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): **October 4, 2007**

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 October 4, 2007, Isis Pharmaceuticals, Inc. ("Isis") announced new results from its Phase 2 clinical trial of ISIS 301012 in patients with heterozygous familial hypercholesterolemia (HeFH) on stable maximally tolerated lipid-lowering therapies presented in a poster session today at the Drugs Affecting Lipid Metabolism (DALM) XVI International Symposium in New York City. 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 October 4, 2007.

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: October 3, 2007

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

INDEX TO EXHIBITS

99.1	Press Release dated October 4, 2007.

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ISIS REPORTS POSITIVE RESULTS OF PHASE 2 STUDY OF ISIS 301012 IN HETEROZYGOUS FH PATIENTS

- **HeFH Patients on Maximally Tolerated Lipid-Lowering Therapies Experienced 46% Further Reductions in LDL-C when Treated with 300 mg/week ISIS 301012 for 13 Weeks**
- **Study Presented in Poster Session Today at DALM Symposium in New York City**
- **Isis Will Host a Conference Call on Monday, October 8, at 8:00 a.m. E.T. at www.isispharm.com**

CARLSBAD, Calif., October 4, 2007 –Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced new results from its Phase 2 clinical trial of ISIS 301012 in patients with heterozygous familial hypercholesterolemia (HeFH) on stable maximally tolerated lipid-lowering therapies presented in a poster session today at the Drugs Affecting Lipid Metabolism (DALM) XVI International Symposium in New York City. These results will also be presented by Dr. John J.P. Kastelein in an oral session at DALM on Saturday at 3:45 p.m. E.T., and Isis will host a conference call Monday morning at 8:00 a.m. E.T. to further discuss the results.

In a randomized, double-blind, placebo-controlled study, HeFH patients being treated with maximally tolerated lipid-lowering therapies were treated with ISIS 301012 for 6 or 13 weeks. Median baseline LDL-C levels for the dose cohorts ranged from 159 — 204 mg/dL. ISIS 301012 add-on treatment produced potent, dose-dependent, prolonged reductions in all atherogenic lipids, and results were consistent with those reported for patients with routine high cholesterol. Furthermore, this study confirmed that ISIS 301012 treatment results in meaningful reductions in Lp(a), another important predictor of cardiovascular disease. These reductions and accompanying improvements in other atherogenic lipid levels were all relative to baseline levels which already reflected the impact of ongoing maximally tolerated lipid-lowering therapies. ISIS 301012 was well tolerated in the study.

According to Evan Stein, M.D., Ph.D., Director, Metabolic and Atherosclerosis Research Center, Cincinnati, Ohio, a principal investigator for the studies, "The performance of ISIS 301012 continues to be extremely encouraging, especially for those of us who care for the many heterozygous FH patients who aren't able to achieve target lipid levels despite being treated with all that we currently have to offer them. The attributes of ISIS 301012, including its effects not only on LDL-C but also on triglycerides and Lp(a) - other important markers of cardiovascular risk, make it all the more promising as a new drug with a unique and complementary profile to available therapies."

ISIS 301012 Coadministered with Maximally Tolerated Lipid-Lowering Therapies

This randomized, placebo-controlled, double-blind, sequential dose-escalation trial included cohorts receiving 6 weeks of treatment at doses of 50, 100, 200 or 300 mg/week. Because ISIS 301012 was well tolerated in the lower dose cohorts and in other ongoing Phase 2 studies, the dosing period for the 300 mg/week cohort was extended to 13 weeks. All patients in the study were diagnosed with heterozygous FH with median baseline levels of LDL-C ranging from 159 — 204 mg/dL while being treated with maximally tolerated doses of lipid-lowering therapies including high-dose statins either alone or in combination with cholesterol absorption inhibitors, bile acid sequestrants or fish oil capsules. At a dose of 300 mg/week for 13 weeks, patients receiving ISIS 301012 achieved median reductions of 43% in apoB and 46% in LDL-C beyond the levels they had already achieved on stable lipid-lowering therapies. ISIS 301012 treatment did not affect HDL-cholesterol (HDL-C) levels.

