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Arrowhead Presents Promising New Preclinical Data on ARC-F12 at AAAAI 2016

PASADENA, Calif.--(BUSINESS WIRE)-- Arrowhead Research Corporation (NASDAQ: ARWR), a biopharmaceutical company developing targeted RNAi therapeutics, today presented additional preclinical data suggesting that ARC-F12, an RNAi therapeutic that inhibits the production of Factor XII (F12), has the potential to treat hereditary angioedema and to prevent thrombosis. Data presented in a poster at the 2016 American Academy of Allergy, Asthma & Immunology Annual Meeting (AAAAI), show that ARC-F12 had the desired effects of significantly reduced swelling in a rat model of edema and inhibition of blood clot formation in a mouse model of thrombosis, without the undesired effect of increased bleeding risk.

In a carrageenan-induced paw edema model in rats, treatment with ARC-F12 seven days prior to carrageenan challenge led to a significant reduction in edema ($p < 0.001$). The reduction in swelling in ARC-F12 treated rats is similar to that seen in rats treated with a kallikrein-targeted antibody. This supports Arrowhead's position that F12 inhibition could be an attractive target for the rare genetic disorder, hereditary angioedema (HAE).

In a mouse model of thrombosis, a dramatic increase in occlusion times was observed in mice receiving ARC-F12. The time to blood flow occlusion is measured as a clinically relevant indicator of physiological response to F12 knockdown and is a measure of the inhibition of thrombus formation. Further, in multiple relevant models of bleeding risk, ARC-F12 did not cause an increase in bleeding times or bleeding risk. Anticoagulants can be used to reduce thrombus formation and thromboembolism occurrence, but also can cause an increase in serious bleeding risk. ARC-F12 may be able to reduce the risk of blood clot formation, without the undesirable bleeding risk caused by anticoagulants.

In vivo studies in wild type mice showed that a single 2 mg/kg dose of ARC-F12 achieved greater than 95% knockdown of F12 levels. In multi-dose primate studies, a 4 mg/kg dose resulted in greater than 90% knockdown with even greater knockdown following subsequent doses. Knockdown was also highly durable with greater than 80% reduction maintained between monthly doses. ARC-F12 appeared to be generally well-tolerated and no drug-related changes in toxicity markers were observed as measured by clinical chemistry and hematologic parameters.

F12 is a key component of the contact activation pathway involved in thrombosis and the kinin-kallekrein system involved in angioedema. It is predominantly produced in the liver and circulates in plasma, so Arrowhead believes that it is a uniquely suited target for an RNAi-therapeutic delivered with the proprietary Dynamic Polyconjugate™ (DPC™) delivery system.

Consistent with its process for all of its RNAi-therapeutic candidates, Arrowhead's discovery of ARC-F12 followed a screening funnel process that includes: bioinformatic selection of RNAi trigger sequences; trigger synthesis and in vitro screening; synthesis of cholesterol-RNAi triggers and in vivo screening; multiple iterations of structure-activity relationship (SAR) studies and in vivo screening to assess various chemical modifications to improve RNAi trigger activity; in vivo screening in non-human primates; efficacy testing in disease relevant models; non-GLP toxicology studies; and lastly, the selection of a lead candidate.

About ARC-F12

Arrowhead's RNAi-based candidate ARC-F12 is in preclinical development as a potential treatment for factor XII (F12) mediated diseases. Arrowhead sees clear unmet need in hereditary angioedema (HAE) and thromboembolic diseases. The biology of factor 12 as part of the coagulation cascade and the kinin-kallikrein system suggest that its reduction through RNAi may present opportunities in both disease areas. The company is currently conducting studies in order to advance ARC-F12 into clinical trials.

About Arrowhead Research Corporation

Arrowhead Research Corporation is a biopharmaceutical company developing targeted RNAi therapeutics. The company is leveraging its proprietary Dynamic Polyconjugate™ delivery platform to develop targeted drugs based on the RNA interference mechanism that efficiently silences disease-causing genes. Arrowhead's pipeline includes ARC-520 and ARC-521 for chronic hepatitis B virus, ARC-AAT for liver disease associated with alpha-1 antitrypsin deficiency, ARC-F12 for

hereditary angioedema and thromboembolic diseases, ARC-LPA for cardiovascular disease, and ARC-HIF2 for renal cell carcinoma.

For more information please visit http://www.arrowheadresearch.com, or follow us on Twitter @ArrowRes. To be added to the Company's email list and receive news directly, please visit http://ir.arrowheadresearch.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 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. Arrowhead Research Corporation's 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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