UNITED STATES
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 13, 2006

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 13, 2006, Isis Pharmaceuticals, Inc. ("Isis") announced new Phase 2 clinical data from ISIS 301012 studies. 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 13, 2006.

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 13, 2006

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

INDEX TO EXHIBITS

99.1 Press Release dated November 13, 2006.

ISIS PHARMACEUTICALS REPORTS ISIS 301012 SIGNIFICANTLY REDUCES ALL ATHEROGENIC LIPIDS WHEN DOSED AS A SINGLE AGENT AND WHEN COADMINISTERED WITH STATINS

- ***ISIS 301012 Lowered LDL-C 62% as Single Agent Dosed for Three Months***
- ***After Only Five Weeks of Treatment, ISIS 301012 Coadministered with Statins Lowered LDL-C 51% Beyond the Levels Achieved with Statins Alone***
- ***ISIS 301012 Was Well-Tolerated in Both Studies***
- ***Webcast Tomorrow, November 13, at 8:00 a.m. E.S.T. at www.isispharm.com***

CARLSBAD, CA, November 12, 2006 - Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced exciting new results from two Phase 2 clinical trials of ISIS 301012 presented today at the American Heart Association Annual Scientific Sessions in Chicago. In the first study reported, patients with high cholesterol on stable doses of statins were treated with ISIS 301012 for five weeks. Patients who received 300 mg/week of ISIS 301012 in this study achieved a 51% reduction in LDL-cholesterol (LDL-C), a 42% reduction in total cholesterol (TC), and a 41% reduction in triglycerides (TG) beyond the levels achieved with statins alone. Isis also presented new results from an ongoing study in which patients with high cholesterol were treated for three months with 300 mg/week of ISIS 301012 as a single agent. Data from this study for dose cohorts through 200 mg/week were previously reported. In this study, increasing the dose of ISIS 301012 to 300 mg/week further reduced atherogenic lipids, with improvements in LDL-C, TC and TG of 62%, 46% and 43%, respectively.

In addition, in these studies ISIS 301012 continued to demonstrate a strong safety profile - as a single agent and when coadministered with statins - in every dose cohort presented. The drug was well-tolerated in both studies.

According to John J.P. Kastelein, M.D., Ph.D., Chairman, Department of Vascular Medicine at the Academic Medical Center in Amsterdam, The Netherlands, "These are quite remarkable results that are very encouraging for further development of ISIS 301012. These new data demonstrate

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pronounced lipid-lowering effects of ISIS 301012, both as a single agent and as an add-on to statin therapy. Further, the drug appears to have a positive safety profile, even at higher doses and when coadministered with statins."

"The guidelines for target cholesterol levels continue to be revised downward," Dr. Kastelein continued. "A significant percentage of at-risk patients are simply not meeting LDL-C targets with current lipid-lowering drugs, so there is a growing need for therapies that can be added to statins to achieve additional reductions in atherogenic lipids. ISIS 301012 shows promise for this group of patients."

Mark Wedel, M.D., J.D., Isis' Chief Medical Officer, added, "We are pleased with the performance of ISIS 301012 in patients, especially with its safety and activity when coadministered with statins demonstrated after only five weeks of treatment. Because ISIS 301012 has a half-life of over 30 days, we are looking forward to seeing results from longer-duration studies where we expect to see even better efficacy than that achieved over this short treatment period. These new data underscore the fact that by inhibiting the production of apoB-100, ISIS 301012 works through a mechanism complementary to statins, enabling effective add-on therapy in patients who have achieved maximal lipid lowering on statins but are unable to reach their desired LDL-C levels."

Isis' Chairman of the Board and Chief Executive Officer, Stanley T. Crooke, M.D., Ph.D, commented, "With these studies, we have answered three important questions: first, with safe doses of ISIS 301012 we can lower atherogenic lipids as or more effectively than any drug currently in use; second, we've shown that ISIS 301012 as an add-on to ongoing statin therapy results in more than double the reduction in atherogenic lipids achieved with ezetimibe or other drugs typically added to statins; third, we have shown that ISIS 301012 is well-tolerated as add-on therapy to statins. We're very excited about these recent results and they set the stage for continued development of this novel lipid-lowering drug."

ISIS 301012 Coadministered with Statins

This randomized, double-blinded, placebo-controlled, dose-escalation study calls for five weeks of therapy at doses of 30, 100, 200, 300 and 400 mg/week. It was recently expanded to include longer-term treatment as well. Patients in the study have LDL-C levels between 100 and 220 mg/dL and have been on stable doses of £ 40 mg of simvastatin or atorvastatin for at least three months. The results of the five week dosing cohorts through 300 mg/week were presented yesterday. At a dose of 300 mg/week, patients receiving ISIS 301012 achieved median reductions of 51% in LDL-C, 42% in TC, 51% in non-HDL-C and 41% in TG beyond the levels they had already achieved on stable statin doses. These results are comparable to the reductions achieved with ISIS 301012 as a single agent and they are consistent with the data suggesting ISIS 301012 acts through a mechanism of lipid lowering that is independent of and complementary to the statin mechanism. The data further demonstrate that when coadministered with a stable dose of statins, ISIS 301012 displays a linear dose response relationship (200 mg/week lowered LDL-C by 30% while 300 mg/week lowered LDL-C by 51%).

