Isis Pharmaceuticals Provides Summary of American Society of Clinical Oncology Data Presentations on Anti-Cancer Antisense Drugs in Development

June 3, 2003

CHICAGO, June 3 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today reported the presentation of results from three studies of its anti-cancer antisense drugs at the 39th Annual Meeting of the American Society of Clinical Oncology (ASCO). Data presented included an overview of the findings previously reported by Isis from a Phase III trial of Affinitak™, an antisense drug which inhibits PKC-alpha, in combination with chemotherapy in patients with non-small cell lung cancer (NSCLC). Also presented were final results from two Phase II studies of ISIS 2503, an antisense agent targeting Ha-ras, in combination with chemotherapy in patients with pancreatic and breast cancers. Principal investigators from each of the studies presented their respective trial results during the ASCO meeting, May 31 - June 3.

Data Presentation Key Highlights

PHASE III TRIAL OF AFFINITAK IN NSCLC

* Results presented from the Phase III trial that evaluated survival of 616 patients who received the chemotherapy regimen of carboplatin and paclitaxel with or without Affinitak were consistent with the study's initial analysis as previously reported in a press release issued on March 17, 2003.

* Affinitak is being developed for the treatment of NSCLC through an alliance between Eli Lilly and Company (NYSE: LLY) and Isis. Lilly is conducting a second Phase III clinical trial that is evaluating Affinitak in combination with Gemzar and cisplation in patients with NSCLC. Lilly and Isis will make development decisions regarding Affinitak based on the results of this trial.

PHASE II TRIAL OF ISIS 2503 IN PANCREATIC CANCER

Key findings were as follows from an open-label Phase II clinical trial of 48 chemotherapy-naive patients with locally advanced or metastatic pancreatic cancer who received ISIS 2503 in combination with Gemzar:

* Six-month survival, the primary endpoint of the study, was achieved by 57.5% of patients. Median survival was 6.6 months.

* The response rate, defined as percent of patients who experienced either a confirmed complete or partial response, was 10% (5 of 48). In total, 71% of patients showed clinical benefit with either a response or stable disease.

* These results compare favorably to historical Gemzar pivotal trial results, where six-month survival was 46%, median survival was 5.65 months, and response rate was 5%.

* The incidence of drug related toxicities in the trial was not meaningfully different from that expected from Gemzar alone.

* Based on these data, the investigators concluded that the combination of ISIS 2503 and Gemzar demonstrated modest activity and warranted further study.

PHASE II TRIAL OF ISIS 2503 IN BREAST CANCER

* In an open-label Phase II clinical trial of 26 patients with metastatic breast cancer who received ISIS 2503 in combination with paclitaxel, the response rate observed was 54% (13 of 24 evaluable patients).

* The most frequent adverse events were complications related to the indwelling catheter used to administer ISIS 2503 and were not related to the drug.

* Investigators concluded that additional trials of ISIS 2503 in combination with paclitaxel in breast cancer were warranted.

Isis is evaluating various strategies, including partnering, for the development of ISIS 2503 in pancreatic and breast cancers as well as in other tumor types.

"We are enthusiastic about the potential for antisense drugs to become important treatment alternatives for patients with cancer," said Jon T. Holmlund, M.D., Isis' Vice President, Development. "We believe the evidence from our trials to date suggests that the first-generation drugs are active. With our partners, Eli Lilly and OncoGenex, we are advancing the development of second-generation drugs targeted to survivin and clusterin, respectively."

ABOUT AFFINITAK

Affinitak is a selective inhibitor of protein kinase C-alpha (PKC-alpha) expression. The PKC protein family plays a role in normal cell function but may also be involved in abnormal cell growth. Affinitak binds to messenger RNA sequence specific to PKC-alpha and thus selectively inhibits production of this protein without inhibiting production of other proteins in the PKC family.

ABOUT ISIS 2503

ISIS 2503 is 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 regulate the process by which cells receive and send signals that affect their behavior. Through an antisense mechanism, ISIS 2503 binds to a 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 family members 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.

ABOUT NSCLC

According to the American Cancer Society, lung cancer is the leading cause of cancer death for both men and women. This year, approximately 171,000 new cases of lung cancer will be diagnosed and about 157,000 Americans will die due to the disease. More people die of lung cancer than of colon, breast and prostate cancers combined. NSCLC is the most prevalent form of lung cancer, accounting for approximately 80 percent of lung cancer diagnoses in the U.S.

ABOUT PANCREATIC CANCER

According to the American Cancer Society, an estimated 30,700 new cases of pancreatic cancer will be diagnosed and an estimated 30,000 deaths are expected in 2003. For all stages combined, the 1-year relative survival rate is 21% and the 5-year rate is about 4%.

ABOUT METASTATIC BREAST CANCER

Metastatic or Stage IV breast cancer is a form of invasive cancer, which spreads to one or more sites in the body distant from the affected breast. According to the American Cancer Society, an estimated 211,000 new cases of invasive breast cancer are expected to occur among women and an estimated 40,200 deaths are anticipated in the United States in 2003. Breast cancer ranks second among cancer deaths in women.

ISIS PHARMACEUTICALS, INC.

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 antisense products in its development pipeline, with two in late-stage development and five in Phase II human clinical trials. Affinitak™ (formerly called LY900003 and ISIS 3521), an inhibitor of PKC-alpha, is in Phase III development 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 1,200 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 diagnosis of infectious organisms and 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 the development and therapeutic potential of Affinitak and ISIS 2503. Any statement describing a goal, expectation, intention or belief of Isis 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. Affinitak has not been proven safe and effective and there are no guarantees that it will receive regulatory approvals or prove to be commercially successful. 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 on Form 10-Q for the period ended March 31, 2003, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

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