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 6, 2012**

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.)

2855 Gazelle Court
Carlsbad, CA 92010
(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 6, 2012, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended June 30, 2012. 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. 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 6, 2012.

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 6, 2012

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 6, 2012.

ISIS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR SECOND QUARTER 2012

- **Conference Call Webcast Monday, August 6, 11:30 a.m. ET at www.isispharm.com**

CARLSBAD, Calif., August 6, 2012 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today reported pro forma net operating income of $6.2 million for the three months ended June 30, 2012 and a pro forma net operating loss (NOL) of $10.0 million for the six months ended June 30, 2012 compared to a pro forma NOL of $11.6 million and $24.9 million for the same periods in 2011. The significant improvement in the Company's operating results was driven primarily by the $25 million milestone payment Isis earned from Genzyme when the FDA accepted the new drug application (NDA) for KYNAMRO™ in the second quarter. The Company ended the second quarter of 2012 with $336 million in cash.

"The planned European and United States launches of KYNAMRO™ will be important milestones for Isis and for antisense technology. KYNAMRO™ commercialization will change our financial position by adding commercial revenue to the steady stream of income we receive from our partnerships," said B. Lynne Parshall, Chief Operating Officer and CFO of Isis. "We have maintained a strong financial position as we have approached this important event while also advancing the rest of our pipeline. We have utilized an innovative and unique business model that has provided us with the cash to expand and mature our industry-leading pipeline. As we look toward the future, in addition to KYNAMRO™ commercial revenue, we have other significant near-term opportunities for continued revenue growth with a wave of potential product launches in the next three to five years. We also look forward to completing clinical studies on several drugs that could be very attractive licensing candidates."

Upcoming Key Milestones

- Present KYNAMRO™ data at the upcoming European Society of Cardiology highlighting the potential of KYNAMRO™ to reduce the need for lipid-apheresis by lowering LDL-C values below thresholds for apheresis eligibility
- Report clinical data from multiple drugs in Isis' pipeline, including ISIS-SMN$_{Rx}$, an antisense drug Isis is evaluating in patients with spinal muscular atrophy
- Initiate a clinical study of ISIS-TTR$_{Rx}$ in patients with familial amyloid polyneuropathy
- Earn a $25 million milestone payment from Genzyme following FDA marketing approval for KYNAMRO™
- Anticipate marketing approval of KYNAMRO™ in the United States and Europe

Financial Results

On a GAAP basis, Isis reported income from operations of $3.7 million for the three months ended June 30, 2012 and a loss from operations of $14.8 million for the six months ended June 30, 2012 compared to a loss from operations of $14.1 million and $30.2 million for the same periods in 2011.

All pro forma amounts referred to in this press release exclude non-cash compensation expense related to equity awards. 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, 2012 was $47.3 million and $70.6 million, respectively, compared to $24.8 million and $46.0 million for the same periods in 2011. 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, Isis' revenue in the first half of 2012 was significantly higher than in the first half of 2011 primarily as a result of the $25 million milestone payment from Genzyme for FDA acceptance of the KYNAMRO™ NDA. Also in the first half of 2012, Isis sold $6.2 million of drug substance to Genzyme to support the planned commercial launch of KYNAMRO™ and began recognizing revenue from the $29 million upfront payment the Company received from Biogen Idec earlier this year. These increases were partially offset when the amortization of the upfront payments associated with the Genzyme collaboration ended in May 2012.

In June 2012, Isis and Biogen Idec entered into a new collaboration and license agreement for the development of a drug to treat myotonic dystrophy (DM1). As part of this collaboration, Isis received a $12 million upfront payment, which Isis will begin amortizing into revenue over five years starting in the third quarter of 2012.

Operating Expenses

On a pro forma basis, operating expenses for the three and six months ended June 30, 2012 were $41.2 million and $80.6 million, respectively, compared to $36.4 million and $70.9 million for the same periods in 2011. The moderately higher expenses in the first half of 2012 were primarily due to higher development costs associated with Isis' maturing pipeline of drugs offset by lower development expenses related to KYNAMRO™ because Genzyme is now sharing these expenses equally with Isis until KYNAMRO™ is profitable. Genzyme is paying all of the marketing and selling expenses until KYNAMRO™ is profitable.

