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): **March 26, 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 the afternoon of March 26, 2007, 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.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated March 26, 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: March 26, 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 March 26, 2007.

STUDY PRESENTED AT ACC SHOWS TREATMENT WITH ISIS 301012 ADDED TO STATINS FOR ONLY 5 WEEKS RESULTS IN 75% OF PATIENTS ACHIEVING LDL-C LEVELS LESS THAN 100 MG/DL AND 50% OF PATIENTS ACHIEVING LDL-C LEVELS OF LESS THAN 70 MG/DL

- ***ISIS 301012 coadministered with statins for only five weeks at 400 mg/week lowered LDL-C 47% beyond the levels achieved with statins alone, with similarly favorable effects on other atherogenic lipids***
- ***ISIS 301012 was well tolerated when coadministered with statins***
- ***Data were presented by lead investigator, Dr. John J.P. Kastelein, at ACC Monday afternoon***

NEW ORLEANS, LA, and CARLSBAD, CA, March 26, 2007 - Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) announced new results from its Phase 2 clinical trial of ISIS 301012 coadministered with statins presented today at the American College of Cardiology Annual Scientific Session (ACC) in New Orleans. In the study, patients with high cholesterol were treated for five weeks with up to 400 mg/week of ISIS 301012 added to ongoing stable doses of statins. Data from this study for dose cohorts through 300 mg/week were previously reported. In the 400 mg/week cohort, ISIS 301012 was well tolerated, and patients dosed per protocol experienced statistically significant median improvements in apoB-100, LDL-cholesterol (LDL-C), and triglycerides (TG) of 51%, 47%, 35%, respectively. Later this year, Isis plans to begin a longer-duration Phase 2 study of ISIS 301012 added to statins in patients with routine high cholesterol to define maintenance doses of ISIS 301012 which are expected to be in the range of 100-200 mg/week.

In this study, at a dose 400 mg/week four of eight patients achieved LDL-C levels below 70 mg/dL and six of eight achieved LDL-C levels below 100 mg/dL. Similarly at a dose of 300 mg/week, three of eight patients achieved LDL-C levels below 70 mg/dL and seven of eight patients achieved LDL-C levels below 100 mg/dL. For High-Risk patients, the recommended target levels of LDL-C are 100 mg/dL, and for Very High-Risk patients a target of less than 70 mg/dL should be seriously considered (see Adult Treatment Panel III Recommendations below). Patients in this cohort had baseline LDL-C levels ranging from 109 – 162 mg/dL and had been on statins for a median duration of four years. These results were achieved with only five weeks of treatment with ISIS 301012.

The most common drug-related adverse events were painless mild to moderate injection site reactions. There was one possibly drug-related serious adverse event reported for the study: a patient in the 400 mg/dL cohort experienced fever more than 12 hours after receiving the first dose and subsequently dropped out of the study. This patient was not included in the per protocol analysis. In this high dose cohort, one patient had consecutive measurements of liver transaminases (ALT) above three times the upper limit of normal (3xULN); the maximal ALT

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observed in the study was 211 IU/L. Importantly, no patients evidenced liver chemistries that would suggest risk of liver injury (extremely high ALT or ALT elevations together with elevations in bilirubin greater than 2xULN). Patients in this study remain in follow-up.

According to John J.P. Kastelein, M.D., Ph.D., Chairman, Department of Vascular Medicine at the Academic Medical Center in Amsterdam, The Netherlands, lead investigator in the study, “ISIS 301012 continues to show exceptional promise as a new lipid-lowering agent. This study demonstrates that as an add-on therapy in patients on statins whose LDL-C levels are not adequately controlled, ISIS 301012 effectively enables patients to achieve target levels of LDL-C. This is an important clinical effect which, together its tolerability and lack of drug interactions, make ISIS 301012 an exciting drug for potential use in combination with other lipid-lowering therapies in the patients unable to derive sufficient benefit from available agents.”

Mark Wedel, M.D., J.D., Isis’ Chief Medical Officer, added, “ISIS 301012 is highly active and well tolerated in combination with statins, both in the routine high cholesterol population represented in this study, as well as in homozygous familial hypercholesterolemic patients on maximal concurrent lipid-lowering therapies. ISIS 301012 continues to perform to our highest expectations, and we are looking forward to taking the next steps toward bringing it to market for patients who need to improve their cholesterol levels. Our next step for the routine high cholesterol population is to conduct a longer-term Phase 2 study in patients in combination with statins, in which we expect to use induction doses of 200 to 300 mg/week and define maintenance doses in the range of 100 to 200 mg/week.”

