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): **August 4, 2011**

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 2.02. Results of Operations and Financial Condition.

On August 4, 2011, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended June 30, 2011. In addition to disclosing results that are determined in accordance with Generally Accepted Accounting Principles (GAAP), the Company also discloses pro forma or non-GAAP results of operations, which are adjusted from GAAP to exclude non-cash compensation expense/benefit. These measures are provided as supplementary information and are not a substitute for financial measures calculated in accordance with GAAP. The Company reports these pro forma results to better enable financial statement users to assess its historical performance and project its future operating results and cash flows. Further, the presentation of Isis' pro forma results is consistent with how Isis' management internally evaluates the performance of its operations. A copy of the release is furnished with this report as an exhibit pursuant to "Item 2.02. Results of Operations and Financial Condition" of Form 8-K in accordance with SEC Release Nos. 33-8216 and 34-47583.

The information in this Current Report on Form 8-K and the Exhibit attached hereto shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934 (the "Exchange Act") or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, regardless of any general incorporation language in such filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated August 4, 2011.

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: August 4, 2011

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

INDEX TO EXHIBITS

99.1	Press Release dated August 4, 2011.

ISIS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR SECOND QUARTER 2011

- **Conference Call Webcast Thursday, August 4, 4:30 p.m. ET at www.isispharm.com**

CARLSBAD, Calif., August 4, 2011 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced its financial results for the quarter ended June 30, 2011. The Company finished the second quarter of 2011 with a pro forma net operating loss (NOL) of $11.6 million and $24.9 million for the three and six months ended June 30, 2011, respectively, compared to a pro forma NOL of $15.5 million and $17.1 million for the same periods in 2010. The Company finished the second quarter of 2011 with more than $395 million in cash. Isis remains on track to meet its 2011 guidance of an NOL in the low $40 million range and a year-end cash balance of more than $350 million.

"We were pleased to announce last week that Genzyme submitted the mipomersen marketing application to the European Medicines Agency and remains on track to submit the US application for marketing approval later this year. Pending regulatory approval, mipomersen will be marketed under the brand name Kynamro™. The Kynamro European regulatory submission is a significant achievement and brings this potentially life-changing drug closer to patients who are at great risk of dying from their cardiovascular disease. We continue to work closely with Genzyme to complete all the steps necessary for a successful approval and launch planned in 2012," said B. Lynne Parshall, COO and CFO of Isis. "We believe the initial commercial opportunities for Kynamro are significant and could provide us with the opportunity to earn significant commercial revenue."

Upcoming Key Milestones

- File for marketing approval for Kynamro™ (mipomersen) in the United States in the fourth quarter of 2011 for patients with homozygous FH.
- Initiate Phase 2 studies on ISIS-CRP_{Rx} in patients with Rheumatoid Arthritis and Multiple Myeloma.

Financial Results

On a GAAP basis, Isis reported a loss from operations of $14.1 million and $30.2 million for the three and six months ended June 30, 2011, respectively, compared to $18.7 million and $23.6 million for the same periods in 2010.

All pro forma amounts referred to in this press release exclude non-cash stock compensation. Please refer to the reconciliation of pro forma and GAAP measures, which is provided later in this release.

Revenue

Revenue for the three and six months ended June 30, 2011 was $24.8 million and $46.0 million, respectively, compared to $23.5 million and $53.4 million for the same periods in 2010. Isis' revenue fluctuates based on the nature and timing of payments under agreements with the Company's partners, including license fees, milestone-related payments and other payments. For example, in the first half of 2011 Isis recognized as revenue a $5 million milestone payment Isis earned from GlaxoSmithKline (GSK) for the initiation of a Phase 1 study for ISIS-TTR_{Rx}. However, revenue in the first half of 2011 included less revenue from Bristol-Myers Squibb and Alnylam Pharmaceuticals compared to the first half of 2010, primarily because amortization of upfront fees from these collaborations ended in 2010, although Isis continues to receive research support from Bristol-Myers Squibb. In the second quarter of 2010, Isis earned $1.9 million from Regulus related to its strategic alliance with Sanofi, which also contributed to lower revenue in the first half of 2011.

Operating Expenses

On a pro forma basis, operating expenses for the three and six months ended June 30, 2011 were $36.4 million and $70.9 million, respectively, compared to $39.0 million and $70.5 million for the same periods in 2010. Isis' operating expenses in the first half of 2011 reflected higher costs associated with Isis' maturing pipeline of drugs offset by lower costs associated with the completion of the mipomersen Phase 3 program that supports the initial regulatory filings. Although Isis' operating expenses were essentially flat compared to 2010, as drugs move forward to more advanced stages of development, including into larger, longer clinical studies, the costs of development will increase. On a GAAP basis, Isis' operating expenses for the three and six months ended June 30, 2011 were $38.9 million and $76.1million, respectively, compared to $42.2 million and $77.0 million for the same periods in 2010.

