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): **May 7, 2013**

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 May 7, 2013, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended March 31, 2013. 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 related to equity awards. The Company is presenting pro forma information excluding the effects of the non-cash compensation expense because the Company believes it is useful for investors in assessing the Company's operating results compared to the prior period. 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 May 7, 2013.

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: May 7, 2013

By: /s/ B. Lynne Parshall
B. LYNNE PARSHALL
Chief Operating Officer

INDEX TO EXHIBITS

99.1	Press Release dated May 7, 2013.

ISIS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR FIRST QUARTER 2013

- **Conference Call Webcast Tuesday, May 7, 4:30 p.m. ET at www.isispharm.com**

CARLSBAD, Calif., May 7, 2013 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today reported pro forma operating income of $4.5 million and pro forma net income of $1.2 million for the three months ended March 31, 2013 compared to a pro forma net operating loss of $16.2 million and a pro forma net loss of $21.7 million for the same period in 2012. The significant improvement in the Company's financial results was driven primarily by milestone payments Isis earned in the first quarter, including a $25 million milestone payment from Genzyme and a $7.5 million milestone payment from GlaxoSmithKline (GSK). In addition, Isis maintained its cash position by ending the first quarter of 2013 with approximately $372 million compared to approximately $374 million at December 31, 2012. On a GAAP basis, Isis reported income from operations of $1.6 million and a net loss of $1.7 million for the three months ended March 31, 2013 compared to a loss from operations of $18.5 million and a net loss of $24.0 million for the same period in 2012.

"The most significant event for Isis this quarter was the approval and launch of KYNAMRO™ in the United States to treat patients with homozygous familial hypercholesterolemia. The approval of KYNAMRO is an important event for these patients who have a severe disease and who struggle daily to control their LDL-C levels. Genzyme has commercially launched KYNAMRO and has physicians qualified under the REMS program. KYNAMRO approval is also an important milestone for Isis and our antisense technology. KYNAMRO is the first systemically delivered antisense drug to be sold commercially and is the culmination of many years of hard work and scientific achievements. We are looking forward to updating you on KYNAMRO's commercial progress later in the year," said B. Lynne Parshall, chief operating officer of Isis. "Isis' value extends well beyond KYNAMRO. We have created a pipeline of promising products to treat severe and rare, neurological, cardiovascular, metabolic and inflammatory diseases, and cancer. Because we have such a robust pipeline, we have numerous events to report throughout the year, including Phase 2 data that we will report within the next couple of months."

"In addition to ending the quarter with both pro forma operating and net income, we maintained our cash position by using only $2 million net during the quarter. We were able to achieve these financial results because of the success of our partnerships with Genzyme and GSK from which we earned $32.5 million in milestone payments in the first quarter. And, we have continued this momentum into the second quarter. We have already received a $30 million upfront fee from Roche for our Huntington's disease program and will earn a $3.5 million milestone payment from Biogen Idec when we dose the first infant with spinal muscular atrophy in the Phase 2 study for ISIS-SMN$_{Rx}$," said Elizabeth L. Hougen, chief financial officer of Isis. "With numerous successful partnerships encompassing multiple drugs, we have continuing opportunities to earn additional milestone payments from our partners as we progress through the year. Our maturing pipeline of unpartnered assets together with our prolific research programs enables us to explore new collaborations as well."

Upcoming Key Milestones

- Report clinical data on ISIS-CRP$_{Rx}$ in patients with rheumatoid arthritis
- Report clinical data on ISIS-APOCIII$_{Rx}$ in patients with high triglycerides

Financial Results

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 months ended March 31, 2013 was $43.4 million compared to $23.2 million for the same period in 2012. Isis' revenue fluctuates based on the nature and timing of payments under agreements with Isis' partners, including license fees, milestone-related payments and other payments. For example, Isis' revenue in the first quarter of 2013 was significantly higher than in the first quarter of 2012 primarily as a result of the $25 million milestone payment from Genzyme for FDA approval of the KYNAMRO NDA and the $7.5 million milestone payment from GSK for the initiation of the Phase 2/3 study of ISIS-TTR$_{Rx}$. Also in the first quarter of 2013, Isis began amortizing revenue from its new alliance with AstraZeneca and its third collaboration with Biogen Idec. Isis' increase in revenue was offset, in part, by the completion of the amortization of the upfront payments associated with Isis' Genzyme collaboration.

Operating Expenses

On a pro forma basis, Isis' operating expenses for the three months ended March 31, 2013 of $38.9 million were essentially flat compared to $39.4 million for the same period in 2012.

On a GAAP basis, Isis' operating expenses for the three months ended March 31, 2013 and 2012 were $41.7 million.

