Arrowhead Pharmaceuticals Hosts Key Opinion Leader Webinar on ARO-ENaC for Treatment of Cystic Fibrosis

July 28, 2020

PASADENA, Calif.--(BUSINESS WIRE)--Jul. 28, 2020-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) is hosting a key opinion leader webinar today at 12:00 PM EDT on ARO-ENaC, the company's investigational RNA interference (RNAi) therapeutic being developed as a treatment for patients with cystic fibrosis (CF).

The webinar features a presentation by Marcus Mall, M.D., professor and director of the Department of Pediatric Pulmonology and Immunology at The Charité University Medical Center Berlin, who will discuss the current treatment landscape and unmet medical need in treating patients with CF. Arrowhead management is providing a review of the ARO-ENaC program, which utilizes Arrowhead's proprietary Targeted RNAi Molecule (TRiM™) platform and is the company's first inhaled RNAi candidate to target pulmonary epithelium. The live webinar and replay may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website.

Key points discussed on the webinar include the following:

Marcus Mall, M.D., professor and director of the Department of Pediatric Pulmonology and Immunology at The Charité University Medical Center Berlin

- The epithelial sodium channel (ENaC) plays an important role in the pathophysiology of CF lung disease and represents a promising alternative target to improve airway surface hydration and mucus clearance in patients, independent of their CFTR genotype
- A substantial number of CF patients (without F508del allele) cannot be treated with current CFTR modulators and could benefit from ENaC inhibition
- Partial rescue of CFTR with current CFTR modulators does not prevent progression of CF lung disease, resulting in an unmet medical need for further improvement of targeted CF therapy
- ENaC inhibition has potential to act synergistically with CFTR modulators by improving the driving force for chloride/fluid secretion mediated by mutant CFTR rescued by CFTR modulators
- ENaC inhibition has potential as a novel therapeutic approach to improve mucus clearance and provide clinical benefits to patients with other muco-obstructive lung diseases, including COPD

Erik Bush, Ph.D., vice president, biology, Arrowhead Pharmaceuticals

- ENaC is a well-validated therapeutic target for cystic fibrosis and muco-obstructive lung disease
- ARO-ENaC overcomes critical limitations of small molecule inhibitors
- ARO-ENaC inhalation silences ENaC expression selectively in the lung, doubling mucociliary clearance for weeks post-dose and preserving clearance in a sheep disease model of mucostasis with no evidence of systemic activity (e.g. electrolyte imbalance)
- Promising results observed in various preclinical toxicology studies

Javier San Martin, M.D., chief medical officer, Arrowhead Pharmaceuticals

- AROENaC1001, a Phase 1/2 study in up to 24 normal healthy volunteers (NHVs) and up to 30 CF patients, is expected to begin dosing in August 2020
- Potential Phase 1/2 readout in the first half of 2021 may include safety in NHVs and patients, and an assessment of lung function in patients measured by forced expiratory volume (FEV1) and lung clearance index (LCI)
- There is a significant and growing population of patients without adequate response to current CF treatment
- Arrowhead is exploring potential accelerated regulatory pathways for patients with the highest unmet need, including Class I patients and other patient subsets with insufficient response to standard of care

CF is a rare disease caused by genetic mutations in the CFTR gene that lead to progressive deterioration in lung function due to poor clearance of mucus and associated recurrent infections. ARO-ENaC is designed to reduce activity of the epithelial sodium channel alpha subunit 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.

Marcus Mall, M.D., is professor and director of the Department of Pediatric Pulmonology and Immunology at The Charité University Medical Center Berlin. Before this appointment, he was head of the Division of Pediatric Pulmonology & Allergy and the Cystic Fibrosis Center at the Department of Pediatrics, University Hospital Heidelberg, Germany, and from 2011 to 2018, director of the Department of Translational Pulmonology at the Heidelberg University Medical School, Heidelberg and member of the Board of Directors of the German Center for Lung Research (DZL). He is an

active member of several professional societies, including the European Cystic Fibrosis Society (ECFS), the European Respiratory Society (ERS) and the American Thoracic Society (ATS). He serves on journal editorial boards and on the Board of the ECFS. Dr. Mall qualified in Medicine at the University of Freiburg, Freiburg, Germany, and received his clinical training at the Universities of Freiburg and Heidelberg, and his postdoctoral training at the University of North Carolina at Chapel Hill, NC, USA, where he was appointed assistant professor of Medicine. In 2005, he received a grant from the European Commission to establish a Marie Curie Excellence Team for CF research at the University of Heidelberg, and in 2009 he was awarded the prestigious Heisenberg Professorship by the German Research Foundation. He is board certified in Pediatrics, Pediatric Pulmonology, Allergology and Infectious Diseases. Dr. Mall's research is focused on the molecular and cellular pathogenesis of CF and other chronic airway diseases, and the development of novel diagnostic approaches and therapeutic strategies. His research has been funded by the German Research Foundation (DFG), the German Ministry for Education and Research (BMBF), the European Commission, and others, and he has received several research awards. During his postdoctoral research, Dr. Mall developed a mouse with airway-specific overexpression of the epithelial sodium channel (βENaC), the first animal model with CF-like lung disease. His current research focus is on interdisciplinary translational research projects, integrating basic research with cohort studies and early phase clinical trials, to improve our understanding of CF lung disease and the translation of research results into the clinic.

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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