



**PRESS RELEASE**

March 22, 2010

**Contact:**  
Brandi Floberg  
The Piacente Group, Inc.  
212-481-2050  
arrowres@tpg-ir.com

**Arrowhead Research Subsidiary, Calando Pharmaceuticals, Provides First Proof  
of RNA Interference in Humans with Systemically Administered siRNA  
Therapeutic; Clinical Trial Results Published in Nature**

*Landmark Caltech-led study shows systemic siRNA delivery, mRNA knockdown, protein knockdown and mRNA cleavage products indicative of RNAi*

*Company to host conference call on Tuesday, March 23 at 1:30 p.m. Pacific time*

**PASADENA, Calif. – March 22, 2010 – Arrowhead Research Corporation (NASDAQ: ARWR)** today announced that the clinical trial being conducted by majority-owned subsidiary, Calando Pharmaceuticals, Inc. has demonstrated systemic delivery of siRNA and the successful “silencing” of a widely recognized cancer gene via RNA interference (RNAi) in humans. This represents a breakthrough for Calando, its proprietary RONDEL™ delivery system, and the field of RNAi. It is thought to be the first ever demonstration in humans of targeted siRNA-containing nanoparticle delivery to tumors using systemic administration, delivery of functional siRNAs, and achievement of specific mRNA and protein reductions via RNAi. Thus far in the trial, no significant drug-related toxicities, known as serious adverse events (SAEs), have been observed that may limit use. Data based on Calando’s study were published in the prestigious journal, *Nature*, on March 21, 2010 in an advance online edition. The article, titled, “Evidence of RNAi in humans from systemically administered siRNA via targeted nanoparticles,” can be viewed at: <http://www.nature.com/nature/journal/vaop/ncurrent/full/nature08956.html>. Further discussion of the article and the data may also be viewed at: <http://www.nature.com/news/2010/100321/full/news.2010.138.html>.

The study was led by Professor Mark E. Davis and a team of scientists at Caltech. It also included researchers and clinicians from UCLA and South Texas Accelerated Research Therapeutics (START), the two sites conducting Calando's clinical trial. The trial, which is investigating the safety and efficacy of drug candidate CALAA-01 and the broader RONDEL nanoparticle delivery system, represented the first time siRNA was systemically administered using a delivery system and the first use of siRNA against cancer in humans. CALAA-01 and the RONDEL™ delivery system widened their lead in the siRNA delivery field with the newly published data, which include:

- Detection of RONDEL siRNA nanoparticles inside cells biopsied from tumors, demonstrating that RONDEL is capable of shuttling siRNA into tumors after being infused into the bloodstream of patients;
- Presence of RONDEL inside tumors in a dose-dependent manner, meaning that the higher a dose administered to a patient, the higher number of nanoparticles reach the intended target;
- Specific reduction in target mRNA (often referred to as “mRNA knockdown”) encoding for the M2 subunit of ribonucleotide reductase (RRM2), a widely-recognized cancer target that CALAA-01 is engineered to decrease;
- Specific reduction in target RRM2 protein levels (often referred to as “protein knockdown”);
- Indication that the mRNA and protein knockdown are mediated by delivered siRNAs and the RNAi mechanism as evidenced by accepted 5'-RACE analysis, proving that RONDEL is capable of enabling RNAi in humans.

For the past decade, the field of RNAi therapeutics has been the focus of much investigational effort and investment. RNAi as a platform is widely considered a potentially revolutionary new way of treating a wide array of diverse diseases, including many conditions that are currently considered “undruggable”. It is an extremely powerful therapeutic tool because the production of any protein can potentially be “turned down” in a very specific way. As a result, investment in RNAi therapeutics has been widespread and is a major focus by most large pharmaceutical companies. However, the promise of RNAi as a new therapeutic class has not yet been realized. This has been, in large part, due to the lack of an effective and safe system for delivering highly fragile siRNA to intended tissues and cells. With its deep expertise and long

experience in drug delivery technology, Calando recognized this opportunity to create significant value, and the current data suggest that it has capitalized on that opportunity.

“This breakthrough evidence provides important validation for siRNA-based therapeutics in general, as well as for our proprietary RONDEL delivery system, and for our lead siRNA therapeutic candidate, CALAA-01,” said Dr. Christopher Anzalone, CEO of Arrowhead. “We congratulate the investigational team for their exceptional work and are gratified that our many years of support and investment in this technology have made this moment in medical history possible. We believe we are nearing the time when siRNA therapeutics can begin to make a historic leap from science to applied medicine, where it can truly make a difference as viable treatments for patients with a variety of prevalent unmet medical needs.

“These important proof-of-concept data position us well as we look to the next phase of Calando’s development. Effective systemic delivery of siRNA has been referred to as the Holy Grail of RNAi therapeutics, and we have now shown that we can accomplish this in humans. We have always believed that great value would be created by the first company to demonstrate the following in humans: (1) siRNA delivery vehicles inside tumor cells; (2) target mRNA knockdown; (3) target protein knockdown; and (4) evidence that effects were mediated by the RNAi mechanism. We have now shown these, so we continue to see Calando as an attractive candidate for partnering and licensing opportunities both with respect to CALAA-01 as a specific drug candidate, as well as with RONDEL as a broad, flexible siRNA delivery system for delivering virtually any other oncology-related siRNA sequence. We are now focused on treating more patients at both UCLA and START. Importantly, we are not seeing drug-related SAEs, so while we have entered a dose range capable of triggering RNAi, we believe we are still far from a maximum tolerated dose (MTD). We intend to continue to escalate doses in search of that MTD.” Dr. Anzalone concluded.

