



Isis Pharmaceuticals Reports Phase II Study Results Of Topical Alicaforseen, ISIS 2302, in Psoriasis

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CARLSBAD, Calif., Feb. 25 /PRNewswire-FirstCall/ -- In a Phase II clinical trial of patients with mild to moderate plaque psoriasis, a topical formulation of alicaforseen (ISIS 2302) demonstrated a statistically significant improvement in Investigator's Global Response Score (IGRS) at week four ($p=0.02$) and a positive trend toward improvement at week eight ($p=0.206$). IGRS is a subjective 0-5 point scale of disease improvement. Additionally, alicaforseen achieved a 31 percent improvement from baseline measurement in plaque induration, or thickness, at both weeks four and eight. This effect was statistically significant ($p=0.013$ and $p=0.034$, respectively), and confirmed trends observed in a prior study. There were no significant adverse events observed in the trial. Alicaforseen drug concentrations observed in skin biopsies also correlated with dose regimen, supporting the potential of antisense topical drugs to treat diseases of the skin. The results of this study were presented in a poster this weekend at the 60th Annual Meeting of the American Academy of Dermatology in New Orleans. As part of its dermatological drug discovery program, Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) is also developing a topical formulation of ISIS 104838, a second-generation antisense inhibitor of TNF-alpha, in psoriasis.

The double-masked, paired-plaque Phase II clinical trial compared four percent topical alicaforseen cream to placebo in 31 patients with mild to moderate plaque psoriasis. In the study, patients applied alicaforseen or placebo to each of two matched psoriatic plaques. Fifteen patients in the study applied the creams once per day. Sixteen patients applied the creams twice per day. Patients were dosed for eight weeks and followed for twelve weeks. Biopsies of plaques from six patients were taken to evaluate the pharmacokinetic properties of alicaforseen. Other endpoints in the study included scaling and erythema, or redness.

"We are encouraged to have observed evidence of activity of topical alicaforseen in psoriasis in two studies. In this latest clinical trial, the drug produced statistically significant reduction in induration and modest therapeutic benefit," said F. Andrew Dorr, M.D., Isis' Vice President and Chief Medical Officer. "Additionally, the drug was very well tolerated, demonstrating that topical antisense drugs may be of value in treating dermatological diseases. We will continue to evaluate the role of ICAM-1 in psoriasis and other skin diseases such as atopic dermatitis. We will also consider future trials to evaluate alicaforseen in combination with other psoriatic medications or in other skin diseases as part of our overall drug discovery and development program in dermatology."

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 products in its development pipeline, with two in late-stage development and six in Phase II human clinical trials. LY900003 (ISIS 3521), an inhibitor of PKC-alpha, is in Phase III trials for non-small cell lung cancer, and alicaforseen (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 nearly 900 issued patents worldwide. Isis' GeneTrove™ division uses antisense to assist pharmaceutical industry partners in validating and prioritizing potential gene targets through customized services and access to an extensive gene function database. 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 development and therapeutic potential of ISIS 2302 and other Isis drugs in psoriasis and diseases of the skin. Any statement describing an 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 Quarterly Report on Form 10Q, for the period ended September 30, 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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