
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, 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 5.02. Election of Director.

On December 14, 2004, the Board of Directors of Isis Pharmaceuticals, Inc. (the "Company") elected Richard D. DiMarchi, Ph.D. as a member of the Company's Board of Directors.

A copy of the press release announcing his election is included with this report as exhibit 99.1

Item 9.01. Financial Statements and Exhibits.

(c) Exhibits.

99.1 Press Release dated December 16, 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: December 16, 2004

By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL

INDEX TO EXHIBITS

99.1 Press Release dated December 16, 2004.

Contact: Kristina Peterson
Navjot Rai
Investor Relations & Corporate Communications
760-603-2331

**RICHARD D. DiMARCHI, Ph.D., JOINS
ISIS PHARMACEUTICALS' BOARD OF DIRECTORS**

Carlsbad, CA –December 16, 2004 -Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that Richard D. DiMarchi, Ph.D., has joined the company's Board of Directors. Dr. DiMarchi is a Professor and the Jack and Linda Gill Distinguished Chair in Biomolecular Science at Indiana University, Bloomington, Indiana. Prior to joining Indiana University, Dr. DiMarchi championed the introduction and integration of cutting-edge biotechnologies, including genomics, proteomics, high-throughput screening, and combinatorial chemistry, while building and leading the biotechnology group at Eli Lilly Research Laboratories, a division of Eli Lilly and Company.

"We are very pleased to have Richard join our Board, as he brings a vast amount of experience and expertise in the areas of drug discovery, development, and commercialization," said Stanley T. Crooke, M.D., Ph.D., Chairman and CEO of Isis Pharmaceuticals. "His leadership and understanding of innovative technologies will be invaluable as we continue to move forward with our second-generation antisense drug development programs."

Over his 22 year tenure at Lilly, Dr. DiMarchi served as Group Vice President Biotechnology and Product Development (1996-2003), Vice President, Endocrine Research and Clinical Investigation (1992-1996), and in additional key positions. Dr. DiMarchi was directly involved in the discovery and development of several Lilly drugs, including Humulin®, Humatrope®, Evista®, Xigris®, and Forteo®. He is a co-inventor of Humalog®, the first biosynthetic protein analog approved for human use.

In addition to his professorship at Indiana University, Dr. DiMarchi continues to be involved in novel drug discovery technologies as a partner of Twilight Venture Fund, LLC in Indianapolis, and as Chairman of Ambrx, a biotechnology company in San Diego. He is a former board member of the Biotechnology Industry Organization (BIO), the industry leading trade group for biotechnology.

Dr. DiMarchi conducted his post-doctoral fellowship at Rockefeller University, received a Ph.D. in Biochemistry from Indiana University and a B.S. in chemistry from Florida Atlantic University. He is the author of more than 150 scientific publications and patents, and is a founding member of the American Peptide Society.

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 10 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 <http://www.isispharm.com>.

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This press release includes forward-looking statements regarding Isis Pharmaceuticals and the company's research, drug discovery, and drug development programs. 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, 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. 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 September 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.

Humulin®, Humatrope®, Evista®, Xigris®, Forteo®, and Humalog® are registered trademarks of Eli Lilly and Company.

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