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

October 18, 2019

PASADENA, Calif.--(BUSINESS WIRE)--Oct. 18, 2019-- 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 its proprietary Targeted RNAi Molecule Platform (TRiM™) platform. The event will feature presentations by Arrowhead's management team andra Goldberg, M.D., the Clarissa and Edgar Bronfman, Jr. Professor of Endocrinology, and the Director of the Division of Endocrinology, Diabetes, and Metabolism at NYU Langone Medical Center.

Presentations will begin at 8:30 a.m. EDT. A live and archived webcast of the event 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: “During the R&D Day, we will discuss our product development strategy as we continue to expand our pipeline and detail the guiding principles that make our R&D organization best-in-class for execution and speed. The clinical data generated to date for multiple drug candidates that leverage our proprietary TRiM™ platform with 432 total doses administered to 214 patients have been very promising. In fact, they have met and, in many areas, exceeded our expectations with respect to tolerability and pharmacologic activity against their respective targets. We now have five candidates in clinical trials, three of which are wholly owned. By the end of 2020, we expect to have at least seven wholly owned candidates in clinical studies, including three in Phase 3 pivotal studies, as well as two partnered programs in Phase 2 studies or later, and drug candidates in four different cell types. We expect to be the first RNAi company in these extra-hepatic cell types. In addition, we continue to make advances to the TRiM™ system, and we are presenting data today demonstrating that a new dimer structure that delivers multiple siRNA sequences together can achieve high levels of knockdown of two different genes simultaneously. These important advances dramatically increase the number of potential diseases that we may be able to address over the coming years.”

Select R&D Day Highlights

ARO-APOC3 and ARO-ANG3

ARO-APOC3 is designed to reduce the 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. ARO-ANG3 is designed to reduce production of angiopoietin-like protein 3 (ANGPTL3), a liver synthesized inhibitor of lipoprotein lipase and endothelial lipase. There is strong genetic validation that loss of function mutations in ANGPTL3 or APOC3 result in improved cardiovascular outcomes relative to the population at large associated with clear lipid phenotypes. These loss of function mutations have not been associated with demonstrated adverse phenotypes. The ability to recapitulate the lipid phenotypes seen in these genetic studies has been demonstrated for antisense, monoclonal antibodies (ANGPTL3 only), and now RNAi. Arrowhead believes that compounds using other mechanisms have vulnerabilities, positioning RNAi as an important potential option. The company will present Phase 1 data for both ARO-APOC3 and ARO-ANG3 on November 18, 2019, in the Late Breaking Science VI: New Frontiers in Lipid Therapy session at the American Heart Association meeting. Presentations will cover full dose response for single doses in healthy volunteers, and will include results for a wide selection of lipids and apolipoproteins.

ARO-AAT

ARO-AAT is the company’s second generation subcutaneously administered RNAi therapeutic being developed as a treatment for liver disease associated with alpha-1 antitrypsin deficiency (AATD), which is a rare genetic disorder that severely damages the liver and lungs of affected individuals. ARO-AAT is designed to reduce production of the mutant Z-AAT protein by silencing the AAT gene in order to potentially prevent accumulation of Z-AAT in the liver, allow clearance of the accumulated Z-AAT protein, prevent repeated cycles of cellular damage, and possibly prevent or even reverse the progression of liver fibrosis. In preclinical studies in PiZ mice, RNAi treatment restored normal hepatocyte ultrastructure. In a Phase 1 clinical study, ARO-AAT administration led to significant reductions in serum AAT levels down to the lower limit of quantitation, with a long duration of effect that supports quarterly or less frequent dosing. Arrowhead is currently conducting the SEQUOIA study (AROAAT2001), an adaptive design, potentially pivotal Phase 2/3 clinical study.

ARO-HSD

ARO-HSD is designed to reduce the production of HSD17B13, a hydroxysteroid dehydrogenase involved in the metabolism of hormones, fatty acids and bile acids. Published human genetic data indicate that a loss of function mutation in HSD17B13 provides strong protection against nonalcoholic steatohepatitis (NASH) cirrhosis and alcoholic hepatitis and cirrhosis. Improvements in NASH and fibrosis were seen with HSD17B13 knockdown in the CDAA diet mouse model, a commonly used NASH model. The in-life phase of the GLP toxicology studies is complete, and Arrowhead expects to file a CTA before year end 2019. With no known plasma readout for activity, the company expects to determine depth and duration of knockdown and dose response using biopsies in a first-in-human trial, expected to begin in the first half of 2020.

ARO-HIF2

ARO-HIF2 is designed to inhibit the production of HIF2α, which has been linked to tumor progression and metastasis in clear cell renal cell carcinoma (ccRCC). 70-80% of kidney cancer are ccRCC. Most of these cases have a mutation that inactivates the Von Hippel-Lindau (VHL) tumor suppressor gene, which regulates the degradation of hypoxia inducible factors (HIFs). VHL inactivation leads to the accumulation of HIFs. In preclinical tumor models, ARO-HIF2 treated groups showed wide-spread tumor destruction, loss of the clear cell characteristic, and areas of apoptosis and necrosis. In addition, ARO-HIF2 led to deep HIF2α mRNA knockdown in tumor and strong tumor growth inhibition with signs of regression in some mice. GLP toxicology studies are complete, and Arrowhead expects to file a CTA before year end 2019.

ARO-ENaC

ARO-ENaC is designed to reduce production of the epithelial sodium channel alpha subunit (αENaC) in the airways of the lung. In cystic fibrosis (CF) patients, increased ENaC activity contributes to airway dehydration and reduced mucociliary transport. Various human genetic studies have validated ENaC as a CF target. The development of inhaled small molecule ENaC inhibitors has been limited by on-target renal toxicity and short duration of action in the lung. Targeted delivery of ARO-ENaC may allow durable, renal-sparing ENaC inhibition in the lung. The mechanism of RNAi-mediated ENaC inhibition could potentially provide clinical benefit to all CF patients, regardless of genotype, and in combination with existing or new CFTR-targeted therapies. ARO-ENaC inhalation led to durable and dose-dependent silencing of pulmonary ENaC expression in rats, and it accelerated mucociliary clearance for weeks post-dose in sheep. In addition, ARO-ENaC preserved lung clearance in a sheep mucostatic model of CF lung disease. IND/CTA-enabling studies are ongoing to support regulatory filings for first-in-human studies in 2020.

Targeted RNAi Molecule Platform (TRiM™)

Arrowhead's Targeted RNAi Molecule, or TRiM™, platform utilizes ligand-mediated delivery and is designed to enable multi-tissue targeting, while being structurally simple. The company has continued to make advances to the platform and can now achieve effective delivery to multiple cell types, including hepatocytes, solid tumors, pulmonary epithelial cells, and skeletal muscle. The second-generation muscle delivery platform can achieve pharmacologic activity of greater than 80% target knockdown with long duration in mice. This muscle delivery platform is now subcutaneous administration compatible, with streamlined manufacturing. In addition, the TRiM™ platform now includes a dimer approach, which provides a potential pathway to achieve maximum therapeutic benefit by simultaneously knocking down two genes with one drug.

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.

Source: Arrowhead Pharmaceuticals, Inc.

View source version on businesswire.com: https://www.businesswire.com/news/home/20191018005154/en/

Source: Arrowhead Pharmaceuticals, Inc.

Arrowhead Pharmaceuticals, Inc.
Vince Anzalone, CFA
626-304-3400
ir@arrowheadpharma.com

Investors and Media:
LifeSci Advisors, LLC
Brian Ritchie
212-915-2578
britchie@lifesciadvisors.com
www.lifesciadvisors.com