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): **April 25, 2008**

ISIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware
(State or Other Jurisdiction of Incorporation)

000-19125	**33-0336973**
(Commission File No.)	(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))

o 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 April 25, 2008, Isis Pharmaceuticals, Inc. and Genzyme Corp. announced today that the FDA has provided guidance regarding approval requirements for mipomersen. A copy of the Press Release related to the guidance 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 April 25, 2008.

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: April 25, 2008

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

INDEX TO EXHIBITS

99.1	Press Release dated April 25, 2008.

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FDA PROVIDES CLARITY TO ISIS REGARDING THE DEVELOPMENT PATH FOR MIPOMERSEN

ISIS TO HOST CONFERENCE CALL TODAY AT 8 A.M. EST

CARLSBAD, Calif. and CAMBRIDGE, Mass., April 25, 2008 – Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) and Genzyme Corp. (Nasdaq: GENZ) announced today that the FDA has provided guidance regarding approval requirements for mipomersen. The FDA has indicated that reduction of LDL-cholesterol is an acceptable surrogate endpoint for accelerated approval of mipomersen for use in patients with homozygous familial hypercholesterolemia (hoFH). The FDA will require data from two ongoing preclinical studies for carcinogenicity to be included in the hoFH filing, which is now anticipated to take place in 2010. A phase 3 study of mipomersen in hoFH is currently enrolling patients.

The companies plan to conduct an outcome trial to support full approval of mipomersen for hoFH and to expand its indication to include other patients with high cholesterol who are at high risk for cardiovascular events. In response to the FDA's guidance, the companies are revising the development plan for mipomersen to accelerate plans for an outcome study. Isis and Genzyme plan to communicate further details of the revised development plan as they are finalized.

"Because our development plan, and our joint plan with Genzyme, has always included outcome studies to maximize the profile and commercial potential of mipomersen, this FDA guidance accelerates these planned studies and simplifies the overall development path for mipomersen," said Dr Stan Crooke, Chairman and Chief Executive Officer of Isis. "Conducting an outcome study in parallel with our continued evaluation of the effects of mipomersen on atherogenic lipids will allow us to submit a much stronger NDA for high risk patients. We are confident that mipomersen will bring benefit to patients with high cholesterol and remain committed to its development and commercialization."

"We are pleased that the FDA has given clear direction on what will be required for the approval of mipomersen, and has acknowledged its potential to help high risk patients whose needs are not being met by current therapies," said Henri A. Termeer, Genzyme's chairman and chief executive

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officer. "Having outcome data earlier on in the development process will be important to patients and serve to enhance the value of this treatment. We plan to engage in discussions with regulatory agencies in Europe and the rest of the world, and look forward to receiving their feedback."

ABOUT MIPOMERSEN

In early 2008, Isis and Genzyme announced that they had entered into a strategic alliance in which Genzyme will develop and commercialize mimpomersen. Final contracts are still being negotiated and are expected to be completed this quarter.

Mipomersen is a second-generation antisense drug that reduces the production of apoB-100, a protein critical to the synthesis and transport of "bad" cholesterol. Cholesterol can be carried in the bloodstream in a variety of forms, with high-density lipoprotein, or HDL-cholesterol, being the good form, and low-density lipoproteins, or LDL-cholesterol, and very low-density lipoproteins, or VLDL-cholesterol, being bad forms directly involved in heart disease. Collectively lowering LDL-cholesterol, VLDL-cholesterol, and other bad forms of cholesterol are a key component in the prevention and management of cardiovascular disease.

Mipomersen is currently in phase 3 development for patients with homozygous familial hypercholesterolemia, a disease which creates a greatly increased risk of premature cardiovascular disease (CVD) and CVD-related death. In phase 2 studies, mipomersen, a weekly injectable therapeutic, was observed to reduce cholesterol and other atherogenic lipids beyond reductions achieved with standard lipid-lowering drugs.

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' majority-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.

ABOUT GENZYME

One of the world's leading biotechnology companies, Genzyme is dedicated to making a major positive impact on the lives of people with serious diseases. Since 1981, the company has grown from a small start-up to a diversified enterprise with more than 10,000 employees in locations spanning the globe and 2007 revenues of $3.8 billion. In 2007, Genzyme was chosen to receive the National Medal of Technology, the highest honor awarded by the President of the United States for technological innovation.

With many established products and services helping patients in nearly 90 countries, Genzyme is a leader in the effort to develop and apply the most advanced technologies in the life sciences.

The company's products and services are focused on rare inherited disorders, kidney disease, orthopaedics, cancer, transplant, and diagnostic testing. Genzyme's commitment to innovation continues today with a substantial development program focused on these fields, as well as immune disease, infectious disease, and other areas of unmet medical need.

Genzyme's press releases and other company information are available at www.genzyme.com and by calling Genzyme's investor information line at 1-800-905-4369 within the United States or 1-678-999-4572 outside the United States.

ISIS SAFE HARBOR STATEMENT

This press release includes forward-looking statements regarding 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, 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, 2007, which is on file with the SEC. Copies of this and other documents are available from the Company.

GENZYME SAFE HARBOR STATEMENT

This press release contains forward-looking statements, including without limitation, statements concerning mipomersen's benefits for patients with high cholesterol, the development plan for mipomersen and FDA's requirements for its approval. These statements are subject to risks and uncertainties that could cause actual results to differ materially from those forecasted. These risks and uncertainties include, among others: the timing of further discussions with FDA regarding the approval of mipomersen; the timing and content of submissions to and decisions made by the FDA relating to mipomersen; further analysis of clinical trial data; the results of other studies; the actual efficacy and safety of mipomersen; and the risks and uncertainties described in Genzyme's SEC reports filed under the Securities Exchange Act of 1934, including the factors discussed under the caption "Risk Factors" in Genzyme's 2007 Annual Report on Form 10K. Genzyme cautions investors not to place substantial reliance on the forward-looking statements contained in this press release. These statements speak only as of today's date and Genzyme undertakes no obligation to update or revise the statements.

CONFERENCE CALL INFORMATION

At 8:00 a.m. Eastern Time Friday, April 25, Isis will conduct a live webcast conference call to discuss the mipomersen regulatory update. Interested parties may access the webcast at http://www.isispharm.com or listen to the call by dialing 877-604-9669. A webcast replay will be available for a limited time.

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