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Arrowhead Presents Data Showing Robust Sustained Anti-viral Effects with ARC-520 in Hepatitis B Infected Chimpanzees

PASADENA, Calif.--(BUSINESS WIRE)-- Arrowhead Research Corporation (NASDAQ: ARWR), a biopharmaceutical company developing targeted RNAi therapeutics, presents data at the AASLD Liver Meeting 2015® in an oral presentation and a poster showing that ARC-520, its drug candidate against chronic hepatitis B infection (HBV), leads to robust, sustained anti-viral effects in chimpanzees with chronic HBV. Arrowhead also describes an important new discovery that HBV DNA integrated into the host genome is likely an important source of HBV surface antigen (HBsAg) production, particularly in chimps that are negative for hepatitis B e-antigen (HBeAg). The company plans to present additional data from this study at the 2015 Hep Dart conference in December demonstrating that two of four HBeAg-positive chimps exhibited signs of immune reactivation, which is believed to be a necessary step toward achieving a functional cure of HBV.

"We believe that these data change current HBV biology dogma," said Bruce D. Given, M.D., Arrowhead's chief operating officer. "We have gained insights about the HBV life cycle during the chimpanzee study, and this has informed our clinical program for ARC-520. In addition, it has enabled us to expand our HBV portfolio to include ARC-521, our new drug candidate that may be highly active against HBsAg in patient populations with higher relative levels of integrated DNA."

ARC-520 led to a dramatic drop in circulating HBsAg, with the degree of HBsAg reduction correlating with HBeAg status. HBeAg-positive and -negative chimps demonstrated HBsAg reductions of 1.5 - 2.7 log (96.8% - 99.8%) and 0.5 - 0.9 log (68.4% - 87.4%), respectively, with an intermediate response in a chimp transitioning from HBeAg positive to negative. In addition, one chimp seroconverted for HBeAg during ARC-520 therapy and had a sustained virologic response with respect to HBeAg, HBV DNA, and HBsAg. This persisted off therapy and through at least 32 weeks after ARC-520 and NUC therapy was removed, which was the last time-point observed. A second chimp demonstrated effects consistent with immunologic reactivation.

In the study, Arrowhead found that the predominant form of liver HBV DNA differed in HBeAg-negative versus HBeAg-positive chimps. Most HBV DNA in HBeAg-positive chimps was cccDNA, while less than 5% of HBV DNA in HBeAg-negative chimps was cccDNA. In addition, Arrowhead found that the HBV RNA profiles in HBeAg-negative chimps were consistent with transcripts arising from integrated DNA. These data and others, strongly suggest that integrated DNA is likely an important source of HBsAg production in HBeAg-negative chimps.

Direct confirmatory data was obtained by treating HBeAg negative chimps with a siRNA designed to target transcripts originating from integrated HBV DNA. Up to an additional 2 logs (99%) of HBsAg knockdown was achieved, resulting in overall relative knockdown levels that are similar to those observed using ARC-520 in HBeAg-positive chimps. Arrowhead has incorporated one of these RNAi triggers and one targeting predominantly cccDNA derived transcripts into a new complementary drug candidate, ARC-521, that is planned to be in clinical trials in 2016.

The study presented at AASLD included 9 chimpanzees chronically infected with HBV. At the beginning of the study four were HBeAg-positive, four were HBeAg-negative, and one was in the process of transitioning from HBeAg-positive to HBeAg-negative. To reduce viral replication prior to treatment with ARC-520, chimps were treated for 8-24 weeks with entecavir (ETV) and in one case with ETV plus tenofovir (TDF). Following the NUC lead-in period, animals were administered ARC-520 intravenously at 4-week intervals (q4w). Dose levels were 2, 3, or 4 mg/kg ARC-520, along with maintenance doses of ETV or ETV and TDF. The response to NUCs during the lead-in period was similar to therapy in humans with deep decreases in serum HBV DNA but minimal effects on HBsAg levels.

Copies of presentation materials can be accessed by visiting the Events section of the company's website at http://ir.arrowheadresearch.com/events.cfm.

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 seroconversion. Arrowhead is conducting Phase 2b multiple dose and combination 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 and ARC-521 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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