Gain on Investments

Isis' gain on investments for the three months ended March 31, 2013 was due to the $1.1 million Isis realized when it sold the stock it held in Sarepta Therapeutics. This gain demonstrates the value that Isis is realizing from its satellite company strategy.

Net Loss

Isis reported a net loss of $1.7 million for the three months ended March 31, 2013 compared to $24.0 million for the same period in 2012. Basic and diluted net loss per share for the three months ended March 31, 2013 was $0.02 per share compared to $0.24 per share for the same period in 2012. Isis' net loss was significantly lower than in 2012 primarily due to the milestone payments it received from its partners in the first quarter.

Balance Sheet

As of March 31, 2013, Isis had cash, cash equivalents and short-term investments of $371.9 million compared to $374.4 million at December 31, 2012 and had working capital of $361.5 million at March 31, 2013 compared to $349.1 million at December 31, 2012. Isis maintained its cash position primarily due to the $32.5 million in milestone payments it received in the first quarter while continuing to invest in its pipeline. Isis' cash at March 31, 2013 does not include the $30 million upfront payment Isis received from Roche for Isis' HTT collaboration. Isis' working capital increased in 2013 primarily due to an increase in current assets resulting from an increase in Isis' investment in Regulus. At March 31, 2013, the carrying value of Isis' investment in Regulus was $44.9 million compared to $33.6 million at December 31, 2012.

Business Highlights

"We have had a number of important accomplishments already this year. Together with Genzyme we brought KYNAMRO to the market in the United States for patients with HoFH. We continued to mature and expand our severe and rare disease franchise, reporting early encouraging data on our first splicing drug, ISIS-SMN$_{Rx}$, in children with spinal muscular atrophy and initiating Phase 2/3 programs for ISIS-SMN$_{Rx}$ with Biogen Idec and ISIS-TTR$_{Rx}$ with GSK. We plan to continue this momentum through the year. Over the next couple of months we plan to report Phase 2 data on both ISIS-CRP$_{Rx}$ and ISIS-APOCIII$_{Rx}$," continued Ms. Parshall.

"We continue to be successful in implementing our business strategy and establishing strategic partnerships that provide us with significant value. The performance of our drugs in the clinic and the broad applicability of our antisense technology have generated significant interest in Isis. One of our partnering goals is to select high-quality partners for our severe neurological disease and cancer programs to augment our own efforts in these two newest areas of our pipeline. We have been successful implementing this strategy. Since January of last year, we have initiated five new partnerships that involve neurological diseases and cancer, bringing in more than $125 million in upfront payments and adding partners that are significantly enhancing our drug discovery and development efforts in these therapeutic areas," continued Ms. Parshall. "We believe that our partnerships are structured to provide the best support and ultimately the best value for each drug. Our partnership with Roche for our Huntington's disease program is a very good example of how we benefit from the expertise and resources that our partner brings while we maintain control over the discovery and early development of the program. We look forward to broadly evaluating this program with Roche and developing antisense drugs to treat Huntington's disease."

Corporate and Drug Development Highlights

- Isis and Genzyme were successful in bringing KYNAMRO to the market in the United States for patients with HoFH. These patients are at high cardiovascular risk and may not be able to reduce their LDL-C sufficiently with currently available lipid-lowering therapies.
    - Genzyme launched KYNAMRO in the United States for the treatment of patients with HoFH.
        - Isis received a $25 million milestone payment from Genzyme related to the marketing approval of KYNAMRO by the FDA.
    - Genzyme continues to enroll the FOCUS FH study, which is designed to provide 60-week safety and efficacy data in FH patients to support an additional regulatory filing. Genzyme reached an agreement with the FDA on the design of the FOCUS FH study via a Special Protocol Assessment, or SPA.
- Isis and its investigators reported positive data from a number of drugs in Isis' pipeline.
    - Dr. Claudia Chiriboga reported Phase 1 data on ISIS-SMN$_{Rx}$ at the American Academy of Neurology. In this open-label study conducted in a small population, ISIS-SMN$_{Rx}$ was well tolerated in children with spinal muscular atrophy (SMA) and functional activity improvements in muscle function were observed in a number of these children.
    - Isis reported positive Phase 1 data on ISIS-CRP$_{Rx}$ demonstrating that, in healthy volunteers, ISIS-CRP$_{Rx}$ can selectively blunt severe increases in CRP following an endotoxin challenge, which produces immune responses similar to those seen with bacterial infections.
    - Isis published data in the journal Circulation Research demonstrating that antisense inhibition of ApoC-III produced significant reductions of ApoC-III and triglycerides in multiple species including man. Isis presented these data in an oral presentation at the 2013 Duell Meeting in March 2013.
- Isis continued to advance its pipeline by initiating clinical studies in numerous disease areas.
    - Isis initiated a Phase 2 study of ISIS-SMN$_{Rx}$ in infants with SMA and will earn a $3.5 million milestone payment from Biogen Idec when the first patient is dosed in this study.
    - Isis initiated a Phase 2/3 study of ISIS-TTR$_{Rx}$ in patients with familial polyneuropathy and received a $7.5 million milestone payment from GlaxoSmithKline related to the initiation of this study.

