Arrowhead Pharmaceuticals Presents Preclinical Data on New RNAi-Based Obesity Program ARO-INHBE

June 24, 2024

PASADENA, Calif.--(BUSINESS WIRE)--Jun. 24, 2024-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced that preclinical data on ARO-INHBE, an investigational RNAi-based medicine for the treatment of obesity and metabolic diseases, were presented at the American Diabetes Association (ADA) 84th Scientific Sessions, which were held June 21-24, in Orlando, FL, and virtually.

The preclinical results demonstrate that ARO-INHBE substantially silenced hepatic expression of the INHBE gene, which has been identified through large genetic studies as a promising target for next generation therapies to address obesity and metabolic diseases. Further, Arrowhead's preclinical research suggests that INHBE knockdown may potentially lead to a suppression in body weight gain, loss of fat mass, and preservation of lean mass. Arrowhead plans to file for regulatory clearance in late 2024 to begin clinical studies of ARO-INHBE.

"There has been a great deal of progress with new agents to treat obesity and metabolic diseases, but significant loss of lean mass and adverse gastrointestinal events at higher dose levels have necessitated the identification of new therapeutic strategies with novel mechanisms of action," said James Hamilton, M.D., chief of discovery and translational medicine at Arrowhead. "ARO-INHBE directly targets hepatic expression of the INHBE gene. Prior genetic studies have associated loss of function mutations in the INHBE gene with reduced levels of abdominal fat and an improved metabolic profile. Our preclinical data presented at ADA suggest that INHBE reduction with siRNA is a promising new approach to address obesity and metabolic diseases and strongly support advancing ARO-INHBE into clinical trials."

In pharmacological studies in obese and diabetic mouse models, INHBE siRNA administration resulted in multiple promising findings, including the following:

- 95% reduction in INHBE mRNA expression
- 19% suppression of body weight compared to saline controls
- 26% loss of fat mass
- Preservation of lean mass

In addition, co-treatment of tirzepatide with INHBE siRNA allowed for the use of a lower tirzepatide dose without compromising its therapeutic effect. These encouraging results suggest that ARO-INHBE has the potential to be a novel therapeutic for metabolic disease.

Details about the ADA presentations are listed below.

American Diabetes Association 84th Scientific Sessions – June 21-24, 2024

Title: **Liver-specific silencing of INHBE with ARO-INHBE, an siRNA therapeutic, for metabolic diseases**
Date: June 24, 2024
Type: Poster

Arrowhead will discuss its growing pipeline of cardiometabolic medicines at two events as part of its 2024 Summer Series of R&D Webinars. The company's lead clinical programs, including the recently completed PALISADE Phase 3 study in familial chylomicronemia with plozasiran, will be highlighted on June 25, 2024, and two preclinical programs addressing obesity and metabolic diseases, including ARO-INHBE, will be discussed on August 15, 2024.

The ADA presentation and the Summer Series of R&D Webinars may be accessed on the Events and Presentations page in 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 X (formerly Twitter) at @ArrowheadPharma or on LinkedIn. 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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