Isis Reports New Data for Mipomersen in Routine High Cholesterol Patients and Provides Cumulative Safety Summary

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- 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 http://www.isispharm.com

CARLSBAD, Calif., Nov 13, 2007 /PRNewswire-FirstCall via COMTEX News Network/ -- 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 http://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	100 mg/week	200 mg/week	300 mg/week	400** mg/week	200*** mg/week

		5 weeks	5 weeks	5 weeks	5 weeks	5 weeks	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% (p5xULN***)	-51%	-42%

** 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 http://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(TM) 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 http://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.

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