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, 2014**

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:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ 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, 2014, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended June 30, 2014. 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 August 4, 2014.

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, 2014

By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL
Chief Operating Officer

INDEX TO EXHIBITS

99.1	Press Release dated August 4, 2014.

Exhibit 99.1

ISIS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR SECOND QUARTER 2014

- **$40 million in milestone payments from partners drives improved quarterly financial performance**

- **Conference Call Webcast Monday, August 4, 10:30 a.m. ET at www.isispharm.com**

CARLSBAD, Calif., August 4, 2014 - Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) today reported pro forma net operating income of $1.1 million and a pro forma net operating loss (NOL) of $21.5 million for the three and six months ended June 30, 2014, respectively, compared to an NOL of $5.3 million and $799,000 for the same periods in 2013. Isis' pro forma operating income in the second quarter of 2014 was primarily driven by more than $40 million of milestone payments from partners the Company earned during the second quarter. On a GAAP basis, Isis reported a loss from operations of $6.7 million and $36.3 million for the three and six months ended June 30, 2014, respectively, compared to a loss from operations of $7.9 million and $6.3 million for the three and six months ended June 30, 2013. Isis ended the first half of 2014 with approximately $591 million in cash, not including approximately $41 million that Isis received after the quarter ended, compared to $657 million at December 31, 2013.

"Our strong financial position demonstrates the value our unique business strategy creates as our pipeline continues to advance. We have initiated the Phase 3 program for ISIS-SMN_{Rx} to treat patients with spinal muscular atrophy. Our Phase 3 clinical study of ISIS-TTR_{Rx} in patients with the polyneuropathy form of transthyretin amyloidosis is enrolling well and patients who have completed the controlled portion of the study can continue to receive treatment in our open-label extension study. Also this year, we plan to initiate the Phase 3 program for ISIS-$APOCIII_{Rx}$ to treat patients with severely elevated triglyceride levels with the first study starting very shortly," said B. Lynne Parshall, chief operating officer of Isis. "By the end of the year, we plan to be conducting Phase 3 programs on a number of different drugs to treat important genetically driven diseases for which antisense may offer a unique therapeutic approach."

"We ended the second quarter with pro forma net operating income of $1.1 million, including more than $40 million in milestone payments reflecting the significant progress our partnered programs are achieving. So far this year, because of our successful execution of our business strategy, we have achieved nearly $75 million in payments from our partners. 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, including an $18 million milestone payment from Biogen Idec when we dose the first infant in our ISIS-SMN_{Rx} Phase 3 study. Further, we maintained our strong cash position by ending the quarter with more than $590 million in cash, which does not include cash from the $40 million in milestone payments we earned late in the second quarter. Because of the timing of these payments, the $40 million will be reflected in our third quarter cash balance," said Elizabeth L. Hougen, chief financial officer of Isis. "We remain on track to meet our financial guidance of a pro forma NOL in the low $50 million range and year end cash in excess of $575 million."

Upcoming Key Milestones

- Initiate an additional Phase 3 clinical study on ISIS-SMN_{Rx}.
- Initiate a Phase 3 clinical program on ISIS-$APOCIII_{Rx}$.
- Report the full data analysis of the Phase 2 study of ISIS-FXI_{Rx} at an upcoming medical meeting.
- Report data from Phase 2 studies of ISIS-SMN_{Rx} in both children and infants with SMA at an upcoming medical meeting.
- Report Phase 2 data from ISIS-$GCCR_{Rx}$ and ISIS-$PTP1B_{Rx}$ in patients with type 2 diabetes.

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 and six months ended June 30, 2014 was $57.1 million and $85.2 million, respectively, compared to $38.1 million and $81.5 million for the same periods in 2013. Isis' revenue fluctuates based on the nature and timing of payments under agreements with its partners and consists primarily of revenue from the amortization of upfront fees, milestone payments and license fees. Isis' revenue from the amortization of payments from its partners was $31.4 million in the first half of 2014, compared to $19.2 million for the same period in 2013, and increased primarily due to the amortization of upfront fees related to the strategic neurology partnership Isis entered into with Biogen Idec in September 2013.

Isis also earned $41.5 million in milestone payments in the first half of 2014, consisting of the following:

- $24.5 million from Biogen Idec related to advancing ISIS-SMN_{Rx}, initiating a Phase 1 study for ISIS-$DMPK_{Rx}$, and validating an undisclosed target to treat a neurological disorder;
- $15 million from AstraZeneca related to initiating a Phase 1 clinical study of ISIS-AR_{Rx}; and
- $2 million from GSK related to advancing ISIS-TTR_{Rx}.

Operating Expenses

On a pro forma basis, Isis' operating expenses for the three and six months ended June 30, 2014 were $56.0 million and $106.8 million, respectively, compared to $43.4 million and $82.3 million for the same periods in 2013. As projected, Isis' operating expenses in 2014 increased due to higher development costs associated with Isis' maturing pipeline of drugs. On a GAAP basis, Isis' operating expenses for the three and six months ended June 30, 2014 were $63.7 million and $121.6 million, respectively, compared to $46.0 million and $87.8 million for the same periods in 2013.

