Isis Initiates Phase 2 Study Of ISIS-FXIRX In Patients Undergoing Knee Replacement Surgery

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CARLSBAD, Calif., Oct. 29, 2012 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced the initiation of a Phase 2 comparator-controlled study evaluating ISIS-FXI$_{Rx}$ in patients undergoing knee replacement surgery, also referred to as total knee arthroplasty (TKA). ISIS-FXI$_{Rx}$ inhibits the production of Factor XI, a coagulation factor produced in the liver that is involved in the formation of clots. In this study, Isis will evaluate the effectiveness of ISIS-FXI$_{Rx}$ in reducing the number of thrombotic events in patients after TKA without increasing bleeding. The combination of robust anti-thrombotic activity with an improved safety profile to currently available anticoagulants could be broadly useful in many therapeutic settings where thrombosis is a serious problem.

"Although there are a number of anti-coagulants on the market today that are considered standard-of-care in multiple therapeutic settings, complications of bleeding associated with these medications remain high and can lead to fatal outcomes," said Harry Buller, Ph.D., M.D., professor of medicine at Academic Medical Center in Netherlands. "Factor XI is an exciting target because it plays a key role in the formation of clots but inhibiting it does not cause bleeding. Humans who are deficient in Factor XI tend to have a lower incidence of stroke and venous thrombosis with no evidence of spontaneous bleeding episodes."

The Phase 2 study is a global, multi-center, open-label, comparator-controlled study in up to 400 patients who are undergoing TKA. The study will compare ISIS-FXI$_{Rx}$ safety and activity to enoxaparin, a commonly used anti-coagulant. In a Phase 1 study in healthy volunteers, ISIS-FXI$_{Rx}$ produced robust dose-dependent, statistically significant reduction of greater than 80 percent in Factor XI activity with no bleeding events observed.

"ISIS-FXI$_{Rx}$ is one of many maturing drugs in our pipeline and represents the broad applicability of our technology to develop novel drugs for many different diseases. We believe that the safety profile observed thus far coupled with the robust activity we have seen for ISIS-FXI$_{Rx}$ in both our Phase 1 study and preclinically, suggest that this drug could have a significant benefit for patients at risk of a thrombotic event. Given the mechanism of Factor XI inhibition, we believe that the drug could be used broadly to prevent deep vein thrombosis or pulmonary embolism in many different therapeutic settings, including stroke, myocardial infarction and with surgeries such as knee or hip replacement, where additional safe and effective anti-thrombotic drugs are needed. Our earlier work suggests that ISIS-FXI$_{Rx}$ could be used in combination with existing therapies," said Sanjay Bhanot, M.D., Ph.D., vice president, clinical development and translational medicine at Isis.

"TKA is one of the leading surgeries performed worldwide each year and is associated with a high incidence of venous thromboembolism," said Brett Monia, Ph.D., senior vice president, antisense drug discovery at Isis. "By evaluating our drug in these patients, we will be able to directly compare the activity and safety of ISIS-FXI$_{Rx}$ to a commonly prescribed anti-coagulant, enoxaparin. With this proof-of-value data in hand, we believe that we will have a robust and comprehensive data package representing a significant licensing opportunity for us."

ABOUT ISIS PHARMACEUTICALS, INC.
Isis is exploiting its leadership position in antisense technology to discover and develop novel drugs for its product pipeline and for its partners. Isis' broad pipeline consists of 25 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, and cancer. Isis' partner, Genzyme, plans to commercialize Isis' lead product, KYNAMRO™, following regulatory approval. Isis' patents provide strong and extensive protection for its drugs and technology. Additional information about Isis is available at www.isispharm.com.

ISIS PHARMACEUTICALS' FORWARD-LOOKING STATEMENT
This press release includes forward-looking statements regarding the discovery, development, activity, therapeutic potential and safety of ISIS-FXI$_{Rx}$. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs, including the planned commercialization of KYNAMRO, 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, 2011 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.

In this press release, unless the context requires otherwise, "Isis," "Company," "we," "our," and "us" refers to Isis Pharmaceuticals and its subsidiaries.

SOURCE Isis Pharmaceuticals, Inc.

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