Net Loss

Isis reported a net loss of $17.9 million and $37.9 million for the three and six months ended June 30, 2011, respectively, compared to $25.2 million and $34.8 million for the same periods in 2010. Basic and diluted net loss per share for the three and six months ended June 30, 2011 was $0.18 per share and $0.38 per share, respectively, compared to $0.25 per share and $0.35 per share for the same periods in 2010. Isis' net loss for the second quarter of 2011 decreased compared to the same period in 2010 primarily due to a decrease in Isis' operating expenses and its share of Regulus' net loss, which reflects additional revenue Regulus earned from its alliance with Sanofi. In the first half of 2011 Isis' net loss increased compared to the same period in 2010 primarily due to a decrease in Isis' revenue offset in part by a decrease in Isis' share of Regulus' net loss as described above.

Balance Sheet

As of June 30, 2011, Isis had cash, cash equivalents and short-term investments of $395.2 million compared to $472.4 million at December 31, 2010 and had working capital of $318.7 million at June 30, 2011 compared to $377.2 million at December 31, 2010. The decrease in cash and working capital primarily relates to cash used to fund Isis' operations.

Isis' leases on its primary research and development facilities expire at the end of 2011. Rather than invest in costly renovations to its existing facilities, the Company chose to consolidate the majority of its operations in a new leased facility that Biomed Realty Trust, Inc. (BMR) constructed. To make the Company's move, scheduled for August 2011, as efficient as possible, Isis requested access to the new facility prior to the completion of construction. To gain early access, Isis agreed to modify its lease to accept additional responsibility. As a result, accounting rules required Isis to record the cost of the facility as a fixed asset with a corresponding liability. Beginning in the third quarter, Isis will depreciate the building over its economic life and Isis' rent payments, which begin on January 1, 2012, will decrease the liability over the term of the lease.

Business Highlights

"The most significant events for Isis this year are the submission of regulatory filings for Kynamro in both Europe and the United States. With the European submission, we are one step closer to commercialization. Together with Genzyme, we have put together a comprehensive package for these filings that includes data from more than 700 mipomersen-treated patients, including a significant number of patients with long-term drug exposure. In all clinical studies conducted, including four Phase 3 studies, we observed an efficacy and safety profile for mipomersen that we believe supports our initial market opportunities. With longer-term dosing, LDL-C reductions are sustained with a safety profile that is consistent with our Phase 3 experience," continued Ms. Parshall. "In addition, together with Genzyme, we are making progress toward initiating additional studies to provide additional patient exposure to support future regulatory filings."

"Already 2011 has been a very successful year, but we have many more events to look forward to as we continue to make significant progress in our pipeline. We anticipate reporting Phase 1 data on several drugs that could provide early evidence of clinical activity supporting disease opportunities that represent very large commercial opportunities. We will also continue to add drugs to our pipeline this year. In short, we are maturing the pipeline as we move important drugs toward the market and expanding our pipeline with the addition of novel drugs in new disease areas. All of these activities are setting the stage for what we hope will be a very exciting 2012," concluded Ms. Parshall.

Corporate and Drug Development Highlights

- Genzyme submitted a marketing application for mipomersen in Europe for patients with homozygous FH and severe heterozygous FH.
- Genzyme announced the brand name, Kynamro, that mipomersen will be marketed under if the necessary approvals are granted
- Data from two Phase 3 studies of mipomersen was presented at the 79th European Atherosclerosis Society Congress. The data highlight the potential of mipomersen in lowering Lp(a) and potentially reducing the necessity for lipid-apheresis.
- Isis initiated Phase 1 studies on ISIS-PTP1B$_{Rx}$ and ISIS-TTR$_{Rx}$, the first drug selected as part of its collaboration with GSK. Upon Phase 1 initiation, Isis earned a $5 million milestone payment from GSK.
- Isis and GSK expanded their collaboration by initiating a sixth program to discover and develop drugs to treat rare and infectious diseases and Isis received a $3 million payment from GSK.
- The Isis and GSK collaboration was awarded the Breakthrough Alliance Award of 2011 as the breakthrough deal of 2010.

Conference Call

At 4:30 p.m. Eastern Time today, August 4, Isis will conduct a live webcast conference call to discuss the earnings release and related activities. Interested parties my listen to the call by dialing 866-543-6407 and refer to passcode "ISIS 2011," or access the webcast at www.isispharm.com. A webcast replay will be available for a limited time at the same address.

About Isis Pharmaceuticals, Inc.

