
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of report (Date of earliest event reported): **February 14, 2005**

ISIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware

(State or Other Jurisdiction of Incorporation)

000-19125

(Commission File No.)

33-0336973

(IRS Employer Identification No.)

**2292 Faraday Avenue
Carlsbad, CA 92008**

(Address of Principal Executive Offices and Zip Code)

Registrant's telephone number, including area code: **(760) 931-9200**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
 - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
 - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
 - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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Item 1.01 **Entry into a Material Agreement.**

On February 14, 2005, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing that it has licensed an anti-cancer antisense drug to and Sarissa, Inc., a biotechnology company emerging from the University of Western Ontario. The drug is an antisense inhibitor of thymidylate synthase (TS), a well-known drug target that protects cancer cells from the effects of several chemotherapy treatments.

Item 9.01. **Financial Statements and Exhibits.**

(c) Exhibits.

99.1 Press Release dated February 14, 2005.

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SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ISIS PHARMACEUTICALS, INC.

Dated: February 10, 2005

By: /s/ B. Lynne Parshall
B. LYNNE PARSHALL
Executive Vice President,
Chief Financial Officer and Director

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99.1 Press Release dated February 14, 2005.

**ISIS PHARMACEUTICALS LICENSES ANTISENSE
ANTI-CANCER DRUG TO SARISSA**

London, Ontario, Canada and Carlsbad, CA, USA, February 14, 2005- Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) and Sarissa, Inc., a biotechnology company emerging from the University of Western Ontario, announced today that Isis has licensed an anti-cancer antisense drug to Sarissa. The drug is an antisense inhibitor of thymidylate synthase (TS), a well-known drug target that protects cancer cells from the effects of several chemotherapy treatments. In preclinical studies, antisense inhibition of TS suppressed human tumor cell growth and overcame tumor cell resistance to marketed TS-targeted drugs.

“This licensing agreement with Isis will enable us to move our oncology drug discovery and development program forward. The combination of our knowledge of the biological role of thymidylate synthase with Isis’ expertise in antisense discovery and development and second-generation chemistry has the potential to yield an exciting and cutting-edge treatment for cancer,” said Mark Vincent M.D., President and CEO of Sarissa. “Looking ahead, we plan to complete a series of preclinical experiments to prepare the drug for IND submission and human clinical trials.”

“This transaction with Sarissa is another example of our successful satellite company partnering program. Through these relationships, we are expanding the reach and potential of antisense therapeutics and participating in the success of multiple companies and products,” said Nicholas Dean, Ph.D., Vice President of Functional Genomics at Isis Pharmaceuticals. “This licensing agreement will allow us to benefit from Sarissa’s expertise and highly focused research efforts in cancer, while Sarissa will benefit from our experience in RNA-based drug discovery and development and access to our intellectual property.”

Under the terms of the agreement, Sarissa will pay Isis a \$1 million upfront fee in exchange for the exclusive, worldwide license to the TS antisense drug. The upfront fee will be paid with a debt instrument which will convert into Sarissa stock upon its successful completion of a venture capital financing. Sarissa will also pay Isis milestone payments for key clinical and regulatory achievements and royalties on product sales. Sarissa will be solely responsible for preclinical and clinical development of the drug.

About Thymidylate Synthase (TS)

TS is an important target in a wide variety of cancers, including colorectal, breast, stomach, esophageal, head and neck cancers, and mesothelioma; it is of increasing importance in non-small cell lung cancer. In addition to interfering with the effectiveness of chemotherapy, the TS gene may also participate in causing cancer. TS is a target for several chemotherapy agents, including 5-fluorouracil (5-FU), pemetrexed (Alimta®), and raltitrexed (Tomudex®).

About Sarissa, Inc.

Sarissa, Inc. was founded by Chief Executive Officer, Mark Vincent, M.D., a medical oncologist and Chief Scientific Officer, James Koropatnick, Ph.D., a cancer research scientist. It has a focus on the antisense down-regulation of thymidylate synthase as a means of chemotherapy potentiation. The Company plans now to leverage its oncology expertise to develop antisense oligonucleotides in the clinic.

About Isis’ Anti-Cancer Drug Discovery and Development Partnerships

Through both strategic partnerships and internal research and development programs, Isis has several ongoing programs focused on identifying antisense drugs for the treatment of a variety of cancers. Isis’ collaboration with Eli Lilly and Company has resulted in two drugs in development that target cancer. LY2181308 is an anti-cancer drug that targets survivin and LY2275796 is an anti-cancer drug that targets eIF-4E. Additionally, with Isis’ assistance, OncoGenex Technologies is developing OGX-011, an anti-cancer drug that targets a protein called clusterin and OGX-225, a cancer drug that targets both Insulin-like Growth Factor Binding Protein-2 (IGFBP-2) and Insulin-like Growth Factor Binding Protein-5 (IGFBP-5). IGFBP-2 and IGFBP-5 are genes involved in regulating growth signals that result in tumor cell growth and the development of metastatic cancer in hormone-regulated tumors such as prostate and breast cancers. Isis is also working with Ercole Biotech on the preclinical development of a Bcl-x antisense drug. This drug inhibits the production of splice variants of the Bcl-x gene; a gene involved in the regulation of apoptosis, or programmed cell death. Internally, Isis continues its drug discovery efforts in oncology with ISIS 345794, a second-generation antisense drug that targets STAT-3. This protein is known to be an important transcription factor that turns on genes required for the division, growth and death of cells. In addition, Isis has several internal and partnered research and development programs to treat metabolic, cardiovascular and inflammatory diseases.

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 10 antisense products in development to treat metabolic, cardiovascular and inflammatory diseases, and cancer. Through its Ibis Therapeutics® program, Isis is developing a biosensor to identify infectious organisms, and is 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 1,500 issued patents worldwide. Additional information about Isis is available at <http://www.isispharm.com>.

This press release includes forward-looking statements regarding Isis Pharmaceuticals and Sarissa’s licensing agreement and the development, therapeutic potential and safety of an antisense drug targeting TS for the treatment of 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, 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. 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 September 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.

Alimta® is a registered trademark of Eli Lilly and Company.

Tomudex® is a registered trademark of AstraZeneca.

