Isis Pharmaceuticals Initiates European Phase III Clinical Trial Of Alicaforsen, ISIS 2302, in Crohn's Disease

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CARLSBAD, Calif., June 25 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today it has initiated a planned second Phase III clinical trial of alicaforsen (ISIS 2302), an antisense inhibitor of Intercellular Adhesion Molecule-1 (ICAM-1), in people with active Crohn's disease. The study will be conducted in Europe and is designed to evaluate the safety and efficacy of alicaforsen. The company initiated a North American Phase III trial of alicaforsen in patients with Crohn's disease in November 2001.

Isis plans to enroll 150 patients at 35 sites in Europe in this randomized, double-masked, placebo-controlled study. As in the North American Phase III trial, the primary endpoint of the study is clinical remission as defined by a Crohn's disease activity index score (CDAI) of less than 150, with no increase in the use of medications or need for surgery. The CDAI is a common clinical scoring system for the severity of symptoms related to Crohn's disease.

Alicaforsen (ISIS 2302) 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 Crohn's disease. It is involved in the recruitment and activation of immune cells associated with the inflammatory response in Crohn's disease. ICAM-1 is part of a molecular family (known as Cellular Adhesion Molecules, or CAMs) that can be found on the surface of virtually every cell in the body, including cells that line the inflamed gastrointestinal (GI) tract. Alicaforsen (ISIS 2302) is also being studied in an enema formulation for patients with ulcerative colitis.

According to the Crohn's and Colitis Foundation of America, Crohn's disease is a chronic inflammatory disease of the GI tract. It predominates in the intestine (ileum) and the large intestine (colon), but may occur in any section of the GI tract. Crohn's disease usually causes diarrhea, abdominal pain, fever and occasional rectal bleeding. It may also cause appetite loss resulting in weight loss. Symptoms can range from mild to severe, but in general people with Crohn's disease can lead active and productive lives.

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 900 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 Crohn's disease and ulcerative colitis. 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, 2001, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

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