Isis Pharmaceuticals Initiates Additional Phase II Clinical Trial Of Alicaforsen, ISIS 2302, In Patients With Ulcerative Colitis

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CARLSBAD, Calif., April 8 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today it has initiated a Phase II clinical trial of alicaforsen (ISIS 2302), an antisense inhibitor of intercellular adhesion molecule-1 (ICAM-1), in people with active ulcerative colitis (UC). The study will compare the safety and efficacy of different dosing-regimens of the enema formulation of alicaforsen to placebo. An intravenous formulation of alicaforsen is being evaluated in a Phase III clinical program in people with Crohn's disease.

"Alicaforsen is one of the most advanced drugs in the company's antisense pipeline," said Mark Wedel, Isis' Vice President of Clinical Research and Chief Medical Officer. "Based on the data from initial studies of this drug for the treatment of Crohn's disease and ulcerative colitis, we are enthusiastic about the potential of alicaforsen in inflammatory bowel disease."

In the randomized, double-masked, placebo-controlled Phase II study approximately 100 patients will be enrolled at sites in the U.S. and Europe. The primary endpoint of the study is improvement in the Disease Activity Index (DAI) upon completion of the six-week dosing period. Patients with an improvement in DAI will be followed for up to a year. DAI is a common clinical index scoring system for the severity of symptoms related to UC. This trial is being conducted in parallel with a Phase II 170-patient study comparing alicaforsen enema to mesalamine enema.

In October 2001, Isis reported results from a six-month, 40-patient Phase II study of alicaforsen enema in UC. In the study, patients demonstrated median improvement in DAI and Clinical Activity Index (CAI) scores (73% and 58%, respectively) after one month of nightly 240 mg alicaforsen enemas. CAI is a commonly used clinical scoring system for the severity of symptoms and quality of life related to UC. The improvements in DAI and CAI were well maintained at month three and month six of the study. No patients in the 240 mg dose group required additional medications during the six-month trial. No serious adverse events were observed in this trial.

Alicaforsen is an antisense inhibitor of ICAM-1, a molecule that plays a key role in a wide range of inflammatory and autoimmune conditions such as UC. ICAM-1 is part of a family of molecules, the cellular adhesion molecules, that can be found on the surface of virtually every cell in the body, including cells that line the colon. It is involved in the production of immune factors that cause the inflammatory response in UC.

According to the Crohn's and Colitis Foundation of America, UC is an inflammatory disease of the colon, the large intestine, which is characterized by inflammation and ulceration of the innermost lining of the colon. Symptoms characteristically include diarrhea, rectal bleeding and abdominal pain. UC disease differs from another inflammatory bowel disease (IBD), Crohn's disease, as it only affects the colon. Up to one million people have IBD, evenly split between Crohn's disease and UC. According to the European Federation of Crohn's and Ulcerative Colitis Associations, a similar number of people are affected in Europe.

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs. The company has commercialized its first product, Vitravene® (fomivirsen), to treat CMV-induced retinitis in AIDS patients. In addition, Isis has 12 antisense products in its development pipeline with two in late-stage development and five in Phase II human clinical trials. Affinitak™, an inhibitor of PKC-alpha, is in a Phase III trial for non-small cell lung cancer and alicaforsen (ISIS 2302), an ICAM-1 inhibitor, is in two Phase III trials for Crohn's disease. Isis has a broad patent estate as the owner or exclusive licensee of nearly 1,200 issued patents worldwide. Isis' GeneTrove™ division uses antisense to assist pharmaceutical industry partners in validating and prioritizing potential gene targets through customized services. Ibis Therapeutics™ is a division focused on the development of a diagnostic tool to detect biological agents and the discovery of small molecule drugs that bind to RNA. Additional information about Isis is available at www.isispharm.com.

This press release contains forward-looking statements about the potential of the investigational compound alicaforsen (ISIS 2302) in the treatment of ulcerative colitis and Crohn's disease and the potential of Isis' drug development programs. Any statement describing a goal, expectation, intention or belief of the company 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 financing such activities. Actual results could differ materially from those projected in this release. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' research and development programs are described in additional detail in the company's Annual Report on Form 10-K for the period ended December 31, 2002, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

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