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Arrowhead Pharmaceuticals Presents New Data on ARC-F12 and ARC-LPA Using DPCsqTM Subcutaneous RNAi Delivery Vehicle

PASADENA, Calif.--(BUSINESS WIRE)-- Arrowhead Pharmaceuticals, Inc. (NASDAQ: ARWR) today delivered oral presentations on ARC-LPA, its preclinical development program targeting lipoprotein (a), for the treatment of cardiovascular disease, and ARC-F12, its preclinical development program targeting factor XII (F12) for the prophylactic treatment of thromboembolism and hereditary angioedema, at the American Heart Association's Scientific Sessions 2016 in New Orleans. These data show advancements being made in the ARC-LPA and ARC-F12 programs and in the development of Arrowhead's proprietary DPC_{sq}^{TM} delivery vehicle designed for subcutaneous administration of RNAi therapeutics.

Chris Anzalone, Ph.D., president and CEO of Arrowhead Pharmaceuticals, said: "We have made rapid advancements to our DPC_{sq}^{TM} subcutaneous RNAi delivery platform. F12 and Lp(a) are both very attractive targets for RNAi, and the data presented today on ARC-F12 and ARC-LPA show substantial improvements in activity over previous generations. In addition, through multiple rounds of SAR studies, substantial gains in potency continue to be made by Arrowhead scientists. Data shown today are from the first and second generation triggers. Studies that are ongoing in NHPs that use our fourth generation RNAi triggers and the DPC_{sq}^{TM} platform, are achieving even higher levels of target knockdown with longer duration using lower and less frequent doses (data not shown)."

The oral poster titled, "**Targeting factor XII (F12) with a novel RNAi delivery platform as a prophylactic treatment for thromboembolism**", describes advancements in the preclinical development of ARC-F12. Key details of the presentation include the following:

- F12 is an attractive target for an RNAi therapeutic
  - It is key component at the top of the contact (intrinsic) coagulation cascade
  - It is predominantly expressed in the liver and circulates in blood
  - Inhibition is genetically validated and deficiency protects from thromboembolic disease but is not associated with either bleeding or thrombotic disorders
- Arrowhead developed RNAi triggers that gave greater than 95% reductions of serum F12 levels after a single subcutaneous injection
- Dose dependent reductions in serum F12 levels were observed with single injections of ARC-F12 of 1 mg/kg and 3 mg/kg leading to mean reductions of 86% and 96% respectively
- A statistically significant reduction (p=0.002) in thrombus weight was observed at greater than 95% F12 knockdown in a rat arterio-venous shunt model
- There was no increased bleeding risk in ARC-F12 treated mice, even with greater than 99% knockdown of F12 levels

The oral presentation titled, "**Targeting apolipoprotein(a) with a novel RNAi delivery platform as a prophylactic treatment to reduce risk of cardiovascular events in individuals with elevated lipoprotein (a)**", describes advancements in the preclinical development of ARC-LPA, which is part of a recently announced license and collaboration agreement with Amgen. Key details of the presentation include the following:

- Lipoprotein (a) [Lp(a)] is an attractive target for an RNAi therapeutic
  - Lp(a) is an independent risk factor for cardiovascular disease through its atherogenic potential
  - Higher levels of Lp(a) correlate with increased risk of cardiovascular disease
  - Lp(a) levels in humans are genetically defined and do not change significantly with diet and exercise
  - Approximately 25% of the U.S. population has greater than 30 mg/dL of Lp(a) (normal levels: 0.1 - 25 mg/dL)
  - It is predominantly expressed in the liver and circulates in blood
- Screening of LPA RNAi triggers in Lp(a) transgenic (Tg) mice identified several that induced substantial and sustained knockdown of serum Lp(a) levels

- Structure activity relationship (SAR) studies assessing structure and chemical modifications identified triggers that achieved greater than 98% maximum knockdown after a single 3 mg/kg SQ dose in Tg mice
- In NHPs, 85-90% reduction of serum Lp(a) levels was observed after three weekly 3 mg/kg SQ doses
- In an atherosclerosis model, data suggest that RNAi triggers can be effectively delivered to a fatty liver using the DPC_{sq}^{TM} platform

A copy of presentation materials will be made available on the Events and Presentations page under the Investors section of the Arrowhead website.

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 ARC-LPA

Arrowhead's RNAi-based candidate ARC-LPA is in preclinical development as a potential treatment for cardiovascular diseases. ARC-LPA is designed to reduce production of apolipoprotein(a), a key component of lipoprotein(a), or Lp(a). Lp (a) levels in humans are genetically defined and higher levels correlate with increased risk of cardiovascular diseases, independent of cholesterol and LDL levels. ARC-LPA is Arrowhead's first drug candidate to use a subcutaneously administered delivery construct.

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. The company's pipeline includes ARC-520 and ARC-521 for chronic hepatitis B virus infection, ARC-AAT for liver disease associated with alpha-1 antitrypsin deficiency, ARC-F12 for hereditary angioedema and thromboembolic disorders, ARC-LPA for cardiovascular disease, and ARC-HIF2 for renal cell carcinoma.

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/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 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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