

# Isis Initiates Phase 1 Clinical Trial of ISIS-FXIRx to Treat Clotting Disorders

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Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced the initiation of a Phase 1 study of ISIS-FXIRx, an antisense drug designed to treat clotting disorders. ISIS-FXIRx inhibits the production of Factor XI, a clotting factor that is an important component of the coagulation pathway. Because of its role in the intrinsic coagulation pathway, inhibition of Factor XI could offer an effective approach for preventing the formation of blood clots with a lower risk of bleeding.

"High levels of Factor XI are a risk factor for aberrant blood clot formation. Blood clot formation is a leading cause of morbidity and mortality associated with vascular diseases, including heart attack, deep vein thrombosis and stroke. Blood clot formation is also a common complication of surgical procedures, especially orthopedic surgeries such as knee or hip replacement. Most commonly used therapies reduce clotting, but also produce an unacceptable increase in bleeding risk," said Brett Monia, Ph.D., Vice President, Drug Discovery and Corporate Development of Isis. "In preclinical studies, ISIS-FXIRx demonstrated potent antithrombotic activity with no increase in bleeding compared with standard anti-clotting agents, including low-molecular weight heparin, warfarin and Factor Xa inhibitors, all of which increased bleeding. Furthermore, humans who are deficient in Factor XI have a lower incidence of thromboembolic events with minimal increase in bleeding risk, providing human genetic validation of this target."

"We have a growing cardiovascular franchise. ISIS-FXIRx broadens our therapeutic approaches in cardiovascular disease beyond lipid management to include anti-thrombotics. The broad applicability of our antisense technology has allowed us to build a pipeline of drugs to improve numerous aspects of cardiovascular disease," said Richard Geary, Ph.D., Senior Vice President, Development of Isis.

## **ABOUT ISIS PHARMACEUTICALS, INC.**

Isis is exploiting its expertise in RNA to discover and develop novel drugs for its product pipeline and for its partners. The Company has successfully commercialized the world's first antisense drug and has 24 drugs in development. Isis' drug development programs are focused on treating cardiovascular, metabolic, and severe neurodegenerative diseases and cancer. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Isis and Alnylam Pharmaceuticals are joint owners of Regulus Therapeutics Inc., a company focused on the discovery, development and commercialization of microRNA therapeutics. Isis also has made significant innovations beyond human therapeutics resulting in products that other companies, including Abbott, are commercializing. As an innovator in RNA-based drug discovery and development, Isis has designed and executed a patent strategy that has provided the Company with strong and extensive protection for Isis' drugs as well as all aspects of antisense drug discovery, development and manufacturing. Additional information about Isis is available at [www.isispharm.com](http://www.isispharm.com).

## **ISIS PHARMACEUTICALS' FORWARD-LOOKING STATEMENT**

This press release includes forward-looking statements regarding Isis Pharmaceuticals and the discovery and development of ISIS-FXIRx for the treatment of clotting disorders. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such drugs. Isis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Isis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2009 and its most recent quarterly report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from the Company.

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