On a GAAP basis, Isis' operating expenses for the three and six months ended June 30, 2012 were $43.6 million and $85.3 million, respectively, compared to $38.9 million and $76.1 million for the same periods in 2011.

Net Loss

Isis reported a net loss of $1.2 million and $25.2 million for the three and six months ended June 30, 2012, respectively, compared to $17.9 million and $37.9 million for the same periods in 2011. Basic and diluted net loss per share for the three and six months ended June 30, 2012 was $0.01 per share and $0.25 per share, compared to $0.18 per share and $0.38 per share for the same periods in 2011. Isis' net loss for the first half of 2012 decreased compared to the same period in 2011 primarily due to a decrease in Isis' net operating loss offset, in part, by additional non-cash interest expense the Company recorded for the long-term liability associated with its new facility.

Balance Sheet

As of June 30, 2012, Isis had cash, cash equivalents and short-term investments of $336.0 million compared to $343.7 million at December 31, 2011 and had working capital of $295.4 million at June 30, 2012 compared to $284.0 million at December 31, 2011. The decrease in cash in the first half of 2012 primarily relates to cash used to fund Isis' operations offset by the $25 million milestone payment Isis received from Genzyme and the $29 million upfront payment Isis received from Biogen Idec. Isis' cash balance at June 30, 2012 does not include the $12 million upfront payment that the Company received in July 2012 from its new collaboration with Biogen Idec to develop and commercialize a drug to treat DM1. Including the $12 million from Biogen Idec, Isis has received more than $875 million from its corporate partnerships since 2007.

Business Highlights

"It has been a very productive first half of 2012 for Isis. We have had many important achievements already this year, including the acceptance of the KYNAMRO™ NDA by the FDA. The KYNAMRO™ NDA filing brings us one step closer to commercializing this important new drug for patients who are at great risk of dying from their cardiovascular disease. KYNAMRO™ represents the first major commercial opportunity for Isis, and we are looking forward to its planned launch in Europe and in the United States," continued Ms. Parshall.

"We have been very successful with our partnerships, bringing in more than $85 million in cash so far this year. The most significant payment was the $25 million milestone payment we received from Genzyme for acceptance of the NDA filing. We also established a new alliance with Biogen Idec valued at up to $271 million, including the $12 million upfront fee we recently received," continued Ms. Parshall. "Our new alliance with Biogen Idec allows us to expand our severe and rare disease franchise to include DM1, a devastating neuromuscular disease. This is the second alliance we have established this year with Biogen Idec, and we benefit tremendously from Biogen Idec's expertise in developing and commercializing drugs to treat neurodegenerative diseases. This expertise complements our ability to discover and develop new antisense drugs to many diseases, including neurodegenerative diseases for which there are limited treatment options and potentially rapid routes to the market."

"We expect an eventful second half of 2012 as we continue to make significant progress in advancing our pipeline. We anticipate reporting clinical data from a number of drugs in our pipeline, advancing several drugs into later-stage clinical studies and continuing to add new drugs to our pipeline. Of course, KYNAMRO™ will remain center stage. We look forward to sharing news about KYNAMRO™ and the rest of our pipeline as the year progresses," concluded Ms. Parshall.

Corporate and Drug Development Highlights

- KYNAMRO™ continues to advance in development and move closer to the market for patients with severe forms of familial hypercholesterolemia (FH; homozygous FH and severe heterozygous FH), at high cardiovascular risk, who cannot reduce their LDL-C sufficiently with currently available lipid-lowering therapies.
  - The FDA accepted for filing the NDA for KYNAMRO™ for the treatment of patients with homozygous FH.
  - Isis received a $25 million milestone payment from Genzyme for the KYNAMRO™ NDA filing.
  - A clinical investigator presented an analysis of Lp(a) data from the KYNAMRO™ Phase 3 program at the European Atherosclerosis Society. The data demonstrated sustained reductions of Lp(a), an independent risk factor for cardiovascular disease.
- Isis received European GMP certification of its manufacturing facility for production of drug substance to support KYNAMRO™ commercial launch.
- Isis initiated a Phase 2 study evaluating ISIS-APOCIII$_{Rx}$ in patients with hypertriglyceridemia, a condition characterized by high levels of triglycerides that is often associated with premature coronary artery disease and pancreatitis.
- Isis formed a new strategic alliance with Biogen Idec to develop and commercialize a drug to treat DM1 that expands Isis' severe and rare disease franchise. Isis received a $12 million upfront payment and is eligible to receive up to an additional $259 million in a licensing fee and milestone payments. Isis will also receive double-digit royalties on product sales.
- Isis and collaborators published a paper in Nature demonstrating that an antisense compound selectively and rapidly reduced target RNA in skeletal muscle and alleviated disease in animal models of DM1.
- Isis and collaborators published a paper in Neuron demonstrating that an antisense compound reversed disease in animal models of Huntington's disease.
- Isis received Orphan Drug Designation in the U.S. for ISIS-TTR$_{Rx}$ for the treatment of TTR amyloidosis.

