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Arrowhead Presents Data on DPC System at TIDES 2012

Delivery polymer provides dramatic reduction in effective dose of Cholesterol-conjugated siRNA

PASADENA, California, May 22, 2012 - Arrowhead Research Corporation (NASDAQ:ARWR) today announced that Darren Wakefield, Ph.D., one of its Senior Scientists at its Madison, WI research and development facility presented data at the TIDES: Oligonucleotide and Peptide Research, Technology and Product Development Conference in Las Vegas, NV. Dr. Wakefield's poster presentation titled, "Liver-targeted and reversibly masked-polycation co-delivery improves cholesterol-conjugated siRNA efficacy," describes the ability of Arrowhead's PBAVE polymer to dramatically decrease the effective dose needed. PBAVE is one of the polymers included in Arrowhead's proprietary Dynamic Polyconjugate (DPC) siRNA delivery platform.

"Linkage to cholesterol is one strategy that has been used by other siRNA therapeutic developers to prolong circulation time and to facilitate uptake into hepatocytes via the LDL receptor," said Dr. Wakefield. "However, three daily injections of 50 mg/kg of cholesterol-conjugated apoB siRNA were previously required to achieve 50% gene silencing. Over the past few years, no real improvements have been reported to optimize the delivery of cholesterol or other lipophilic siRNA conjugates in vivo. Using our delivery technology, we are able to achieve similar gene silencing with a dramatically lower dose. This demonstration is one example of the potential of our DPC platform to broaden the utility and safety of siRNA therapeutics."

Arrowhead's chemists employed a new delivery approach to achieve similar gene silencing after a single injection of 0.2 mg/kg of cholesterol-conjugated siRNA, a 750-fold improvement in effective dose. This enhanced efficacy is attained by the co-delivery of an asiologlycoprotein receptor (ASGPr)-targeted and reversibly-masked cationic polymer, PBAVE. The injection of cholesterol-conjugated siRNA and modified-polymer can be temporally separated up to four hours without significant effects on gene silencing, suggesting that delivery does not depend on the association of targeted PBAVE and the cholesterol-conjugated siRNA in the blood. Genetic knockout of the ASGPr eliminates effective delivery of the cholesterol-conjugated siRNA, indicating that delivery depends on proper targeting of the PBAVE polymer.

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 targeted therapeutics company with development programs in oncology, obesity, and infectious disease. The company leverages its platform technologies to design and develop peptide-drug conjugates (PDCs) which specifically home to cell types of interest while sparing off-target tissues, creates targeted drugs based on the gene silencing RNA interference (RNAi) mechanism, and works with partners to create improved versions of traditional small molecule drugs.

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

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