Arrowhead Pharmaceuticals Presents Interim Clinical Data on ARO-CFB for the Treatment of Complement Mediated Diseases

December 11, 2024

- Interim data from Phase 1/2a study demonstrate near complete inhibition in hemolytic activity and functional activity of alternative complement pathway

PASADENA, Calif.--(BUSINESS WIRE)--Dec. 11, 2024-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced interim results from a Phase 1/2a clinical study of ARO-CFB, the company's investigational RNA interference (RNAi) therapeutic targeting complement factor B being developed as a potential treatment for complement mediated diseases. The data were presented today, December 11, 2024, at the 8th Complement-Based Drug Development Summit being held in Boston.

"Dysregulated activation of the complement system can lead to progression of certain renal diseases, either by playing a directly pathogenic role, or by amplifying or exacerbating the inflammatory and damaging impact of non-complement disease triggers. In a Phase 1/2a clinical study, ARO-CFB treatment in healthy volunteers achieved deep and durable reductions in the liver production of complement factor B (CFB), which is involved in alternative complement pathway activation and associated with pathogenesis of diseases involving complement activation. Circulating levels of CFB protein were reduced by a mean of up to 90% to date, with additional data from higher doses levels pending, and a duration of response greater than 3 months," said James Hamilton, M.D., MBA, Chief of Discovery and Translational Medicine at Arrowhead. "ARO-CFB also demonstrated dramatic reductions in measures of alternative complement pathway activation, with mean reductions at or approaching 100% in AH50 and Wieslab AP at multiple dose levels. These interim results in healthy volunteers give us confidence in the potential of ARO-CFB as we seek to complete Part 1 of the study over the coming months, and subsequently look ahead to Part 2 of the study in patients with immunoglobulin A nephropathy, which is the most common glomerular disease worldwide."

Select ARO-CFB Results

In the ongoing AROCFB-1001 study, ARO-CFB achieved the following key results in normal healthy volunteers as of the interim data cutoff - 15 November 2024:

- ARO-CFB led to dose dependent reductions in circulating CFB protein by up to 90% with greater than 3 months duration
  - 90% mean reduction achieved after a single dose of 400 mg
  - 90% mean reduction achieved after two doses of 100 mg
- Single and multiple doses of ARO-CFB led to near complete inhibition of alternative pathway activity based on Wieslab AP
  - 100% mean reduction achieved by week 4 after a single dose at both 200 mg and 400 mg doses
  - 92% and 100% mean reductions were achieved after two doses at 100 mg and 200 mg, respectively
- Single and multiple doses of ARO-CFB led to near complete inhibition of alternative pathway hemolytic activity, measured by AH50

Safety and Tolerability Results

ARO-CFB has been generally well-tolerated to date with safety data supportive of further clinical development. There have been no treatment emergent adverse events (TEAE) leading to study or study drug discontinuation with most TEAEs being mild in severity.

About ARO-CFB

ARO-CFB is designed to reduce hepatic expression of complement factor B (CFB), which plays an important regulatory role in amplifying complement alternative pathway activation and has been identified as a promising therapeutic target. ARO-CFB is being developed as a potential treatment for complement mediated kidney diseases such as immunoglobulin A nephropathy (IgAN), which is the most common glomerular disease worldwide and carries a high lifetime risk of progression to end-stage renal disease. Additionally, ARO-CFB may have clinical applications in non-renal diseases involving complement activation.

About the AROCFB-1001 Phase 1/2 Study

AROCFB-1001 (NCT06209177) is an ongoing Phase 1/2a dose-escalating study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of ARO-CFB in up to 66 normal healthy volunteers (NHV) and patients with complement mediated kidney disease. In Part 1 of the study, NHVs will receive either one or two doses of ARO-CFB or placebo. In Part 2 of the study, adult patients with IgAN will receive 3 open-label doses of ARO-CFB. The study is designed to assess safety and tolerability and key pharmacodynamic parameters, including the change and percent change from baseline over time in serum CFB, and alternative complement pathway activity via AH50 and Wieslab AP.

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.

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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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