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Arrowhead Presents New Clinical Data Demonstrating a Sustained Host Response in Hepatitis B Patients Following RNAi Therapy

— Up to 5.0 log10 reduction in HBsAg observed; data presented at HEP DART 2017 —

PASADENA, Calif.--(BUSINESS WIRE)-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) presented new data from the company's Phase 2 clinical study in patients that received multiple doses of ARC-520, the company's prior generation RNAi-based clinical candidate against chronic hepatitis B infection (HBV). A maximum reduction from baseline in HBV surface antigen (HBsAg) of 5.0 log10 was achieved seven months following the administration of the last dose of ARC-520, with the lowest absolute level observed being just above the lower limit of HBsAg quantitation. These data, presented at the 22nd biennial HEP DART meeting held in Kona, Hawaii, from Dec. 3-7, indicate that multiple doses of an RNAi-based therapy may lead to a host response that is sustained after therapy is concluded.

Bruce D. Given, M.D., chief operating officer and head of R&D for Arrowhead Pharmaceuticals, said: "We believe that achieving a functional cure of chronic hepatitis B infection will require a sustained host response, which is likely to be immune mediated. In our Phase 2 study of ARC-520, multiple patients saw continued reductions in key HBV markers long after ARC-520 treatment ceased. These data represent the first clinical evidence that an RNAi-based approach can lead to the type of favorable sustained host response that we have always believed is possible. Achieving this result with ARC-520, which was not designed for activity against HBV s-antigen produced by integrated DNA, provides us with further confidence that our new RNAi-based compound, ARO-HBV, which is designed to silence the production of all HBV gene products, including transcripts derived from integrated DNA, has a good chance of being a backbone therapy for combinations intended to cure chronic HBV."

In an oral presentation titled, "Looking Back to Move Forward - Designing Next Gen RNAi for HBV," Dr. Given showed key evidence for the first time that 2 of 3 (66.7%) HBV e-antigen (HBeAg) positive patients and 2 of 5 (40%) HBeAg negative patients treated with an RNAi-based therapy achieved a sustained host response off therapy. This was characterized by continued reduction of multiple HBV viral markers, including HBsAg, and coinciding with an increase in circulation of liver enzyme alanine aminotransferase (ALT), indicative of host response. The new data from Heparc-2001, the company's Phase 2 open-label extension study of ARC-520 in combination with entecavir in 8 patients, follows patients over 7 months after the last ARC-520 dose was administered, which is the last time point currently available.

In the 4 patients that appeared to have a sustained host response, observed reductions in HBsAg were 5.0, 3.1, 2.4, and 0.6 log10 from baseline. In addition, these patients achieved absolute levels of HBsAg of 58, 2.6, 0.36, and 0.051 IU/ml. The lower limit of quantitation for this measurement of HBsAg is 0.05 IU/ml, below which would be deemed seroclearance. These patients also achieved reductions in HBV DNA to below the level of quantitation, and deep reductions in core-related antigen (HBcrAg), and HBeAg, with many at or below their respective lower limits of quantitation.

Dr. Given also presented select preclinical data on ARO-HBV, a new therapy for patients with chronic HBV that utilizes the company's next generation Targeted RNAi Molecule (TRiM™) platform. Notably, 3 doses of ARO-HBV in wild type pHBV mice led to reductions in HBV DNA of 3.44 log10 and both HBsAg and HBeAg dropped below the lower limit of quantitation (reductions of greater than 3.0 log10 and greater than 2.2 log10, respectively).

In addition, Arrowhead created a mutated pHBV mouse model that eliminates the HBx trigger site to simulate HBV patients with high levels of integrated HBV DNA relative to cccDNA. In this model, a single dose of ARO-HBV led to a reduction in HBsAg of 2.95 log10. The duration of effect was long, with a HBsAg reduction of approximately 2.0 log10 still observed 8 weeks after the dose.

ARO-HBV is designed to silence the production of all HBV gene products, including transcripts derived from integrated DNA, with the goal of getting to a level where patients' immune systems can reconstitute, leading to a sustained host response and ultimately a functional cure. Arrowhead's learnings from multiple clinical studies of prior generation compounds, ARC-520 and ARC-521, and the extensive non-clinical research completed in multiple species, including long-term treatment of chimpanzees, have guided the rapid development of ARO-HBV. The results presented with respect to ARC-520 are not necessarily predictive of ARO-HBV results.

GLP-toxicology studies are being conducted and Arrowhead is manufacturing the drug supply necessary to begin clinical studies of ARO-HBV. The company anticipates filing a Clinical Trial Application by the second quarter of 2018.

Slides from Dr. Given's presentation may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website.

About Arrowhead Pharmaceuticals

Arrowhead Pharmaceuticals develops medicines that treat intractable diseases by silencing the genes that cause them. Using a broad portfolio of RNA chemistries and efficient modes of delivery, Arrowhead therapies trigger the RNA interference mechanism to induce rapid, deep, and durable knockdown of target genes. RNA interference, or RNAi, is a mechanism present in living cells that inhibits the expression of a specific gene, thereby affecting the production of a specific protein. Arrowhead's RNAi-based therapeutics leverage this natural pathway of gene silencing.

For more information, please visit www.arrowheadpharma.com, or follow us on Twitter @ArrowheadPharma. To be added to the Company's email list and receive news directly, please visit http://ir.arrowheadpharma.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 the safety and efficacy of our product candidates, the duration and impact of regulatory delays in our clinical programs, 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. Our 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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