Arrowhead to Present Late-Breaking Clinical Data on ARO-AAT and ARO-HBV at AASLD Liver Meeting® 2018

October 11, 2018

PASADENA, Calif.--(BUSINESS WIRE)--Oct. 11, 2018-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) will make two late-breaking poster presentations at The Liver Meeting® 2018, the Annual Meeting of the American Association for the Study of Liver Disease (AASLD) being held on November 9-13, 2018, in San Francisco. The abstracts became available today on the Online Planner on the AASLD website.

ARO-HBV Presentation Details

First Results with RNA interference (RNAi) in Chronic Hepatitis B (CHB) Using ARO-HBV

- Publication Number: LB-25
- Session: Late-Breaking Poster Session
- Session Date and Time: November 12, 2018 from 8:00 AM to 5:30 PM PT
- Location: Moscone Center North/South Building, Hall C
- Authors: Dr. Edward J. Gane, *et al.*

Abstract

Background: RNAi has shown promise as a potential component of finite therapy for patients with chronic hepatitis B (CHB) based on its ability to silence HBV mRNA thereby reducing all viral products, most notably HBsAg. Clinical utility has been limited by IV delivery and/or safety concerns. ARO-HBV is composed of two siRNAs, each directly conjugated to N-acetyl galactosamine to drive hepatocyte delivery. Administered subcutaneously (SQ), it is designed to silence all mRNA from cccDNA and host integrated viral DNA, without need for additional delivery elements.

Methods: Normal healthy volunteer (NHV) cohorts (4 active, 2 placebo) received single SQ doses of 35, 100, 200, 300 or 400 mg. CHB cohorts 2b-5b (n=4, HBeAg pos or neg, NUC treated or not on NUCs) received monthly doses x 3 of 100, 200, 300 or 400 mg. Cohorts of HBeAg pos, NUC naïve and experienced CHB (cohorts 8, 9 respectively, n=4 each) are receiving 300 mg monthly x 3. NUC untreated receive NUCs from day 1. Results reported are from 28 days after 3rd dose (day 85) when available or most recent.

Results: No serious AEs or dropouts in NHVs or CHBs have been reported. AEs were mild and similar in occurrence for active or placebo. Injection site AEs (all mild) occur in ~11% of injections. For cohorts 2b-5b (n=16 active), 14 were BLQ for HBV DNA and 13 were HBeAg negative at baseline; 14 on chronic NUCs. In CHB, mean (max) log10 reductions in HBsAg were: 100 mg 2.0 (4.0) through Day 85, 200 mg 1.6 (2.2) through Day 85, 300 mg 1.5 (2.2) through Day 85 and 400 mg 1.7 (3.0) through day 71 in cohorts 2b-5b and 1.5 (3.0) in cohort 8 through day 43 and 1.0 (1.3) through day 15 in cohort 9. All patients reaching day 85 have > 1.0 log10 reduction in HBsAg with additional HBsAg decreases observed after the second and third doses. Of these 24 CHB, 21 had HBsAg >100 IU/ml at baseline and currently 17 have achieved HBsAg <100, 7 ≤10, 4 ≤1. In CHB with other viral parameters above LLOQ at baseline, all have improved following ARO-HBV, including reduction to BLQ in: HBV DNA (2 of 7), HBV RNA (8 of 14), HBeAg (0 of 11) and HBcrAg (3 of 15).

Conclusions: ARO-HBV has been well tolerated in NHVs and CHB. ~11% of SQ injections were associated with mild injection site AEs. Monthly RNAi with ARO-HBV effectively reduces all measurable viral products, including HBsAg. ARO-HBV has characteristics desirable for RNAi to become a cornerstone therapy in finite regimens aimed at HBsAg clearance in CHB.

ARO-AAT Presentation Details

A Phase 1 Single and Multiple Dose-Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Effect of ARO-AAT on Serum Alpha-1 Antitrypsin levels in Normal Adult Volunteers

- Publication Number: LB-9
- Session: Late-Breaking Poster Session
- Session Date and Time: November 12, 2018 from 8:00 AM to 5:30 PM PT
- Location: Moscone Center North/South Building, Hall C
- Authors: Dr. Christian Schwabe, *et al.*

Abstract

Background: Alpha-1 antitrypsin deficiency (AATD) is an autosomal co-dominant genetic disorder causing liver disease in children and adults. Alpha-1 antitrypsin (AAT) is a glycoprotein produced primarily in hepatocytes. The PiZ mutation causes improper AAT folding and impaired secretion by hepatocytes leading to accumulation in the liver of AAT aggregates known as globules. Accumulated globules can lead to a recurrent cycle of hepatic injury, fibrosis, cirrhosis and hepatocellular carcinoma. ARO-AAT is a hepatocyte targeted RNAi therapeutic designed to silence production of Z-AAT protein with the intent of reducing liver globules. In a mouse model, reduced liver Z-AAT synthesis correlated to reduced serum AAT and reduced Z-AAT globules prevented progression and development of AATD-associated liver disease.

Methods: 45 healthy volunteers (age 18-52) received escalating single or multiple doses of ARO-AAT by subcutaneous injection. Subjects were randomized (4 placebo:4 active) to receive single 35 mg doses of ARO-AAT or placebo. Multi-dose cohorts (4 placebo:4 active) received three doses every 28 days at doses of 100, 200 or 300 mg. In parallel, open label cohorts enrolled 4 subjects each receiving a single dose of ARO-AAT at 100, 200 and 300 mg to assess single dose duration of response. Assessments included safety (including pulmonary function tests), tolerability, pharmacokinetics, and pharmacodynamics. Subjects were evaluated through at least Day 29 (35 mg single dose cohort) or Day 113 (open label and multi-dose cohorts) or until AAT levels returned to 20% below baseline or above 90 mg/dL.

Results: No deaths, SAEs or severe AEs have been reported. The most common AEs were headache (22%) and rhinorrhea (13%). Single dose serum AAT mean nadir reductions from baseline of 79%, 87%, >91% and >91% were reported at 35, 100, 200 and 300 mg respectively. Multi-dose mean nadir serum AAT reductions were >91% at all dose levels with most subjects BLQ. Maximum AAT reduction across all cohorts was >94%. A greater than 90% reduction was sustained for at least 8 weeks following the last dose in the lowest multi-dose cohort (100 mg), the only cohort with data of this duration.

Conclusions: ARO-AAT has been well tolerated at doses as high as 300 mg given three times every 28 days. Maximum nadir reduction of >94% from baseline indicates potent siRNA inhibition of hepatic AAT synthesis. Based on duration of response, quarterly or less frequent dosing appears feasible.

A copy of the presentation materials may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website after the presentations conclude.

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/email-alerts.

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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