

Lilly Initiates Clinical Trials on Second Cancer Drug Discovered in Isis Collaboration

February 1, 2006

Isis Earns Milestone Payment From Lilly

CARLSBAD, Calif., Feb. 1 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that Eli Lilly and Company (NYSE: LLY) has initiated clinical trials of LY2275796 in cancer patients. LY2275796, a second-generation antisense drug, targets eukaryotic initiation factor-4E (eIF-4E), a protein involved in the translation of key growth and survival factors that contribute to tumor progression and the spread of cancers. LY2275796 was discovered in the Isis-Lilly drug discovery collaboration, and is the second antisense drug candidate from this strategic alliance to advance into Phase 1 development. Lilly will pay Isis \$750,000 for the accomplishment of this milestone. In addition, Lilly is funding the development of LY2275796 and will make additional payments on the achievements of certain development and regulatory milestones, and royalties on product sales to Isis.

"Advancing our second drug into clinical trials from the Isis-Lilly collaboration is an important milestone in the discovery and development of novel antisense drugs to treat significant diseases," said C. Frank Bennett, Ph.D., Senior Vice President, Antisense Research at Isis. "eIF-4E is a drug target that oncologists believe may play a key role in initiating and maintaining various cancers, yet considered 'undruggable' with traditional drug discovery technologies. Our specific and potent antisense drug has the potential to help patients suffering from cancer, including breast, head and neck, colon, prostate, bladder, and lung cancer."

ABOUT LY2275796 AND eIF-4E

LY2275796 targets eIF-4E, a protein that is increased in a variety of cancers, including breast, head and neck, prostate, lung, bladder, colon, thyroid and non-Hodgkin's lymphomas. The molecule facilitates the synthesis of tumor angiogenic factors (factors that facilitate the growth of new blood vessels to support the development and progression of tumors), growth factors and survival factors by selectively enhancing their translation. Based on scientific literature, there is a strong indication that eIF-4E may act as a critical "switch" in cancer progression.

ABOUT ISIS PHARMACEUTICALS, INC.

Isis is exploiting its expertise in RNA to discover and develop novel drugs for its product pipeline and for its partners. The Company has successfully commercialized the world's first antisense drug and has 12 antisense drugs in development to treat metabolic, cardiovascular, ocular and inflammatory diseases, and cancer. In its Isis division, Isis is developing and commercializing the TIGER biosensor system, a revolutionary system to identify infectious organisms. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of approximately 1,500 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

This press release includes forward-looking statements regarding Isis' collaboration with Eli Lilly and the development of LY2275796 to treat cancer. Any statement describing Isis' goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' goals. 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 in the endeavor of building a business around such products. Isis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Isis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2004, and its quarterly report on Form 10-Q for the quarter ended September 30, 2005, which are on file with the SEC. Copies of these and other documents are available from the Company.

SOURCE Isis Pharmaceuticals, Inc.

02/01/2006

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02/01/2006 07:00 EST <http://www.prnewswire.com>