Arrowhead Pharmaceuticals Presents New Preclinical Data on ARO-ENaC for Treatment of Cystic Fibrosis

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PASADENA, Calif.--(BUSINESS WIRE)--May 21, 2018-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced the presentation of new preclinical data on ARO-ENaC, formerly referred to as ARO-Lung1, for the treatment of cystic fibrosis (CF), at the American Thoracic Society (ATS) 2018 International Conference in San Diego, CA. ARO-ENaC is the first product candidate to leverage the Targeted RNAi Molecule (TRiM™) platform targeting the pulmonary epithelium to address diseases of the lung.

ARO-ENaC is an inhaled RNA interference (RNAi) therapeutic targeting the epithelial sodium channel alpha subunit (αENaC) for the treatment of CF, a rare disease caused by a genetic mutation that leads to mucus buildup in the lungs and pancreas. CF patients can have difficulty breathing and experience frequent and persistent lung infections. Increased ENaC activity contributes to drying mucus in the airway and a reduced ability of the lung to clear toxins and infectious agents. Inheritance of poorly functioning ENaC genes by CF patients leads to milder lung disease.

Researchers have been interested in developing therapeutics that decrease ENaC activity in CF patients. However, the development of inhaled small molecule inhibitors has been limited by their short duration of action and unwanted effects resulting from ENaC inhibition in the kidney. ARO-ENaC is designed specifically to address those deficiencies by selectively reducing ENaC in the lung, while sparing the kidney, with a long duration of effect.

Christopher Anzalone, Ph.D., president and chief executive officer at Arrowhead, said, “The Targeted RNAi Molecule, or TRiM™, platform has several important advantages over the prior generation and competing technologies, including the ability to target tissues and diseases outside of the liver. ENaC is a genetically and biologically validated target for cystic fibrosis with a profile that we believe is well-suited for an RNAi-based intervention. We view ARO-ENaC as an important proof of concept for future TRiM™ enabled candidates targeting additional pulmonary diseases.”

A poster titled, “Targeting αENaC with an epithelial RNAi trigger delivery platform for the treatment of cystic fibrosis,” was presented by Erik Bush, Ph.D., Arrowhead’s director of extra-hepatic targeting. Dr. Bush’s presentation contained new preclinical data on ARO-ENaC and advancements being made with the TRiM™ platform. The data presented included the following:

- Integrin αvβ6 receptor ligands improve endocytosis of RNAi triggers in cultured epithelial cells
- Conjugates employing targeting ligands to the integrin αvβ6 receptor improve functional delivery of an αENaC RNAi trigger to the pulmonary epithelium after inhalation, producing deeper and more consistent reduction of whole lung αENaC mRNA at lower doses
- Loss of airway epithelial αENaC protein expression is observed at exposures that produce approximately 50% reduction in whole lung αENaC mRNA, with remaining protein expressed in alveolar epithelium
- Reduction of lung αENaC mRNA expression is durable, maintaining greater than the target level of 50% knockdown at 3 weeks post-dose and requiring 6-7 weeks for recovery to baseline expression
- Aerosol inhalation improves delivery efficiency approximately tenfold over intratracheal administration
- Conjugates were well-tolerated with no observed changes in renal αENaC mRNA expression
- The ability of the TRiM™ platform to facilitate functional delivery of RNAi triggers to the lung suggests that additional therapeutic targets in the pulmonary epithelium could be considered, particularly those that are currently inaccessible to traditional small molecule or antibody approaches

A copy of presentation materials may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website.

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 future success of our scientific studies, our ability to successfully develop 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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