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): **May 20, 2009**

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 May 20, 2009, Isis Pharmaceuticals, Inc. and Genzyme Corp. announced that the phase 3 study of mipomersen in patients with homozygous familial hypercholesterolemia (hoFH) met its primary endpoint, with a 25 percent reduction in LDL cholesterol after 26 weeks of treatment, vs. 3 percent for placebo ($p<0.001$). A copy of the Press Release related to these data 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 May 20, 2009.

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: May 20, 2009

By: /s/ B. Lynne Parshall
B. LYNNE PARSHALL

Chief Operating Officer,
Chief Financial Officer and Director

INDEX TO EXHIBITS

99.1	Press Release dated May 20, 2009.

Exhibit 99.1

Genzyme and Isis Announce that Mipomersen Phase 3 Study in Patients with Homozygous Familial Hypercholesterolemia Met Primary Endpoint

- **25 Percent LDL-C Reduction in Very High-Risk Patient Population**

CAMBRIDGE, Mass. & CARLSBAD, Calif.—(BUSINESS WIRE)—Genzyme Corp. (NASDAQ: GENZ) and Isis Pharmaceuticals Inc. (NASDAQ: ISIS) today announced that the phase 3 study of mipomersen in patients with homozygous familial hypercholesterolemia (hoFH) met its primary endpoint, with a 25 percent reduction in LDL cholesterol after 26 weeks of treatment, vs. 3 percent for placebo ($p<0.001$). This study also met each of its three secondary endpoints of reduction in apolipoprotein B, total cholesterol and non-HDL cholesterol (all $p<0.001$).

Although the patients were on maximally tolerated statins and other lipid-lowering therapies, their average LDL-C at baseline was greater than 400 mg/dL. The reductions observed in the study were in addition to those achieved with the patients' existing therapeutic regimen. Full data from the study will be presented at a future medical meeting.

"These are promising results for a very high-risk patient population that is in great need of new treatment options," said Genzyme Chief Medical Officer Richard A. Moscicki, M.D. "This is one of the largest studies of hoFH patients ever conducted, and we are very encouraged by these robust data and the emerging profile of the drug. With these results, we remain on-track with our development plan for mipomersen."

Consistent with previous studies evaluating mipomersen, the most commonly observed adverse events were injection site reactions, flu-like symptoms and elevations in liver transaminases. Of the 34 patients treated with mipomersen, 28 completed the study. One patient discontinued due to elevations in liver transaminases.

"The results announced today are good news for patients with hoFH," said John J. P. Kastelein, M.D., Ph.D., Professor of Medicine and Chairman of the Department of Vascular Medicine at the Academic Medical Centre Amsterdam. "The currently available treatments do not provide the magnitude of lipid lowering that these patients need, leaving them at extraordinarily high risk of cardiovascular events. Mipomersen has the potential to change the standard of care for hoFH patients, whose life expectancies are limited due to the severity of this disease."

"This is a historic moment for Isis and antisense technology as this study represents the first successful phase 3 trial with a systemically delivered antisense drug," said Isis Pharmaceuticals Chairman and CEO Stanley T. Crooke, M.D., Ph.D. "This drug exemplifies the potential of the antisense drug discovery platform pioneered by Isis. We look forward to benefitting patients in need with mipomersen and other drugs in our pipeline."

The trial was a randomized, double-blind, placebo-controlled study that enrolled 51 hoFH patients, aged 12 and older. Seven patients were aged 12 to 17. Patients were randomized 2:1 to receive a 200 mg dose of mipomersen or placebo via weekly injections for 26 weeks. The trial was conducted at 10 sites in seven countries in North America, Europe, Asia, South America and Africa.

Data from this phase 3 study of mipomersen in patients with hoFH will form the basis of Genzyme's initial regulatory filing for marketing approval, which is anticipated in the second half of 2010.

About Familial Hypercholesterolemia (FH)

FH is a genetic disorder in which patients are unable to properly metabolize LDL cholesterol, resulting in elevated LDL-C levels. FH patients experience a markedly increased risk of premature cardiovascular disease (CVD) and CVD-related death. There are two forms of FH: homozygous (hoFH), where the same defective gene is inherited from both parents, or heterozygous (heFH), where the defective gene is inherited from only one parent so that some function is preserved.

The homozygous form of FH is a very rare condition estimated to affect approximately one in a million people. HoFH patients can have LDL-C levels greater than 600 mg/dL and are at very high risk for early coronary events and sudden death. Because many patients are resistant to the lipid-lowering effects of currently available therapies, effective treatment of hoFH patients is difficult. HeFH is a more common form of the disorder, with a prevalence of approximately one in 500, and results in untreated LDL cholesterol levels of approximately 300 mg/dL, double those of the general population.

About Mipomersen

Mipomersen is a first-in-class apo-B synthesis inhibitor currently in late-stage development. It is intended to reduce LDL-C by preventing the formation of atherogenic lipoproteins. Genzyme and Isis are currently conducting several clinical trials of mipomersen, including:

· A phase 3 study in patients with heterozygous FH;

· A phase 3 study in patients with severe hypercholesterolemia;

· A phase 3 study in hypercholesterolemic patients at high risk for coronary heart disease; and

· A phase 2 study in high-risk, high-cholesterol patients who are intolerant to statins.

Data from these trials are expected to be available at the time of the initial hoFH regulatory filing, and will continue to build the body of clinical evidence around the treatment's value in managing high-risk, high-cholesterol patients.

In 2008, Genzyme and Isis completed a licensing agreement that provides Genzyme with exclusive worldwide rights to mipomersen, which was discovered and initially developed by Isis.

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 11,000 employees in locations spanning the globe and 2008 revenues of $4.6 billion.

With many established products and services helping patients in approximately 100 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 immune disease, and diagnostic testing. Genzyme's commitment to innovation continues today with a substantial development program focused on these fields, as well as cardiovascular disease, neurodegenerative diseases, 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.

About Isis

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 19 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. 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 is the owner or exclusive licensee of over 1,600 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

Genzyme Safe Harbor Statement

This press release contains forward-looking statements regarding Genzyme's business plans and strategies including, without limitation, statements about the presentation of the data from the mipomersen Phase 3 clinical study; the expected timing of the mipomersen development plan and regulatory filings; and the potential uses and benefits of mipomersen. 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 actual timing of the completion of the analysis of the clinical study results; Genzyme's ability to accurately understand and predict the outcome and impact of its clinical studies related to mipomersen; Genzyme's ability to continue to support its clinical and other development efforts related to mipomersen; the actual efficacy and safety of mipomersen; the outcome of discussions with regulatory authorities regarding clinical studies 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 Quarterly Report on Form 10-Q for the period ended March 31, 2009. Genzyme cautions investors not to place undue reliance on the forward-looking statements contained in this press release. These statements speak only as of the date of this press release and Genzyme undertakes no obligation to update or revise the statements.

Isis Safe Harbor Statement

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 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, 2008, 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" refers to Isis Pharmaceuticals and its subsidiaries and joint venture.