Net Loss

Isis reported a net loss of $12.1 million and $43.4 million for the three and six months ended June 30, 2014, respectively, compared to $10.1 million and $11.8 million for the same periods in 2013. Basic and diluted net loss per share for the three and six months ended June 30, 2014 was $0.10 per share and $0.37 per share, respectively, compared to $0.09 per share and $0.11 per share for the same periods in 2013. Isis' net loss increased in the first half of 2014 primarily due to the planned increase in operating expenses associated with the Company's maturing pipeline of drugs.

Balance Sheet

As of June 30, 2014, Isis had cash, cash equivalents and short-term investments of $590.8 million compared to $656.8 million at December 31, 2013 and had working capital of $605.0 million at June 30, 2014 compared to $637.7 million at December 31, 2013. The decrease in cash and working capital primarily relates to cash used to fund Isis' operations. Isis' cash balance at June 30, 2014 does not include approximately $41 million in payments that it recognized into revenue in the second quarter and received in the third quarter.

Business Highlights

"We have had a successful start to the year. We reported positive Phase 2 data from five of the drugs in our pipeline. These data highlight the potential of our antisense technology to create drugs to treat a wide range of diseases, including type 2 diabetes, high triglycerides and orphan diseases, like SMA and FCS, where there are no therapeutic options. We advanced two partnered drugs into clinical development for which we earned $29 million in milestone payments from our partners at Biogen Idec and AstraZeneca. In addition, our unpartnered drugs continued to advance. Our Lp(a) drug, ISIS-APO(a)$_{Rx}$, entered Phase 2 clinical trials and we plan to begin Phase 3 clinical trials for ISIS-APOCIII$_{Rx}$ shortly," continued Ms. Parshall. "We look forward to continuing this momentum in the second half of this year."

Corporate and Drug Development Highlights

- Isis reported positive clinical results from five drugs in later-stage development. These data exemplify the broad applicability and potential for antisense drugs to provide therapeutic benefit to many different diseases.
  - Isis reported positive Phase 2 data on ISIS-APOCIII$_{Rx}$ in patients with high to extremely high triglyceride levels as a single agent and in combination with fibrates. In these studies, patients experienced substantial reductions of triglyceride and apoC-III levels with significant increases in HDL-cholesterol. These Phase 2 data were presented at the Arteriosclerosis, Thrombosis and Vascular Biology and the National Lipid Association meetings.
  - Isis presented positive results from both of the ongoing multiple-dose open label Phase 2 studies of ISIS-SMN$_{Rx}$ in infants and children with SMA, which were consistent with earlier reported data. In these studies, Isis reported increases in muscle function scores in infants and children treated with ISIS-SMN$_{Rx}$. These Phase 2 data were presented at the American Academy of Neurology meeting.
  - Isis reported positive Phase 2 data for ISIS-GCGR$_{Rx}$ in patients with type 2 diabetes. In this study, patients with type 2 diabetes uncontrolled on stable metformin therapy experienced up to a 2.25 percentage point mean reduction in HbA1c levels after 13 weeks of dosing. These Phase 2 data were presented at the American Diabetes Association Scientific Sessions.
  - Isis reported positive top-line Phase 2 clinical results for ISIS-FXI$_{Rx}$ in patients undergoing total knee replacement. In this study, ISIS-FXI$_{Rx}$-treated patients experienced a dose-dependent decrease in venous thromboembolism and numerically fewer bleeding events compared to patients treated with enoxaparin.
  - Isis reported Phase 2 results showing that ISIS-CRP$_{Rx}$ produced statistically significant mean reductions of CRP protein of 65% with reductions as great as 84% in patients with atrial fibrillation (AF). In addition, two patients who had elevated levels of CRP (>5 mg/L) experienced a reduction of CRP that was associated with a decline to zero in overall AF burden while on treatment.
- Isis continued to advance its pipeline of drugs.
  - Isis initiated a Phase 3 study, ENDEAR, of ISIS-SMN$_{Rx}$ in infants with SMA and will earn an $18 million milestone payment upon dosing of the first infant. This is the first of several planned studies in a broad and comprehensive late-stage clinical development program for ISIS-SMN$_{Rx}$.
  - Isis initiated a Phase 2 study of ISIS-APO(a)$_{Rx}$ in patients with high levels of lipoprotein(a), an independent risk factor for cardiovascular disease.
  - Isis initiated a Phase 1 study of ISIS-PKK$_{Rx}$, an antisense drug to treat patients with hereditary angioedemia, and a Phase 1 study of ISIS-DMPK$_{Rx}$, an antisense drug to treat patients with myotonic dystrophy type 1.
  - AstraZeneca initiated a Phase 1 study of ISIS-AR$_{Rx}$, an antisense drug discovered by Isis to treat patients with cancer.
  - Isis added a new drug, ISIS-HTT$_{Rx}$, to its pipeline. ISIS-HTT$_{Rx}$ is part of Isis' alliance with Roche and is in development to treat patients with Huntington's Disease.
- Isis and its partners were recognized by the drug development community for Isis' innovative and collaborative alliances and Isis' commitment to developing drugs to treat patients with serious, unmet medical needs.
  - Isis and Genzyme received the 2014 Partners in Progress Corporate Award from the National Organization for Rare Disorders (NORD) for the development and approval of KYNAMRO, a drug selected for being a very important orphan therapy to reach the market in the United States. This award honors companies that have brought important and innovative treatments to market for patients with rare disorders.
  - Isis' and Biogen Idec's innovative collaboration was voted breakthrough alliance of 2014 by Thomson Reuters Recap.
  - Frank Bennett, Ph.D., Isis' senior vice president, research, was a recipient of the Commitment to a Cure Award by the ALS Association for his and Isis' research and commitment to develop a treatment for amyotrophic lateral sclerosis (ALS).

