November 10, 2014

Arrowhead Presents Data on ARC-520 and ARC-AAT at AASLD The Liver Meeting® 2014

- ARC-520 shows statistically significant reduction in HBsAg through day 43 after a single injection ($p < 0.05$)

- Repeat dosing of ARC-AAT in primates shows reduction of approximately 90% of serum alpha 1 antitrypsin (AAT) with long duration of effect suggesting that monthly or less frequent dosing may be sufficient for sustained suppression of hepatic AAT production

- ARC-AAT abstract highlighted in the AASLD President's Press Conference as a promising new treatment

- Arrowhead will host an investor event and presentation to discuss results that will be webcast at 8:00 p.m. EST

PASADENA, Calif.--(BUSINESS WIRE)-- Arrowhead Research Corporation (NASDAQ: ARWR), a biopharmaceutical company developing targeted RNAi therapeutics, today announced that initial data from the ongoing Phase 2a study of ARC-520, its RNAi therapeutic candidate for the treatment of chronic hepatitis B (HBV) infection, was presented today in the late-breaking poster session at the 2014 American Association for the Study of Liver Diseases (AASLD) Liver Meeting in Boston. Arrowhead also delivered a plenary presentation with new preclinical efficacy data on ARC-AAT, its RNAi therapeutic candidate for the treatment of liver disease associated with Alpha-1 antitrypsin deficiency.

The Company will host an investor event and presentation to discuss these results that will be webcast tonight at 8:00 p.m. EST. Investors may access the webcast and presentation slides on the Events page of the Company's website at http://ir.arrowheadresearch.com/events.cfm. An audio only version of the live webcast may also be accessed by calling 844-825-4406 toll-free from the U.S., or 315-625-3230 for international callers, using conference ID 31449966. An archive of the call will be available for seven days and may be accessed by calling 855-859-2056 or 404-537-3406. Copies of the AASLD poster and plenary presentation will also be available to view on the Events page of the Company's website.

"We presented some important advancements today for both ARC-520 and ARC-AAT," said Christopher Anzalone, Ph.D., Arrowhead's President and Chief Executive Officer. "These programs and our expanding pipeline of RNAi therapeutics continue to generate exciting data that further validate the utility of the DPC delivery system. We have seen clear activity across multiple preclinical models and are now seeing activity in humans. We are still dose escalating in the ARC-520 Phase 2a, where dosing is complete in the 3 mg/kg cohort and screening has begun for 4 mg/kg. We believe that the initial data from the first two dose cohorts as well as safety data from the Phase 1 volunteer study are encouraging and support advancement of the program into multi-dose Phase 2b studies. We are currently preparing regulatory filings for the ARC-520 Phase 2b and the ARC-AAT Phase 1, both of which we expect to be filed this quarter. We intend to initiate those studies soon after receiving regulatory permission to begin."

ARC-520 Data

In a Late-Breaking Poster titled, **"Phase II, dose ranging study of ARC-520, a siRNA-based therapeutic, in patients with chronic hepatitis B virus infection,"** interim data on ARC-520 was presented by Man-Fung Yuen, M.D., Ph.D., Chair of Gastroenterology and Hepatology, and Li Shu Fan Medical Foundation Professor in Medicine, The University of Hong Kong, and a principal investigator for the study. The poster included up-to-date safety data on ARC-520 from this study, an ongoing Phase 2a multicenter, randomized, double-blind, placebo-controlled, dose-escalation study, as well as a recently completed Phase 1 normal volunteer study.

The nine dose group, Phase 1, normal volunteer trial was designed to characterize the safety profile of ARC-520 across a range of doses and evaluate pharmacokinetics. It was a single-center, randomized, double-blind, placebo-controlled, single dose-escalation, first-in-human study of ARC-520 administered intravenously to healthy adult volunteers for which partial data has been previously reported. All subjects received either placebo or ARC-520 in doses ranging from 0.01 mg/kg to 4.0 mg/kg. The study successfully enrolled all 54 subjects (36 received ARC-520, 18 placebo). The Phase 2a study has enrolled three dose cohorts including 24 patients, 18 receiving drug and 6 receiving placebo. Unblinded data is available for the first two cohorts. Cohort 3 data collection is ongoing and this cohort remains blinded. Full results for the first two dose cohorts at 1.0 mg/kg and 2.0 mg/kg and partial (blinded) safety results from the 3.0 mg/kg dose cohort were included in the poster.

In both studies, there have been no reports of serious AEs, no dose limiting toxicities, no discontinuations due to AEs, and a modest overall occurrence rate of AEs without a clear dose-related increase in frequency or severity. There has been a modest occurrence rate of non-clinically significant abnormal laboratory tests. There were no reported drug related or clinically significant differences for vital signs or ECGs between subjects receiving drug versus placebo. To date, ARC-520 when administered as a single dose up to 4.0 mg/kg to healthy volunteers and up to 3.0 mg/kg to patients with chronic HBV appears to be well tolerated.

Arrowhead also reported initial results for depth and duration of hepatitis B surface antigen (HBsAg) reduction in the Phase 2a study. In cohort 1 (1.0 mg/kg), the mean nadir of HBsAg was -39% (range -22 to -57) with a mean change on day 85 of -31% (range -14 to -39). In cohort 2 (2.0 mg/kg), the mean nadir of HBsAg was -51% (range -46 to -59) with a mean change on day 85 of -22% (range -7 to -40). For cohort 2, the percent reduction in HBsAg was statistically significant versus placebo ($p < 0.05$) for days 3 through 43 post-dose. For cohort 2, the mean day of HBsAg nadir was day 33 with a range of day 8 to day 57.