Table 1: ISIS 301012 Coadministered with Statins, Median Percent Reductions from Baseline,

Day 59*

	Placebo	30 mg/week	100 mg/week	200 mg/week	300 mg/week
# of patients	9	8	8	8	8
ApoB	-6%	0% (p=0.54)	-20% (p=0.18)	-24% (p=0.05)	-52% (p=0.0006)
LDL-C	-4%	4% (p=0.23)	-22% (p=0.05)	-30% (p=0.002)	-51% (p=0.0005)
Total Cholesterol	-3%	5% (p=0.61)	-15% (p=0.02)	-20% (p=0.03)	-42% (p=0.0006)
Non-HDL-C	-8%	8% (p=0.23)	-20% (p=0.10)	-26% (p=0.07)	-51% (p=0.0003)
Triglycerides	-24%	4% (p=0.12)	4% (p=0.14)	-20% (p=0.90)	-41% (p=0.15)
HDL-C	12%	1% (p=0.09)	-4% (p=0.05)	-2% (p=0.04)	5% (p=0.24)

* 30 days post dosing p value = vs. placebo

ISIS 301012 as a Single Agent

This randomized, double-blinded, placebo-controlled, dose-escalation trial treated patients with high cholesterol (stable LDL-C ³ 130 mg/dL) for three months with ISIS 301012 as a single agent. In April, results for the first three dose cohorts through 200 mg/week were presented. Today the data from the 300 mg/week dose cohort were presented, documenting median reductions of 62% in LDL-C,

46% in TC, 54% in non-HDL-C and 43% in TG. These data demonstrate that in contrast to statins, ISIS 301012 causes linearly increasing reductions of atherogenic lipids as doses are increased.

Table 2: ISIS 301012 as a Single Agent, Median Percent Reductions from Baseline, Day 99*

	Placebo	50 mg/week	100 mg/week	200 mg/week	300 mg/week
# of patients	8	8	8	8	8
ApoB	7%	-22% (p=0.07)	-23% (p=0.001)	-47% (p=0.0002)	-61% (p=0.0003)
LDL-C	2%	-12% (p=0.33)	-22% (p=0.01)	-42% (p=0.0002)	-62% (p=0.0003)
Total Cholesterol	6%	-12% (p=0.33)	-15% (p=0.09)	-34% (p=0.0002)	-46% (p=0.0003)
Non-HDL-C	4%	-17% (p=0.25)	-21% (p=0.02)	-44% (p=0.0002)	-54% (p=0.0003)
Triglycerides	-13%	-7% (p=0.65)	-22% (p=0.54)	-46% (p=0.02)	-43% (p=0.04)
HDL-C	2%	9% (p=0.28)	5% (p=0.40)	-1% (p=0.72)	-15%** (p=0.009)

* 14 days post dosing p value = vs. placebo

** HDL-C measurements for this study were performed using a direct method that can be inaccurate when LDL-C levels are low. Parallel evaluation of the 300 mg/week cohort in this study using a common precipitation method showed an 11% increase in HDL-C.

The safety data for ISIS 301012 continue to show that the drug is well-tolerated. In both studies, the most common adverse events were injection site reactions, categorized as mild and painless, that did not interfere with treatment. No clinically significant effects on liver function tests were observed.

More about Phase 2 Trials for ISIS 301012

Both studies for which data were presented are continuing with patients currently being enrolled in the 400 mg/week dose cohort of the single agent study and the 400 mg/week dose cohort for the five-week coadministration with statins study. Extended three-month treatment periods are planned for subsequent cohorts of 200 and 300 mg/week doses in the statin coadministration study.

In addition to the two studies described above, ISIS 301012 is currently being evaluated in Phase 2 dose escalation studies in patients with homozygous and heterozygous Familial Hypercholesterolemia (FH). Data from these trials, in which patients are being dosed with ISIS 301012 as an add-on to their existing lipid-lowering therapies, are expected late in 2006 or early 2007. ISIS 301012 has been

granted orphan drug status for the treatment of homozygous FH and Isis plans to begin registration-directed studies for FH in 2007.

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.

The National Cholesterol Education Program’s Adult Treatment Panel updated LDL-C target for High-Risk patients is less than 100 mg/dL. For Moderately High-Risk patients, the target is less than 130 mg/dL. Over 20 million Americans in the High-Risk and Moderately High-Risk categories are failing to meet their LDL-C targets using currently available lipid-lowering therapies.

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.

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 14 drugs in development. Isis' drug development programs are aimed at treating cardiovascular, metabolic and inflammatory diseases. Isis' partners are focused in disease areas such as ocular, viral and neurodegenerative diseases, and cancer. In its Ibis Biosciences™ division, Isis 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 approximately 1,500 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

This press release includes forward-looking statements regarding the development, therapeutic potential and safety of ISIS 301012 targeting apoB-100 and in treating high cholesterol and cardiovascular disease. Any statement describing Isis' goals, expectations, 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. 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, 2005, and its quarterly report on Form 10-Q for the quarter ended September 30, 2006, which are on file with the SEC. Copies of these and other documents are available from the Company.

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Contacts:

Kate Winkler Corcoran, Ph.D.
Vice President, Corp. Development
Isis Pharmaceuticals, Inc.
+1 760 603.2712

William C. Craumer
Executive Director, Corp. Communications
Isis Pharmaceuticals, Inc.
+1 760 603.2773