

## Sirna Therapeutics Selects Development Candidate for Its Hepatitis C Antiviral Program

### Systemically Delivered siRNA Designed to Dramatically Reduce Drug Resistant Variants

SAN FRANCISCO, Dec. 21 /PRNewswire-FirstCall/ -- Sirna Therapeutics, Inc. (Nasdaq: RNAI), a leading RNAi therapeutics company, announced today that it has selected Sirna-AV34, a systemically delivered, chemically modified short interfering RNA (siRNA) compound, as its candidate for advancement to human clinical testing against Hepatitis C virus. Sirna completed its preclinical evaluation of the efficacy of Sirna-AV34 and has begun cGMP manufacturing for its Phase I clinical studies. Sirna expects to initiate IND-enabling toxicology studies in the first quarter of 2006 followed by the filing of an Investigational New Drug (IND) application with the U.S. Food and Drug Administration (FDA) by the fourth quarter of 2006.

Sirna-AV34 is a systemically delivered, nanoparticle-based therapeutic targeting the Hepatitis C virus. The compound consists of multiple individual, chemically modified, siRNA sequences which target highly conserved sequences in the Hepatitis C viral genome. Sirna-AV34 is designed to inhibit viral replication and dramatically reduce the selection of drug resistant mutant variants. The design principles used in Sirna-AV34 were validated by demonstrating reduction in escape mutation frequency in the Hepatitis C virus sub-genomic replicon system in vitro. No existing therapeutic approach has the potential to broadly inhibit Hepatitis C viral replication while reducing the probability of drug resistant variants.

"We are extremely pleased by the significant progress of our Hepatitis C antiviral program," stated Sirna Senior Vice President and Chief Scientific Officer, Barry Polisky, PhD. "The selection of Sirna-AV34 as our clinical candidate reflects two major accomplishments of our research team. The first is the design, chemical modification and synthesis of a stable and potent siRNA compound which is effective broadly against the Hepatitis C virus. The second is the development of a proprietary nanoparticle delivery technology capable of efficient and specific delivery of the siRNA compound to hepatocytes. These two achievements have provided us with a unique opportunity to bring this groundbreaking therapy to the clinic."

Sirna has completed its preclinical evaluation including demonstration of systemic efficacy in both rodent and non-human primate animal models. As previously reported in a rodent model of Hepatitis B virus used as a surrogate for Hepatitis C virus, Sirna demonstrated that a chemically optimized and encapsulated siRNA had significant antiviral activity and prolonged duration of effect in vivo. Recent data from a non-human primate model of Hepatitis C replication demonstrated that Sirna's systemically delivered siRNA compound dramatically suppressed Hepatitis C viral titers via an RNA interference mechanism.

"We are very excited to be moving a systemically delivered siRNA towards the clinic," stated Roberto Gueriolini, MD, Senior Vice President and Chief Medical Officer. "Since the current treatments for chronic Hepatitis C remain highly unsatisfactory, we believe that the application of an siRNA compound targeting multiple components of the viral genome will result in a significant advancement in the treatment of this disease."

Sirna-AV34 will be manufactured at Sirna's cGMP facilities in Boulder, Colorado for both Phase I enabling toxicology studies and Phase I human clinical testing.

#### About Sirna Therapeutics

Sirna Therapeutics is a clinical-stage biotechnology company developing RNAi-based therapies for serious diseases and conditions, including age-related macular degeneration (AMD), hepatitis B and C, dermatology, asthma, Huntington's disease, diabetes and oncology. Sirna Therapeutics has presented interim Phase I clinical trial data for its most advanced compound, Sirna-027, a chemically optimized siRNA targeting the clinically validated vascular endothelial growth factor pathway to treat AMD. Sirna-027, which has been partnered with Allergan, Inc., has been shown to be safe and well tolerated with a trend toward visual acuity improvement and demonstrated biological activity. Sirna has a leading intellectual property portfolio in RNAi with 45 issued patents and over 250 pending applications worldwide. More information on Sirna Therapeutics is available on the Company's web site at <http://www.sirna.com>.

#### Safe Harbor Statement

Statements in this press release which are not strictly historical are "forward-looking" statements which should be considered as subject to many risks and uncertainties. For example, Sirna's ability to develop a treatment for Hepatitis C will require additional, much more costly clinical trials, the results of which are highly uncertain. Moreover, Sirna's ability to develop products and operate as a going concern requires significant cash to fund its operating programs. Additional risks and uncertainties include Sirna's early stage of development and short operating history, Sirna's history and expectation of losses and need to raise capital, Sirna's need to obtain clinical validation and regulatory approval for products, Sirna's need to obtain and protect intellectual property, risk of third-party patent infringement claims, Sirna's need to attract and retain qualified personnel, Sirna's need to engage collaborators, availability of materials for product

manufacturing, the highly competitive nature of the pharmaceutical market, the limited trading volume and history of volatility of Sirna's common stock, Sirna's concentration of stock ownership, and risks from relocating Sirna headquarters. These and additional risk factors are identified in Sirna's Securities and Exchange Commission filings, including the Forms 10-K and 10-Q and in other SEC filings. Sirna undertakes no obligation to revise or update any forward-looking statements in order to reflect events or circumstances that may arise after the date of this release.

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