    - AstraZeneca initiated a Phase 1b/2a study of ISIS-STAT3$_{Rx}$ in patients with advanced metastatic hepatocellular carcinoma.
    - Isis initiated a Phase 1 study of ISIS-APOA$_{Rx}$, an antisense drug designed to reduce levels of Lp(a), an atherogenic lipoprotein.
- Isis formed a new alliance with Roche to discover and develop antisense drugs to treat Huntington's disease.
    - Isis received a $30 million upfront payment and is eligible to receive up to $362 million in a license fee, pre-licensing and post-licensing milestone payments, including up to $80 million in commercial milestones.

- In addition, Isis is eligible to receive up to $136.5 million in milestone payments for each additional drug successfully developed plus up to $50 million in commercial milestones if a drug using Roche's proprietary brain shuttle technology is successfully commercialized.
- Isis is also eligible to receive tiered royalties on sales of drugs arising from the alliance.

Conference Call

At 4:30 p.m. Eastern Time today, May 7, 2013, Isis will conduct a live webcast conference call to discuss this earnings release and related activities. Interested parties may listen to the call by dialing 1-866-652-5200 and provide the conference identification number "10028266", 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 28 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, and cancer. Isis' partner, Genzyme, is commercializing Isis' lead product, KYNAMRO™, in the United States for the treatment of patients with HoFH. Genzyme is also pursuing marketing approval of KYNAMRO in other markets. Isis' patents provide strong and extensive protection for its drugs and technology.

FORWARD-LOOKING STATEMENT

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. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs, including the commercial potential 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, 2012 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.

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

	Three months ended, March 31,	
	2013	2012
	(unaudited)	
Revenue:		
Research and development revenue under collaborative agreements	$ 41,921	$ 21,818
Licensing and royalty revenue	1,439	1,417
Total revenue	43,360	23,235
Expenses:		
Research and development	38,312	38,714
General and administrative	3,423	2,976
Total operating expenses	41,735	41,690
Income (loss) from operations	1,625	(18,455)
Other income (expense):		
Equity in net loss of Regulus Therapeutics Inc.	—	(976)
Investment income	376	600
Interest expense	(4,795)	(5,179)
Gain on investments, net	1,058	17
Loss before income tax expense	$ (1,736)	$ (23,993)
Income tax benefit (expense)	64	(2)
Net loss	$ (1,672)	$ (23,995)
Basic and diluted net loss per share	$ (0.02)	$ (0.24)
Shares used in computing basic and diluted net loss per share	101,875	100,157

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

	Three months ended, March 31,	
	2013	2012
	(unaudited)	
As reported operating expenses according to GAAP	$ 41,735	$ 41,690
Excluding compensation expense related to equity awards	(2,869)	(2,267)
Pro forma operating expenses	$ 38,866	$ 39,423
As reported income (loss) from operations according to GAAP	$ 1,625	$ (18,455)
Excluding compensation expense related to equity awards	(2,869)	(2,267)
Pro forma income (loss) from operations	$ 4,494	$ (16,188)
As reported net loss according to GAAP	$ (1,672)	$ (23,995)
Excluding compensation expense related to equity awards	(2,869)	(2,267)
Pro forma net income (loss)	$ 1,197	$ (21,728)

Reconciliation of GAAP to Pro Forma Basis

As illustrated in the Selected Financial Information in this press release, pro forma operating expenses, pro forma income (loss) from operations, and proforma net income (loss) 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 results 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)

	March 31, 2013	December 31, 2012
	(unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	$ 371,911	$ 374,446
Investment in Regulus Therapeutics Inc.	44,863	33,622
Other current assets	15,055	15,370
Property, plant and equipment, net	89,694	91,084
Other assets	31,438	31,164
Total assets	$ 552,961	$ 545,686
Liabilities and stockholders' equity:		
Other current liabilities	$ 35,051	$ 38,397
Current portion of deferred contract revenue	35,244	35,925
2 3/4% convertible senior notes	145,533	143,990
Long-term obligations, less current portion	77,226	77,952
Long-term deferred contract revenue	58,816	66,656
Stockholders' equity	201,091	182,766
Total liabilities and stockholders' equity	$ 552,961	$ 545,686

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