Arrowhead Announces Positive Interim Results from Phase 1b Study of ARO-HIF2 for Treatment of Clear Cell Renal Cell Carcinoma

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PASADENA, Calif.--(BUSINESS WIRE)--Jul. 6, 2021-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today announced positive interim results from the first two cohorts of AROHIF21001, a Phase 1b dose-finding clinical study of ARO-HIF2, the company's investigational RNA interference (RNAi) therapeutic being developed as a treatment for patients with clear cell renal cell carcinoma (ccRCC). ARO-HIF2 is the first tumor-targeted investigational medicine to utilize Arrowhead's proprietary Targeted RNAi Molecule (TRiM™) platform in a clinical trial. Arrowhead is currently enrolling the third planned patient cohort of AROHIF21001 and the company intends to present additional data at an appropriate medical congress.

James Hamilton, M.D., MBA, senior vice president of discovery and translational medicine at Arrowhead, said: "The AROHIF21001 Phase 1b study is designed to evaluate safety as well as preliminary pharmacodynamics and efficacy in an advanced ccRCC patient population. We believe that in the first two dose cohorts investigational ARO-HIF2 is showing clear signs of meaningful target engagement and some potentially early signs of efficacy in at least one patient. This is an encouraging start for the study. Specifically, in seventeen patients treated with investigational ARO-HIF2, nine had tumor biopsy material that could be evaluated. Seven of these nine tumor samples demonstrated reductions in HIF2α protein, as measured by immunohistochemistry H-score. The mean of these reductions was -48% with a range from -9% to -82%. In addition, one patient achieved a partial response with tumor shrinkage of approximately 65% and four additional patients in cohort 2 remain on study drug with stable disease. Tumors typically have a high level of heterogeneity and the patients in AROHIF21001 have advanced ccRCC and have failed multiple lines of treatment including checkpoint inhibitors and anti-VEGF regimens, so these early results in a heavily pre-treated population are encouraging for investigational ARO-HIF2 and our tumor-targeted platform broadly. ARO-HIF2 has been generally well-tolerated and we look forward to continued dose escalation."

Key Results from AROHIF21001

- 17 patients have been enrolled to receive intravenous injections of 225 mg weekly (cohort 1, n=7) or 525 mg weekly (cohort 2, n=10)
- The study has progressed to a dose of 1050 mg weekly (cohort 3), which is currently enrolling patients
- HIF2α protein H-score was assessed via immunohistochemistry
    - 9 of 17 patients had tumor samples that could be evaluated
    - 7 of 9 demonstrated reductions in HIF2α
        - Reductions ranged from -9% to -82% with a mean reduction of -48%
- Efficacy was assessed by Response Evaluation Criteria in Solid Tumors (RECIST)
    - In cohort 2, one subject had a partial response with approximately 65% tumor shrinkage and 5 had a best response of stable disease
    - 4 subjects in cohort 2 remain on drug with stable disease with treatment durations between 12 and 24 weeks
- To date, investigational ARO-HIF2 has been generally well tolerated at doses of up to 525 mg weekly
    - No cases of anemia related to drug have been reported

AROHIF21001 (NCT04169711) is a Phase 1b dose-finding clinical study in patients with advanced ccRCC to evaluate the safety of ARO-HIF2 and to determine the recommended Phase 2 dose. Secondary objectives include the assessment of pharmacokinetics and preliminary efficacy, based on Response Evaluation Criteria in Solid Tumors (RECIST). Exploratory objectives for AROHIF21001 are post-dose tumoral expression of HIF genes in response to treatment with ARO-HIF2, change in Karnofsky Performance Status (KPS), correlation of tumor response based on RECIST with tumor HIF2α gene expression and tumor integrin expression, correlation of integrin expression with changes in HIF gene expression, evaluation of serum biomarkers of ARO-HIF2 activity, correlation of RCC-related gene expression to ARO-HIF2 activity, and evaluation of plasma and urine metabolites.

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," "intend," "plan," "project," "could," "estimate," or "continue" 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 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, 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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