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## Arrowhead Presents Data on DPC System and Hepatitis B Program at CLINAM 2012

## Preclinical studies show substantial reduction of serum HBsAg, HBV DNA and dramatically decreased HBV RNA and DNA in liver

**PASADENA, California, May 9, 2012 — Arrowhead Research Corporation (NASDAQ:ARWR)** today announced that David Lewis, Ph.D., Vice President Biology and Site Head of its Madison, WI research and development facility presented data at the European Foundation for Clinical Medicine Conference in Basel, Switzerland. Dr. Lewis' presentation, "DPC Technology for Safe and Effective siRNA Delivery" described the development and capabilities of Arrowhead's Dynamic Polyconjugate (DPC) siRNA delivery platform, as well as the system's deployment in the development of a new treatment for chronic Hepatitis B.

Dr. Lewis reported data from Arrowhead's preclinical HBV program that support Arrowhead's clinical strategy for the development of an effective siRNA-based therapeutic for the treatment of patients with chronic HBV infection. Single-dose injections of hepatocyte-targeted anti-HBV siRNA DPCs in a replication-competent, transiently transgenic HBV mouse model resulted in a multi-log reduction of serum HBsAg and serum HBV DNA. Using a transgenic mouse model of chronic HBV infections in viral transcripts, viral replicative DNA intermediates, and intracellular HBV core antigen were observed in the liver after two weekly doses. In multi-dose studies in mice carrying a hepatocyte-specific reporter gene fused to HBV sequences, four biweekly injections of anti-HBV siRNA DPCs resulted in a multi-log reduction in gene expression over 2 months without changes in toxicity markers. Safety studies performed in non-human primates have shown DPCs to be highly effective and well tolerated.

According to the World Health Organization, about 2 billion people worldwide have been infected with the virus and about 350 million live with chronic infection. An estimated 600,000 persons die each year due to the acute or chronic consequences of hepatitis B.

"Current treatments for HBV are poorly tolerated and fail to adequately reduce circulating Hepatitis B Surface Antigen (HBsAG), which is thought to hinder the immune system's ability to eradicate the virus," said Dr. Lewis. "RNAi has the potential to be much more effective through its ability to not only knock down the replication of the virus but crucially reduce the expression of viral proteins as well, including HBsAG. It is believed this will clear the way for the patient's immune system to mount an effective response to the infection."

Full data from these experiments will be submitted for publication.

## About the Dynamic PolyConjugate siRNA Delivery Platform

Achieving safe and effective in vivo delivery of siRNA to the appropriate tissue and cell type is the primary barrier to development of RNAi as a therapeutic modality. Dynamic PolyConjugate (DPC) technology overcomes this barrier. Key features of the DPC technology include:

- New classes of membrane-active and biodegradable polymers,
- Reversible chemical masking of the polymers so that membrane-lytic activity is revealed only in the acidic environment of endosomes, and
- The ability to attach ligands to guide the polymer and the siRNA cargo to specific cell types in vivo..

The utility of this technology has been demonstrated by ligand-mediated delivery of siRNA to liver hepatocytes in mice, rats, and non-human primates resulting in high-level knockdown of the targeted gene. Importantly, DPCs display a low toxicity profile enabling siRNA redosing and long-term target gene knockdown.

## About Arrowhead Research Corporation

Arrowhead Research Corporation is a clinical stage nanomedicine company developing innovative therapies at the interface of biology and nanoengineering. Arrowhead's world-class capabilities and intellectual property covering nucleic acid delivery, siRNA chemistry, and tissue targeting allow it to design and develop therapeutic agents for a wide range of diseases. The

company's lead products include CALAA-01, an oncology drug candidate based on the gene silencing RNA interference (RNAi) mechanism, and Adipotide<sup>™</sup>, an antibesity peptide that targets and kills the blood vessels that feed white adipose tissue. Arrowhead is leveraging its proprietary Dynamic PolyConjugate (DPC), Liposomal Nanoparticle (LNP), and RONDEL<sup>™</sup> deliver platforms to support its own pipeline of preclinical and clinical candidates and to secure external partnerships and collaborations with biotech and pharmaceutical companies.

For more information please visit <u>http://www.arrowheadresearch.com</u>, or follow us on Twitter <u>@ArrowRes</u>. To be added to the Company's email list to receive news directly, please send an email to <u>ir@arrowres.com</u>

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