



PRESS RELEASE
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NEW RESEARCH PUBLISHED ON IMPACT OF TARGETING ON BIODISTRIBUTION AND EFFICACY OF siRNA USING CALANDO PHARMACEUTICALS siRNA DELIVERY TECHNOLOGY

PASADENA, Calif.—September 25, 2007—Calando Pharmaceuticals, a leading siRNA therapeutics company and a majority-owned subsidiary of Arrowhead Research Corporation (NASDAQ: ARWR) announced the publication of a study in the Proceedings of the National Academy of Sciences (PNAS) the scientific journal of the NAS. Dr. Mark Davis, professor of chemical engineering at Caltech, and his colleagues at UCLA used Calando's proprietary RONDEL™ polymer technology for delivering siRNA in mice. Dr. Davis is a founder and Chief Scientific Advisor to Calando and to Insert Therapeutics, Inc., another majority-owned subsidiary of Arrowhead.

The paper, entitled "Impact of tumor-specific targeting on the biodistribution and efficacy of siRNA nanoparticles measured by multimodality *in vivo* imaging", was published online in the Early Edition of the PNAS on September 17, 2007. In the study, Dr. Davis and his colleagues used positron-emission tomography (PET) and bioluminescent imaging (BLI) to quantify biodistribution and function in mice of siRNA nanoparticles formulated with Calando's proprietary RONDEL™ polymer technology for delivering siRNA and other nucleic acids. Some were targeted with transferrin, an iron-carrying protein, and others were not. While all the particles – targeted and not – accumulated to a similar extent in tumors, the targeted particles reduced the BLI signal from tumor cells by 50% relative to the non-targeted particles. These results show that the advantages of targeted nanoparticles appear to be associated with uptake into tumor cells, and not to overall tumor localization.

"This work reveals that the primary advantage of targeted nanoparticles for tumor-specific delivery of siRNA is the enhanced uptake in tumor cells rather than altered biodistribution," said Mark Davis. "The conclusions should be applicable to nanoparticle delivery systems in general, and they emphasize why targeted particles should show greater efficacy than non-targeted particles."

“This study demonstrates the importance of including a targeting ligand for achieving efficacy in tumor cell gene inhibition with siRNA,” said John Petrovich, President and CEO of Calando Pharmaceuticals. “Calando plans to file an investigational new drug (IND) application with the US Food and Drug Administration for a Phase I clinical trial in cancer with what we believe will be the first targeted, systemically-delivered siRNA, using a similar formulation carrying siRNA RRM2, a protein essential to cell replication in tumors”.

Established in 1914, PNAS is one of the world’s most-cited multidisciplinary scientific serial publications. Coverage in PNAS includes research reports, commentaries, reviews, perspectives and colloquium papers that span the biological, physical and social sciences, as well as the actions of the Academy. PNAS is published weekly in print, and daily online in PNAS Early Edition at <http://www.pnas.org>.

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About RNA Interference (RNAi)

RNA interference, or RNAi, is a naturally occurring mechanism within cells for selectively silencing and regulating specific genes. Since many diseases are caused by the inappropriate activity of specific genes, the ability to silence genes selectively through RNAi could provide a new way to treat a wide range of human diseases. RNAi is induced by small, double-stranded RNA molecules. One method to activate RNAi is with chemically synthesized small interfering RNAs, or siRNAs, which are double-stranded RNAs that are targeted to a specific disease-associated gene. The siRNA molecules are used by the natural RNAi machinery in cells to cause highly targeted gene silencing.

About Calando Pharmaceuticals Inc.

Calando Pharmaceuticals Inc. (www.calandopharma.com), a majority owned subsidiary of Arrowhead Research Corporation (NASDAQ: ARWR), is using its proprietary technologies in targeted polymeric delivery systems and siRNA design to design and create new, targeted siRNA therapeutics. The company is pursuing this goal through its internal research and development and also through collaborations and partnerships with pharmaceutical and biotechnology companies.

Calando Technology

Calando’s cyclodextrin-containing polymers form the foundation for its two-part siRNA delivery system. The first component is a linear, cyclodextrin-containing polycation that, when mixed with small interfering RNA (siRNA), binds to the anionic “backbone” of the siRNA. The polymer and siRNA self-assemble into nanoparticles of approximately 50-80 nm diameter that fully protect the siRNA from nuclease degradation in serum. The siRNA delivery system has been designed to allow for intravenous injection. Upon delivery to the target cell, the targeting ligand binds to membrane receptors on the cell surface and the RNA-containing nanoparticle is taken into the cell by endocytosis. There, chemistry built into the polymer functions to unpackage the siRNA from the delivery vehicle. In addition to targeting tumors, the targeting of liver cells has also been accomplished *in vivo*.

Safe Harbor Statement under the Private Securities Litigation Reform Act of 1995:

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 future success of our clinical studies, our ability to successfully develop and manufacture products, rapid technological change in our industry, changes in demand for our future products, legislative, regulatory and competitive developments and general economic conditions. Our Annual Report on Form 10-K, and other SEC filings discuss these and other important risk

factors that may affect our business, results of operations and financial condition. We undertake no obligation to revise or update publicly any forward-looking statements for any reason.

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