Arrowhead Pharmaceuticals Initiates Phase 1/2a Study of ARO-ALK7 for the Treatment of Obesity

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- ARO-ALK7 is the first investigational RNAi therapeutic to enter clinical studies that targets a gene expressed in adipose tissue
- Study initiation highlights Arrowhead's leadership in the delivery of siRNA to multiple tissues and cell types throughout the body utilizing its proprietary and differentiated Targeted RNAi Molecule (TRiM™) platform
- In preclinical studies, ARO-ALK7 silenced Activin receptor-like kinase 7 (ALK7) expression in adipose tissue, which led to reduced body weight and fat mass with preservation of lean muscle

PASADENA, Calif.--(BUSINESS WIRE)--Jun. 2, 2025-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced that it has dosed the first subjects in a Phase 1/2a clinical trial of ARO-ALK7, the company's investigational RNA interference (RNAi) therapeutic being developed as a potential treatment for obesity. ARO-ALK7 is designed to intervene in a known pathway that signals the body to store fat in adipose tissue. The study initiates in otherwise healthy obese subjects using single and multiple escalating doses of ARO-ALK7 monotherapy and is expected to progress rapidly to investigate combinations of ARO-ALK7 with tirzepatide in obese patients with and without type 2 diabetes.

"Arrowhead's two clinical stage RNAi-based obesity programs, ARO-ALK7 and ARO-INHBE, intervene in a known pathway that signals the body to store fat in adipose tissue. Both programs have strong genetic validation and promising results in preclinical studies, which suggest that silencing the respective genes may lead to reduced body weight and potentially preserve lean muscle mass resulting in improved body composition," said James Hamilton, M.D., Chief Medical Officer and Head of R&D. "This ongoing Phase 1/2a clinical study will evaluate single and multiple ascending doses of ARO-ALK7 as monotherapy in otherwise healthy obese volunteers as well as multiple doses in obese patients with or without type 2 diabetes in combination with incretin therapy."

About ARO-ALK7

ARO-ALK7 is designed to silence adipocyte expression of the ACVR1C gene to reduce production of Activin receptor-like kinase 7 (ALK7), which acts as a receptor in a pathway that regulates energy homeostasis in adipose tissue. In large genetic datasets, reduced ACVR1C expression has been associated with healthier adipose distribution and reduced risk of obesity-related metabolic complications. In preclinical animal studies, ALK7 silencing in adipose tissue led to reduced body weight and fat mass with preservation of lean muscle. Treatment with investigational ARO-ALK7 has the potential to reduce visceral adiposity and improve lipid and glycemic parameters.

About the AROALK7-1001 Phase 1/2 Study

AROALK7-1001 (NCT06937203) is a Phase 1/2a first-in-human dose-escalating study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of ARO-ALK7 in up to 90 adult volunteers with obesity. Part 1 of the study is designed to assess single and multiple doses of ARO-ALK7 monotherapy, and Part 2 of the study is designed to assess ARO-ALK7 in combination with tirzepatide, a subcutaneously administered GLP-1/GIP receptor co-agonist that has been approved in the United States and the European Union for management type 2 diabetes mellitus since 2022 and weight management since 2023/2024 respectively.

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, LinkedIn, Facebook, and Instagram. 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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