
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 10, 2011**

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 8.01. Other Events.

On January 10, 2011, Isis Pharmaceuticals, Inc. announced that it will hold a conference call focused on Genzyme's recent regulatory discussions with the FDA about the mipomersen NDA filing. A copy of the press release related to this announcement is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated January 10, 2011.

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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: January 10, 2011

By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL

Chief Operating Officer,

Chief Financial Officer and Director

INDEX TO EXHIBITS

99.1 Press Release dated January 10, 2011.



**ISIS PHARMACEUTICALS TO DISCUSS PRODUCTIVE REGULATORY DISCUSSIONS REGARDING THE MIPOMERSEN NDA FILING
IN A CONFERENCE CALL TODAY, JANUARY 10TH AT 9:00 A.M. ET**

Carlsbad, Calif., January 10, 2011 — Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced today that it will hold a conference call focused on Genzyme's recent regulatory discussions with the FDA about the mipomersen NDA filing.

Genzyme plans to communicate at its JP Morgan presentation Tuesday that:

- It had a productive meeting with the FDA.
- Based on FDA feedback, it believes the mipomersen package for HoFH is sufficient for filing.
- Due to the size of the severe HeFH population, the FDA provided guidance for additional 12 month exposure data before the mipomersen filing for severe HeFH. The Genzyme team is working with the FDA to further define the study required. FDA acknowledged that an outcome study may not be feasible in severe HeFH patients due to the size of the population.
- The EU filing continues on track toward a 1H filing for HoFH and may include severe HeFH.
- As Genzyme incorporates the FDA feedback, it will determine the timing for the US HoFH filing, which may shift to the second half of the year.

Conference Call

At 9:00 a.m. Eastern Time Monday, January 10, 2011, Isis will conduct a live webcast conference call. Interested parties may listen to the call by dialing 866-788-0544 and refer to passcode "ISIS 2011" or access the webcast at www.isispharm.com. A webcast replay will be available for a limited time at the same address.

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 24 drugs in development. Isis' drug development programs are focused on treating cardiovascular, metabolic, and severe neurodegenerative diseases and cancer. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Isis and Alnylam Pharmaceuticals are joint owners of Regulus Therapeutics Inc., a company focused on the discovery, development and commercialization of microRNA therapeutics. Isis also has made significant innovations beyond human therapeutics resulting in products that other companies, including Abbott, are commercializing. As an innovator in RNA-based drug discovery and development, Isis has designed and executed a patent strategy that has provided the Company with strong and extensive protection for Isis' drugs as well as all aspects of antisense drug discovery, development and manufacturing. Additional information about Isis is available at www.isispharm.com.

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This press release includes forward-looking statements regarding Isis' collaboration with Genzyme Corporation, its financial and business development activities, and the development, activity, therapeutic potential and safety of mipomersen in treating patients with high cholesterol. 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. 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 drugs. 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, 2009 and its most recent quarterly report on Form 10-Q, 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, including Regulus Therapeutics Inc.

Isis Pharmaceuticals is a registered trademark of Isis Pharmaceuticals, Inc. Regulus Therapeutics is a trademark of Regulus Therapeutics Inc.

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