Isis is exploiting its leadership position in antisense technology to discover and develop novel drugs for its product pipeline and for its partners. Isis' broad pipeline consists of 24 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic and severe and rare/neurodegenerative diseases, and cancer. Isis' partner, Genzyme, plans to commercialize Isis' lead product, mipomersen, following regulatory approval, which is expected in 2012. Isis' patents provide strong and extensive protection for its drugs and technology. Additional information about Isis is available at **www.isispharm.com**.

Forward Looking Statements

This press release includes forward-looking statements regarding Isis Pharmaceuticals' financial position and outlook, Isis' business, the planned commercialization of mipomersen, and the therapeutic and commercial potential of Isis' technologies and products in development, including the business of Regulus, Isis' jointly owned subsidiary. 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. 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 drugs. 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, 2010 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., its jointly owned subsidiary.

ISIS PHARMACEUTICALS, INC.
SELECTED FINANCIAL INFORMATION
Condensed Consolidated Statements of Operations
(In Thousands, Except Per Share Data)

	Three months ended, June 30,		Six months ended, June 30,	
	2011	2010	2011	2010
	(unaudited)		(unaudited)	
Revenue:				
Research and development revenue under collaborative agreements	$ 24,305	$ 21,143	$ 44,319	$ 49,699
Licensing and royalty revenue	518	2,360	1,651	3,730
Total revenue	24,823	23,503	45,970	53,429
Expenses:				
Research and development	36,009	39,124	70,254	71,111
General and administrative	2,874	3,051	5,884	5,869
Total operating expenses	38,883	42,175	76,138	76,980
Loss from operations	(14,060)	(18,672)	(30,168)	(23,551)
Other income (expense):				
Equity in net loss of Regulus Therapeutics Inc.	(1,033)	(3,942)	(1,889)	(5,428)
Investment income	616	859	1,321	1,814
Interest expense	(3,437)	(3,261)	(6,851)	(6,498)
Gain (loss) on investments, net	34	(136)	(285)	(1,146)
Loss before income tax expense	(17,880)	(25,152)	(37,872)	(34,809)
Income tax expense	(9)	(2)	(11)	(2)
Net loss	$ (17,889)	$ (25,154)	$ (37,883)	$ (34,811)
Basic and diluted net loss per share	$ (0.18)	$ (0.25)	$ (0.38)	$ (0.35)
Shares used in computing basic and diluted net loss per share	99,602	99,091	99,586	99,052

Isis Pharmaceuticals, Inc.
Reconciliation of GAAP to Pro Forma Basis:
Condensed Consolidated Operating Expenses and Loss From Operations
(In Thousands)

	Three months ended, June 30,		Six months ended, June 30,	
	2011	2010	2011	2010
	(unaudited)		(unaudited)	
As reported operating expenses according to GAAP	$ 38,883	$ 42,175	$ 76,138	$ 76,980
Excluding compensation expense related to stock options	(2,500)	(3,132)	(5,232)	(6,488)
Pro forma operating expenses	$ 36,383	$ 39,043	$ 70,906	$ 70,492
As reported loss from operations according to GAAP	$ (14,060)	$ (18,672)	$ (30,168)	$ (23,551)
Excluding compensation expense related to stock options	(2,500)	(3,132)	(5,232)	(6,488)
Pro forma loss from operations	$ (11,560)	$ (15,540)	$ (24,936)	$ (17,063)

Reconciliation of GAAP to Pro Forma Basis

As illustrated in the Selected Financial Information in this press release, pro forma operating expenses and pro forma loss from operations were adjusted from GAAP to exclude compensation expense related to stock options, which are non-cash. Isis has regularly reported non-GAAP measures for operating expenses and loss from operations as pro forma results. These measures are provided as supplementary information and are not a substitute for financial measures calculated in accordance with GAAP. Isis reports these pro forma results to better enable financial statement users to assess and compare its historical performance and project its future operating results and cash flows. Further, the presentation of Isis' pro forma results is consistent with how Isis' management internally evaluates the performance of its operations.

Condensed Consolidated Balance Sheets
(In Thousands)

	June 30, 2011 (unaudited)	December 31, 2010
Assets:		
Cash, cash equivalents and short-term investments	$ 395,184	$ 472,353
Other current assets	15,536	10,784
Property, plant and equipment, net	88,010	35,703
Other assets	30,842	31,637
Total assets	$ 529,572	$ 550,477
Liabilities and stockholders' equity:		
Other current liabilities	$ 23,261	$ 31,388
Current portion of deferred contract revenue	68,719	74,502
2 5/8% convertible subordinated notes	137,073	132,895
Long-term obligations, less current portion	64,187	15,867
Investment in Regulus Therapeutics Inc.	2,759	870
Long-term deferred contract revenue	21,356	50,413
Stockholders' equity	212,217	244,542
Total liabilities and stockholders' equity	$ 529,572	$ 550,477

###