

# 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 3, 2006**

## 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 8.01. Other Events.

On October 3, 2006, Isis Pharmaceuticals, Inc. ("Isis") filed a press release announcing recent developments related to its Ibis Biosciences™ division ("Ibis"), including the following updates:

- Isis has received its first commercial order for Ibis T5000™ Biosensor Systems;
- Isis successfully completed the first phase of its Challenge Grant from the National Institute of Allergy and Infectious Disease (NIAID), a part of the National Institutes of Health (NIH), and has been granted funding for the second and third phases of the Grant which includes installing an Ibis T5000 Biosensor System at Johns Hopkins University Medical Center; and
- Isis recently received a contract from the U.S. Government to perform forensic analyses of up to 10,000 samples in its Ibis T5000 Assay Services Laboratory.

A copy of the release is attached hereto as Exhibit 99.1 and incorporated herein by reference.

\* \* \* \* \*

This report includes forward-looking statements regarding the development and commercialization of the Ibis T5000 Biosensor System and the revenue potential of certain government contracts. 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, 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, 2005, and its quarterly report on Form 10-Q for the quarter ended June 30, 2006, which are on file with the SEC. Copies of these and other documents are available from Isis.

#### Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated October 3, 2006.

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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 3, 2006

By: /s/ B. Lynne Parshall

**B. LYNNE PARSHALL**

Executive Vice President,

Chief Financial Officer and Director

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**INDEX TO EXHIBITS**

99.1 Press Release dated October 3, 2006.

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**ISIS PHARMACEUTICALS RECEIVES FIRST COMMERCIAL ORDER FOR  
IBIS T5000 BIOSENSOR SYSTEMS**

- *Government Agency to Purchase Two Ibis T5000 Biosensor Systems for Human Forensics*
- *Ibis T5000 Biosensor System to be Installed at Johns Hopkins*
- *Ibis Awarded Up to \$1.9 Million Government Contract for Assay Services*
- *Live Webcast on Isis' Ibis Biosciences Business Plan - Today at 12:00 pm Eastern Time*

**CARLSBAD, Calif., October 3, 2006** - Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that it has received its first commercial order for Ibis T5000™ Biosensor Systems. A U.S. government agency has ordered two Ibis T5000 systems for human forensics applications. The purchase agreement marks an important milestone for Isis' Ibis Biosciences™ division (Ibis), which has worked closely with government collaborators to expand the Ibis T5000 capabilities to include forensics. Isis plans to complete installation of the first system before the end of the year, and to install the second system early in 2007. Further details about the agreement were not disclosed.

The Ibis T5000 Biosensor Systems will be used by this initial customer for high-throughput forensic analysis of human mitochondrial DNA (mtDNA) to genotype and identify individuals based on unique patterns of genetic variation. MtDNA analysis is often used in cases involving the identification of human remains or missing persons where nuclear DNA is either too degraded or too scarce to employ standard analytical methods. Compared to traditional sequencing methods for mtDNA analysis, the Ibis T5000 is automated and high-throughput, allowing numerous samples to be analyzed rapidly and accurately. In a related agreement, Ibis was recently awarded a research contract to support the continued development of advanced capabilities in the field of mtDNA forensics using the Ibis T5000 Biosensor System.

Isis also announced today that it successfully completed the first phase of its Challenge Grant from the National Institute of Allergy and Infectious Disease (NIAID), a part of the National Institutes of Health (NIH), and has been granted funding for the second and third phases of the Grant which includes installing an Ibis T5000 Biosensor System at Johns Hopkins University Medical Center. The purpose of the Grant is to develop and validate a broad range of respiratory and blood-borne infectious agents, including bacteria and viruses on the NIAID priority list. The milestones for the first phase involved development of assays for identification, strain typing, virulence and drug resistance of important human pathogens. In addition to deployment of an Ibis T5000, the second and third phases of the Grant — approximately \$2.5 million — include funding for the purchase of assay kits to analyze human samples in validation studies.

“Demand is growing for solutions that can quickly identify emerging pathogens,” according to Garth Ehrlich, Ph.D., Executive Director, Center for Genomic Sciences, Allegheny Singer Research Institute /Allegheny General Hospital, an industry expert in infectious disease research. “Governments, organizations like the CDC (Centers for Disease Control), hospitals and health providers throughout the world need better tools to deal with the growing risks associated with SARS-like epidemics and hospital infections. The Ibis T5000 Biosensor System represents a compelling approach for addressing these intractable challenges.”

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In addition, Isis announced today that Ibis recently received a contract from the U.S. Government to perform forensic analyses of up to 10,000 samples in its Ibis T5000 Assay Services Laboratory. Revenue from this contract could be up to \$1.9 million. This assay service capability represents a key part of the Ibis business strategy, as it not only has the potential to be an important revenue-generating opportunity for the business, but also represents an important resource for customers evaluating the capabilities of the system and collaborating in applications development.

