ISIS Pharmaceuticals Reports Positive Phase 1 Data Demonstrating ISIS-PKK Rx Produces Significant Reductions in Prekallikrein Levels

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CARLSBAD, Calif., Feb. 24, 2015 /PRNewswire/ -- Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today positive results from a Phase 1 study with ISIS-PKK$_{Rx}$. In this study, healthy volunteers treated with ISIS-PKK$_{Rx}$ achieved dose-dependent reductions of up to 95 percent in prekallikrein, or PKK. ISIS-PKK$_{Rx}$ is a RNA-targeted antisense drug designed to inhibit the production of PKK for the prophylactic treatment of hereditary angioedema (HAE). HAE is a severe and 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 airway.

"Despite currently available prophylactic therapies, we believe that there remains a significant need for patients with HAE. PKK is a protein produced in the liver that plays an important role in the activation of inflammatory mediators associated with acute attacks of HAE. Since the inappropriate activation of PKK leads to HAE, these data could be predictive of the potential benefit we hope to see in patients with HAE," said Brett Monia, Ph.D., senior vice president of antisense drug discovery at Isis Pharmaceuticals. "We are very encouraged with these early clinical data demonstrating that ISIS-PKK$_{Rx}$ can significantly and dose-dependently lower its target, PKK. In addition to the robust PKK lowering we observed in this study, ISIS-PKK$_{Rx}$ was well tolerated and the safety profile observed to date supports our plan to evaluate ISIS-PKK$_{Rx}$ as prophylaxis for patients who suffer from HAE attacks. We plan to initiate a Phase 2 study later this year."

The Phase 1 study of ISIS-PKK$_{Rx}$ was a blinded, placebo-controlled, dose-escalation study in healthy volunteers. The study was designed to assess the safety, tolerability and pharmacokinetics of ISIS-PKK$_{Rx}$. ISIS-PKK$_{Rx}$ was evaluated in single and multiple doses ranging from 50 mg per week up to 400 mg per week for the single dose and 100 mg up to 400 mg for the multiple doses. After only 3 weeks of dosing, subjects in the 100, 200, 300 and 400 mg multiple-dose cohorts displayed a mean reduction of PKK of 33, 69, 87 and 92 percent, respectively, from baseline. In this study, ISIS-PKK$_{Rx}$ was generally well tolerated.

"ISIS-PKK$_{Rx}$ is a new addition to our severe and rare disease franchise, and one that we plan to develop into later-stage clinical studies on our own. We have the internal resources and capabilities to easily and rapidly move this program forward in patients with HAE," said B. Lynne Parshall, chief operating officer at Isis Pharmaceuticals. "ISIS-PKK$_{Rx}$ is also a product of our improved second generation, or generation 2-plus, technology, which enables us to consistently develop more potent and better tolerated drugs."

ABOUT ISIS PHARMACEUTICALS, INC.

Isis is exploiting its leadership position in RNA-targeted technology to discover and develop novel drugs for its product pipeline and for its partners. Isis' broad pipeline consists of 34 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®, in the United States and other countries for the treatment of patients with homozygous FH. Isis has numerous drugs in Phase 3 development in severe/rare diseases and cardiovascular diseases. These include ISIS-APOCIII$_{Rx}$, a drug Isis is developing through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with severely high triglycerides, such as patients with familial chylomicronemia syndrome; ISIS-TTR$_{Rx}$, a drug Isis is developing with GSK to treat patients with the polyneuropathy form of TTR amyloidosis; and, ISIS-SMN$_{Rx}$, a drug Isis is developing with Biogen Idec to treat infants and children with spinal muscular atrophy, a severe and rare neuromuscular disease. 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 and commercial potential and safety of ISIS-PKK$_{Rx}$ 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.

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