Calando’s RONDEL siRNA delivery platform is designed to self-assemble with any siRNA therapeutic and to easily incorporate many different targeting molecules, making the platform potentially applicable to many disease indications beyond cancer. Importantly, the sugar-based system has not shown the immune system activation caused by other lipid-based siRNA delivery systems in pre-clinical and clinical development.

## **Conference Call**

Arrowhead Research will conduct a conference call on Tuesday, March 23, 2010 at 1:30 p.m. Pacific time to discuss the data and its implications. To participate in the conference call, please dial (877) 407-4134 toll free from the US or Canada, or (201) 689-8430 from outside the US. Investors may also access a live audio web cast of this conference call on the Company's website at [www.arrowheadresearch.com](http://www.arrowheadresearch.com).

A replay of the webcast will be available approximately two hours after the conclusion of the call. The webcast replay will remain available for 90 days. An audio replay will also be available approximately two hours after the conclusion of the call and will be made available until Friday, March 26, 2010. The audio replay can be accessed by dialing 877-660-6853 toll free from the US or Canada, or 201-612-7415 internationally, and entering account number 356 and encore passcode number 347571.

## **About RONDEL™**

Calando's RONDEL delivery system extends the reach of RNAi therapeutics by answering the new field's most pressing need — an effective and safe systemic delivery method.

The RONDEL system takes advantage of molecular forces that generate self-assembly of an siRNA containing nanoparticle therapeutic. Comprised of three components and siRNA, the system is engineered to form targeted, stabilized, siRNA-containing nanoparticles of less than 100nm in diameter that target specific tissues and fully protect the siRNA from degradation in serum.

Upon delivery to the target cell, the nanoparticle binds to membrane receptors on the cell surface and the siRNA-containing nanoparticle is taken into the cell by endocytosis. There, chemistry built into the system unpacks the siRNA from the delivery vehicle. The siRNA is deposited into the cytoplasm of the cell where it can access the cellular machinery for RNA interference.

Benefits of the RONDEL system include more effective delivery, modular design to allow easy exchange of the active siRNA ingredient and targeting agent, fewer immune reactions and increased stability. RONDEL is also designed to work with human physiology and cell biology to overcome the extra- and intra-cellular barriers to siRNA delivery.

## **About CALAA-01**

CALAA-01, Calando's leading drug candidate, is a combination of RONDEL™ and a patented siRNA targeting the M2 subunit of ribonucleotide reductase, a clinically-validated cancer target. Ribonucleotide reductase catalyzes the conversion of ribonucleosides to deoxyribonucleosides and is necessary for DNA synthesis and replication; it is a critical component in the proliferation of cancer cells. Calando's siRNA and CALAA-01 have demonstrated potent anti-proliferative activity across multiple types of cancer cells. The targeting agent in CALAA-01 is transferrin, a blood plasma protein for iron delivery. Transferrin receptors have been shown to be up regulated in many types of cancer cells.

### **About the CALAA-01 Phase I Trial**

This is an open-label, dose-escalating study of the safety of intravenous CALAA-01 in adults with solid tumors refractory to standard-of-care therapies. Patients who satisfy the inclusion and exclusion criteria receive two, 21-day cycles of CALAA-01. A cycle consists of four infusions administered on days 1, 3, 8, and 10 followed by 11 days of rest. If safe, a second 21-day cycle is administered consisting of infusions on days 22, 24, 29, and 31 followed by 11 days of rest. For information about the CALAA-01 clinical trials, please visit [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

### **About Arrowhead Research Corporation**

Arrowhead Research Corporation ([www.arrowheadresearch.com](http://www.arrowheadresearch.com)) (NASDAQ: ARWR) is a nanotechnology company commercializing new technologies in the areas of life sciences and electronics. Arrowhead is seeking to build value for shareholders through the progress of its subsidiaries and investments. Currently, Arrowhead is focused primarily on its two majority owned subsidiaries; Unidym, a leader in carbon nanotube technology for electronic applications, and Calando, at the forefront of clinical application of RNAi delivery technology. Arrowhead also has minority investments in two privately held nanobiotech companies.

### **About Calando Pharmaceuticals, Inc.**

Calando ([www.calandopharma.com](http://www.calandopharma.com)), a majority-owned subsidiary of Arrowhead Research Corporation, is a clinical stage nanobiotechnology company at the forefront of RNAi therapeutics. Calando develops nanoparticle therapeutics that use patented sugar (cyclodextrin)-based polymer technologies as a drug delivery system for siRNA. Engineered to reduce the debilitating effects of cancer treatment, the proprietary molecules are designed to improve the safety and efficacy of cancer therapeutics using siRNA as the active ingredient. The target-agnostic platform technology has the potential to be applied to a wide range of diseases beyond cancer as well as to therapeutic classes beyond siRNA therapeutics.

### **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. For example, there can be no assurance that Calando's technology will be successfully developed or that early-stage clinical results will be replicated in larger subsequent trials. Arrowhead Research Corporation's Annual Report on Form 10-K and 10-K/A, recent and forthcoming Quarterly Reports on Form 10-Q and 10-Q/A, recent Current Reports on Forms 8-K and 8-K/A, our Registration Statements on Form S-1, and other SEC filings discuss these and other important risk factors that may affect our business, results of operations and financial condition. We disclaim any intent to revise or update publicly any forward-looking statements.*

###