
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): **October 6, 2004**

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 October 6, 2004, Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced that its Ibis program has been granted three new government contracts valued at up to \$10 million for the continued development of its TIGER biosensor technology. TIGER, which stands for Triangulation Identification Genetic Evaluation of Risks, is a research program initially sponsored by the Defense Advanced Research Projects Agency (DARPA) under a subcontract from San Diego-based Science Applications International Corporation (SAIC) for bioweapons defense.

Item 9.01 Financial Statements and Exhibits.

(c) Exhibits.

99.1 Press Release dated October 6, 2004.

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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: October 5, 2004

By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL

Executive Vice President,

Chief Financial Officer and Director

99.1

Press Release dated October 6, 2004.

Contact: Kristina Peterson
Isis Pharmaceuticals, Inc.
(760) 603-2521

**ISIS PHARMACEUTICALS' TIGER PROGRAM AWARDED GOVERNMENT
CONTRACTS FOR UP TO \$10 MILLION**

*NIAID Contract to Develop Vaccine Screening Application Creates
New Commercial Prospect for Technology*

CARLSBAD, CA, October 6, 2004 - Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that its Ibis program has been granted three new government contracts valued at up to \$10 million for the continued development of its TIGER biosensor technology. TIGER, which stands for Triangulation Identification Genetic Evaluation of Risks, is a research program initially sponsored by the Defense Advanced Research Projects Agency (DARPA) under a subcontract from San Diego-based Science Applications International Corporation (SAIC) for bioweapons defense. The TIGER program is also funded by the Centers for Disease Control and Prevention (CDC) for epidemiological surveillance applications, the Federal Bureau of Investigation (FBI) for the development of a microbial agent database, and by the National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health, for biological products screening. The development of these various applications significantly broadens and enhances TIGER's commercial value and opportunity in the government, research instrument, and medical and diagnostic markets. Together with prior awards, Ibis has received contracts for up to \$65 million in funding from multiple government agencies.

The development of TIGER's biological products screening application will be funded by a contract from the NIAID. Currently, there are few tests available that can specifically assess particular safety issues that are unique to cell substrates used in vaccine manufacturing, such as the identification of unknown or novel microbes that have the potential to contaminate vaccine cell lines and substrates. The TIGER biosensor has the potential to simultaneously identify a broad array of infectious agents, including previously unknown and newly emerging organisms that might be contaminating such cell substrates.

Under the NIAID award, Isis will develop an application to use its TIGER technology to assess the safety of investigational vaccines and the components used for the manufacturing of biological products by identifying foreign infectious organisms that may be present. Using TIGER, Isis will develop protocols and procedures for vaccine screening that provide meaningful, relevant information to regulatory agencies and vaccine manufacturers on how to adequately assess the risk of vaccines produced in new cell substrates.

"We are very pleased to apply the strength of TIGER technology for high-priority, NIAID health safety initiatives aimed at ensuring vaccine safety, and with the opportunity to develop a new commercial application for our biosensor," said David J. Ecker, Ph.D., Isis Vice President and President of Ibis Therapeutics.

Additionally, Ibis Therapeutics[®] received an award from the FBI to continue ongoing development of the Microbial Rosetta Stone (MRS) informational databases on microbial agents for law enforcement use. The MRS program is for information management and a database of biological threat agents, their DNA sequences, and effects that can be used by law enforcement officials to confer deterrence and support forensic investigations. Additional information about this award is available at <http://www.fedbizopps.gov>.

Isis was also awarded a third contract from an undisclosed government agency.

"With the receipt of these new government contracts, we continue to execute our business strategy, which is to secure supplemental government funding to develop additional applications for TIGER, broaden our base of government customers, generate revenue and continually enhance the technology's potential for success in the large research instrument and clinical diagnostics commercial markets," Dr. Ecker continued.

ABOUT TIGER AND THE IBIS PROGRAM

Isis' Ibis program has expanded on Isis' RNA-based drug discovery and development expertise in order to revolutionize the identification and treatment of infectious diseases. The program's goals are to create a platform technology, TIGER, that can rapidly and accurately identify a broad range of organisms in a single test and to develop small molecule antibacterial and antiviral drugs that bind to RNA. To accomplish these tasks, Ibis scientists integrate functional genomics, bioinformatics and RNA-focused chemistry programs with novel high-throughput, mass spectrometry-based screening methods.

The key benefit of the TIGER biosensor is that in a single test, without culturing, the system is capable of simultaneously identifying infectious agents, including previously unknown and newly emerging organisms. The technology development program combines Ibis' expertise in microbial genome sequence analysis and advanced mass spectrometry technology with SAIC's advanced signal processing capabilities.

In October 2001, DARPA commissioned Isis to design a sensor for environmental surveillance capable of detecting a biological attack. DARPA continues to fund the ongoing development of Isis' TIGER biosensor, and has successfully transitioned a TIGER system to the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) for government-sponsored research programs.

The Ibis program has received research funding from several government entities, including DARPA, the CDC, the NIH, the FBI, National Institutes of Standards and Technology and USAMRIID.

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 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 1,400 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 TIGER biosensor technology and products, as well as Isis' plans and goals for the program. 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.

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