New Affinitac(TM) Data in Non-Small Cell Lung Cancer Presented at ASCO

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Chemotherapy Naive and Extensively Pretreated Patients

ORLANDO, Fla., May 20 /PRNewswire-FirstCall/ -- Affinitac™, an investigational targeted therapy used in combination with chemotherapy, demonstrated high rates of tumor response and stable disease in the treatment of non-small cell lung cancer (NSCLC), according to results from separate ongoing Phase II trials presented at the 38th Annual Meeting of the American Society of Clinical Oncology (ASCO). NSCLC is the most common form of lung cancer, affecting more than one million people worldwide.

Affinitac (formerly LY900003) is being developed for the treatment of NSCLC through an alliance between Eli Lilly and Company (NYSE: LLY) and Isis Pharmaceuticals, Inc. (Nasdaq: ISIS). This antisense agent targets a specific molecule called protein kinase c-alpha, or PKC-alpha, which has been implicated in tumor development and maintenance.

The new findings on Affinitac, presented at ASCO on Sunday, May 19, are from ongoing, Phase II clinical trials. The first presentation involved results from a study in which Affinitac is being evaluated in combination with Gemzar® (gemcitabine hydrochloride) and cisplatin in previously untreated patients with advanced NSCLC. The second presentation involved results from a study in which Affinitac is being studied in combination with docetaxel in previously treated patients with NSCLC. These Phase II trials were initiated in 2001. Enrollment in both trials has been completed, and patient monitoring continues to determine median survival and time to disease progression.

Non-Small Cell Lung Cancer Phase II Trial of Affinitac, Gemzar and

cisplatin

In the Phase II NSCLC study of Affinitac combined with Gemzar and cisplatin, 93% of the 55 chemotherapy naive patients enrolled had Stage IV disease. Forty-eight patients were evaluable for response, the primary endpoint of the study. In total, 87% had a tumor response or stable disease. One patient experienced a complete response and 17 patients experienced a partial response, resulting in an objective response rate (complete plus partial responses) of 37%.

The safety profile observed in the study did not appear to be meaningfully different from that of Gemzar and cisplatin alone. As with the Gemzar and cisplatin chemotherapy regimen, thrombocytopenia, a decrease in the number of platelets in the blood, was commonly observed, but not associated with severe clinical consequences.

"We are encouraged by the early data from this study as the combined rates of response and stable disease suggest that the vast majority of patients are experiencing some benefit from this regimen. The addition of Affinitac to Gemzar and cisplatin appears to add no significant toxicities," said Paul Ritch, M.D., Professor of Medicine, Division of Neoplastic Diseases, Medical College of Wisconsin. "Moreover, these response data are reminiscent of the previous experience with Affinitac in combination with carboplatin and paclitaxel in patients with non-small cell lung cancer. We are optimistic that this study, as it matures, may also produce prolonged survival and time to progression."

Non-Small Cell Lung Cancer Phase II Trial of Affinitac and docetaxel

This ongoing trial involves 57 patients with advanced previously treated NSCLC who are receiving Affinitac plus docetaxel. Fifty-four percent of patients enrolled had previously received two or more chemotherapy regimens, which is substantially greater than in previous studies of docetaxel alone. The response rate of the 52 evaluable patients to date is 15.4%, with 44.2% of patients experiencing stable disease, for a total rate of response plus stable disease of 59.6%.

Affinitac appears to add no significant toxicity to docetaxel in these extensively pretreated patients. The most commonly reported adverse events have been neutropenia and thrombocytopenia, which appear to be similar to what is expected with docetaxel alone.

"The response rates achieved in this group of patients with highly advanced disease compares favorably to responses observed in patients who had been exposed to fewer chemotherapy treatments and higher doses of docetaxel. Further, it appears that Affinitac can be added to this chemotherapeutic agent without adding to toxicity for patients. Tolerability is an important factor in this very ill patient population," said Melvin Moore, M.D., Research and Therapeutic Committee Director, Georgia Cancer Specialists, "We are encouraged by these early results, and continued follow-up for survival and time to progression is in progress."

Other Research

Both of the Phase II studies described above build on Affinitac data presented at the American Association for Cancer Research (AACR), the National Cancer Institute (NCI) and the European Organization for Research and Treatment of Cancer (EORTC) annual conference in Miami late last year. At this conference, results were presented from a Phase II study that evaluated Affinitac in combination with the chemotherapy regimen of carboplatin and paclitaxel in patients with previously untreated NSCLC. A 15.9-month median survival was observed, as well as a median time to tumor progression of 6.3 months, and responses or stable disease in 83% of patients.

Isis completed enrollment of a randomized Phase III clinical trial of Affinitac in combination with carboplatin and paclitaxel in NSCLC in January 2002, approximately 15 months after its initiation. The 600 patient Phase III trial is evaluating the ability of Affinitac plus carboplatin and paclitaxel to safely prolong patients' lives. In addition, Lilly has formally launched a planned global clinical trial of Affinitac in combination with Gemzar and cisplatin in the treatment of NSCLC. The study's primary endpoint is survival.

Non-Hodgkin's Lymphoma Phase II Trial of Affinitac

Isis has completed a Phase II trial of Affinitac as a single agent in patients with low-grade non-Hodgkin's lymphoma. The results of this study and an earlier trial will be presented on Tuesday, May 21 in an afternoon poster session at ASCO.

ASCO Wrap-up Conference Call

Isis will conduct a live webcast conference call to review the Affinitac data presented at ASCO. In order to summarize all the data presented, the webcast call will take place on Tuesday, May 21 at 4:30 pm Eastern time. To participate over the internet go to www.isispharm.com. A replay of the webcast will be available at this address for up to 30 days.

Affinitac is an antisense compound. Antisense compounds use the specificity of the genetic code to prevent the production of disease-causing proteins. Specifically, Affinitac 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. Affinitac 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.

According to the American Cancer Society, lung cancer is the leading cause of cancer death for both men and women. This year, approximately 170,000 new cases of lung cancer will be diagnosed and about 155,000 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 75 percent of lung cancer diagnoses in the U.S.

Lilly, a leading innovation-driven corporation is developing a growing portfolio of best-in-class pharmaceutical products by applying the latest research from its own worldwide laboratories and from collaborations with eminent scientific organizations. Headquartered in Indianapolis, Ind., Lilly provides answers -- through medicines and information -- for some of the world's most urgent medical needs.

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 six in Phase II human clinical trials. Affinitac™, 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 a Phase III trial in 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 concerning the development and therapeutic potential of Affinitac. Any statement describing a goal, expectation, intention or belief of Isis or Lilly 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. Affinitac 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 the research of Lilly or Isis research and development programs are described in additional detail in the companies' Annual Reports on Form 10-K, for the period ended December 31, 2001, and subsequent quarterly reports on Form 10-Q which are on file with the U.S. Securities and Exchange Commission, copies of which are available from both companies.

Affinitac™, a trademark of Eli Lilly and Company, is an investigational cancer compound being developed through an alliance between Lilly and Isis Pharmaceuticals, Inc. and marketed globally by Lilly.

Gemzar® (gemcitabine hydrochloride, Lilly)

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