Isis Pharmaceuticals Achieves Milestone in Antisense Drug Discovery Collaboration With Eli Lilly and Company

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CARLSBAD, Calif., April 21 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that it has achieved a significant milestone in the development of ISIS 23722, as part of its broad antisense drug discovery collaboration with Eli Lilly and Company (NYSE: LLY). ISIS 23722 is the first compound from the partnership to be selected for clinical development by Lilly. As a result of the achievement, Isis will receive a $1.5 million payment from Lilly.

Based on a robust preclinical data package, Lilly plans to advance ISIS 23722, a second-generation antisense agent, into investigational new drug (IND) enabling studies. In preclinical studies, ISIS 23722 demonstrated activity in multiple in vivo models of cancer. ISIS 23722 targets survivin, a molecule that allows the survival of cells that would normally undergo programmed cell death. When cancer cells grow, they appear to need the help of survivin. The molecule is abundant in many types of cancers, including colon, brain, lung, skin and others, but nearly nonexistent in normal cells.

"The collaboration has produced compelling preclinical data suggesting ISIS 23722 may be useful in the treatment of a variety of tumor types," said Stanley T. Crooke, M.D., Ph.D., Isis' Chairman and CEO. "We are pleased with the rapid progress of our drug discovery collaboration with Lilly in cancer and other therapeutic areas."

In addition to the payment for this milestone, Lilly will fund the continued development of ISIS 23722. The licensing of ISIS 23722 to Lilly was a component of the cancer drug discovery collaboration the companies previously initiated. The oncology relationship builds on a broad, ongoing strategic alliance previously established by the companies to discover antisense drugs in the areas of inflammatory and metabolic diseases.

Antisense inhibitors work at the molecular level by binding to messenger RNA to interrupt the process by which disease-related proteins are produced. Antisense inhibitors can be used as functional genomics tools or as drugs. Antisense drugs can be designed to treat a wide range of diseases. Due to their gene selectivity, they have the potential to be highly effective and less toxic than traditional small molecule drugs.

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 antisense products in its development pipeline with two in late-stage development and five in Phase II human clinical trials. Affinitak™, an inhibitor of PKC-alpha, is in a Phase III trial for non-small cell lung cancer and alicaforsen (ISIS 2302), an ICAM-1 inhibitor, is in two Phase III trials for Crohn's disease. Isis has a broad patent estate as the owner or exclusive licensee of nearly 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 development of a diagnostic tool to detect biological agents 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 ISIS 23722 and the collaboration between Isis Pharmaceuticals and Eli Lilly and Company. Any statement describing a goal, expectation, intention or belief of Isis is a forward- looking 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 Isis' Annual Report on Form 10-K for the period ended December 31, 2002, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from Isis.

Vitravene® is a registered trademark of Novartis AG.

GeneTrove™ and Ibis Therapeutics™ are trademarks of Isis Pharmaceuticals, Inc. Affinitak™, a trademark of Eli Lilly and Company, is a investigational cancer compound being developed through an alliance between Lilly and Isis Pharmaceuticals, Inc. and marketed globally by Lilly.

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