Isis Pharmaceuticals to Manufacture Affinitac™ for Eli Lilly and Company

October 1, 2002

For Initial Commercialization

CARLSBAD, Calif., Oct. 1 /PRNewswire-FirstCall/ --
Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that it will manufacture Affinitac™ for the product launch period for Eli Lilly and Company. Affinitac, an antisense drug, is in Phase III human clinical trials and is being developed by Lilly and Isis for the treatment of patients with non-small cell lung cancer. Lilly will market the product worldwide.

Affinitac is the first anticancer agent in a fundamentally new class of drugs, called antisense. Affinitac selectively inhibits the production of protein kinase C-alpha (PKC-alpha), a molecule implicated in tumor development and maintenance. Antisense drugs are designed to have a high degree of target specificity that may provide them with a substantial advantage over traditional small molecule drugs in many difficult-to-treat diseases.

Under the terms of the agreement, Lilly will provide approximately

$21 million in the form of a loan to fund a new manufacturing suite dedicated to Affinitac. The facility is under construction on Isis' Carlsbad campus and will be located in an existing building. Isis will continue to manufacture Affinitac for clinical use and will now also produce product for commercial use for approximately a three-year period, after which Lilly plans to assume responsibility for manufacturing. The loan to Isis will be repaid with Affinitac success milestones and other product-related cash inflows.

We are pleased to contribute to the early commercial success of Affinitac and with the tremendous value this transaction offers Isis, said B. Lynne Parshall, Isis' Executive Vice President and CFO. This agreement has the potential to generate up to $120 million in revenue to Isis over the next three years, if the Affinitac new drug application is successfully submitted to the FDA in 2003, the drug is approved based on positive results from Isis' Phase III study and its market penetration is in line with our projections. These manufacturing revenues, the expenses for the costs of goods and the associated profits will be new elements on our financial statements and the profits represent another opportunity to further enhance our financial position.

Ms. Parshall continued, Furthermore, we benefit from the investment that Lilly is making to significantly expand our manufacturing facility, as this facility will be available to us to support the development and commercialization of Isis' future antisense drugs.

The processes involved in manufacturing antisense drugs compare favorably to those of traditional small molecule drugs or protein therapeutics, as antisense technology offers many advantages in efficiency. Unlike other drugs, antisense drugs share a common chemistry, so the manufacturing processes can be standardized very effectively. Antisense drugs are synthetic molecules, not biologic, so the expensive equipment and processes for fermentation, as needed with protein therapeutics, are not required.

Isis will conduct a live webcast conference call to discuss this press release on Tuesday, October 1, at 10:00 am Eastern time. To participate over the Internet, go to our website at www.isispharm.com or http://www.firstcallevents.com/service/ajwz366212839gf12.html . A replay of the webcast will be available at this address for up to 30 days.

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® (formivirsen), 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™ (formerly called LY900003 and 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 1000 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 commercial and therapeutic potential of Affinitac and the potential of Isis' manufacturing capabilities. 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 10-K 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.

Vitravene® is a registered trademark of Novartis AG.

GeneTrove™ and Ibis Therapeutics™ are trademarks of Isis

Pharmaceuticals, Inc.

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.

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