Table 1: ISIS 301012 in HeFH Patients on Maximally Tolerated Lipid-Lowering Therapies, Summary of Results. Median % changes from baseline at primary endpoint*

Per Protocol	Placebo	50 mg/week	100 mg/week	200 mg/week	300 mg/week	
# of patients (treatment duration)	8 (8 for 6 weeks, 2 for 13 weeks)	7 (6 weeks)	8 (6 weeks)	9 (6 weeks)	8 (6 weeks)	8 (13 weeks)
ApoB	-6%	-9% (p=0.69)	-9% (p=0.57)	-20% (p=0.02)	-33% (p=0.01)	-43% (p=0.02)
LDL-C	-5%	-12% (p=0.12)	-11% (p=0.19)	-20% (p=0.03)	-36% (p=0.003)	-46% (p=0.03)
Non-HDL-C	-6%	-10% (p=0.23)	-6% (p=0.57)	-26% (p=0.04)	-30% (p=0.01)	-39% (p=0.03)
HDL-C	11%	-7% (p=0.28)	-1% (p=0.28)	-4% (p=0.28)	10% (p=0.88)	5% (p=0.97)
ApoA-1	-1%	-1% (p=0.78)	0% (p=0.88)	-5% (p=0.56)	1% (p=0.96)	-2% (p=0.81)
TC	-2%	-11% (p=0.19)	-5% (p=0.44)	-24% (p=0.04)	-22% (p=0.007)	-31% (p=0.03)
TG	-17%	5% (p=1.00)	6% (p=0.16)	-25% (p=0.14)	-27% (p=0.51)	-24% (p=0.46)
Lp(a)	-3%	0% (p=0.84)	-19% (p=0.16)	-17% (p=0.14)	-25% (p=0.03)	-37% (p=0.37)

p value = vs. placebo

*Primary endpoint analysis was Study Day 43 for the 6 week treatment cohorts, and Day 99 for the 13 week treatment cohort.

There were no Serious Adverse Events in the study, and the most common Adverse Event was transient, painless erythema at the site of injection. There was no effect on liver synthetic function as indicated by changes in bilirubin and albumin levels and prothrombin time. Three patients treated with the 300 mg/week dose experienced mild elevations of liver transaminases above three times the upper limit of normal; the maximal ALT observed in the study was 216 IU/L. Patients in this study remain in follow-up or are participants in the ongoing Open-Label Extension study.

ABOUT ISIS 301012 AND CHOLESTEROL

ISIS 301012 is a second-generation antisense drug that reduces the production of apoB-100, a protein critical to the synthesis and transport of “bad” cholesterol and a target that has proved to be undruggable using traditional, small-molecule approaches. Cholesterol can be carried in the bloodstream in a variety of forms, with high-density lipoprotein, or HDL-C, being the good form, and low-density lipoproteins, or LDL-C, and very low-density lipoproteins, or VLDL-C, being bad forms directly involved in heart disease. Collectively, LDL-C, VLDL-C, and other bad forms of cholesterol are referred to as “non-HDL-C.” The lowering of non-HDL-C is a key component in the prevention and management of cardiovascular disease. Isis plans to develop ISIS 301012 as the drug of choice for patients who are unable to achieve target cholesterol levels with statins alone or who are intolerant of statins. For future studies, including the registration studies for FH and the long-term coadministration study planned for patients with routine high cholesterol, both expected to begin this year, Isis has selected 200 mg/week as its development dose.

ABOUT FAMILIAL HYPERCHOLESTEROLEMIA

Familial hypercholesterolemia is a genetic condition that results in markedly elevated LDL-C levels beginning at birth and heart attacks at an early age. People with the disease have consistently high levels of LDL-C, which leads to premature atherosclerosis of the coronary arteries. Current therapies for FH are inadequate, and the most severely affected patients may need apheresis, an expensive and time-consuming procedure that removes the “bad” cholesterol from the blood. Homozygous FH is rare,

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affecting about one in one million people, but heterozygous FH is much more common with a prevalence of approximately one in every 500 people.

Conference Call Information

At 8:00 a.m. Eastern Time Monday, October 8, Isis will conduct a live webcast conference call to discuss ISIS 301012 results. Interested parties may access the webcast at http://www.isispharm.com or listen to the call by dialing 888-211-7384 (U.S.) / 913-312-0380 (International). A replay will be available for a limited time.

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 17 drugs in development. Isis’ drug development programs are focused on treating cardiovascular and metabolic diseases. Isis’ partners are developing drugs for a wide variety of diseases. Ibis Biosciences, Inc., Isis’ wholly owned subsidiary, is developing and commercializing the Ibis T5000™ Biosensor System, a revolutionary system to identify infectious organisms. 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 http://www.isispharm.com.

This press release includes forward-looking statements regarding the development, activity, therapeutic potential and safety of ISIS 301012 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 or projections. 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, in developing and commercializing systems to identify infectious organisms that are effective and commercially attractive, 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, 2006, and its quarterly report on Form 10-Q for the quarter ended June 30, 2007, which are on file with the SEC. Copies of this 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.

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