Isis Pharmaceuticals Reports Preliminary Phase II Data On ISIS 2503 Plus Chemotherapy in Pancreatic Cancer

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Trial Continues

CARLSBAD, Calif., April 10 /PRNewswire-FirstCall/ -- In a planned interim analysis of a Phase II trial of the antisense anti-cancer compound ISIS 2503 in combination with gemcitabine, clinical investigators observed six months or longer survival in patients with pancreatic cancer, surpassing the primary endpoint of the study's defined criteria for success. The Phase II trial design and endpoints of improvement in patient survival and in patient response rates were established by the North Central Cancer Trial Group (NCCTG), a leading North American cancer research group with a research base located at Mayo Cancer Center in Rochester, Minnesota. The NCCTG is conducting the Phase II study. Data from this interim analysis were presented yesterday at the 93rd Annual Meeting of the American Association for Cancer Research (AACR) in San Francisco, by Steven R. Alberts, M.D., a Mayo Clinic oncologist and lead researcher on this study. ISIS 2503 is being developed by Isis Pharmaceuticals, Inc. (Nasdaq: ISIS).

The NCCTG's predetermined criteria for success at the interim analysis of the Phase II trial was the survival of nine or more patients for six months or longer. The prospectively planned interim analysis of this open-label Phase II trial was performed after the first 20 patients were enrolled in the study, received treatment with ISIS 2503 and gemcitabine, a standard chemotherapy agent, and completed six months of follow-up. The median survival time for these 20 patients at the time of the interim analysis in the trial was 6.7 months, with 60 percent of patients (12 of 20) surviving six months or longer.

The interim analysis also evaluated patient response rates. Twenty percent of patients receiving ISIS 2503 in the study achieved a complete or partial response. Complete response is defined as no detectable evidence of cancer by standard medical techniques. Partial response is a 50 percent or greater reduction in measurable tumor size on X-ray. The safety profile observed in the study to date does not appear to be meaningfully different from that of gemcitabine alone.

"Pancreatic cancer is one of the most difficult cancers to treat, and new therapies are needed. While the data from this Phase II trial are early, ISIS 2503 plus gemcitabine appears to be a promising combination that warrants further study," said Dr. Alberts.

In total, 48 patients with locally advanced or metastatic pancreatic cancer have been enrolled in this trial. Each patient receives a 6 mg/kg/day dose of ISIS 2503 through continuous intravenous infusion for two weeks of a three week cycle, as well as standard doses of gemcitabine on days one and eight. Patients in the trial have had no prior chemotherapy treatment for advanced disease. Results for the entire group of patients are likely to be presented at a scientific meeting late this year or early 2003.

"We are encouraged by the data reported yesterday, as they suggest that ISIS 2503 may be of value in this deadly disease. ISIS 2503 is the second anti-cancer drug to emerge from Isis' extensive pipeline, and one of eight promising antisense products in human clinical trials for a variety of important therapeutic areas," said F. Andrew Dorr, M.D., Isis' Vice President and Chief Medical Officer. "We look forward to continuing the development of this drug in pancreatic cancer as well as other tumor types."

Beyond pancreatic cancer, Isis is evaluating the activity of ISIS 2503 in combination with chemotherapy in two Phase II clinical trials in patients with either metastatic breast or non-small cell lung cancer.

ISIS 2503 is an antisense anti-cancer compound that inhibits the expression of Harvey-ras or H-ras, a molecule known to be involved in the development and maintenance of human cancers. H-ras is a member of the ras family of proteins, which also include N-ras, Ki-rasA, and Ki-rasB, that regulate the process by which cells receive and send signals that affect their behavior. Through an antisense mechanism, ISIS 2503 binds to an mRNA sequence specific to Ha-ras, and thus selectively inhibits production of this protein without inhibiting production of other proteins in the ras family. The specificity of antisense technology makes it possible to inhibit a single family member that may play a role in disease while allowing other members of the family to continue to perform normal cellular functions. This high degree of selectivity may provide antisense drugs substantial advantage over traditional small molecule drugs in many difficult to treat diseases.

According to the American Cancer Society (ACS), pancreatic cancer is the fourth leading cause of cancer death in men and women. The ACS estimates that in 2002, about 30,300 people in the U.S. will be diagnosed with pancreatic cancer and about 29,700 will die of the disease. Less than two out of every 10 patients with cancer of the pancreas live at least one year after the cancer is found, but only a very few will survive for five years.

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 13 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 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 ISIS 2503 in the treatment of pancreatic and other types of cancer. 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 10K, 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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