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Arrowhead Presents Data Suggesting ARC-520 Induces Therapeutic Flare in Chronic Hepatitis B

Presentation at the Annual Meeting of the American Association for the Study of Liver Diseases (AASLD) demonstrates reduction of key HBV antigens and DNA, and evidence of immune reactivation in a chimpanzee with chronic HBV infection

PASADENA, Calif. — November 4, 2013 — Arrowhead Research Corporation (NASDAQ: ARWR), a biopharmaceutical company developing targeted RNAi therapeutics, today announced that it presented new data on ARC-520, its clinical candidate for the treatment of chronic hepatitis B virus, at the 2013 AASLD Annual Meeting. The data demonstrate that intravenous administration of two doses (2 mg/kg, 3 mg/kg) of ARC-520 in a chimpanzee chronically infected with HBV, resulted in substantial and sustained reductions in HBV DNA, HBeAg, and HBsAg, which did not return to baseline until study day 43, 43, and 71 respectively. In addition, an increase in serum alanine transaminase (ALT) occurred 4 weeks after the last dose, coincident with the nadir of circulating HBsAg. This is suggestive of a therapeutic immunological flare, which is thought to be part of a cascade that under chronic therapy may lead to HBsAg seroconversion and functional cure. Robert E. Lanford, Ph.D., of the Texas Biomedical Research Institute where the study was conducted, presented these data and the poster was selected as a Presidential Poster of Distinction indicating that it was in the top 10% of all abstracts selected for poster presentation.

“This study would have been important if ARC-520 just demonstrated safe and effective HBsAg reduction because this is thought to be a necessary step in achieving a functional cure,” said Dr. Lanford. “What is really exciting about these data, however, is that we appear to have seen immune de-repression, the next step toward HBsAg seroconversion and functional cure. The timing of the ALT rise and associated increases in key chemokine/cytokine mRNAs suggest that they were related to the therapy-induced reduction in circulating HBsAg and represented an immunological event.”

The study was a proof-of-concept antiviral efficacy trial for ARC-520, which is composed of 2 cholesterol-conjugated siRNAs and the hepatocyte-targeted membrane-lytic Dynamic Polyconjugate (DPC) delivery vehicle. It was conducted at the Texas Biomedical Research Institute in a single chimpanzee chronically infected with HBV since 1979 (chimpanzee 4x0139; genotype B; viral load ~$1.3x10^{10}$ GE/ml; HBsAg 824 µg/ml). Activity was monitored using serum levels of HBV DNA, HBeAg, and HBsAg. Safety was monitored using CBC, blood chemistries, and serum levels of 39 cytokines and chemokines. Liver histology, viral antigens, and host transcripts were monitored in the liver.

Arrowhead previously reported initial data through day 29 of this study. The animal was monitored at additional time points through day 85 to assess duration of effect for ARC-520 and other outcome measures. HBV DNA levels dropped by 17-fold by day 4, exhibited a 36-fold decline following the second dose, and returned to baseline by day 43. HBeAg levels declined by more than one log by day 4 and returned to baseline by day 43. HBsAg levels declined gradually reaching a 5.2-fold reduction on day 29 and did not return to baseline until day 71. HBsAg is a serum lipoprotein complex and has a significant half-life in circulation, thus declines for this marker were more gradual but also more sustained. An increase in ALT was observed near the HBsAg nadir.

“This is an important addition to our data set and a milestone for the development plan of ARC-520,” said Christopher Anzalone, Ph.D., Arrowhead’s President and CEO. “We successfully completed enrollment in a Phase 1 clinical study in healthy volunteers with initial data indicating that ARC-520 is generally safe and well tolerated in humans. We will be filing with Hong Kong regulatory authorities this quarter to enable a Phase 2a study in patients with chronic HBV infection.”

Arrowhead also recently presented a poster at the 2013 International Meeting on Molecular Biology of Hepatitis B Viruses. The data presented indicate that treatment with ARC-520 in combination with entecavir appears to be additive and possibly synergistic. These results support plans to initiate a Phase 2a study of ARC-520 in combination with entecavir, pending regulatory approval.

Copies of both poster presentations can be found on the Presentations and Events page of the Arrowhead website at www.arrowheadresearch.com/presentations.

About ARC-520

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. 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 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. In a chimpanzee chronically infected with HBV and high viremia and antigenemia, ARC-520 induced rapid and deep reductions in HBV DNA, e-antigen, and s-antigen. Arrowhead has completed enrollment in a phase 1 single ascending dose study in normal volunteers, which the company expects to follow with a phase 2a study in chronic HBV patients.

About Arrowhead Research Corporation

Arrowhead Research Corporation is a biopharmaceutical company developing targeted RNAi therapeutics. The company is leveraging its proprietary drug delivery technologies to develop targeted drugs based on the RNA interference mechanism that efficiently silence disease-causing genes. Arrowhead technologies also enable partners to create peptide-drug conjugates that specifically home to cell types of interest while sparing off-target tissues. Arrowhead's pipeline includes clinical programs in chronic hepatitis B virus and obesity and partner-based programs in 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 to receive news directly, please send an email to ir@arrowres.com

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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