Arrowhead Presents New Clinical Data on ARO-HIF2 at ASCO GU 2022

February 17, 2022

PASADENA, Calif.--(BUSINESS WIRE)--Feb. 17, 2022-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) today announced positive interim results from 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). The data presented provide initial proof of target engagement based on reductions in hypoxia inducible factor-2 alpha (HIF2α) expression, as well as an acceptable safety profile in response to escalating doses of ARO-HIF2. The data are being presented by James Brugarolas, M.D., Ph.D, Professor at University of Texas Southwestern Medical Center and investigator in the study, in a poster presentation at the 2022 American Society of Clinical Oncology Genitourinary Cancers Symposium (ASCO GU), being held February 17-19, 2022, in San Francisco, CA and online.

Presentation Details:

Title: **Initial results from the phase 1 study of ARO-HIF2 to silence HIF2-alpha in patients with advanced ccRCC (AROHIF21001)**
Authors: James Brugarolas, et al.
Session: Poster Session C: Renal Cell Cancer; Adrenal, Penile, Urethral, and Testicular Cancers
Abstract Number: 339
Poster Number: F9

Key results from AROHIF21001 as of December 1, 2021 data cut:

Pharmacodynamics and Efficacy

- Tumoral expression of HIF2α protein was assessed via immunohistochemistry
  - Among patients with evaluable biopsy, 9/14 showed reductions in HIF2α protein
  - Responders in Cohort 1 (225 mg, n=3), Cohort 2 (525 mg, n=4), and Cohort 3 (1050 mg, n=2) achieved mean reductions of HIF2α protein of -45%, -57%, and -80%, respectively
- Tumoral expression of HIF2α messenger RNA (mRNA) was assessed by quantitative polymerase chain reaction (qPCR)
  - Among patients with evaluable biopsy, 9/9 showed reductions in HIF2α mRNA
  - Cohort 1, Cohort 2, and Cohort 3 achieved mean reductions of HIF2α mRNA of -38%, -28%, and -44%, respectively
- Efficacy was assessed by Response Evaluation Criteria in Solid Tumors (RECIST)
  - Disease control rate (complete response + partial response + stable disease) was 39% (10 of 26) across all cohorts
  - Objective response (complete response + partial response) was 8% (2 of 26), with one patient in Cohort 2 and one patient in Cohort 3 achieving a partial response

Safety

- ARO-HIF2 was generally well-tolerated in patients. Anemia and hypoxia, frequently reported on-target adverse events (AEs) with small molecule HIF2α inhibitors, were reported in 12% of patients
- Five serious AEs in 5 patients were reported by investigators as possibly drug related, including myocarditis (in a patient with a history of TKI induced cardiomyopathy), demyelinating neuropathy (in a patient with autoimmune sequelae due to checkpoint inhibitors), chronic inflammatory demyelinating polyradiculoneuropathy (in a patient with distant history of checkpoint inhibitor use), hypoxia (in a patient with a pulmonary infiltrate), and acute hypoxemic respiratory failure (in a patient with progressive lung metastatic disease)

A copy of the presentation materials with full data may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website.

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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