Isis Pharmaceuticals Initiates Phase II Clinical Trial of Alicaforsen, ISIS 2302, in Patients With Ulcerative Colitis

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CARLSBAD, Calif., Nov. 21 /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 an enema formulation of alicaforsen to mesalamine enema, a widely used topical medication for UC. An intravenous formulation of alicaforsen is being evaluated in a Phase III clinical program in people with Crohn's disease.

"The early clinical data on the enema formulation of alicaforsen in ulcerative colitis are exciting. We are pleased to move this drug forward in development and to continue to expand the types of diseases that may be treated with this novel compound," said F. Andrew Dorr, M.D., Isis' Vice President and Chief Medical Officer. "Current treatment options for ulcerative colitis are limited, and we are optimistic that alicaforsen may be able to help address this critical medical need."

The randomized, double-masked, active-controlled Phase II study is planned to enroll approximately 170 patients at 25 U.S. sites. Patients will be given alicaforsen enema or mesalamine enema once nightly for six weeks. The primary endpoint of the study is improvement in the Disease Activity Index (DAI) upon completion of the six-week dosing period and during a 12-month follow-up period. DAI is a common clinical index scoring system for the severity of symptoms related to UC.

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. Alicaforsen was well tolerated during the study.

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, Crohn's disease, as it only affects the colon. UC affects approximately 500,000 people in the United States.

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® (formivirsen), to treat CMV-induced retinitis in AIDS patients. In addition, Isis has 13 antisense products in its development pipeline, with two in late-stage development and six in Phase II human clinical trials. Affinitac™ (formerly called LY900003 and ISIS 3521), an inhibitor of PKC-alpha, is in Phase III trials for non-small cell lung cancer, and alicaforsen (ISIS 2302), an ICAM-1 inhibitor, is in Phase III human clinical trials for Crohn's disease. Isis has a broad patent estate, as the owner or exclusive licensee of more than 1000 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 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 and quarterly report on Form 10-Q for the periods ended December 31, 2001 and Sept. 30, 2002, respectively, which are on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

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