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 5, 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 5, 2007, Isis Pharmaceuticals, Inc. ("Isis") announced the first safety results from its ongoing Phase 2 open-label extension (OLE) study of ISIS 301012 in patients with familial hypercholesterolemia (FH) on stable maximally tolerated lipid-lowering therapies. 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 5, 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 5, 2007.

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ISIS REPORTS THAT ISIS 301012 IS WELL TOLERATED IN PATIENTS TREATED FOR FIVE OR MORE MONTHS

- **Twelve of Sixteen FH Patients in an Ongoing Open-Label Extension Study Have Been Dosed With ISIS 301012 for Approximately Five Months or More, and Four Have Been Dosed for More Than Six Months**
- **Isis Will Host a Conference Call on Monday, October 8, at 8:00 a.m. E.T. at www.isispharm.com**

CARLSBAD, Calif., October 5, 2007 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced the first safety results from its ongoing Phase 2 open-label extension (OLE) study of ISIS 301012 in patients with familial hypercholesterolemia (FH) on stable maximally tolerated lipid-lowering therapies. In addition, yesterday Isis announced results from a placebo-controlled Phase 2 study of ISIS 301012 in patients with heterozygous FH that were presented in a poster session today at the Drugs Affecting Lipid Metabolism (DALM) XVI International Symposium in New York City. Collectively, these results will 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 discuss the results.

The ongoing Phase 2 OLE study includes 16 FH patients who had completed one of Isis' initial Phase 2 studies in FH patients and who subsequently enrolled in this open-label extension study. ISIS 301012 continues to be well tolerated by these patients with extended exposures and in the presence of continued maximally tolerated lipid-lowering therapies. As of September 17, four patients had received more than six months of weekly doses of ISIS 301012 over the course of both initial and OLE studies, and 12 of the 16 patients had total exposures of approximately five months or more. No new types of adverse events were observed with extended dosing or repeat exposures, no worsening of injection site reactions, and no increase in the frequency or severity of liver transaminase elevations.

John J.P. Kastelein, M.D., Ph.D., Chairman, Department of Vascular Medicine at the Academic Medical Center in Amsterdam, The Netherlands, also a principal investigator for the studies, commented, "We are particularly pleased to have had such an uneventful experience with patients in the long-term study. Until now, the longest exposures to ISIS 301012 had been three months, and now to have patients dosed for a total of more than six months without any tolerability issues is quite reassuring. Of course, we will all be eager to see more patients and longer exposure times to strengthen our confidence that ISIS 301012 could truly be a transformational new drug for the treatment of refractory high cholesterol."

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

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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, 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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