Arrowhead Pharmaceuticals Hosts R&D Day on Pipeline of RNAi Therapeutics

October 16, 2018

PASADENA, Calif.--(BUSINESS WIRE)--Oct. 16, 2018-- Arrowhead Pharmaceuticals Inc. (NASDAQ: ARWR) is hosting a Research & Development (R&D) Day today in New York to discuss its emerging pipeline of RNAi therapeutics that leverage the Company's proprietary Targeted RNAi Molecule (TRiM™) platform. In addition to senior members of the Arrowhead team, the R&D Day includes Ira J. Goldberg, M.D., Bronfman Professor of Medicine, Chief of the Division of Endocrinology, Diabetes, and Metabolism, New York University Langone School of Medicine.

Presentations will begin at 1:00 p.m. EDT. A live and archived webcast of the event, with slides, may be accessed on the Events and Presentations page under the Investors section of the Arrowhead website.

Chris Anzalone, Ph.D., president and chief executive officer of Arrowhead Pharmaceuticals, said: "We have made great progress since we unveiled our proprietary TRiM™ platform just a year ago. Our first two candidates, ARO-AAT and ARO-HBV, have advanced into clinical studies with speed and precision and the initial data have been very promising. In addition, our ability to target extrahepatic tissues is expanding. This now includes lung, tumor, and today we will show initial data demonstrating good knockdown in multiple muscle types. With this validation and the forthcoming capital from the ARO-HBV partnership with Janssen, we confidently enter the next phase of rapid growth for Arrowhead. Looking forward, we expect to accomplish the following: file 2-3 new CTAs every year; target a new cell type with the TRiM™ platform every 18 months; and, have 10 TRiM™ enabled candidates in clinical studies by the end of 2020."

Select R&D Day Highlights

ARO-APOC3

ARO-APOC3 is designed to reduce production of Apolipoprotein C-III (apoC-III), a component of triglyceride rich lipoproteins (TRLs) including very low density lipoprotein (VLDL) and chylomicrons and is a key regulator of triglyceride metabolism. The company believes that knocking down the hepatic production of apoC-III may result in enhanced triglyceride metabolism and clearance of VLDL and chylomicron remnants. Elevated triglyceride levels are an independent risk factor for cardiovascular disease. Severely elevated triglycerides (often over 2,000 mg/dL) in patients with familial chylomicronemia syndrome (FCS), a rare genetic disorder, can result in potentially fatal, acute pancreatitis. Arrowhead has conducted work in multiple preclinical models, including in transgenic mice, cynomolgus monkeys (cynos), and high fructose fed rhesus monkeys that suggest ARO-APOC3 strongly reduces the liver production of apoC-III and has a desired effect on serum triglyceride levels. The company will present additional data, including liver biopsy measurements in cynos, in an oral presentation at the American Heart Association (AHA) meeting on November 12, 2018. In addition, a CTA filing is planned for late 2018 to request approval to begin a Phase 1, single and multiple ascending dose study in heathy volunteers and in patients with elevated triglycerides.

ARO-ANG3

ARO-ANG3 is designed to reduce production of angiopoietin-like protein 3 (ANGPTL3), a liver synthesized inhibitor of lipoprotein lipase and endothelial lipase. ARO-ANG3 is being developed for the treatment of dyslipidemias and metabolic diseases. ANGPTL3 inhibition has been shown to lower serum LDL, serum and liver triglyceride and has genetic validation as a novel target for cardiovascular disease. In multiple animal models, ARO-ANG3 led to deep ANGPTL3 knockdown in both Western diet or chow-fed mice and significant improvements in lipid parameters. A CTA was recently filed to begin AROANG1001, a Phase 1 single and multiple dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamic effect of ARO-ANG3 in adult healthy volunteers and dyslipidemic patients. The study is designed to enroll up to 70 subjects. Arrowhead will also present additional data at the AHA meeting on November 12, 2018.

Targeted RNAi Molecule Platform (TRiM ™)

Arrowhead's Targeted RNAi Molecule platform, or TRiM™, utilizes ligand-mediated delivery and is designed to enable multi-tissue targeting, while being structurally simple. TRiM™ represents an evolution in RNAi therapeutics from biologic complexity to small molecule precision and execution. It was designed to optimize potency, activity, durability, and safety. Important differentiators of the TRiM™ platform include:

- TRiM™ platform demonstrates versatility for both hepatic and extrahepatic targets
  - Potency, activity, durability and safety
  - Speed and high success rates
- Hepatocyte targets
  - Expertise in RNAi chemistry and biology
  - We have yet to encounter a hepatocyte gene that we could not knock down effectively and with a wide therapeutic index
- Extrahepatic targets
  - Requires all TRiM™ platform modules to be fully optimized
  - Expertise in uncovering ligand/receptor pairs
  - Expertise in ligand designs to enable maximal uptake through endocytosis
- Successful extrahepatic, systemic delivery of RNAi triggers via IV and subcutaneous administrations in ccRCC
- Expanding extrahepatic capabilities to now include delivery to the lung, tumor, and muscle tissue

ARO-ENaC Gen 1

ARO-ENaC is designed to reduce production of the epithelial sodium channel alpha subunit (αENaC) in the airways of the lung. In cystic fibrosis patients, increased ENaC activity contributes to airway dehydration and reduced mucociliary transport. ENaC inhibitors promise a genotype-agnostic therapeutic approach for potentially all CF patients, including those with Class I mutations that produce no CFTR protein. Inhaled small molecule inhibitors transiently improve lung mucociliary clearance, but they are rapidly absorbed and systemic exposure results in renal ENaC inhibition and hyperkalemia. Inhalation of aerosolized ARO-ENaC Gen 1 selectively and durably silences ENaC mRNA expression in the rat lung while sparing the kidney. In addition, improved mucociliary clearance was observed in sheep two weeks after inhalation of aerosolized ARO-ENaC Gen 1. Work on a next-generation ARO-ENaC is focused on further increasing potency to produce in vivo clearance increases similar to short-acting small molecule ENaC inhibitors. A CTA is planned for ARO-ENaC in 2019. The platform may also be adapted to additional therapeutic targets in the pulmonary epithelium, particularly those that are currently inaccessible to traditional small molecule or antibody approaches.

ARO-HIF2

ARO-HIF2 is designed to inhibit the production of HIF2α, which has been linked to tumor progression and metastasis, for the treatment of clear cell renal cell carcinoma (ccRCC). Arrowhead believes it is an attractive target for intervention because most ccRCC tumors express a mutant form of the Von Hippel-Landau protein that is unable to degrade HIF-2α, leading to its accumulation during tumor hypoxia and promoting tumor growth. ARO-HIF2 has demonstrated effective tumor delivery and deep HIF2α mRNA knockdown in tumors. In addition, ARO-HIF2 led to inhibition of tumor growth and improved overall survival in tumor models. Initial rat exploratory toxicity studies predict that ARO-HIF2 may have a wide safety margin. Additional data is planned to be presented as a late-breaking poster at the EORTC/AACR/NCI symposium being held November 13-16, 2018. A CTA is planned for ARO-HIF2 in 2019.

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 likelihood and timing of the receipt of future milestone and licensing fees, the future success of our scientific studies, our ability to successfully develop and commercialize 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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