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, 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 November 13, 2007, Isis Pharmaceuticals, Inc. ("Isis") announced new results from its Phase 2 clinical trial of mipomersen (ISIS 301012) in patients with routine high cholesterol, as well as provided an integrated Phase 1 & Phase 2 safety summary for the drug. 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, 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: November 13, 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 November 13, 2007.

Isis Pharmaceuticals' Contacts:
Kristina Lemonidis
Associate Director, Investor Relations
760-603-2490

Amy Blackley, Ph.D.
Manager, Corporate Communications
760-603-2772

ISIS REPORTS NEW DATA FOR MIPOMERSEN IN ROUTINE HIGH CHOLESTEROL PATIENTS AND PROVIDES CUMULATIVE SAFETY SUMMARY

- **Patients on stable doses of statins treated for 3 months with 200 mg/week mipomersen experienced 48% further reduction in LDL-cholesterol**
- **Integrated Phase 1 & 2 safety update continues to support mipomersen's favorable safety profile**
- **Isis hosting Analyst & Investor Day today — webcast live at 9:00 a.m. EST at www.isispharm.com**

CARLSBAD, Calif., November 13, 2007 — Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) announced new results from its Phase 2 clinical trial of mipomersen (ISIS 301012) in patients with routine high cholesterol, as well as providing an integrated Phase 1 & Phase 2 safety summary for the drug. Data are being presented in conjunction with Isis' Analyst & Investor Day today in New York, which will be webcast live at 9:00 a.m. EST at www.isispharm.com.

Eight patients with routine high cholesterol on stable doses of less than or equal to 40 mg/day of statins were treated with 200 mg/week mipomersen for three months. Results were compared with those from 14 placebo-treated patients. All patients remained on stable statin therapy throughout the study. Mipomersen treatment resulted in a 42% reduction in apoB and a 48% reduction in LDL-C, beyond reductions achieved with statin therapy alone. Previously, Isis reported results from the dose escalation portion of the study. With five weeks of treatment at 200 mg/week reductions in apoB and LDL-C were 24% and 30% respectively, so, as predicted, extending treatment with mipomersen from five weeks to 13 weeks led to further reductions in apoB and LDL-C. Mipomersen was well tolerated throughout the study.

Further, Isis reported results of an integrated safety analysis including data from more than 250 subjects treated with mipomersen in Phase 1 and Phase 2 studies. This analysis demonstrates that mipomersen has been well tolerated and that treatment with mipomersen did not result in evidence of liver toxicity. Among all subjects who received mipomersen, there were no instances of transaminase (ALT) elevations associated with two-fold increase in bilirubin or any other signs or symptoms of liver dysfunction. While on treatment, 3% of subjects treated with placebo and 3% of subjects treated with 200 mg/week mipomersen experienced ALT elevations of 150-250 IU/L. During the entire study periods, including dosing plus 90 day follow up, 5% and 7% of subjects treated with placebo or 200 mg/week of mipomersen, respectively, experienced ALT elevations of 150-250 IU/L. The most common adverse event was mild to moderate injection site reactions.

According to Jeffrey Jonas, M.D., Executive Vice President, Isis Pharmaceuticals, "Our clinical experience continues to demonstrate the lipid-lowering activity of mipomersen, which has been equally effective across multiple patient populations both as a single agent and in combination with lipid-lowering

---

therapies. Furthermore, mipomersen's lipid-lowering effects have been highly predictable. As we expected, extending treatment from five to 13 weeks results in further lipid lowering, increasing LDL-C reductions from 30% to 48%.

"In addition, we have now dosed over 250 subjects with mipomersen and are able to present an extensive integrated safety summary. We have explored a full dose range for mipomersen as a single agent and in combination with moderate to maximal lipid-lowering therapies, and we have exposed subjects to aggressive loading and induction schedules. Mipomersen continues to display an attractive safety profile. The primary adverse event in our studies has been mild to moderate injection site reactions, which represent cosmetic inconveniences rather than safety concerns. We have not observed elevations in liver enzymes associated with increases in bilirubin or other signs or symptoms of liver dysfunction. During treatment and follow-up periods, subjects who received 200 mg/week mipomersen, our Phase 3 dose, experienced mild ALT elevations of 3-5xULN, similar to those in subjects who received placebo. These data are particularly impressive when one considers the fact that every subject was evaluated weekly and all ALT elevations were counted, whether confirmed or not. Based on this experience, we are very encouraged by mipomersen's overall safety and efficacy profile," concluded Dr. Jonas.

