HepaSense Initiates Phase II Clinical Trial of ISIS 14803 in Hepatitis C

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CARLSBAD, Calif., March 21 /PRNewswire-FirstCall/ -- HepaSense™, Ltd., a joint venture of Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) and Elan Corporation, plc (NYSE: ELN) ("Elan"), of Dublin, Ireland, announced today that it has initiated a Phase II clinical trial of ISIS 14803 in patients with chronic Hepatitis C Virus infections (HCV). The Phase II clinical trial will evaluate the safety and tolerability of ISIS 14803, an antisense drug that inhibits HCV replication, when administered by intravenous infusion (IV).

The open-label, dose escalation Phase II study is planned to enroll 40 patients at six sites across the U.S. Two dosing regimens of ISIS 14803 administered IV over 12 weeks will be studied. The primary endpoint in the clinical trial is reduction in viral titer, or level of virus in blood.

"We are pleased to continue the development of ISIS 14803 in HCV, a disease where improved therapies are much needed. We observed encouraging results in the initial Phase I/II trial that provided us with a foundation for further study of this drug," said F. Andrew Dorr, M.D., Isis' Vice President and Chief Medical Officer. "Results from this study, in which patients will receive doses of ISIS 14803 for three months, will help us determine the next steps in developing this drug."

Ivan Lieberburg, Elan's Chief Scientific and Medical Officer stated, "Isis' approach to HCV therapy is unique in the field and we look forward to the results of this study."

In June 2001, HepaSense reported preliminary data from a small group of patients in a Phase I/II clinical trial in which ISIS 14803 demonstrated antiviral activity by reducing viral titers in patients with drug-resistant chronic HCV. Patients in the study received escalating doses of ISIS 14803 by IV for one month. All patients in the report had the most common and drug resistant form of HCV, genotype 1, and all but one patient had failed previous interferon-based therapy. Clinical trials of ISIS 14803 using Elan's MEDIPAD™ Drug Delivery System, a minimally invasive microinfusion pump, are planned for the future.

Hepatitis C causes chronic inflammation of the liver that can go undetected for months or years but is frequently progressive, resulting in life-threatening impairment of liver function. Persistent liver inflammation causes ongoing injury to the cells of the liver. It can lead to liver scarring called cirrhosis, liver failure, possibly liver cancer and death due to the complications of these hepatic insults. Liver complications of chronic HCV infections are the most frequent indication for liver transplants.

According to the National Institute of Diabetes, Digestive and Kidney Diseases (NIDDK), HCV is one of the most important causes of chronic liver disease in the U. S. It accounts for approximately 20 percent of acute viral hepatitis, 60 to 70 percent of chronic hepatitis, and 30 percent of cirrhosis, end-stage liver disease, and liver cancer. Nearly four million Americans, or 1.8 percent of the U.S. population, have antibody to HCV (anti-HCV), indicating ongoing or previous infection with the virus. HCV causes an estimated 8,000 to 10,000 deaths annually in the U.S.

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 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 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. 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 concerning HepaSense and the profile and development of ISIS 14803 and its prospects, planned development activities and therapeutic potential for our pipeline products. 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, the reader is 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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