Conference Call

At 10:30 a.m. Eastern Time today, August 4, 2014, 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 877-443-5662 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 32 drugs to treat a wide variety of diseases with an emphasis on cardiovascular, metabolic, severe and rare diseases, including neurological disorders, and cancer. Isis' partner, Genzyme, is commercializing Isis' lead product, KYNAMRO®, in the United States and other countries for the treatment of patients with homozygous FH. Isis' patents provide strong and extensive protection for its drugs and technology. Additional information about Isis is available at www.isispharm.com.

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 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, 2013, 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.

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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,	
	2014	2013	2014	2013
Revenue:	(unaudited)		(unaudited)	
Research and development revenue under collaborative agreements	$ 56,628	$ 37,615	$ 76,177	$ 79,285
Licensing and royalty revenue	448	477	9,060	2,166
Total revenue	57,076	38,092	85,237	81,451
Expenses:				
Research, development and patent expenses	59,264	42,631	112,712	80,944
General and administrative	4,462	3,389	8,842	6,811
Total operating expenses	63,726	46,020	121,554	87,755
Loss from operations	(6,650)	(7,928)	(36,317)	(6,304)
Other income (expense):				
Investment income	671	589	1,328	967
Interest expense	(4,961)	(4,808)	(9,904)	(9,603)
Gain (loss) on investments, net	(260)	840	137	1,898
Loss before income tax benefit	(11,200)	(11,307)	(44,756)	(13,042)
Income tax benefit (expense)	(881)	1,181	1,395	1,244
Net loss	$ (12,081)	$ (10,126)	$ (43,361)	$ (11,798)
Basic and diluted net loss per share	$ (0.10)	$ (0.09)	$ (0.37)	$ (0.11)
Shares used in computing basic and diluted net loss per share	117,588	108,539	117,359	105,225

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

	Three months ended, June 30,		Six months ended, June 30,	
	2014	2013	2014	2013
	(unaudited)		(unaudited)	
As reported operating expenses according to GAAP	$ 63,726	$ 46,020	$ 121,554	$ 87,755
Excluding compensation expense related to equity awards	(7,708)	(2,636)	(14,777)	(5,505)
Pro forma operating expenses	$ 56,018	$ 43,384	$ 106,777	$ 82,250
As reported loss from operations according to GAAP	$ (6,650)	$ (7,928)	$ (36,317)	$ (6,304)
Excluding compensation expense related to equity awards	(7,708)	(2,636)	(14,777)	(5,505)
Pro forma income (loss) from operations	$ 1,058	$ (5,292)	$ (21,540)	$ (799)
As reported net loss according to GAAP	$ (12,081)	$ (10,126)	$ (43,361)	$ (11,798)
Excluding compensation expense related to equity awards	(7,708)	(2,636)	(14,777)	(5,505)
Pro forma net loss	$ (4,373)	$ (7,490)	$ (28,584)	$ (6,293)

Reconciliation of GAAP to Pro Forma Basis

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

	June 30, 2014 (unaudited)	December 31, 2013
Assets:		
Cash, cash equivalents and short-term investments	$ 590,835	$ 656,761
Investment in Regulus Therapeutics Inc.	56,678	52,096
Other current assets	58,284	26,653
Property, plant and equipment, net	86,321	86,198
Other assets	25,659	25,448
Total assets	$ 817,777	$ 847,156
Liabilities and stockholders' equity:		
Other current liabilities	$ 49,256	$ 49,677
Current portion of deferred contract revenue	51,560	48,135
2 3/4% convertible senior notes	153,700	150,334
Long-term obligations, less current portion	76,014	77,830
Long-term deferred contract revenue	120,387	142,790
Stockholders' equity	366,860	378,390
Total liabilities and stockholders' equity	$ 817,777	$ 847,156

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