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# 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): **May 24, 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 Material Agreements.**

On May 24, 2005, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing that it has entered into a multi-year drug discovery collaboration with Pfizer Inc. to identify second-generation antisense drugs for the treatment of ophthalmic disease. In addition, the Company intends to present certain information related to this collaboration at its upcoming annual meeting of stockholders.

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

(c) Exhibits.

- 99.1 Press Release dated May 24, 2005.
- 99.2 Slide for annual meeting of stockholders.

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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: May 24, 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 May 24, 2005.
- 99.2 Slide for annual meeting of stockholders.

Contact: Claudine Prowse, Ph.D.  
Isis Pharmaceuticals, Inc.  
760-603-2331

**ISIS PHARMACEUTICALS ANNOUNCES COLLABORATION WITH PFIZER TO DISCOVER ANTISENSE DRUGS FOR THE TREATMENT OF EYE DISEASE**

**CARLSBAD, CA, May 24, 2005** – Isis Pharmaceuticals Inc. (NASDAQ: ISIS) has entered into a multi-year drug discovery collaboration with Pfizer Inc (NYSE: PFE) to identify second-generation antisense drugs for the treatment of ophthalmic disease. Under the terms of the agreement, Isis will receive a technology access fee of \$1 million, research funding, and milestone payments. In addition, Isis will receive royalties on the sale of drugs resulting from the collaboration.

Using Isis' proprietary second-generation antisense platform, the companies will work together to identify antisense drugs against targets selected by Pfizer. Pfizer will be responsible for clinical development and commercialization of the antisense drugs. Pfizer may develop the antisense drugs identified in the collaboration for all human health indications.

"Isis has already shown that antisense drugs can be effective in treating ocular diseases, having discovered and developed Vitravene<sup>®</sup>. We are excited to contribute to Pfizer's leading ophthalmology program and at the same time work with a recognized expert to extend the technology beyond our primary therapeutic focus," said C. Frank Bennett, Isis' Vice President of Antisense Research.

"This new collaboration reflects our active strategy to work with recognized leaders such as Pfizer to broaden and deepen our antisense pipeline moving forward. Because the antisense technology platform that Isis has pioneered allows us to very rapidly discover highly selective drugs to almost any gene target, we are able not only to keep our own pipeline full, but also provide drug candidates to partners," added Dr. Bennett.

**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 11 antisense products in development to treat metabolic, cardiovascular and inflammatory diseases, and cancer. Through its Ibis division, Isis is developing a 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 <http://www.isispharm.com>.

This press release includes forward-looking statements concerning Isis' collaboration with Pfizer Inc and the development, therapeutic potential and safety of antisense drugs in treating

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ophthalmic disease. 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 discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, in developing and commercializing technology and systems used to identify infectious agents, and in the endeavor of building a business around such products and services. Our forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Although our forward-looking statements reflect the good faith judgment of our management, these statements can only be based on facts and factors currently known by us. 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, 2004, and quarterly report on Form 10-Q for the quarter ended March 30, 2005, which are on file with the U.S. Securities and Exchange Commission (SEC). Copies of these and other documents are available from the company.

Vitravene<sup>®</sup> is a registered trademark of Novartis AG

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# Multi-year Drug Discovery and Development Collaboration with Pfizer

## Creating Second-generation Antisense Drugs for Ocular Diseases

- **Work with recognized expert to extend the technology beyond Isis' primary therapeutic focus**
- **Expand the application of oligonucleotide drugs for treatment ocular diseases**
  - ◆ **Vitravene™**
  - ◆ **Macugen®**
- **Payments to Isis**
  - ◆ **Technology access fee, support and milestones for research**
  - ◆ **Up to \$80 million in development and sales milestones for three successful drugs in ocular indications**
  - ◆ **Additional milestones for other indications**
  - ◆ **Royalties**
- **Pfizer will develop and commercialize drugs from the collaboration**



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