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# Arrowhead Receives Regulatory Clearance to Begin Additional Phase 2b Studies of Hepatitis B Candidate ARC-520

PASADENA, Calif.--(BUSINESS WIRE)-- Arrowhead Research Corporation (NASDAQ: ARWR), a biopharmaceutical company developing targeted RNAi therapeutics, today announced that its Clinical Trial Application for ARC-520, its clinical candidate for chronic hepatitis B infection (HBV), has been approved by Germany's Federal Institute for Drugs and Medical Devices. The company now has regulatory clearance in Germany for two additional Phase 2b multiple-dose studies of ARC-520 to be conducted in parallel. Arrowhead awaits final IRB approval from the sites, which are expected shortly, and in addition, the company is engaged with regulatory authorities from Hong Kong and South Korea to open additional sites for these studies. Arrowhead will provide guidance in the future on timing for release of data from these studies.

"ARC-520 is leading the way in studying the use of RNAi drugs as new treatment options for chronic HBV. We are very pleased to receive regulatory clearance in Europe to conduct the parallel design Phase 2b multiple-dose studies that we proposed," said Bruce D. Given, M.D., Arrowhead's Chief Operating Officer. "We view these studies as the front end of a set of global multiple-dose studies designed to identify the right agents, doses, and regimens that can achieve functional cures. Based on multiple-dose data from our recently disclosed chimpanzee study and the long duration of activity ARC-520 has demonstrated in the single-dose Phase 2a study in patients, we are starting with doses of 1mg/kg and 2mg/kg in parallel. We have incorporated an interim analysis in both studies to get an early read on whether we may want to interrogate higher doses. ARC-520 continues to be well tolerated and we have not seen any signal suggesting that we are approaching a maximum tolerated dose through 4mg/kg, the highest dose studied in humans to date."

The studies titled Heparc-2002 and Heparc-2003 will enroll patients with chronic HBV infection that are e-antigen (HBeAg) negative and HBeAg positive, respectively. Each study is a multicenter, randomized, double-blind, placebo-controlled, multi-dose study intended to evaluate two dose levels in parallel of ARC-520 in combination with entecavir or tenofovir in patients with immune active chronic HBV infection. The 2002 and 2003 studies are planned to enroll up to 60 and 90 patients, respectively. In each study, patients will be randomized to receive four doses, once every 4 weeks, of either 1 mg/kg ARC-520, 2 mg/kg ARC-520, or placebo at a ratio of 1:1:1.

For each patient, the duration of the study is approximately 33 weeks, from screening to the Day 169 follow-up visit. For each study, a planning interim analysis will be performed when 54 patients have completed their Day 71 visit. This analysis will be used to plan future studies only and will not impact the enrollment or conduct of Heparc-2002 and -2003. Based on the interim results, the company will decide whether higher multiple-doses would be likely to lead to increased activity, in which case higher doses may be evaluated in one or more additional studies.

The primary objective of the 2002 and 2003 studies is to evaluate the depth of hepatitis B surface antigen (HBsAg) decline in response to multiple doses of ARC-520 compared to placebo as a measure of drug activity. Secondary objectives include the assessment of safety and tolerability and multi-dose pharmacokinetics of ARC-520 when co-administered with entecavir or tenofovir, in addition to other exploratory objectives.

**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 interferenc

mechanism that efficiently silences disease-causing genes. Arrowhead's pipeline includes ARC-520 for chronic hepatitis B virus and ARC-AAT for liver disease associated with Alpha-1 antitrypsin deficiency.

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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*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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