Arrowhead believes that this is the first time that a reduction in HBsAg mediated through RNA interference has been demonstrated in patients with chronic HBV infection. This study is ongoing with follow up continuing on Cohort 3 (3.0 mg/kg) and recruitment underway for a fourth cohort of patients at 4.0 mg/kg.

Preparations are underway to initiate a series of multi-dose Phase 2b studies of ARC-520, for which the Company plans to file with regulatory authorities in the fourth quarter of 2014. These studies are planned to have clinical sites in the US, Western Europe, Asia, and potentially other countries and/or regions. Several studies are currently contemplated, including ARC-520 in combination with entecavir or tenofovir as well as combination studies that add an immunostimulatory agent.

ARC-AAT Data

Arrowhead also presented data on ARC-AAT, its clinical candidate for the treatment of liver disease associated with Alpha-1 Antitrypsin Deficiency (AATD), a rare genetic disease that severely damages the liver and lungs of affected individuals. These patients synthesize a mutant form of AAT (Z-AAT) in the liver which is poorly secreted and accumulates, resulting in liver injury. The goal of treatment with ARC-AAT is to silence production of Z-AAT thereby preventing further accumulation of Z-AAT in the liver and potentially reversing pre-existing liver injury and fibrosis.

The presentation in the prestigious Plenary Session titled, "**A hepatocyte-targeted RNAi-based treatment for liver disease associated with alpha-1 antitrypsin deficiency**," was presented by Christine Wooddell, Ph.D., Group Leader, Arrowhead Research. AASLD President Dr. Adrian Di Bisceglie, MD, FACP also highlighted the presentation, along with just ten others, in the President's Press Conference as a program that holds great promise for patients.

In preclinical studies with PiZ mice, which are genetically modified to produce the mutant human AAT (Z-AAT), ARC-AAT induced a greater than 95 percent reduction in circulating AAT after a single dose with a long duration of effect. Area covered by Z-AAT globules and globule size within the liver were significantly reduced after a single dose of ARC-AAT at day 15 post-dose ($p < 0.005$) and day 29 post-dose ($p < 0.01$). Multi-dose studies in PiZ mice showed that ARC-AAT was effective at reducing and preventing Z-AAT aggregates in the liver. At week 13 of the study, after 4 biweekly doses, the ARC-AAT treated group show 99% less soluble (monomer) Z-AAT and 79% less insoluble (polymer) Z-AAT, normalized to a saline control group. Thus, injection of ARC-AAT in transgenic mice expressing human Z-AAT resulted in prevention and reduction of Z-AAT globules and, importantly, liver inflammation.

In primate studies, a 90% reduction of AAT in serum was observed after a single injection, which persisted for over ten weeks with greater than 80 percent knockdown observed at the six-week time point. Multi-dose studies in primates showed a sustained reduction of AAT with once every six weeks dosing, suggesting that once monthly or less frequent dosing may be sufficient to maintain approximately 80-90% knockdown in humans. The treated animals showed no changes in clinical chemistry (ALT, AST, BUN, Creatinine), indicating that ARC-AAT appeared to be well tolerated at these optimal therapeutic dose levels.

About ARC-520

Arrowhead's RNAi-based candidate ARC-520 is designed to treat chronic HBV infection by reducing the expression and release of new viral particles and key viral proteins. The goal is to achieve a functional cure, which is an immune clearant state characterized by hepatitis B s-antigen negative serum with or without sero-conversion. The siRNAs in ARC-520 intervene at the mRNA level, upstream of where nucleotide and nucleoside analogues act. In transient and transgenic mouse models of HBV infection, a single co-injection of Arrowhead's Dynamic Polyconjugate (DPC) delivery vehicle with cholesterol-conjugated siRNA targeting HBV sequences resulted in multi-log knockdown of HBV RNA, proteins and viral DNA with long duration of effect. Arrowhead has completed enrollment in a Phase 1 single ascending dose study in normal volunteers. The company is conducting a single dose Phase 2a study in chronic HBV patients, and expects to follow with multi-dose, multi-national Phase 2b studies. Approximately 350 million people worldwide are chronically infected with the hepatitis B virus. Chronic HBV infection can lead to cirrhosis of the liver and is responsible for 80% of primary liver cancers globally.

About ARC-AAT

Arrowhead has developed ARC-AAT for the treatment of liver disease associated with Alpha-1 Antitrypsin Deficiency (AATD), a rare genetic disease that severely damages the liver and lungs of affected individuals. ARC-AAT employs a novel unlocked nucleobase analog (UNA) containing RNAi trigger molecule designed for systemic delivery using the Dynamic Polyconjugate delivery system. ARC-AAT is highly effective at knocking down the Alpha-1 antitrypsin (AAT) gene transcript and reducing the hepatic production of the mutant AAT (Z-AAT) protein. Reduction of liver production of the inflammatory Z-AAT protein, which has been clearly defined as the cause of progressive liver disease in AATD patients, is important as it is expected to halt the progression of liver disease and potentially allow fibrotic tissue repair. The Company plans to file with regulatory authorities in the fourth quarter of 2014 and commence clinical studies shortly after receiving permission to begin.

About Arrowhead Research Corporation

Arrowhead Research Corporation is a biopharmaceutical company developing targeted RNAi therapeutics. The company is leveraging its proprietary Dynamic Polyconjugate delivery platform to develop targeted drugs based on the RNA interference mechanism that efficiently silences disease-causing genes. Arrowhead's pipeline includes ARC-520 for chronic hepatitis B virus, ARC-AAT for liver disease associated with Alpha-1 antitrypsin deficiency, and partner-based programs in obesity and oncology.

For more information please visit http://www.arrowheadresearch.com, or follow us on Twitter @ArrowRes. To be added to the Company's email list and receive news directly, please visit http://ir.arrowheadresearch.com/alerts.cfm.

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