Conference Call

At 11:30 a.m. Eastern Time today, August 6, Isis will conduct a live webcast conference call to discuss this earnings release and business highlights. Interested parties may listen to the call by dialing 877-556-5921 and refer to passcode "ISIS 2012," 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 25 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, and cancer. Isis' partner, Genzyme, plans to commercialize Isis' lead product, KYNAMRO™, in the United States and Europe following regulatory approval. 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, 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, including the planned commercialization of KYNAMRO™, 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, 2011 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.

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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,	
	2012	2011	2012	2011
	(unaudited)		(unaudited)	
Revenue:				
Research and development revenue under collaborative agreements	$ 47,140	$ 24,305	$ 68,957	$ 44,319
Licensing and royalty revenue	200	518	1,618	1,651
Total revenue	47,340	24,823	70,575	45,970
Expenses:				
Research and development	40,435	36,009	79,149	70,254
General and administrative	3,209	2,874	6,185	5,884
Total operating expenses	43,644	38,883	85,334	76,138
Income (loss) from operations	3,696	(14,060)	(14,759)	(30,168)
Other income (expense):				
Equity in net loss of Regulus Therapeutics Inc.	(163)	(1,033)	(1,139)	(1,889)
Investment income	477	616	1,077	1,321
Interest expense	(5,219)	(3,437)	(10,398)	(6,851)
Gain (loss) on investments, net	2	34	19	(285)
Loss before income tax expense	(1,207)	(17,880)	(25,200)	(37,872)
Income tax expense	—	(9)	(2)	(11)
Net loss	$ (1,207)	$ (17,889)	$ (25,202)	$ (37,883)
Basic and diluted net loss per share	$ (0.01)	$ (0.18)	$ (0.25)	$ (0.38)
Shares used in computing basic and diluted net loss per share	100,213	99,602	100,185	99,586

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,	
	2012	2011	2012	2011
	(unaudited)		(unaudited)	
As reported operating expenses according to GAAP	$ 43,644	$ 38,883	$ 85,334	$ 76,138

Excluding compensation expense related to equity awards	(2,460)	(2,500)	(4,727)	(5,232)
Pro forma operating expenses	$ 41,184	$ 36,383	$ 80,607	$ 70,906
As reported income (loss) from operations according to GAAP	$ 3,696	$ (14,060)	$ (14,759)	$ (30,168)
Excluding compensation expense related to equity awards	(2,460)	(2,500)	(4,727)	(5,232)
Pro forma income (loss) from operations	$ 6,156	$ (11,560)	$ (10,032)	$ (24,936)

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 equity awards, 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.

Isis Pharmaceuticals, Inc.
Condensed Consolidated Balance Sheets
(In Thousands)

	June 30, 2012 (unaudited)	December 31, 2011
Assets:		
Cash, cash equivalents and short-term investments	$ 336,029	$ 343,664
Other current assets	14,390	16,475
Property, plant and equipment, net	94,008	96,615
Other assets	27,967	28,140
Total assets	$ 472,394	$ 484,894
Liabilities and stockholders' equity:		
Other current liabilities	$ 32,065	$ 39,528
Current portion of deferred contract revenue	22,998	36,584
2 5/8% convertible subordinated notes	146,031	141,448
Long-term obligations, less current portion	79,708	74,002
Investment in Regulus Therapeutics Inc.	5,563	4,424
Long-term deferred contract revenue	31,715	17,474
Stockholders' equity	154,314	171,434
Total liabilities and stockholders' equity	$ 472,394	$ 484,894

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