met
- Rolling Review, enabling a drug company to submit completed sections of its New Drug Application (NDA) for review by FDA, rather than waiting until every section of the NDA is completed before the entire application can be reviewed. NDA review usually does not begin until the drug company has submitted the entire application to the FDA.[1]

SEQUOIA (NCT03945292) is a placebo-controlled, adaptive design Phase 2/3 study to evaluate the safety, efficacy, and tolerability of ARO-AAT administered subcutaneously to 120 patients with AATD-associated liver disease. Doses will be administered on day 1, 29, and approximately every 12 weeks thereafter. The four-arm placebo-controlled Part A component of the study will feed seamlessly into a two-arm placebo-controlled Part B component. The primary objective for Part A is to select a single dose level for use in Part B of the study based on a combined evaluation of safety and pharmacodynamic dose response in each Part A cohort using change from baseline in soluble liver mutant AAT (Z-AAT), insoluble liver Z-AAT, and serum AAT levels as pharmacodynamic metrics. The primary objective for Part B is to evaluate efficacy, as assessed by the proportion of ARO-AAT treated patients relative to placebo achieving a 2-point improvement in a histologic grading scale of AATD-associated liver disease, and no worsening of liver fibrosis on end of study biopsy.

AROAAT2002 (NCT03946449) is a pilot open-label, multi-dose Phase 2 study to assess changes in a histologic grading scale in response to ARO-AAT administration in up to 12 patients with AATD-associated liver disease. Doses will be administered on day 1, 29, and approximately every 12 weeks thereafter. The histologic grading score will be assessed at weeks 24 and 72 for cohort 1 and weeks 48 and 96 for cohort 2. Multiple secondary and exploratory objectives will also be assessed throughout the study.

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.

Source: Arrowhead Pharmaceuticals, Inc.

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[1] https://www.fda.gov/patients/fast-track-breakthrough-therapy-accelerated-approval-priority-review/fast-track (accessed June 25, 2019)

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