Arrowhead Presents Data on Pulmonary Pipeline at ERS 2023

September 11, 2023

- Arrowhead Expands the Reach of RNAi Therapies to Address Diseases in the Lung

- Late-Breaking Clinical Data for ARO-RAGE for Treatment of Asthma Demonstrate Deep and Durable Gene Silencing

- Promising Preclinical Data Across Multiple Gene Targets Suggest Potentially Broad Applications for Arrowhead's TRiM™ Platform

PASADENA, Calif.--(BUSINESS WIRE)--Sep. 11, 2023-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today announced data on its pipeline of pulmonary targeted RNA interference (RNAi) therapeutic candidates, including clinical results for ARO-RAGE, being presented at the European Respiratory Society (ERS) International Congress 2023 in Milan, Italy. In an ongoing Phase 1/2 clinical trial, ARO-RAGE, Arrowhead's investigational RNAi therapeutic for the treatment of inflammatory lung diseases, achieved mean target gene knockdown of up to 90% with a maximum of 95% after a single inhaled administration.

Interim results from the healthy volunteer portion of the ARORAGE-1001 Phase 1/2 clinical trial show that ARO-RAGE reduced soluble RAGE (sRAGE) concentration in bronchoalveolar lavage fluid (BALF) and serum in a dose-dependent manner. Reduction of serum sRAGE was similar in healthy volunteers and in patients with asthma at the 44 mg dose level. Additional dose cohorts are ongoing. Based on interim blinded safety results from the ongoing study, ARO-RAGE has been well-tolerated to date in healthy volunteers and asthma patients.

"Today we announced additional data on multiple programs from our emerging pipeline of first-in-class pulmonary targeted RNAi therapeutic candidates at the European Respiratory Society International Congress. Clinical results from the ARO-RAGE Phase 1/2 study are highly encouraging and demonstrate a significant level of target gene knockdown with a duration of effect that may enable a long dosing interval possibly up to once every two months," said Javier San Martin, M.D., chief medical officer at Arrowhead. "In addition, the preclinical data presented at ERS suggest that the TRiM™ platform can achieve compelling results across multiple additional gene targets in the lung, including MUC5AC, MMP7, and our newest program against thymic stromal lymphopoietin (TSLP), a clinically well validated target."

Arrowhead Abstracts at ERS 2023

A Clinical-Stage Inhaled RNAi Therapeutic for Pulmonary Inflammation Mediates Durable RAGE Silencing in Nonhuman Primates
Poster Session 146, Sept. 10, 2023, 12:30-14:00 CEST

A Lung-Targeted RNAi Therapeutics Delivery Platform Compatible with Subcutaneous Administration Mediates Pulmonary RAGE Silencing in Rodents and Nonhuman Primates
Poster Session 146, Sept. 10, 2023, 12:30-14:00 CEST

Silencing TSLP Expression with a Lung-targeted RNAi Molecule Suppresses Pulmonary Allergic Inflammation
Poster Session 146, Sept. 10, 2023, 12:30-14:00 CEST

A First-in-human Study of ARO-RAGE, an RNAi Therapy Designed to Silence Pulmonary RAGE Expression
Late Breaking Abstract, Sept. 11, 2023, 11:00-12:15 CEST

A Clinical-stage RNAi Therapeutic Candidate for IPF Mediates Durable MMP7 Silencing in Nonhuman Primates and Human Lung Tissue
Poster Session 383, Sept. 12, 2023, 8:00-9:30 CEST

Presentation slides and posters may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website.

About Pulmonary TRiM ™Platform

Arrowhead's pulmonary Targeted RNAi Molecule (TRiM™) delivery platform facilitates selective delivery of therapeutic small interfering RNAs (siRNAs) to the lung epithelium via an integrin $\alpha_V\beta_6$ targeting moiety, mediating durable gene silencing upon inhalation. The pulmonary TRiM™ delivery platform is also compatible with subcutaneous administration and is capable of effectively silencing gene expression in the lung in rodents and non-human primates. While inhaled dosing offers a convenient local delivery solution, systemic administration would offer additional flexibility for some therapeutic applications. Subcutaneous administration in humans is currently being evaluated in a clinical trial.

About ARO-RAGE

ARO-RAGE is an investigational RNAi therapeutic targeting the receptor for advanced glycation end-products (RAGE) as a potential treatment for inflammatory lung diseases. RAGE is implicated as an upstream mediator of Type-2 and non-Type-2 inflammatory cascades and is involved in the pathogenesis of asthma and numerous inflammatory diseases. Silencing RAGE expression via RNAi is designed to reduce the amount of RAGE protein expressed on pulmonary epithelial cells. Reduced RAGE expression in the pulmonary epithelium may result in reduction of RAGE-dependent inflammatory pathways, leading to decreased exacerbation frequency and improved airflow in patients with asthma.

About the ARORAGE-1001 Phase 1/2 Study

ARORAGE-1001 (NCT05276570) is a Phase 1/2a, randomized, double-blinded, placebo-controlled study in normal healthy volunteers (NHV), Part 1, and in patients with inflammatory lung disease, Part 2. The single ascending dose portion of the study includes 5 sequentially enrolled NHV cohorts with escalating single-dose levels. The multiple ascending dose portion of the study includes 5 NHV cohorts, 3 asthma patient cohorts, and 1 cystic

fibrosis patient cohort. The objectives of the study include the assessment of safety and tolerability, pharmacokinetics, and pharmacodynamics of ARO-RAGE in NHVs and patients with inflammatory lung disease.

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," "continue," "target," "forecast" or "continue" or the negative of these words or other variations thereof or comparable terminology 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 forward-looking statements include, but are not limited to, statements about the initiation, timing, progress and results of our preclinical studies and clinical trials, and our research and development programs; our expectations regarding the potential benefits of the partnership, licensing and/or collaboration arrangements and other strategic arrangements and transactions we have entered into or may enter into in the future; our beliefs and expectations regarding milestone, royalty or other payments that could be due to or from third parties under existing agreements; and our estimates regarding future revenues, research and development expenses, capital requirements and payments to third parties. 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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