

# 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 28, 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))

#### **Item 1.01. Entry into a Material Definitive Agreement.**

On July 28, 2006, Isis Pharmaceuticals, Inc. entered into a strategic alliance with Bruker Daltonics for manufacturing and distribution of Isis' Ibis T5000™ biosensor system. In this strategic alliance, Bruker Daltonics will be the exclusive worldwide manufacturer of the Ibis T5000 biosensor system, which incorporates Bruker Daltonics' micrOTOF™ ESI-TOF mass spectrometer. Bruker Daltonics will also be responsible for order processing, system installations and service in North America, Europe and the Middle East. In Europe and the Middle East, Bruker Daltonics will have exclusive rights to sell Ibis T5000 systems and Ibis infectious organism identification kits for various government applications, and non-exclusive rights to sell to all other customers, including clinical, pharmaceutical and academic researchers for all other applications except diagnostics. Outside of Bruker Daltonics' exclusive market, Isis may sell Ibis T5000s and its infectious organism identification kits. A copy of this press release is attached to this Report as Exhibit 99.1.

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

(d) Exhibits.

99.1 Press Release dated July 31, 2006.

2

#### **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 28, 2006

By: /s/ B. Lynne Parshall

INDEX TO EXHIBITS

99.1 Press Release dated July 31, 2006.

Contact:  
 Michael Willett  
 Investor and Public Relations Officer  
 Bruker Daltonics  
 Tel. 978-663-3660, ext. 1411  
 Email: [ir@bruker-biosciences.com](mailto:ir@bruker-biosciences.com)

Kate Corcoran, Ph.D.  
 Vice President, Corporate Development  
 Isis Pharmaceuticals  
 760-603-2331

**BRUKER DALTONICS AND ISIS PHARMACEUTICALS ENTER  
 INTO MANUFACTURING AND DISTRIBUTION AGREEMENT FOR IBIS T5000  
 BIOSENSOR SYSTEM**

**BILLERICA, Mass. & CARLSBAD, Calif., July 31, 2006** - Bruker Daltonics, a subsidiary of Bruker BioSciences (Nasdaq: BRKR), and Isis Pharmaceuticals (Nasdaq: ISIS) announce today a strategic alliance for manufacturing and distribution of Isis' Ibis T5000™ biosensor system. The Ibis T5000, developed by Isis' Ibis Biosciences™ division, is a universal biosensor system that can simultaneously identify thousands of types of infectious organisms in a sample, without needing to know beforehand what might be present in the sample.

In this strategic alliance, Bruker Daltonics will be the exclusive worldwide manufacturer of the Ibis T5000 biosensor system, which incorporates Bruker Daltonics' micrOTOF™ ESI-TOF mass spectrometer. Bruker Daltonics will also be responsible for order processing, system installations and service in North America, Europe and the Middle East. In Europe and the Middle East, Bruker Daltonics will have exclusive rights to sell Ibis T5000 systems and Ibis infectious organism identification kits for various government applications, and non-exclusive rights to sell to all other customers, including clinical, pharmaceutical and academic researchers for all other applications except diagnostics. Outside of Bruker Daltonics' exclusive market, Isis may sell Ibis T5000s and its infectious organism identification kits.

The Ibis T5000 utilizes the Triangulation Identification for the Genetic Evaluation of Risks (T.I.G.E.R.) methodology, which is a combination of genomics, mathematical modeling, mass spectrometry and molecular amplification, to generate a "fingerprint" of each bacterium or virus, allowing it to identify virtually any bacteria or virus present in a sample. In addition, the Ibis T5000 biosensor system can rapidly identify or classify organisms that are newly-emerging, genetically altered or unculturable. The Ibis T5000 biosensor works with many different types of infectious samples from human samples, such as throat swabs or sputum, to environmental samples, such as soil or air. The Ibis T5000 is currently designated for Research Use Only (RUO) and has not been approved for any regulated uses, including *in vitro* diagnostics.

