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): **August 4, 2010**

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 August 4, 2010, Isis Pharmaceuticals, Inc. and Genzyme Corp. announced results of two phase 3 studies of mipomersen in patients who had high cholesterol levels while on maximally tolerated lipid-lowering therapy. 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 August 4, 2010.

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: August 4, 2010

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

Chief Financial Officer and Director

INDEX TO EXHIBITS

99.1	Press Release dated August 4, 2010.

For Immediate Release
August 4, 2010

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Genzyme and Isis Report Results of Two Phase 3 Trials of Mipomersen

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Studies Meet Primary Endpoints with 36 and 37 Percent LDL-C Reductions in Severe Hypercholesterolemia and High-Risk Patients

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Companies Complete Phase 3 Studies Planned to Support Initial Filings

CAMBRIDGE, Mass. and CARLSBAD, Calif. — Genzyme Corp. (NASDAQ: GENZ) and Isis Pharmaceuticals Inc. (NASDAQ: ISIS) today announced results of two phase 3 studies of mipomersen in patients who had high cholesterol levels while on maximally tolerated lipid-lowering therapy. In the study of patients with severe hypercholesterolemia, mipomersen reduced LDL-C, the primary endpoint, by 36 percent compared with a 13 percent increase for placebo. In the study of patients with high cholesterol at high cardiovascular risk, mipomersen reduced LDL-C by 37 percent compared with a 5 percent reduction for placebo. Both studies met all of their secondary endpoints. Frequently observed adverse events were injection site reactions, flu-like symptoms and elevations in liver transaminases, as seen in previous studies.

With these studies, the companies have completed the four phase 3 studies that are planned to be included in the initial U.S. and E.U. regulatory filings for mipomersen. These filings, expected in the first half of 2011, will seek approval for the treatment of patients with homozygous familial hypercholesterolemia (FH), and may also include patients with severe hypercholesterolemia. The two previous phase 3 studies of mipomersen, which focused on patients with homozygous and heterozygous FH, also met their primary and secondary endpoints.

“We are pleased with the robust efficacy of mipomersen across all four phase 3 trials. These data, along with the emerging safety profile, support our focused approach on patients at highest cardiovascular risk who are in the greatest need of new treatments,” said Genzyme Senior Vice President John Butler. “With completion of these studies, we remain on-track with our plans for mipomersen.”

Phase 3 Study in Patients with Severe Hypercholesterolemia

This double-blind, placebo-controlled trial included 58 patients with severe hypercholesterolemia who were already taking maximally tolerated lipid-lowering medications. Severe hypercholesterolemia patients were defined as those who have LDL-C levels $\geq$ 200 mg/dL with baseline cardiovascular disease (CVD) or LDL-C levels $\geq$ 300 mg/dL without CVD. Patients were randomized 2:1 to receive 200 mg dose of mipomersen or placebo weekly for 26 weeks. This study was conducted at 26 sites in North America, Europe and South Africa.

Patients treated with mipomersen had an average LDL-C at baseline of 276 mg/dL. At the end of the trial, these patients had an average LDL-C level of 175 mg/dL, representing an average LDL-C reduction of 101 mg/dL (36 percent). The reductions observed in the study were in addition to those achieved with the patients’ existing maximally tolerated lipid-lowering regimens. The trial also met each of its three secondary endpoints with statistically significant reductions in apo-B, non-HDL-cholesterol and total cholesterol. Study results are based on an intent-to-treat analysis (full analysis set). Detailed results will be submitted for presentation at a medical meeting.

Of the 39 patients treated with mipomersen, 27 completed treatment; of the 19 patients treated with placebo, 18 completed treatment. Eight of the discontinuations in the mipomersen group were reported as being related to adverse events, the nature of which was generally similar to previous studies. The placebo discontinuation was reported as being related to an adverse event. There was one death in the study due to acute coronary syndrome in a patient treated with mipomersen that was reported as unrelated to treatment.

Elevations in liver transaminases (ALTs) in patients treated with mipomersen were observed that were generally similar in character with those seen in other studies. In this study, 15 percent of patients had persistent ALT elevations above 3X ULN (three times the upper limit of normal) during the treatment period. Persistent is defined as consecutive elevations at least one week apart. No patients had changes in laboratory tests indicative of clinically significant hepatic dysfunction, and there were no Hy’s Law cases.

“There are patients, such as those with familial hypercholesterolemia, who are on maximally tolerated doses of currently available medications and still are very far from appropriate target goals,” said James A. Underberg, M.D., of the New York University Center for Cardiovascular Disease Prevention. “For these high risk patients, there exists a tremendous need for additional lipid lowering therapies.”

