Arrowhead Pharmaceuticals Announces Topline Results from Part 2 of Phase 1/2 Study of ARO-C3 in Patients with IgA Nephropathy

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- ARO-C3 achieved deep and sustained reductions in alternative pathway complement activity and proteinuria

- Mean sustained reductions in C3 of ≥87%, AH50 of ≥76%, Wieslab AP of ≥89% through week 24

- Mean reduction in spot urine protein-to-creatinine ratio (UPCR) of 41% by week 24

PASADENA, Calif.--(BUSINESS WIRE)--Mar. 10, 2025-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today announced topline results from Part 2 of a Phase 1/2 clinical study of ARO-C3, the company's investigational RNA interference (RNAi) therapeutic designed to reduce liver production of complement component 3 (C3) as a potential therapy for various complement mediated diseases. The company plans to present additional results at a medical meeting in 2025.

Select Phase 1/2 Study Results

- Patients with IgA nephropathy (IgAN) (n=14) received subcutaneous doses of ARO-C3 (400 mg) on Days 1, 29, and 113 and were followed through Day 169
- Pharmacodynamic effects
  - Maximum mean reduction in C3 of 89% and mean sustained reduction of greater than 87% from baseline through week 24
  - Maximum mean reduction in serum AH50 (alternative pathway hemolytic assay) of 85% and mean sustained reduction greater than 76% from baseline through week 24
  - Maximum mean reduction in Wieslab AP (alternative pathway) of 100% and mean sustained reduction greater than 89% from baseline through week 24
  - Duration of effect supportive of once every three month or less frequent subcutaneous dosing in later stage studies
- Effects on proteinuria
  - Mean reduction in spot UPCR of 41% and maximum individual reduction of 89% from baseline by week 24
- Safety and Tolerability
  - ARO-C3 was generally well-tolerated in patients with IgAN
  - No serious or severe treatment emergent adverse events (TEAE) and no TEAEs that led to study or study drug discontinuation
  - The only TEAEs reported in more than 1 subject were headache, cough, and nasopharyngitis
  - No infections with encapsulated organisms

"ARO-C3 has shown potent and consistent results in normal healthy volunteers and now in patients with IgA nephropathy, including up to 89% mean reduction of complement component 3 (C3), which led to reductions of 85% in AH50 and 100% in Wieslab AP, both markers of alternative pathway complement activity. Such durable and near complete inhibition of the alternative complement pathway achieved with infrequent subcutaneous dose administration may be advantageous," said James Hamilton, M.D., MBA, Chief Medical Officer and Head of R&D. "In addition, proteinuria, a surrogate marker of renal injury in IgAN, improved with a 41% reduction in spot UPCR. We look forward to sharing more data from the Phase 1/2 clinical study of ARO-C3 at an upcoming medical meeting in 2025."

About ARO-C3

ARO-C3 is designed to reduce hepatocyte production of complement component 3 (C3) as a potential treatment for various complement mediated renal diseases. Dysregulated activity of the complement system can play a primary pathogenic role and can contribute to tissue injury and progression of disease. By silencing C3, investigational ARO-C3 has the potential to treat complement-mediated renal diseases by modulating activation of the complement cascade.

About the AROC3-1001 Phase 1/2a Study

AROC3-1001 (NCT05083364) is a Phase 1/2a first-in-human dose-escalating study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics in adult healthy volunteers (HVs) and in adult patients with complement-mediated renal disease. In Part 1 of the study, HVs receive either one or two doses of ARO-C3 or placebo. In Part 2 of the study, adult patients with C3 Glomerulopathy (C3G) and IgA Nephropathy (IgAN) receive 3 open-label doses of ARO-C3.

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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