
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): **July 21, 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.)

1896 Rutherford Road

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 July 20, 2005, Isis Pharmaceuticals, Inc., through its Ibis division (the "Company"), was granted a contract for approximately \$2.6 million from the Defense Advanced Research Projects Agency (DARPA) under a subcontract from San Diego-based Science Applications International Corporation (SAIC). On July 21, 2005, the Company issued a press release announcing its Ibis division has been granted contracts for approximately \$5 million, which amount includes the DARPA contract, from several government agencies to continue advancing development of applications to support the initial operations of the TIGER (Triangulation Identification for Genetic Evaluation of Risks) biosensor system.

Item 9.01. Financial Statements and Exhibits.

(c) Exhibits.

99.1 Press Release dated July 21, 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: July 21, 2005

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

INDEX TO EXHIBITS

99.1 Press Release dated July 21, 2005.

Contact: Navjot Rai
Investor Relations & Corporate Communications
760-603-2331

**ISIS PHARMACEUTICALS AWARDED APPROXIMATELY \$5 MILLION FROM
GOVERNMENT AGENCIES TO ADVANCE ADDITIONAL APPLICATION DEVELOPMENT
FOR TIGER BIOSENSOR SYSTEM**

Government Partners Include DARPA and Department of Homeland Security

CARLSBAD, Calif., July 21, 2005 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that its Ibis division has been granted contracts for approximately \$5 million from several government agencies to continue advancing the development of applications and to support the initial operations of the TIGER (Triangulation Identification for Genetic Evaluation of Risks) biosensor system. Funding was granted by several government agencies including the Defense Advanced Research Projects Agency (DARPA) and the Department of Homeland Security (DHS), under subcontracts from San Diego-based Science Applications International Corporation (SAIC). The TIGER biosensor system is a revolutionary system for the identification of infectious organisms as it can simultaneously identify thousands of infectious organisms without having to know or suspect what may or may not be present in a sample.

“In addition to advancing application development, this funding also allows us to further prepare our government customers for the delivery of TIGER biosensor systems,” said David J. Ecker, Ph.D., Isis’ Vice President and Chief Scientific Officer of Ibis. “The first three TIGER biosensor systems planned for delivery will each be used for a different application, which is a testament to the versatility of the TIGER technology.”

Ibis plans to deliver TIGER biosensor systems this year to the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), who will use it for biological warfare defense; to the Naval Health Research Center and Centers for Disease Control and Prevention (CDC), who will each use it for epidemiological surveillance, and to the Department of Homeland Security, who will use it for microbial forensics.

“The funding we have received from our government partners has allowed us to build a broadly applicable, high-throughput system for the identification of infectious organisms for a variety of applications,” said Michael Treble, Isis’ Vice President and President of Ibis. “In addition to advancing applications for our government customers, we are capitalizing on the utility of the TIGER biosensor system and developing applications for the pharmaceutical and healthcare sectors for use in pharmaceutical process control, healthcare-associated infections and infectious disease diagnostics.”

From inception through March 31, 2005, Ibis has earned \$38.5 million in revenue from government partners. An additional \$13.0 million is committed under existing contracts and grants, with the potential for added funding.

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ABOUT TIGER AND THE IBIS DIVISION

The Ibis division has developed the TIGER (Triangulation Identification for Genetic Evaluation of Risks) biosensor system, a revolutionary system to identify infectious organisms. Ibis plans to commercialize the TIGER biosensor system to government customers for use in biowarfare defense, epidemiological surveillance and forensics; and to non-government customers for use in pharmaceutical process control, hospital-associated infection control, and infectious disease diagnostics. Additional information about Isis’ Ibis division can be found at www.ibistiger.com or accessed from Isis’ homepage at www.isispharm.com.

The Ibis division has been funded by U.S. government agencies including the Defense Advanced Research Projects Agency (DARPA), the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), the Federal Bureau of Investigation (FBI), and the Department of Homeland Security (DHS), and others.

ABOUT ISIS PHARMACEUTICALS, INC.

Isis Pharmaceuticals, Inc. 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 11 antisense drugs in development to treat metabolic, cardiovascular and inflammatory diseases, and cancer. In its Ibis 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 more than 1,500 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

This press release includes forward-looking statements regarding the development and commercialization of Isis Pharmaceuticals’ TIGER biosensor system and related products, as well as the Company’s plans and goals for the program. 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 developing and commercializing systems to identify infectious organisms that are effective and commercially attractive, 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 March 31, 2005, which are on file with the SEC. Copies of these and other documents are available from the Company.

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