According to Michael Treble, President of Ibis and Vice President of Isis, “We’re pleased to announce the first commercial order for the Ibis T5000 Biosensor System. This order reflects the successful implementation of our strategy to work closely with key investigators to develop applications for the Ibis T5000. When the applications are successfully completed, we can then convert our collaborators into commercial customers and pursue new markets with validated assays. We’re also very pleased to be installing an Ibis T5000 at Johns Hopkins. Working with the clinical staff at this prestigious institution allows us to continue to expand the capabilities of the Ibis T5000 in the highest-quality manner.”

Treble continued, “These commercial milestones are key accomplishments for the Ibis business. Together, the purchase order, research commitment, second and third phases of the Challenge Grant, and large-scale sample screening agreement represent revenue of up to \$5.5 million. We hope to continue to achieve additional commercial milestones as we complete 2006 and enter 2007. We believe the Ibis T5000 Biosensor System has the potential to revolutionize human forensics and identification of infectious organisms.”

Isis recently announced that Bruker Daltonics, a subsidiary of Bruker Biosciences Corporation, will provide worldwide manufacturing, installation, support services and order processing for the Ibis T5000. Over the coming months, Isis will transition manufacturing responsibility for the Ibis T5000 instruments to Bruker, and Bruker will build and install future Ibis T5000 instruments. Ibis will build and install these first commercial instruments during the transition period. Ibis will develop, manufacture and supply assay kits for the Ibis T5000 and will provide related applications support. Initially, Bruker will focus its sales effort for Ibis T5000 Biosensor Systems and assay kits in Europe and in the Middle East and Ibis will focus on North America. Today’s announcement follows last week’s European introduction of the Ibis T5000 Biosensor System.

Ibis’ commercial activity in forensics builds upon its government-funded application development in biowarfare defense, disease surveillance and epidemiology. Going forward, Ibis intends to expand its commercial activity into hospital markets where the Ibis T5000 can be used to identify sources of and monitor control of hospital-associated infections (HAI), also known as nosocomial infections. In addition to pathogen identification, the system can provide rapid strain typing, resistance profiling and information on the presence of virulence markers associated with particularly aggressive infections. Ibis Biosciences also plans to leverage the unique benefits of the Ibis T5000 Biosensor System to enter the diagnostics market with a partner in the future.

### **Webcast of Ibis Division Strategy**

Isis will provide additional detail about its Ibis Biosciences business, and Ibis biosensor technology, markets and commercialization strategy in a presentation that will be webcast today, October 3, 2006, beginning at 12:00 PM Eastern Time. The live webcast can be accessed at [www.isispharm.com](http://www.isispharm.com) and will be archived on the investor page of Isis' website.

### **How the System Works**

The Ibis T5000 Biosensor System is an automated system for high-throughput identification and characterization of bacterial, viral and other infectious organisms, and forensic analysis of human DNA. The system uses broad-range primers to amplify genomic regions that are, in part, shared by groups of related organisms. Mass spectrometric analysis enables determination of base composition without sequencing, while proprietary analytical algorithms establish the identity of the organism(s) in the sample. The Ibis T5000 is

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unique in its ability to rapidly identify organisms without knowing specifically which organism it is trying to identify. Traditional technology is typically limited to testing for the presence of a single organism or small set of organisms. If the expected organism is not detected, additional tests are required to identify what organism or organisms may be present. The Ibis T5000 overcomes these limitations.

### **ABOUT IBIS T5000 BIOSENSOR SYSTEM AND ISIS' IBIS BIOSCIENCES DIVISION**

Ibis Biosciences, a division of Isis Pharmaceuticals, has developed the Ibis T5000 Biosensor System for rapid identification and characterization of infectious agents. The Ibis T5000 is capable of identifying virtually all bacteria, virus and fungi, and can provide high-resolution information about drug resistance, virulence and strain type of these pathogens. Commercial applications for the Ibis T5000 Biosensor System include epidemiologic surveillance, monitoring of pandemic diseases, identification of emerging or previously unknown pathogens, forensic characterization of human samples, identification of sources of hospital-associated infections, and, in the future, human infectious disease diagnostics. Bruker Daltonics, a subsidiary of Bruker BioSciences Corporation, is globally responsible for manufacture, order processing, installation and service of Ibis T5000 instruments. Ibis Biosciences develops, manufactures and markets Ibis T5000 assay kits. Additional information about Isis' Ibis division can be found by selecting the Ibis Biosciences link from Isis' homepage at [www.isispharm.com](http://www.isispharm.com).

The Ibis Biosciences division has received development funding from 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), the Department of Homeland Security (DHS), and others.

### **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 15 drugs in development. Isis' drug development programs are aimed at treating cardiovascular, metabolic and inflammatory diseases. Isis' partners are focused in disease areas such as inflammatory, ocular, viral and neurodegenerative diseases, and cancer. 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](http://www.isispharm.com).

This press release includes forward-looking statements regarding the development and commercialization of the Ibis T5000 Biosensor System and the revenue potential of certain government contracts. 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, 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

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ended December 31, 2005, and its quarterly report on Form 10-Q for the quarter ended June 30, 2006, which are on file with the SEC. Copies of these and other documents are available from the Company.

Ibis Biosciences<sup>TM</sup> is a trademark of Isis Pharmaceuticals, Inc.  
Ibis T5000<sup>TM</sup> is a trademark of Isis Pharmaceuticals, Inc.

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