Table 1: Mipomersen in Routine High Cholesterol Patients Coadministered with Statins
Summary of Results. Median % changes from baseline at primary endpoint.*

Per Protocol	Placebo	30 mg/week 5 weeks	100 mg/week 5 weeks	200 mg/week 5 weeks	300 mg/week 5 weeks	400† mg/week 5 weeks	200‡ mg/week 13 weeks
# of patients	11	8	8	16	8	8	8
ApoB	-1%	0% (p=0.80)	-20% (p=0.03)	-24% (p=0.004)	-52% (p<0.0001)	-51% (p=0.0004)	-42% (p<0.0001)
LDL-C	-4%	4% (p=0.31)	-22% (p=0.01)	-30% (p=0.002)	-51% (p<0.0001)	-47% (p=0.008)	-48% (p<0.0001)
VLDL-C	7%	8% (p=0.84)	10% (p=0.66)	-25% (p=0.38)	-63% (p=0.08)	-69% (p=0.02)	-17% (p=0.80)
Non-HDL-C	-1%	8% (p=0.44)	-20% (p=0.02)	-22% (p=0.02)	-51% (p<0.0001)	-49% (p=0.008)	-30% (p=0.006)
HDL-C	9%	1% (p=0.24)	-4% (p=0.15)	6% (p=0.23)	5% (p=0.41)	6% (p=0.60)	-4% (p=0.33)
ApoA-1	0%	0% (p=0.59)	-6% (p=0.66)	1% (p=0.93)	2% (p=0.67)	-6% (p=0.43)	-5% (p=0.04)
TC	2%	5% (p=0.72)	-15% (p=0.005)	-13% (p=0.009)	-42% (p<0.0001)	-34% (p=0.0001)	-23% (p=0.0001)
TG	0%	4%	4%	-25%	-41%	-35%	-15%

	(p=0.60)	(p=0.52)	(p=0.38)	(p=0.04)	(p=0.02)	(p=0.92)

P value = vs. placebo
*Primary endpoint analysis was 30 day post last dose, Day 59, in cohorts treated for 5 weeks and 14 days post last dose, Day 99, in the cohort treated for 13 weeks
†Per protocol, analysis excludes one patient enrolled in the 400 mg/week cohort who dropped out after receiving only one dose of study drug
‡Statistical analysis of the 200 mg/week dose group treated for 13 weeks is versus a pooled placebo from all cohorts (n=14)

Table 2: Mipomersen Phase 1 and Phase 2 Summary of On-Treatment ALT Elevations *
Percentage of subjects with ALT elevations

Max ALT†	Placebo (N=40)	30/50 mg/week (N=35)	100 mg/week (N=35)	200 mg/week (N=87)	>=300 mg/week (N=106)
150-250 IU/L (3xULN-5xULN‡)	3%	3%	0	3%	7%
>250 IU/L (>5xULN‡)	0%	0%	0%	0%	0%

*On-treatment period encompasses the treatment period from first dose to last dose
† Each subject is counted only once at maximum ALT reading
‡ULN is defined to be 50 IU/L

Table 3: Mipomersen Phase 1 and Phase 2 Summary of Entire Study ALT Elevations *
Percentage of subjects with ALT elevations on-treatment or during 90 days following the last study dose

Max ALT†	Placebo (N=40)	30/50 mg/week (N=35)	100 mg/week (N=35)	200 mg/week (N=87)	>=300 mg/week (N=106)
150-250 IU/L (3xULN-5xULN‡)	5%	9%	0%	7%	14%
>250 IU/L (>5xULN‡)	0%	0%	0%	1%	4%

† Each subject is counted only once at maximum ALT reading
‡ULN is defined to be 50 IU/L

ABOUT MIPOMERSEN AND CHOLESTEROL
Mipomersen, formerly 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 mipomersen as the drug of choice for patients who are unable to achieve target cholesterol levels with statins alone or who are intolerant of statins. Isis is developing mipomersen at a dose of 200 mg/week in its ongoing and future studies.

Analyst & Investor Day Information
At 9:00 a.m. Eastern Standard Time Tuesday, November 13, Isis will conduct a live webcast presentation of its Analyst & Investor Day. Interested parties may access the webcast at www.isispharm.com. A replay of the webcast will be available on Isis’ web site 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 18 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. Isis is a joint owner of Regulus Therapeutics LLC, a joint venture focused on the discovery, development and commercialization of microRNA therapeutics. 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 www.isispharm.com.

This press release includes forward-looking statements regarding 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, 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, 2006, and its quarterly report on Form 10-Q for the quarter ended September 30, 2007, 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,” “Company,” “we,” “our,” and “us” refers to Isis Pharmaceuticals and its subsidiaries.

###