Arrowhead Pharmaceuticals Hosts R&D Day on Emerging Pipeline of Pulmonary Targeted RNAi Therapeutics

May 26, 2022

PASADENA, Calif.--(BUSINESS WIRE)--May 26, 2022-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) is hosting a pulmonary research & development (R&D) Day today in New York City to discuss its emerging pipeline of pulmonary targeted RNA interference (RNAi) therapeutic candidates that leverage its proprietary Targeted RNAi Molecule (TRIM™) platform. The event will feature presentations by Arrowhead's management team and key opinion leaders, Mario Castro, M.D., MPH (University of Kansas Medical Center) and Matthias Salathe, M.D. (University of Kansas Medical Center), who will discuss the current treatment landscape and unmet medical need in treating patients with muco-obstructive and inflammatory pulmonary diseases.

Presentations will begin at 10:00 a.m. ET. A live and archived webcast of the event may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website.

Arrowhead will describe the development of investigational candidates:

- ARO-MUC5AC, designed to reduce expression of mucin 5AC (MUC5AC) as a potential treatment for various muco-obstructive pulmonary diseases
- ARO-RAGE, designed to reduce expression of the receptor for advanced glycation end products (RAGE) as a potential treatment for various obstructive inflammatory pulmonary diseases
- ARO-MMP7, Arrowhead's newest and previously undisclosed candidate designed to the reduce expression of matrix metalloproteinase 7 (MMP7) as a potential treatment for idiopathic pulmonary fibrosis (IPF)

The company will also discuss learnings from its first pulmonary clinical candidate, ARO-ENaC, that led to enhanced candidate and platform designs that have the potential to offer improved potency, duration, and the flexibility of subcutaneous as well as inhaled delivery.

"Today we're discussing ARO-MUC5AC, ARO-RAGE, and ARO-MMP7, three of our pulmonary candidates. These are each potentially important new investigational medicines that seek treat muco-obstructive and inflammatory lung diseases and IPF in fundamentally new ways," said Chris Anzalone, Ph.D., president and chief executive officer of Arrowhead. "The pulmonary targeted TRiM™ platform has come a long way since our first clinical candidate, ARO-ENaC. We now have improved siRNA triggers with longer pharmacodynamic duration allowing less frequent dose administration and a lower cumulative exposure in planned tox studies, thus less likely to overload lung clearance mechanisms. This gives us increased confidence as we move forward with upcoming clinical studies and additional toxicology studies."

Select R&D Day Highlights

ARO-RAGE

ARO-RAGE is an investigational medicine that aims to be a better anti-inflammatory therapy with broader anti-inflammatory effects than current biologics and with a more convenient inhaled mode of administration. Preclinical studies have yielded highly positive results. Single inhaled doses of ARO-RAGE in rats and primates led to reductions of greater than 90% in lung RAGE mRNA and in serum sRAGE protein, a circulating biomarker for RAGE target engagement in the lung. Pharmacodynamic response appears to be highly durable enabling bimonthly or quarterly dosing. In a rat model of allergic asthma, silencing RAGE in the lung effectively reduced inflammatory cell recruitment and cytokines, supporting the rationale for targeting RAGE in inflammatory lung disease. Subcutaneous administration also achieved deep and sustained reduction in RAGE expression, expanding the flexibility of the TRiM™ platform.

ARO-MUC5AC

ARO-MUC5AC is the first investigational medicine to directly silence pathologic MUC5AC expression and potentially address muco-obstructive disease, characterized by mucus hypersecretion, in a fundamentally different way than current therapies. Preclinical results have shown deep silencing of up to 70-90% of induced MUC5AC expression in mice and primates. In a sheep model of allergic asthma, ARO-MUC5AC administration effectively preserved airway function.

ARO-MMP7

ARO-MMP7 is Arrowhead's previously undisclosed investigational medicine being developed as a potential treatment for IPF. MMP7 plays multiple roles in IPF pathogenesis, including promoting inflammation and aberrant epithelial repair and fibrosis. Silencing MMP7 expression in a rat IPF model reduced inflammatory cell infiltration, limited lung fibrosis, and preserved pulmonary function. Additional data on this program will be presented at the European Respiratory Society (ERS) International Congress being held September 4-6, 2022.

Non-clinical Toxicology

Arrowhead's first clinical candidate, ARO-ENaC, using the lung targeted TRiM™ platform was voluntarily paused in 2021 based on non-clinical findings showing adverse local lung effects seen in chronic rat (6-month) and primate (9-month) GLP toxicology studies. The company believes that the mechanism underlying ARO-ENaC chronic toxicology findings are consistent with lung macrophage overload, which has been widely studied for over 40 years and extensively described in the literature. Arrowhead believes that a lower cumulative dose in future chronic toxicology studies

decreases the risk of adverse findings. For example, the planned 6-month rat ARO-MUC5AC and ARO-RAGE dose levels and dose intervals yield a cumulative dose well below the threshold where adverse findings were seen in the ARO-ENaC 6-month rat 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. Any statements contained in this release except for historical information may be deemed to be forward-looking statements. Without limiting the generality of the foregoing, words such as "may," "will," "expect," "believe," "anticipate," "hope," "intend," "plan," "project," "could," "estimate," or "continue" are intended to identify such forward-looking statements. In addition, any statements that refer to projections of our future financial performance, trends in our business, expectations for our product pipeline or product candidates, including anticipated regulatory submissions and clinical program results, prospects or benefits of our collaborations with other companies, or other characterizations of future events or circumstances are forward-looking statements. 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 numerous factors and uncertainties, including the impact of the ongoing COVID-19 pandemic on our business, the safety and efficacy of our product candidates, decisions of regulatory authorities and the timing thereof, 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, the enforcement of our intellectual property rights, and the other risks and uncertainties described in our most recent Annual Report on Form 10-K, subsequent Quarterly Reports on Form 10-Q and other documents filed with the Securities and Exchange Commission from time to time. We assume no obligation to update or revise forward-looking statements to reflect new events or circumstances.

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