

## Isis Pharmaceuticals Initiates Phase 1 Study of ISIS-PKK Rx

May 20, 2014

CARLSBAD, Calif., May 20, 2014 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that it initiated a Phase 1 clinical study of ISIS-PKK<sub>Rx</sub>. ISIS-PKK<sub>Rx</sub> is an antisense drug in development to treat patients with hereditary angioedema (HAE). HAE is a rare genetic disease that is characterized by rapid and painful attacks of inflammation in the hands, feet, limbs, face, abdomen, larynx and trachea. HAE affects approximately 20,000 patients in the United States and Europe and can be fatal if swelling occurs in the larynx. ISIS-PKK<sub>Rx</sub> is designed to alter the course of HAE and therefore has the potential to be best-in-class for the treatment of HAE.



"ISIS-PKK<sub>Rx</sub> targets the prekallikren (PKK), a protein produced in the liver that plays an important role in the activation of inflammatory mediators associated with acute attacks of HAE. This is a well-validated pathway and one that is easily accessible using our antisense technology. In our preclinical models of HAE, we observed significant reductions of PKK that were associated with the amelioration of symptoms of disease, including the prevention of tissue swelling," said Brett Monia, Ph.D., senior vice president of antisense drug discovery at Isis. "By inhibiting the production of PKK, we believe that ISIS-PKK<sub>Rx</sub> could be a best-in-class prophylactic treatment for patients with HAE."

ISIS-PKK<sub>Rx</sub> is a wholly owned Isis drug in development for the prevention of HAE attacks. HAE is a rare and severe disease in which patients have acute, frequent, debilitating and sometimes fatal attacks. ISIS-PKK<sub>Rx</sub> is an antisense drug designed to reduce the production of PKK in the liver and therefore alter the course of disease in patients who have severe HAE attacks. Isis plans to complete the Phase 1 study of ISIS-PKK<sub>Rx</sub> and initiate a Phase 2 study in patients with HAE.

### **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 32 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, including neurological disorders, and cancer. Isis' partner, Genzyme, is commercializing Isis' lead product, KYNAMRO<sup>®</sup>, in the United States and other countries for the treatment of patients with homozygous FH. Isis' patents provide strong and extensive protection for its drugs and technology. 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 the discovery, development, activity, therapeutic and commercial potential and safety of ISIS-PKK<sub>Rx</sub> for the treatment of patients with HAE. 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, 2013, 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.

Isis Pharmaceuticals<sup>®</sup> is a registered trademark of Isis Pharmaceuticals, Inc. KYNAMRO<sup>®</sup> is a registered trademark of Genzyme Corporation.

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