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Arrowhead Reports Peak Reduction in HBsAg of Up to 99% (1.9 log) After a Single Dose with Hepatitis B Candidate ARC-520 in Treatment Naïve Cohort of Phase 2a Study

- Single-dose Reductions in HBeAg of up to 98% (1.7 log) also achieved

- Multi-dose studies in chimpanzees showed peak reduction in HBsAg of up to 99.8% (2.7 log)

- Company hosts an analyst and investor day today to discuss results

PASADENA, Calif.--(BUSINESS WIRE)-- Arrowhead Research Corporation (NASDAQ: ARWR), a biopharmaceutical company developing targeted RNAi therapeutics, is hosting an analyst day today in New York, with a presentation starting at 11:00 a.m. EDT to discuss top-line findings from the Heparc-2001 Phase 2a clinical study of ARC-520, its candidate for the treatment of chronic hepatitis B infection. Additionally, the company will discuss findings from a study of 9 chimpanzees that have been treated monthly with ARC-520 for between 6 and 11 months with a background therapy of nucleotide/nucleoside analog inhibitors (NUCs) tenofovir and/or entecavir.

Key findings:

Arrowhead's proprietary DPC™ platform can effectively and consistently knock down target genes in humans
HBV E-antigen positive (HBeAg-positive) patients on a background of chronic entecavir receiving a 4 mg/kg single-dose of ARC-520 showed a mean maximal 92% (1.2 log) reduction in circulating HBeAg and a best reduction of 98% (1.7 log). Similar mean maximal reductions were also demonstrated in HBV core-related antigen (HBcrAg) from both HBeAg-negative and -positive patients. ARC-520 is designed to silence all gene products expressed by HBV cccDNA, so this data suggests that it may be substantially disrupting additional viral functions.

ARC-520 achieves significant HBV s-Antigen (HBsAg) reductions in humans, particularly in treatment naïve, HBeAg-positive patients
In a cohort of NUC-naïve, HBeAg-positive patients, best peak HBsAg reduction has been 99% (1.9 log) and the mean maximum HBsAg reduction has been 1.05 log through 15 days post ARC-520 treatment. This open-label cohort is fully enrolled; data collection is ongoing and will be continued through Day 85 post ARC-520 treatment. These reductions are substantially higher than results from NUC treatment-experienced cohorts.

Arrowhead identifies a large target HBV population for ARC-520 and describes a new paradigm for the HBV lifecycle
Arrowhead's long-term chimp study and findings from the clinical study suggest that HBV cccDNA decreases during the HBV lifecycle, especially with the transition from HBeAg-positive to -negative. HBV DNA integrated into host DNA appears to maintain significant HBsAg production as cccDNA declines. This process is accelerated with NUC treatment. ARC-520 specifically targets cccDNA, and NUC-naïve HBeAg-positive patients are expected to be richest in cccDNA. It is estimated in the U.S. that 95% of people chronically infected with HBV are currently NUC-naïve and at least 50% of them are likely to be HBeAg-positive. While it is unknown what impact ARC-520's broad based effects on HBV biology will have on the sero-clearance process in any of the HBV subgroups, the effect on HBsAg in NUC-naïve HBeAg-positive patients makes this group especially attractive to study and a key focus for multi-dose studies going forward.

ARC-520 induces deep HBsAg reduction in chronically HBV infected chimps and 1 of 4 HBeAg-positive chimps demonstrated signs of immune reactivation during therapy
9 chimps were first suppressed with NUCs and then treated with 6 - 11 monthly doses of ARC-520. 4 HBeAg-positive chimps demonstrated 99% (2 log) mean peak reduction in HBsAg, and 1 of the 4 experienced signs of immune reactivation during therapy; 4 HBeAg-negative chimps demonstrated 81% (0.7 log) mean peak reduction in HBsAg; and 1 chimp transitioning from HBeAg-positive to HBeAg-negative demonstrated peak HBsAg reduction of 87% (0.9 log).

ARC-520 has been well tolerated
84 humans have received ARC-520 and to date no adverse events have been rated as serious or severe, no discontinuations have occurred due to an adverse event, and no laboratory results have indicated any end organ toxicity. Additionally, 9 chimps received 6-11 monthly doses of ARC-520 and no safety signals were detected in any chimp.

Arrowhead expands its HBV portfolio by nominating an additional clinical candidate that is complementary to ARC-520
ARC-520 will continue development including focus on the significant market of e-antigen positive treatment-naïve chronic HBV patients. ARC-521 is being developed to target cccDNA and also, integrated DNA, which appears to be a more significant producer of HBsAg in patients who have been treated with NUCs or who are e-antigen negative. In HBeAg-negative chimps predicted to have higher levels of integrated DNA, administration of the integrant-targeted siRNA in ARC-521 led to 99% (2 logs) of additional HBsAg reduction. The Company expects to file an IND or equivalent for ARC-521 by mid-2016.

Quotes:

Christopher Anzalone, Ph.D., president and CEO of Arrowhead, said, "These are exciting data that represent a significant leap forward for our DPC™ platform, ARC-520, and the HBV field. We have achieved the highest knockdown ever reported in humans with RNAi and a safety profile that continues to be excellent. We are optimistic that this will ultimately translate into powerful clinical outcomes for ARC-520 and follow-on candidates against multiple indications."

Robert Gish, M.D., clinical professor of medicine (consultant) at Stanford Hospital and Medical Center, said, "These animal and single-dose human studies with ARC-520 in chronic hepatitis B infected individuals provide compelling evidence about a multi-pronged antiviral effect that will accelerate new studies with multiple doses and combination therapy to move forward."

Robert Lanford, Ph.D., director at the Southwest National Primate Research Center, said, "I have been extremely impressed by the potency of ARC-520 and its ability to reduce multiple viral proteins. The results from the study in chimpanzees have revealed some important new insights about HBV biology and have introduced new ideas about effective ways to intervene in the HBV lifecycle."

A live and archived version of the webcast, including presentation slides, will be available on the events section of the Company's website at ir.arrowheadresearch.com/events.cfm. To access an audio only version of the live presentation, dial 855-215-6159 toll-free from the U.S. or 315-625-6887 for international callers and enter Conference ID 19541930.

About ARC-520

Arrowhead's RNAi-based candidate ARC-520 is being investigated in the treatment of chronic HBV infection. The small interfering RNAs (siRNAs) in ARC-520 intervene at the mRNA level, upstream of the reverse transcription process where current standard of care nucleotide and nucleoside analogues act. Arrowhead is investigating ARC-520 specifically, to determine if it can be used to achieve a functional cure, which is an immune clearant state characterized by hepatitis B s-antigen negative serum with or without sero-conversion. Arrowhead has completed a Phase 1 single ascending dose study in normal volunteers and the company is conducting single dose Phase 2a studies and multiple dose Phase 2b studies in chronic HBV patients. Approximately 350-400 million people worldwide are chronically infected with the hepatitis B virus, which can lead to cirrhosis of the liver and is responsible for 80% of primary liver cancers globally.

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, ARC-F12 for hereditary angioedema and thromboembolic diseases, and ARC-HIF2 for renal cell carcinoma.

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.

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. 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 various factors and uncertainties, including our ability to finance our operations, the future success of our scientific studies, our ability to successfully develop drug candidates, the timing for starting and completing clinical trials, rapid technological change in our markets, and the enforcement of our intellectual property rights. Arrowhead Research Corporation's most recent Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q discuss some of the important risk factors that may affect our business, results of operations and financial condition. We assume no obligation to

update or revise forward-looking statements to reflect new events or circumstances.

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