Arrowhead Presents Preclinical Data on ARO-DUX4 at FSHD Society International Research Congress

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PASADENA, Calif.--(BUSINESS WIRE)--Jun. 25, 2021-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today presented preclinical data on the development of ARO-DUX4, the company's investigational RNA interference (RNAi) therapeutic being developed as a treatment for patients with facioscapulohumeral muscular dystrophy (FSHD), at the 28th Annual FSHD Society International Research Congress. Arrowhead intends to file for regulatory clearance in the third quarter of 2021 to begin clinical studies of ARO-DUX4.

James Hamilton, M.D., MBA, senior vice president of discovery and translational medicine at Arrowhead, said: "Preclinical development of ARO-DUX4 has produced very promising results that we believe strongly support advancement into clinical testing. In our preclinical studies in relevant models, ARO-DUX4 achieved deep knockdown of DUX4 and its target genes. Importantly, in a transgenic mouse model of FSHD, treatment with ARO-DUX4 prevented and reversed tamoxifen-induced increases in DUX4 and DUX4 target gene expression. In addition, ARO-DUX4 prevented and reversed DUX4-induced body weight loss, muscle fibrosis, and rotarod performance loss. Collectively, these preclinical results suggest that ARO-DUX4 achieved good target engagement, which led to a downstream beneficial physiological change. We look forward to initiating our clinical program and translating these results into humans. A significant unmet need exists in FSHD, an indication with no currently available treatments."

Preclinical data demonstrated that Arrowhead's Targeted RNAi Molecule (TRiM™) muscle delivery platform can achieve functional delivery to various types of skeletal muscle. Using RNAscope to detect RNAi, after a single 3 mg/kg intravenous (IV) dose in a mouse, 76-99% of myofibers in gastrocnemius contained TRiM™ RNAi. In addition, nonhuman primates receiving three doses of 10 mg/kg (day 1, 7, and 28) of a TRiM™ RNA targeting myostatin achieved 79% serum myostatin knockdown with a greater than 70% reduction still being observed at week 12.

ARO-DUX4 also achieved dose-dependent knockdown of DUX4 and a deep reduction of DUX4 target gene expression in differentiated FSHD patient-derived myotubes. Additionally, ARO-DUX4 was evaluated in a transgenic FSHD-like mouse model, which has muscle-specific expression of human DUX4 and increased expression of DUX4 target genes. These animals develop a FSHD-like muscle phenotype which includes functional loss. In this model, ARO-DUX4 treatment:

- Prevented and reversed a tamoxifen-induced increase in DUX4 and DUX4 target gene expression
- Prevented DUX4-induced body weight loss
- Reversed DUX4-induced body weight loss by day 17 allowing a return to baseline body weight by day 22
- Prevented and reversed muscle fibrosis
- Prevented rotarod performance loss
- Reversed rotarod performance loss by day 15

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

FSHD is an autosomal dominant disease associated with the failure to maintain complete epigenetic suppression of DUX4 expression in differentiated skeletal muscle, leading to overexpression of DUX4, which is myotoxic and can lead to muscle degeneration. As DUX4 expression is recognized as the cause of muscle pathology in FSHD patients, Arrowhead believes that the selective targeting and knockdown of DUX4 using RNAi may prevent or reverse downstream myotoxicity and lead to muscle repair and improvement in muscle function in patients. There are currently no effective treatments specifically for FSHD.

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. Any statements contained in this release except for historical information may be deemed to be forward-looking statements. Without limiting the generality of the foregoing, words such as "may," "will," "expect," "believe," "anticipate," "intend," "plan," "project," "could," "estimate," or "continue" are intended to identify such forward-looking statements. In addition, any statements that refer to projections of our future financial performance, trends in our business, expectations for our product pipeline or product candidates, including anticipated regulatory submissions and clinical program results, prospects or benefits of our collaborations with other companies, or other characterizations of future events or circumstances are forward-looking statements. 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 numerous factors and uncertainties, including the impact of the ongoing COVID-19 pandemic on our business, 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, the enforcement of our intellectual property rights, and the other risks and uncertainties described in our most recent Annual Report on Form 10-K, subsequent Quarterly Reports on Form 10-Q and other documents filed with the Securities and Exchange Commission from time to time. We assume no obligation to update or revise forward-looking statements to reflect new events or circumstances.

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