

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): **December 14, 2007 (December 11, 2007)**

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 5.02. Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

On December 14, 2007 Isis Pharmaceuticals, Inc. ("Isis") announced that its Board of Directors has promoted B. Lynne Parshall, J.D. to Chief Operating Officer, effective immediately. Ms. Parshall retains her position as Chief Financial Officer, and is a Director of Isis.

Ms. Parshall, age 52, joined Isis in November 1991, and she has served as Director since 2000, Executive Vice President since 1995, Chief Financial Officer since 1994 and Secretary 1991. Ms Parshall is currently responsible for overseeing the operations of finance, legal, patents, manufacturing and business development and is also very involved in Isis' corporate communications activities. Previously, Ms. Parshall was a Partner with the firm of Cooley Godward LLP, now Cooley Godward Kronish LLP, where she represented several health care companies in a general practice specializing in corporate partnering and other technology-based transactions. Ms. Parshall received her J.D. at Stanford Law School, Stanford, California and her B.A. from Harvard University, Cambridge, Massachusetts. Ms. Parshall is on the board of CardioDynamics International Corporation and is a Trustee of The Bishop School in La Jolla. Ms. Parshall is also a member of the Licensing Executives Society and a member of the American, California, and San Diego bar associations.

A copy of Isis' press release regarding Ms. Parshall's promotion is attached hereto as Exhibit 99.1.

Related Party Transactions and Retention and Change of Control Agreements

As previously disclosed in Isis' Proxy Statement for its 2007 Annual Meeting of Stockholders:

Isis has entered into indemnity agreements with each of its executive officers and Directors, including Ms. Parshall, which provide, among other things, that Isis will indemnify her, under the circumstances and to the extent provided for therein, for expenses, damages, judgments, fines and settlements she may be required to pay in actions or proceedings which she is or may be made a party by reason of her position as a Director, officer or other agent of Isis, and otherwise to the fullest extent permitted under Delaware law and Isis' bylaws. Isis' bylaws provide that it will indemnify its Directors and executive officers, including Ms. Parshall, to the fullest extent not prohibited by Delaware law or any other applicable law, except that Isis will generally not be required to indemnify a Director or executive officer in connection with any proceeding initiated by such Director or executive officer.

In February 2006, Isis amended its agreement with Ms. Parshall to continue her April 2003 retention agreement. Specifically, Isis agreed to continue to provide Ms. Parshall the following severance benefits: Ms. Parshall will be eligible to receive a severance payment equal to (i) 18 months of her then-current base salary in the event that her employment is terminated without cause and (ii) 30 months of her then-current base salary in the event that her employment

is terminated as a result of a change of control. As a condition to receiving payments under each the retention and change of control agreement, Ms. Parshall is required to return all of Isis' property and information and sign an agreement releasing Isis from liability. This agreement will remain in effect as long as Ms. Parshall continues to be employed by Isis.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated December 14, 2007.

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: December 14, 2007

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

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99.1 Press Release dated December 14, 2007

**Isis Pharmaceuticals' Contacts:**

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 Manager, Corporate Communications
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**ISIS ANNOUNCES APPOINTMENT OF B. LYNNE PARSHALL
 AS CHIEF OPERATING OFFICER**

CARLSBAD, Calif., December 14, 2007 — Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced that its Board of Directors has promoted B. Lynne Parshall, J.D. to Chief Operating Officer, effective immediately. Ms. Parshall retains her position as Chief Financial Officer, and is a Director of the Company.

“This promotion is well-deserved, and appropriately reflects the scope of Lynne’s responsibilities at Isis,” commented Stanley Crooke, M.D., Ph.D., Isis’ President and CEO. “Lynne has been an integral part of Isis’ management team for many years, and has been performing COO functions now for quite some time. This promotion recognizes her outstanding contributions and the nature of her current role with the Company.”

Ms. Parshall joined Isis in November 1991, and she has served as Director since 2000, Executive Vice President since 1995, Chief Financial Officer since 1994 and Secretary since 1991. Ms. Parshall is currently responsible for overseeing the operations of finance, legal, patents, manufacturing and business development and is also very involved in the Company’s corporate communications activities. Previously, Ms. Parshall was a Partner with the firm of Cooley Godward LLP, now Cooley Godward Kronish LLP, where she represented several health care companies in a general practice specializing in corporate partnering and other technology-based transactions. Ms. Parshall received her J.D. at Stanford Law School, Stanford, California and her B.A. from Harvard University, Cambridge, Massachusetts. Ms. Parshall is on the board of CardioDynamics International Corporation and is a Trustee of The Bishop School in La Jolla. Ms. Parshall is also a member of the Licensing Executives Society and a member of the American, California, and San Diego bar associations.

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 18 drugs in development. Isis’ drug development programs are focused on treating cardiovascular and metabolic diseases. Isis’ partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Ibis Biosciences, Inc., Isis’ wholly owned subsidiary, is developing and commercializing the Ibis T5000™ Biosensor System, a revolutionary system to identify infectious organisms. Isis is a joint owner of Regulus

Therapeutics LLC, a joint venture focused on the discovery, development and commercialization of microRNA therapeutics. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of over 1,500 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

This press release includes forward-looking statements regarding Isis Pharmaceuticals and the Company’s business. Any statement describing Isis’ goals, expectations, financial or other projections, 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, 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, 2006, and its quarterly report on Form 10-Q for the quarter ended September 30, 2007, which are on file with the SEC. Copies of these and other documents are available from the Company.

In this press release, unless the context requires otherwise, “Isis,” “Company,” “we,” “our,” and “us” refers to Isis Pharmaceuticals and its subsidiaries.

Isis Pharmaceuticals is a registered trademark of Isis Pharmaceuticals, Inc. Ibis Biosciences and Ibis T5000 are trademarks of Ibis Biosciences, Inc. Regulus Therapeutics is a trademark of Regulus Therapeutics LLC.

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