Arrowhead Pharmaceuticals Files for Regulatory Clearance to Begin Phase 1/2a Study of ARO-ENaC for Treatment of Cystic Fibrosis

April 10, 2020

PASADENA, Calif.--(BUSINESS WIRE)--Apr. 10, 2020-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today announced that it has filed an application for clearance to begin a Phase 1/2a clinical trial of ARO-ENaC, the company's investigational RNA interference (RNAi) therapeutic being developed as a treatment for patients with cystic fibrosis (CF), which is a rare disease caused by genetic mutations that lead to progressive deterioration in lung function due to poor clearance of mucus and associated recurrent infections. ARO-ENaC utilizes Arrowhead's proprietary Targeted RNAi Molecule (TRiM ™) platform and is the company's first inhaled RNAi candidate to target pulmonary epithelium.

Chris Anzalone, Ph.D., president and chief executive officer of Arrowhead, said: "ARO-ENaC is Arrowhead's second investigational RNAi therapeutic utilizing the TRiM ™ platform to target tissues outside of the liver and the first to target a disease of the lungs. This CTA filing is the culmination of years of work by Arrowhead scientists to optimize our TRiM ™ based lung targeting program. We have always believed that for RNAi to reach its full potential, it needs to reach disease targets throughout the body. Arrowhead is leading the RNAi field towards that goal, which holds the promise of helping a vast number of patients and addressing many diseases that currently do not have adequate treatment options."

Pending clearance, Arrowhead intends to proceed with AROENaC1001, a Phase 1/2a dose-escalating study to evaluate the safety, tolerability, and pharmacokinetic effects of ARO-ENaC in normal healthy volunteers and to evaluate the safety, tolerability, and efficacy in patients with CF. Exploratory objectives in patients with CF include assessing the effects of ARO-ENaC on changes in lung clearance index (LCI) and evaluating changes in forced expiratory volume (FEV1)

Javier San Martin, M.D., chief medical officer at Arrowhead, said: "The epithelial sodium channel, ENaC, has been a target of great interest due to its potential to help many CF patients. In animal models, ARO-ENaC reduced ENaC activity in the lung, but avoided silencing renal ENaC expression, which has historically been a key safety limitation for prior investigational small molecule ENaC inhibitors. ARO-ENaC has the potential to be a genotype-agnostic therapy, which may prove useful in combination with existing or new CFTR-targeted therapies. In addition, our preclinical studies have indicated that ARO-ENaC has an extended duration of action that enables once every 3-4 weeks or even less frequent administration, which may minimize treatment burden for patients with CF. We are excited to begin, pending regulatory clearance, the AROENaC1001 clinical study, which is designed to assess safety, tolerability, and pharmacokinetics and potentially provide an accelerated assessment of efficacy in patients with CF."

The application for approval of the clinical trial is being submitted to a local Ethics Committee and to the New Zealand Medicines and Medical Devices Safety Authority for review by the Standing Committee on Therapeutic Trials.

ARO-ENaC is designed to reduce activity of the epithelial sodium channel alpha subunit (αENaC) in the airways of the lung. In patients with CF, CFTR dysfunction causes increased ENaC activity which contributes to airway dehydration and reduced mucociliary transport. This predisposes patients to persistent lung infections, structural damage, and progressive loss of pulmonary function. ENaC has been extensively explored as a potential therapeutic target for CF, but the development of inhaled small molecule ENaC inhibitors has been limited by on-target renal toxicity and short duration of action in the lung.

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.

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