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): January 22, 2007

ISIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware

(State or Other Jurisdiction of Incorpo ration)

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:

o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

o 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 8.01. Other Events.

On January 22, 2007, Isis Pharmaceuticals, Inc. (the "Company") announced that Jeffrey M. Jonas, M.D. will join Isis on February 1, 2007 as Executive Vice President. In this position, Dr. Jonas will lead Clinical Development, Preclinical Development, Regulatory Affairs, and Quality Assurance and Compliance at Isis. He will be broadly responsible for the entire pipeline, both partnered and unpartnered, and contribute to portfolio management. Along with Stanley T. Crooke, M.D., Ph.D., Chairman and CEO, and Lynne Parshall, J.D., Executive Vice President, Dr. Jonas will be a principal representative of the Company interacting with investors and partners, working with Kate Corcoran, Ph.D., Vice President, Corporate Development.

A copy of the Company's press release dated January 22, 2007, relating to Dr. Jonas' appointment is attached hereto as Exhibit 99.1.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated January 22, 2007.

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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.

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INDEX TO EXHIBITS

99.1 Press Release dated January 22, 2007.



ISIS ANNOUNCES APPOINTMENT OF JEFFREY M. JONAS, M.D. AS EXECUTIVE VICE PRESIDENT

CARLSBAD, Calif., January 22, 2007 — Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced today that Jeffrey M. Jonas, M.D. will join Isis on February 1, 2007 as Executive Vice President. In this position, Dr. Jonas will lead Clinical Development, Preclinical Development, Regulatory Affairs, and Quality Assurance and Compliance at Isis. He will be broadly responsible for the entire pipeline, both partnered and unpartnered, and contribute to portfolio management. Along with Stanley T. Crooke, M.D., Ph.D., Chairman and CEO, and Lynne Parshall, J.D., Executive Vice President, Dr. Jonas will be a principal representative of the Company interacting with investors and partners, working with Kate Corcoran, Ph.D., Vice President, Corporate Development.

Prior to joining Isis Pharmaceuticals, Dr. Jonas was Chief Medical Officer and Executive Vice President at Forest Laboratories, Inc., responsible for Clinical Development, Medical Affairs, Pharmacovigilence and External Scientific Affairs. Dr. Jonas joined Forest in 2003 as VP, Central Nervous System Area. In 2005, he was promoted to Senior VP, Clinical Development. In 2006, he was promoted to his current position. Dr. Jonas' initial experience in the pharmaceutical industry began in 1991 at Upjohn Laboratories initially as Director of Psychopharmacology and after several promotions ultimately as Chief Medical Officer and VP, Clinical Development. He has been responsible for numerous successful INDs and NDAs for drugs in a wide range of therapeutic classes.

In addition, Dr. Jonas has been a successful entrepreneur. He founded and led AVAX Technologies, a leader in autologous cell therapy and individualized therapy. During his tenure, he led AVAX through several successful financings, including an initial public offering in 1997. In 2001, he founded SCEPTOR Industries, a biotechnology company involved in biodefense surveillance.

Dr. Jonas has published more than 70 scientific papers and chapters and has received a number of awards. Dr. Jonas received his M.D. from Harvard Medical School in 1979, completed a residency in

psychiatry at Harvard following which he was Chief Resident in psychopharmacology at McClean Hospital, Harvard Medical School.

"The Board, Lynne, and I are extraordinarily pleased that Dr. Jonas is joining Isis. Jeff's appointment comes at a key moment in our history when antisense technology is validated and we have multiple drugs designed to treat multiple diseases in clinical development. Jeff's training and experience nicely complement the skills of the rest of our team, Mark Wedel, Senior VP and Chief Medical Officer and Art Levin, Senior VP, Preclinical Development," commented Dr. Stanley Crooke.

"Thanks to Mark Wedel's outstanding leadership, our clinical development group has become one of the core strengths of Isis. Art Levin has been a leader at Isis for more than a decade and has created an outstanding preclinical R&D organization that has pioneered the development of antisense technology and our drugs. Thus, Jeff joins a strong organization, and his appointment brings to Isis additional senior experience in drug development," said Dr. Crooke.

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 ocular, viral and neurodegenerative diseases, and cancer. In its Ibis BiosciencesTM division, Isis is developing and commercializing the Ibis T5000TM 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.

This press release includes forward-looking statements regarding Isis Pharmaceuticals and the Company's business. 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, 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

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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 September 30, 2006, which are on file with the SEC. Copies of these and other documents are available from the Company.

Ibis T5000, Ibis Biosciences and Isis Pharmaceuticals are trademarks or registered trademarks of Isis Pharmaceuticals, Inc.

Kate Corcoran, Ph.D. Vice President, Corporate Development

William Craumer Executive Director, Corporate Communications

Isis Pharmaceuticals, Inc. +1-760-603-2331