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): **November 17, 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 November 17, 2009, Isis Pharmaceuticals, Inc. and Genzyme Corp. announced that data from the phase 3 study of mipomersen in patients with homozygous familial hypercholesterolemia (hoFH) were presented today at the American Heart Association's Scientific Sessions. 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 November 17, 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: November 17, 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 November 17, 2009.

For Immediate Release
November 17, 2009

Genzyme Contacts:
Erin Emlock (Media)
(617) 768-6923

Leah Monteiro (Investors)
(617) 768-6602

Isis Contacts:
Amy Blackley, Ph.D. (Media)
(760) 603-2772

Kristina Lemonidis (Investors)
(760) 603-2490

Data from Mipomersen Phase 3 Trial in hoFH Patients Presented at AHA

Study Meets Primary Endpoint with 25 Percent LDL Reduction in Very High-Risk Patient Population

CAMBRIDGE, Mass. and CARLSBAD, Calif. — Genzyme Corp. (NASDAQ: GENZ) and Isis Pharmaceuticals Inc. (NASDAQ: ISIS) announced that data from the phase 3 study of mipomersen in patients with homozygous familial hypercholesterolemia (hoFH) were presented today at the American Heart Association's Scientific Sessions. The study met its primary endpoint in an intent-to-treat analysis, with a 25 percent reduction in LDL-cholesterol after 26 weeks of treatment, vs. 3 percent for placebo ($p<0.001$) which constitutes an average reduction greater than 100 mg/dL. The trial also met each of its secondary endpoints.

This phase 3 study in hoFH patients, one of the largest trials to date in this rare population, was designed to test the efficacy and safety of adding mipomersen to substantial lipid-lowering therapy. Patients' average LDL-C at baseline was greater than 400 mg/dL. All but one of the patients were being treated with lipid-lowering therapy (50/51, 98 percent), of whom 11 (22 percent) were taking a statin alone and 39 (78 percent) were taking a statin in combination with at least one other lipid-lowering agent, most commonly ezetimibe (37/50, 74 percent). The LDL-C reductions observed in the study were in addition to those achieved with the patients' existing therapeutic regimen.

"These results are good news for patients with hoFH," said Professor Frederick J. Raal, Ph.D., Director of the Carbohydrate and Lipid Metabolism Research Unit at the University of the Witwatersrand in South Africa, and the study's primary investigator. "These patients are at very high risk of cardiovascular events despite being on currently available treatments, and their life expectancies are limited due to the severity of the disease. Mipomersen has the potential to change the standard of care for hoFH patients."

The trial met all of its secondary and tertiary endpoints, suggesting that mipomersen may offer potential benefits to patients beyond LDL-C reduction. Patients treated with mipomersen experienced a 27 percent reduction in apolipoprotein B vs. 3 percent for placebo; a 21 percent reduction in total cholesterol vs. 2 percent for placebo; and a 25 percent reduction in non-HDL cholesterol vs. 3 percent for placebo (all $p<0.001$).

Reductions were observed in other atherogenic lipids, including: Lp(a) by 31 percent and VLDL-C by 17 percent (both $p<0.01$ vs. placebo); and triglycerides by 18 percent ($p=0.013$ vs. placebo). Apo B, Lp(a) and triglycerides are all generally accepted risk factors for cardiovascular disease.

Mipomersen patients' HDL-C levels increased 15 percent ($p=0.035$ vs. placebo), which combined with the LDL-C reductions observed, resulted in improved LDL/HDL ratios, a ratio considered an important measure of cardiovascular risk. Mipomersen patients' LDL/HDL ratios decreased by 34% ($p<0.001$ vs. placebo).

"Mipomersen could represent a significant advance for hoFH patients, who are in great need of new treatment options," said John P. Butler, President of Genzyme's Cardiometabolic and Renal business. "We are excited about this therapy's potential and are making excellent progress in our development plan for bringing it to the market."

Consistent with previous studies evaluating mipomersen, the most commonly observed adverse events were injection site reactions (77 percent for mipomersen vs. 24 percent for placebo), flu-like symptoms (29 percent for mipomersen vs. 24 percent for placebo) and elevations in liver transaminases (12 percent $\geq$ 3 X ULN for mipomersen vs. none for placebo.)