ISIS 301012 Coadministered with Statins

This randomized, double-blinded, placebo-controlled, dose-escalation study initially included five weeks of treatment at doses of 30, 100, 200, and 300 mg/week. Because ISIS 301012 was well tolerated in these cohorts, the study was expanded to include a 400 mg/week five-week treatment group and two longer-term treatment cohorts; results of dose cohorts through 300 mg/week were presented previously, results from the 400 mg/week cohort were presented today, and results from the longer-term cohorts will be presented later in the year. Patients in the five-week study had median baseline LDL-C levels between 107 and 168 mg/dL and had been on stable doses of </= 40 mg of simvastatin or atorvastatin for at least three months, with a median statin treatment duration of 4 years. At a dose of 400 mg/week, patients receiving ISIS 301012 achieved median reductions of 51% in apoB, 47% in LDL-C, and 35% in TG beyond the levels they had already achieved on stable statin doses. ISIS 301012 treatment had no effect on HDL-cholesterol levels (HDL-C).

Interestingly, in this short-term study, increasing the dose from 300 mg/week to 400 mg/week did not result in further lipid lowering activity represented as median % changes from baselines. This apparent plateau in % reductions may be due to the higher baseline values in the 300 mg/week cohort relative to the 400 mg/week cohort. Indeed, the 400 mg/week cohort did achieve lower median absolute levels of both apoB (55 mg/dL at 400 mg/week versus 61 mg/dL at 300 mg/week) and LDL-C (67 mg/dL at 400 mg/week versus 76 mg/dL at 300 mg/week) than the 300 mg/week cohort.

Table 1: ISIS 301012 Coadministered with Statins, Summary of Results. Median % changes from baseline at primary endpoint*

Per Protocol	Placebo	30 mg/week	100 mg/week	200 mg/week	300 mg/week	400 mg/week
# of patients	13	8	8	16	8	8

ApoB	-1%	0%(p=0.80)	-20%(p=0.03)	-24%(p=0.004)	-52%(p<0.0001)	-51%(p=0.0004)
LDL-C	-4%	4%(p=0.31)	-22%(p=0.01)	-30%(p=0.002)	-51%(p<0.0001)	-47%(p=0.008)
VLDL-C	7%	8%(p=0.84)	10%(p=0.66)	-25%(p=0.38)	-63%(p=0.08)	-69%(p=0.02)
Non-HDL-C	-1%	8%(p=0.44)	-20%(p=0.02)	-22%(p=0.02)	-51%(p<0.0001)	-49%(p=0.008)
HDL-C	9%	1%(p=0.24)	-4%(p=0.15)	6%(p=0.23)	5%(p=0.41)	6%(p=0.60)
ApoA-1	0%	0%(p=0.59)	-6%(p=0.66)	1%(p=0.93)	2%(p=0.67)	-6%(p=0.43)
TC	2%	5%(p=0.72)	-15%(p=0.005)	-13%(p=0.009)	-42%(p<0.0001)	-34%(p=0.0001)
TG	0%	4%(p=0.60)	4%(p=0.52)	-25%(p=0.38)	-41%(p=0.04)	-35%(p=0.02)
ApoB:ApoA-1	-1%	0%(p=0.97)	-15%(p=0.01)	-28%(p=0.006)	-55%(p<0.0001)	-45%(p=0.0008)
TC:HDL-C	-6%	0%(p=0.27)	-15%(p=0.36)	-14%(p=0.06)	-41%(p<0.0001)	-38%(p=0.01)

p value = vs. placebo
*Primary endpoint analysis was 30 days post last dose, Day 59

Table 2: ISIS 301012 Coadministered with Statins, Absolute ApoB and LDL-C Reductions. Absolute levels of ApoB and LDL-C in mg/dL at baseline and primary endpoint*.

		Placebo	30 mg/wk	100 mg/wk	200 mg/wk	300 mg/wk	400 mg/wk
ApoB	Baseline	105	95	106	103	133	108
	Primary Endpoint*	105	98	82	73	61	55
LDL-C	Baseline	131	107	134	128	168	134
	Primary Endpoint*	130	114	96	87	76	67

*Primary endpoint analysis was 30 days post last dose, Day 59

Table 3: ISIS 301012 Coadministered with Statins, Patients at Target. Number of patients (%) in each cohort at target lipid levels at the primary endpoint*.

