

Isis Pharmaceuticals Licenses Second Antisense Anti-Cancer Drug Candidate to Lilly for Clinical Development

September 20, 2004

CARLSBAD, Calif., Sept. 20 /PRNewswire-FirstCall/ -- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that Eli Lilly and Company (NYSE: LLY) licensed LY2275796, a second-generation antisense anti-cancer drug candidate for clinical development. LY2275796 targets eukaryotic initiation factor-4E (eIF-4E), a protein involved in the translation of key growth and survival factors that drive tumor progression, angiogenesis and metastases. The compound was discovered in the Isis -- Lilly drug discovery collaboration, and is the second antisense drug candidate from this broad, strategic alliance to be licensed to Lilly for development. Isis will receive a \$750,000 payment from Lilly for the license.

"Our collaboration with Lilly is productive and we are pleased to contribute new, cutting-edge drug candidates to Lilly's oncology portfolio. Already, we have successfully licensed this compound and LY2181308, a second-generation drug candidate against the cancer target survivin, which is planned to enter Phase 1 trials later this year. We are optimistic that additional drug candidates will emerge from the alliance not only for cancer, but also for inflammatory and metabolic diseases," said C. Frank Bennett, Ph.D., Isis' Vice President, Antisense Research. "eIF-4E and survivin are drug targets that have been of great interest to the pharmaceutical industry and the oncology community at large, yet considered 'undruggable' with traditional small molecule compounds. However, using our proprietary second-generation chemistry, the collaboration readily identified selective and potent inhibitors to these targets."

Lilly will fund the continued development of LY2275796 and under the terms of the companies' alliance, Lilly will pay Isis development and regulatory milestones and royalties on potential product sales. The Isis -- Lilly oncology relationship, initiated in June 2002 and extended earlier this year, builds on an ongoing alliance previously established by the companies to discover antisense drugs in the areas of inflammatory and metabolic diseases.

ABOUT LY2275796 AND eIF-4E

LY2275796 targets eIF-4E, a protein that is upregulated or overexpressed 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 Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs for its pipeline and for its partners. The company has successfully commercialized the world's first antisense drug and has 12 antisense products in development to treat metabolic, cardiovascular, inflammatory and viral diseases and cancer. Through its Ibis Therapeutics® program, Isis is developing a biosensor to identify infectious organisms, and discovering small molecule drugs that bind to RNA. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of more than 1,400 issued patents worldwide. Additional information about Isis is available at <http://www.isispharm.com>

This press release includes forward-looking statements regarding Isis' collaboration with Eli Lilly and Company and the development, therapeutic potential and safety of LY2275796 targeting eIF-4E and LY2181308 targeting survivin in treating cancer. Any statement describing our 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' clinical goals. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of developing technology and systems used to identify infectious agents, in discovering and commercializing drugs that are safe and effective for use as human therapeutics and in the endeavor of building a business around such products and services. Actual results could differ materially from those discussed in this press 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 year ended December 31, 2003, and quarterly report on Form 10-Q for the quarter ended June 30, 2004, which are on file with the U.S. Securities and Exchange Commission. Copies of these and other documents are available from the company.

Ibis Therapeutics® is a registered trademark of Isis Pharmaceuticals, Inc.

SOURCE Isis Pharmaceuticals, Inc.

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