Phase 3 Study in Hypercholesterolemic Patients at High Risk of Developing Coronary Heart Disease

This double-blind, placebo-controlled trial included 158 patients with hypercholesterolemia (LDL-C $\geq$ 100 mg/dL) and at high risk of developing coronary heart disease (CHD) who were taking a maximally tolerated dose of a statin. Patients were randomized 2:1 to receive a 200 mg dose of mipomersen or placebo weekly for 26 weeks. This study was conducted at 43 sites in the United States and Canada. This was the first study of mipomersen designed to evaluate patients with diabetes. More than 50 percent of patients in the study had type 2 diabetes.

Patients treated with mipomersen had an average LDL-C at baseline of 123 mg/dL. At the end of the study, these patients had an average LDL-C level of 75 mg/dL, representing an average LDL-C reduction of 48 mg/dL (37 percent). Half of the mipomersen-treated patients achieved LDL-C levels of less than 70 mg/dL, a recognized treatment goal for high-risk patients. The reductions observed in the study were in addition to those achieved with the patients' existing maximally tolerated statin regimens. The trial also met each of its three secondary endpoints with statistically significant reductions in apo-B, non-HDL-cholesterol and total cholesterol. Study results are based on an intent-to-treat analysis (full analysis set). Detailed results will be submitted for presentation at a medical meeting.

Of the 105 patients treated with mipomersen, 60 completed treatment; of the 53 patients treated with placebo, 44 completed treatment. Twenty-six of the discontinuations in the mipomersen group were reported as being related to adverse events, the nature of which was generally similar to previous studies. Two of the discontinuations in the placebo group were reported as being related to adverse events. There was one death in the study due to acute myocardial infarction in a patient treated with placebo.

Elevations in ALTs in patients treated with mipomersen were observed that were generally similar in character with those seen in other studies. In this study, 10 percent of patients had persistent ALT elevations above 3X ULN during the treatment period. Persistent is defined as consecutive elevations at least one week apart. In many cases, these elevations were associated with increased hepatic fat content, as measured by MRI. No patients had changes in laboratory tests indicative of clinically significant hepatic dysfunction, and there were no Hy's Law cases.

"The completion of these phase 3 studies is a significant milestone for the mipomersen program, for antisense technology and for patients in need," said Isis Pharmaceuticals Chairman and CEO Stanley T. Crooke. "Mipomersen's lipid-lowering activity demonstrates the value antisense drugs can bring to patients. Our robust pipeline is evidence of the efficiency of our technology and the potential value we can create."

Late-Stage Development Plan

Genzyme's initial U.S. and E.U. regulatory filings for mipomersen will seek marketing approval for the treatment of patients with the genetic disease homozygous FH (hoFH). These initial filings may also include patients with severe hypercholesterolemia. In the first half of 2011, Genzyme expects to submit the initial U.S. and E.U. filings, and to have made progress toward filing in other major international markets.

As previously reported, the phase 3 study of mipomersen in hoFH patients met its primary endpoint with 25 percent LDL-C reduction, and results were presented at last year's American Heart Association meeting. Genzyme and Isis in February reported that the phase 3 study of mipomersen in heFH met its primary endpoint with a 28 percent LDL-C reduction, and data will be presented at the European Society of Cardiology meeting this month. In addition, studies are ongoing and planned to evaluate alternative dosing regimens.

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 lipids. It acts by decreasing the production of apo-B, which provides the structural core for all atherogenic lipids, including LDL-C, which carry cholesterol through the bloodstream.

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 12,000 employees in locations spanning the globe and 2009 revenues of $4.5 billion. In 2010, Genzyme was named to the Fortune 500.

With many established products and services helping patients in 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. 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 23 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 is the owner or exclusive licensee of approximately 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 regarding mipomersen including, without limitation, statements about its potential uses, the expected timing of regulatory filings in the U.S. and E.U., and the studies that are expected to form a basis of the regulatory filings. 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: that regulatory authorities determine additional clinical studies of mipomersen are needed to support a 2011

filing; that Genzyme is unable to continue to support its clinical and other development efforts related to mipomersen; that regulatory authorities determine mipomersen's safety profile does not support approval for treatment of any or all of the targeted population; 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/A for the period ended March 31, 2010. 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 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.

Conference Call Information

Genzyme and Isis will host a conference call today at 8:30 a.m. Eastern. To participate in the call, please dial 1-517-308-9370 and refer to pass code "Genzyme." This call will also be webcast live on the investor events section of www.genzyme.com and on www.isispharm.com A replay of this call will be available by dialing 1-203-369-0784. Replays of the call and the webcast will be available until midnight on August 12, 2010.

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