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 21, 2009**

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 21, 2009, Isis Pharmaceuticals, Inc. ("Isis") announced positive top-line results from a Phase 2 study evaluating the safety and efficacy of ISIS 113715 in patients with type 2 diabetes. 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 21, 2009.

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 21, 2009

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

INDEX TO EXHIBITS

99.1 Press Release dated October 21, 2009.

Exhibit 99.1

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ISIS PHARMACEUTICALS REPORTS POSITIVE PHASE 2 DATA FOR ISIS 113715 IN PATIENTS WITH TYPE 2 DIABETES

Full Data to Be Presented At Upcoming Medical Meeting

Conference Call Webcast and Slide Presentation Wednesday, October 21, 4:30 p.m. EDT at www.isispharm.com

CARLSBAD, Calif., October 21, 2009 – Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) today announced positive top-line results from a Phase 2 study evaluating the safety and efficacy of ISIS 113715 in patients with type 2 diabetes. ISIS 113715 is a novel insulin sensitizer that reduces the expression of protein tyrosine phosphatase-1B (PTP-1B). The study showed consistent and statistically significant reductions in multiple short and intermediate measures of glucose control. In addition to lowering blood glucose, ISIS 113715 caused statistically significant and clinically meaningful reductions in LDL cholesterol. Consistent with the preclinical data with ISIS 113715, a tendency toward weight loss was observed even in this short-term study without strict dietary control. The effect of ISIS 113715 on weight was preceded by a statistically significant increase in circulating adiponectin, a hormone that is increased with weight loss. ISIS 113715 demonstrated a favorable safety profile with no exacerbation of sulfonylurea-induced hypoglycemia or other clinically significant adverse effects. The full details of the data will be presented at a future medical meeting.

"Although the study completed is only 13 weeks in duration, I am encouraged by the safety and efficacy data," said Robert Henry, M.D., Professor of Medicine, University of California at San Diego and Chief, Section of Diabetes, Endocrinology and Metabolism at VA San Diego. "If the profile of ISIS 113715 seen in this study is confirmed in longer-term trials, the drug could be an important addition to the care of type 2 diabetic patients."

The analysis demonstrated statistically significant reductions in multiple indices of glucose control as compared to placebo in patients with type 2 diabetes on stable doses of sulfonylurea. The measures of glucose control evaluated were – fasting serum glucose (FSG), a spot measure of glucose control; weekly self monitored blood glucose (SMBG), a one week average of daily fasting glucose measurements; fructosamine, a measure of glucose over the preceding 2-4 weeks; and glycated albumin, a measure of average glucose over the preceding 4 weeks. In the 200 mg/week cohort, there was a 25 mg/dL decrease in averaged weekly fasting SMBG ($p=0.026$ versus placebo) and a 25 umol/L decrease in serum fructosamine ($p=0.009$ versus placebo). Further, glycated albumin was also statistically significantly reduced and similar results were observed for fasting blood glucose.

Consistent, but less robust effects on all of these parameters were also observed in the 100 mg/week cohort. The fifth measure of glucose control in the study, hemoglobin A1c (HbA1c), a measure of average glucose control over the preceding 8-12 weeks, failed to reach statistical significance due to the delay in onset of glucose control as accumulation of ISIS 113715 to active concentrations took more than 6 weeks.

ISIS 113715 was well-tolerated. The most common adverse events were mild injection site reactions. There were no drug-related serious adverse events, no severe hypoglycemia, no clinically significant alterations in kidney or liver function even in patients who entered the trial with mild renal dysfunction, and no other clinically significant adverse effects were observed in subjects exposed to ISIS 113715. From both the 100 mg and 200 mg per week treatment groups, there were only three terminations in the study due to adverse events, one for uncontrolled diabetes, one for a rash following the first subcutaneous dose and one for a moderate injection site reaction in a subject with inadequately controlled diabetes.

"We are pleased that this study has confirmed that ISIS 113715, a first in class PTP-1B inhibitor, is well tolerated and has a unique profile," said Sanjay Bhanot, M.D., Ph.D., Vice President of Metabolic Disorders and Translational Medicine at Isis. "An insulin sensitizer that normalizes glucose without exacerbating hypoglycemia, that also reduces LDL-C levels and weight would be a significant advance in the treatment of patients with type 2 diabetes, who frequently are obese and at high cardiovascular risk."

The trial was a randomized, double-blind, placebo-controlled Phase 2 study that had 76 evaluable patients with well-established type 2 diabetes who had uncontrolled blood sugar despite treatment with stable doses of sulfonylurea. Patients were randomized 2:1 to receive either placebo (n=26) or ISIS 113715 100 mg (n=24), 200 mg (n=26) once-weekly subcutaneously for three months in addition to their stable doses of sulfonylurea. Patients entering the study had average HbA1c levels of 8.8%, average fasting glucose levels of approximately 196 mg/dL, and average LDL-C levels of approximately 128 mg/dL. The trial was conducted in several countries in Eastern Europe, including Romania, Poland and Russia. Study end points evaluated included HbA1c, FSG, SMBG, lipids, Apo B-100, adiponectin, fructosamine and glycated albumin.

Conference Call

At 4:30 p.m. Eastern Time today, October 21, 2009, Isis will conduct a live webcast and slide presentation conference call to discuss the positive top-line results from a Phase 2 study evaluating the safety and efficacy of ISIS 113715 in patients with type 2 diabetes. Interested parties may listen to the call by dialing 866-788-0545 and refer to passcode "ISIS 2009" or access the webcast with or without audio at www.isispharm.com. A webcast replay will be available for a limited time at the same address.

About ISIS 113715

ISIS 113715 is a second-generation antisense drug that inhibits PTP-1B, an enzyme that is a key mediator of insulin resistance. Insulin resistance is one of two main defects in patients with type 2 diabetes. The inhibition of PTP-1B may allow insulin receptors to be more active, allowing for more sugar uptake into cells, thereby lowering blood sugar levels in the bloodstream. ISIS 113715 may offer new treatment to patients who do not respond adequately to currently available therapies such as glitazones, sulfonylureas, metformin, and GLP-1 based 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 19 drugs in development. Isis' drug development programs are focused on treating cardiovascular, metabolic and severe neurodegenerative diseases and cancer. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Isis and Alnylam Pharmaceuticals are joint owners of Regulus Therapeutics Inc., a company focused on the discovery, development and commercialization of microRNA therapeutics. Isis also has made significant innovations beyond human therapeutics resulting in products that other companies, including Abbott, are commercializing. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of over 1,600 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 113715 in treating type 2 diabetes. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and

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should be considered an at-risk statement. 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, 2008, and its most recent quarterly report on Form 10-Q, 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, including Regulus Therapeutics Inc.

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