Of the 34 patients treated with mipomersen, 28 completed the study. Reasons for withdrawal from the mipomersen group were: injection site reactions (2), elevations in liver transaminases (1), rash (1), personal reasons (1), and non-compliance (1).

Four patients had elevations in liver transaminases above 3 X ULN (three times the upper limit of normal), three of whom reached between 5 and 8 X ULN. None of these patients, including the patient who discontinued the study, had changes in other laboratory tests to indicate hepatic dysfunction, i.e., Hy's Law. In all cases, transaminases returned to entry criteria by the end of planned clinical observations.

"Mipomersen continues to provide an exciting example of the potential of Isis' antisense technology platform to create potent and specific drugs that could play an important role in the treatment of disease," said Stanley Crooke, Chairman and Chief Executive Officer of Isis Pharmaceuticals. "Apo-B, the target of mipomersen, is a very attractive target for lowering atherogenic lipids, but has been an inaccessible target using traditional drug discovery methods until now. Mipomersen is representative of Isis' leadership in the field of RNA targeted therapeutics."

Development Plan

Genzyme's initial U.S. and E.U. regulatory filings for mipomersen will seek marketing approval for the treatment of patients with hoFH. These two filings may also include patients with severe hypercholesterolemia. A phase 3 study of mipomersen in patients with severe hypercholesterolemia is fully enrolled with 58 patients and data are anticipated in mid-2010.

With the completion of enrollment of this study, the last of the four phase 3 studies that will form the basis for the first regulatory filings, Genzyme continues to refine and expand the regulatory and commercial strategy for mipomersen. By mid-2011, Genzyme expects to have filed for approval in the U.S. and E.U. and to have made progress toward filing in other major international markets.

The companies have also completed enrollment in a phase 3 trial of mipomersen in patients with heterozygous FH; there are 124 patients in this study and results are expected in the first quarter of 2010. In addition, a phase 3 trial in hypercholesterolemic patients at high risk for coronary heart disease is now fully enrolled with 158 patients, and data are anticipated in mid-2010.

As Genzyme and Isis investigate mipomersen's potential in patient populations beyond hoFH, the companies are continuing to improve the treatment's tolerability profile and are planning two new studies exploring alternative dosing regimens. The first, a phase 1 trial, is expected to begin during the first quarter of next year. This trial will compare a 30 mg daily injection, a 70 mg injection three times a week, and a 200 mg weekly injection, each with placebo. This study will be followed by a longer trial in patients examining the efficacy and safety of alternative dosing regimens.

Data from these and other ongoing studies of mipomersen will inform the design of an outcome study to support mipomersen's use in a broader group of at-risk, high cholesterol patients.

About the phase 3 study in hoFH patients

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.

Professor Raal presented the overall study results at AHA. Study investigator Dr. William Cromwell, Chief of the Division of Atherosclerosis and Lipoprotein Disorders at the Presbyterian Cardiovascular Institute in Charlotte, North Carolina, also presented at AHA on the effects of mipomersen on Lp(a) within the trial.

All study participants had the option of enrolling in an open-label extension trial. The extension study's efficacy measurements include percent reduction of LDL-C, apo-B and non-HDL-C at various points through at least 52 weeks of treatment. Of the 28 patients treated with mipomersen who completed the initial trial, 23 enrolled in the extension study; of the 17 placebo patients, 16 enrolled in the extension.

About Familial Hypercholesterolemia

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 Lp(a)

Lp(a) is a lipoprotein particle that is found in atherosclerotic plaques and appears to play a role in complications at these plaque sites. Studies have shown that increased levels of Lp(a) are associated with increased vascular risk due to the proatherogenic and prothrombotic effects of the lipoprotein. Lp(a) is now generally recognized as an independent cardiovascular risk factor. In view of observed associations of high levels of Lp(a) with vascular disease, research suggests that treatments to reduce Lp(a) levels could be clinically beneficial.

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, 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 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 potential uses and benefits of mipomersen; the expected timing of regulatory filings for mipomersen; and the design of future clinical studies of mipomersen and the expected timing of such studies. 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 efficacy and safety of mipomersen; the actual timing and results of the clinical studies; 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 outcome of discussions with regulatory authorities regarding clinical

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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 September 30, 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, Isis' 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.

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