"Utilizing our mass spectrometry instrumentation, the Ibis division at Isis Pharmaceuticals has pioneered a universal biosensor system that with the appropriate reagents and databases has the potential to meet unmet infectious disease identification needs both in the government and in important clinical and pharmaceutical research markets," said Frank Laukien, President of Bruker Daltonics. "The Ibis T5000 system can identify or classify and quantify a broad range of pathogens, and also can yield details on strain type and drug resistance. In the future, this additional information can potentially support rapid, informed responses, for instance, in

---

monitoring infectious disease outbreaks or in identifying the sources of hospital-acquired infections. Our strategic alliance will allow Ibis to take advantage of our instrument manufacturing capabilities, global distribution channels and service network, while we benefit from Ibis' technology expertise and the outstanding capabilities of the Ibis T5000 biosensor system."

"This alliance is a major milestone in commercializing our Ibis T5000 biosensor system. We have been working with Bruker Daltonics for over nine years and as the relationship has evolved, Bruker was an obvious partner for the manufacturing, distribution and service of the Ibis T5000 biosensor system," said Michael Treble, President of the Ibis Biosciences division and Vice President of Isis Pharmaceuticals. "Combining Bruker Daltonics' worldwide presence and instrument manufacturing expertise with our proprietary infectious disease identification technology is a key component of our commercialization strategy for the Ibis T5000 system. We anticipate that this relationship will immediately help us with this year's planned commercialization to our early-access customers, and overall we expect that working with Bruker Daltonics will expand the reach of the Ibis T5000 biosensor system within the U.S. and overseas markets for various government and medical research applications."

**ABOUT THE IBIS T5000 BIOSENSOR SYSTEM AND IBIS BIOSCIENCES DIVISION**

Isis' Ibis Biosciences division has developed the Ibis T5000 biosensor system, which uses the Triangulation Identification for the Genetic Evaluation of Risks (T.I.G.E.R.) methodology to identify infectious organisms. Isis plans to commercialize the Ibis T5000 biosensor system and associated reagents 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 by selecting the Ibis Biosciences link from Isis' homepage at [www.isispharm.com](http://www.isispharm.com).

The Ibis Biosciences 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), the Department of Homeland Security (DHS), and others.

**ABOUT BRUKER BIOSCIENCES**

Bruker BioSciences Corporation in Billerica, Massachusetts is the parent company of Bruker AXS Inc., Bruker Daltonics Inc. and Bruker Optics, Inc. Bruker AXS is a leading developer and provider of life science, materials research and industrial X-ray analysis tools. Bruker Daltonics is a leading developer and provider of innovative life science tools based on mass spectrometry, and also offers a broad line of nuclear, biological and chemical (NBC) detection

products for homeland security. Bruker Optics is a leading developer, manufacturer and provider of research, analytical and process analysis instruments and solutions based on infrared and Raman molecular spectroscopy technology. For more information, please visit [www.bruker-biosciences.com](http://www.bruker-biosciences.com)

#### **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. In its Ibis Biosciences division, Isis is developing and commercializing the Ibis T5000 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 approximately 1,500 issued patents worldwide. Additional information about Isis is available at [www.isispharm.com](http://www.isispharm.com).

#### **CAUTIONARY STATEMENT OF ISIS AND BRUKER BIOSCIENCES**

This press release includes forward-looking statements regarding Isis' agreement with Bruker Daltonics and the development and commercialization of the Ibis T5000 biosensor system and related products, as well as both companies' plans and goals for the alliance. Any statement describing Isis' or Bruker's goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. 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' and Bruker's 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' and Bruker's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis and Bruker. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks are described in additional detail in Isis' and Bruker's respective annual reports on Form 10-K for the year ended December 31, 2005, and their respective quarterly reports on Form 10-Q for the quarter ended March 31, 2006, which are on file with the SEC. Copies of these and other documents are available from the companies.

Ibis Biosciences™ is a trademark of Isis Pharmaceuticals, Inc.

Ibis T5000™ is a trademark of Isis Pharmaceuticals, Inc.

###

---