



Drug Delivery System Unlocks Promise of RNAi Therapeutics

Calando's siRNA Delivery System
Provides First in Human
Demonstration of siRNA activity
using Targeted Delivery and
Systemic Administration

Calando Pharmaceuticals is a clinical stage oncology drug delivery company at the forefront of RNA interference (RNAi), a recently discovered cellular mechanism with the potential to provide powerful new treatments for diseases such as cancer, hepatitis, HIV and others. The lack of an effective delivery method has been a key roadblock to the development of RNAi-based drugs. Calando's ongoing Phase I trial is providing data that demonstrates the effectiveness of its RONDEL™ drug delivery vehicle in overcoming this difficulty and validates the use of siRNA gene specific therapeutic. Calando's Phase I trial 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. Calando expects to announce complete trial results in 2010.

RNA Interference

RNAi is a naturally occurring mechanism for the regulation of gene expression that has the potential to selectively inhibit the activity of, or "silence," any gene. Since many diseases are the result of inappropriate gene activity, RNAi presents the potential for a new and powerful treatment of a variety of human diseases by "turning-off" or "silencing" genes in a sequence specific manner. The mechanism is mediated by a form of RNA called siRNA (small interfering RNA). Successful application of siRNA therapeutics represents an entirely new and potentially more effective method for treating diseases.

Landmark Clinical Results

In April 2008, Calando initiated a Phase 1 clinical trial in patients with its lead RNAi product candidate, CALAA-01. CALAA-01 is a formulation of a proprietary siRNA targeting cancer with Calando's RONDEL siRNA delivery components. In a publication of the prestigious journal of science, *Nature*, a Caltech-led team of scientists and clinicians report preliminary results from the Phase 1 clinical trial of CALAA-01.

Study data show:

- ◆ Delivery of functional siRNA to tumor cells
- ◆ RNAi mediated mRNA knock-down
- ◆ RNAi mediated protein knock-down
- ◆ Sequence specific mRNA cleavage fragments

Analysis was performed on biopsy samples obtained from melanoma patients before and after treatment. Samples were blinded and independently verified.

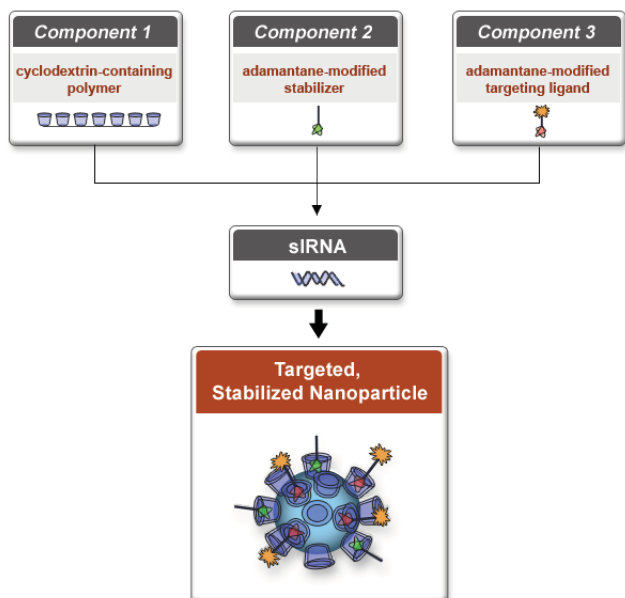
CALAA-01 is showing a strong safety profile with no significant dose limiting toxicities observed so far in the trial.

About RONDEL

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 during systemic administration.

Upon delivery to the target cell, the nanoparticle binds to 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 enters 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 agents, 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.



Financial Implications

Calando's RONDEL delivery system extends the reach of RNAi therapy by answering the new field's most pressing need — an effective and safe systemic delivery method. For the past decade, siRNA therapeutics has been the focus of intense investigational effort and an estimated nearly \$3 billion of investment. RNAi therapeutics is widely considered to have the potential to be the next major drug development engine after small molecules and recombinant proteins. As a result, investment in RNAi therapeutics has been widespread, including most of the major pharmaceutical companies. In order to unlock its full potential, systemic delivery technologies that allow the siRNA to reach its site of desired activity are critically needed. It is expected that technologies that can provide proof-of-concept for such gene knockdown in man will be highly valued by the field. The study data are expected to make Calando an attractive partnering or acquisition target for the many pharma and biotech companies active in the field.



Calando is a majority-owned subsidiary of Arrowhead Research Corporation (NASDAQ: ARWR).

This document 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 current expectations and speak only as of the date hereof. Actual results may differ materially and adversely from those expressed in any forward-looking statements as a result of various factors and uncertainties. Arrowhead Research's most recent Annual Report on Form 10-K and subsequent Quarterly Reports on Form 10-Q and other SEC filings discuss some of the important risk factors that may affect its business, results of operations and financial condition. Arrowhead undertakes no obligation to revise or update publicly any forward-looking statements for any reason.