Parameter	Target*	Placebo	30 mg/wk	100 mg/wk	200 mg/wk	300 mg/wk	400 mg/wk
# of patients		13	8	8	16	8	8
LDL-C	<100 mg/dL	3 (23%)	2 (25%)	3 (38%)	9 (56%)	7 (88%)	6 (75%)
	< 70 mg/dL	0	0	0	3 (19%)	3 (38%)	4 (50%)
Non-HDL-C	<130 mg/dL	4 (31%)	5 (63%)	5 (63%)	11 (69%)	7 (88%)	6 (75%)
ApoB	< 90 mg/dL	3 (23%)	2 (25%)	4 (50%)	10 (63%)	7 (88%)	6 (75%)
ALL TARGETS	LDL-C<100 Non-HDL-C<130 ApoB<90	2 (15%)	2 (25%)	3 (38%)	8 (50%)	7 (88%)	6 (75%)

*Primary endpoint analysis was 30 days post last dose, Day 59

Table 4: ISIS 301012 Coadministered with Statins, Laboratory Findings. Number of patients with ALT elevations >/= 3xULN (maximal ALT observed = 211 IU/L).

ALT Elevations Single† / Consecutive‡	Placebo (n = 3)	30 mg (n = 8)	100 mg (n = 8)	200 mg (n =16)	300 mg (n = 8)	400 mg (n = 8)
Primary Endpoint (Day 1 to 59)	0 / 0	0 / 0	0 / 0	1 / 0	0 / 1	1 / 0
Primary Follow-up (Day 60 to 87)	0 / 0	0 / 0	0 / 0	0 / 1	0 / 0	0 / 0
Long term F/U (Day 88 to 199)	0 / 0	0 / 0	0 / 0	0 / 0	NA	NA

†Single = elevation that returned to below 3xULN by the next visit at least 7 days later
‡Consecutive = elevation that was observed in two measures at least 7 days apart
Primary endpoint period was 30 days post last dose, Day 59
Primary follow-up period was from primary endpoint to 8 weeks post last dose
NA = data not available, cohorts remain in follow-up

Presentation Details

Date:	Monday, March 26, 2007
Session:	820: Clinical Trials of Lipid-Lowering Therapy (4:00 - 5:30 p.m. CT)
Track:	ACC.Vascular Disease, Hypertension, and Prevention
Room:	Auditorium B
Presentation:	820-6
Time:	4:45 - 5:00 p.m.
Speaker:	Dr. John J.P. Kastelein
Title:	ISIS 301012, an Antisense Inhibitor of Apolipoprotein B, Produces Significant Additional Reduction of Low-Density Lipoprotein Cholesterol and Apolipoprotein B in Hypercholesterolemic Subjects on Statins Not Meeting Target

More about Phase 2 Trials for ISIS 301012

Additional data from two studies evaluating ISIS 301012's safety and lipid lowering activity were presented at the ACC. This morning in an oral session, results of an ongoing trial of ISIS 301012 added to maximal lipid lowering therapies in homozygous familial hypercholesterolemia (FH) patients were reported. Results of polygenic hypercholesterolemic patients treated with up to 400 mg/week of ISIS 301012 for up to three months as a single agent are the subject of a v-cast poster presentation. Results for the extended three-month treatment cohorts at 200 and 300 mg/week doses in the statin coadministration study are expected later in the year. Also later in the year, results from an ongoing double-blind, placebo-controlled, dose-escalation study in patients with heterozygous FH will be reported.

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

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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.

Adult Treatment Panel III Recommendations

The National Cholesterol Education Program's Adult Treatment Panel III guidelines for target LDL-C levels High-Risk patients is less than 100 mg/dL, with an optional target of less than 70 mg/dL. For Moderately High-Risk patients, the target is less than 130 mg/dL. Over 20 million people in the U.S. in the High-Risk and Moderately High-Risk categories are failing to meet recommended LDL-C targets using currently available lipid-lowering therapies.

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 cancer, and inflammatory and other 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 www.isispharm.com.

This press release includes forward-looking statements regarding the development, activity, therapeutic potential and safety of ISIS 301012 in treating 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, which is on file with the SEC. Copies of this and other documents are available from the Company.

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