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): **November 7, 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:

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 November 7, 2014, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended September 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 November 7, 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: November 7, 2014

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

INDEX TO EXHIBITS

99.1	Press Release dated November 7, 2014.

Exhibit 99.1

ISIS PHARMACEUTICALS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR THIRD QUARTER 2014

· **Conference Call Webcast Friday, November 7, 11:30 a.m. ET at www.isispharm.com**

CARLSBAD, Calif., November 7, 2014 - Isis Pharmaceuticals, Inc. (NASDAQ: ISIS) today reported a pro forma net operating loss (NOL) of $13.4 million and $34.9 million for the three and nine months ended September 30, 2014, respectively, compared to an NOL of $22.7 million and $23.5 million for the same periods in 2013. Isis' revenue increased by more than 20% during the first nine months of 2014 compared to 2013 primarily due to the successes of its partnered programs as they advanced through research and development. In addition to the increase in revenue, Isis had a planned increase in operating expenses primarily associated with its late-stage clinical programs. On a GAAP basis, Isis reported a loss from operations of $21.5 million and $57.8 million for the three and nine months ended September 30, 2014, respectively, compared to a loss from operations of $25.5 million and $31.8 million for the three and nine months ended September 30, 2013. Isis ended the third quarter with $592 million in cash, compared to $657 million at December 31, 2013.

"We have had a very successful year and, with a number of exciting events on the horizon, the remainder of 2014 promises to be equally eventful. Just last month, we reported encouraging results from our ISIS-SMN_{Rx} drug in infants and children with spinal muscular atrophy. We initiated the Phase 3 study on ISIS-SMN_{Rx} in infants with SMA this summer and plan to initiate the Phase 3 study in children with SMA by the end of this year. We continue to treat patients with the polyneuropathy form of transthyretin amyloidosis in our Phase 3 study of ISIS-TTR_{Rx}. Many patients have completed all 15 months of treatment in the Phase 3 ISIS-TTR_{Rx} study and are receiving drug in the open-label extension study. We also initiated a Phase 3 clinical trial of ISIS-$APOCIII_{Rx}$ for patients with familial chylomicronemia syndrome, a rare genetic disorder resulting in extremely high triglyceride levels. We are pleased to now be conducting three Phase 3 programs, while we also mature the rest of our pipeline. We have a number of additional activities related to our pipeline to look forward to before the end of the year," said B. Lynne Parshall, chief operating officer of Isis Pharmaceuticals.

"The success of the drugs in our pipeline has contributed significantly to our financial performance this year and is strong evidence that our business strategy is working. Our business model is designed to generate substantial amounts of cash and revenue from our partners as our programs succeed. Already this year, including to date in the fourth quarter, we have generated more than $160 million from our partners. We expect to continue this momentum through the end of this year and beyond. We have numerous opportunities to earn milestone payments between now and the end of the year, including a $27 million milestone payment from Biogen Idec when we initiate the Phase 3 CHERISH study on ISIS-SMN_{Rx} in children with SMA," said Elizabeth L. Hougen, chief financial officer of Isis Pharmaceuticals. "As a result of our successes so far this year, we expect to improve upon 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-$APOCIII_{Rx}$ in patients with high triglycerides and on ISIS-SMN_{Rx} in children with SMA.
- Report the full data analysis of the Phase 2 study of ISIS-FXI_{Rx} at an upcoming medical meeting.
- Report Phase 2 data from ISIS-$PTP1B_{Rx}$ and ISIS-$GCCR_{Rx}$ 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 nine months ended September 30, 2014 of $44.1 million and $129.3 million, respectively, was significantly higher than revenue for the same periods in 2013 of $23.6 million and $105.0 million, respectively. 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 $46.0 million in the first nine months of 2014, compared to $29.8 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 $66.5 million from milestone payments in the first nine months of 2014, consisting of the following:

- $43 million from Biogen Idec related to advancing ISIS-SMN$_{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}$;
- $4.5 million from GSK related to advancing the Phase 3 study of ISIS-TTR$_{Rx}$ and advancing ISIS-GSK4$_{Rx}$; and
- $4 million from Achaogen when Achaogen initiated a Phase 3 study of plazomicin.

Already in the fourth quarter, Isis has earned $23 million in milestone payments from GSK for advancing ISIS-TTR$_{Rx}$ and for designating ISIS-GSK5$_{Rx}$ as a development candidate. Isis has also earned a $10 million milestone payment from Biogen Idec and a $7.5 million milestone payment from AstraZeneca as the partnered programs in these alliances advanced. Isis will recognize all of these milestone payments in its fourth quarter 2014 financial results.

Operating Expenses

On a pro forma basis, Isis' operating expenses for the three and nine months ended September 30, 2014 were $57.4 million and $164.2 million, respectively, compared to $46.3 million and $128.5 million for the same periods in 2013. As projected, Isis' operating expenses in 2014 increased due to higher development costs associated with Isis' maturing pipeline of drugs, including costs associated with its Phase 3 programs for ISIS-TTR$_{Rx}$, ISIS-SMN$_{Rx}$ and ISIS-APOCIII$_{Rx}$. As drugs move forward to more advanced stages of development, including into larger, longer clinical studies, the costs of development increase. In addition to the Phase 3 programs Isis is conducting, Isis initiated Phase 2 studies for several drugs in its pipeline in the second half of 2013, which are ongoing, and advanced several drugs in clinical development in the third quarter of 2014. On a GAAP basis, Isis' operating expenses for the three and nine months ended September 30, 2014 were $65.6 million and $187.1 million, respectively, compared to $49.1 million and $136.8 million for the same periods in 2013.

Net Loss

Isis reported a net loss of $26.7 million and $70.0 million for the three and nine months ended September 30, 2014, respectively, compared to $24.6 million and $36.4 million for the same periods in 2013. Basic and diluted net loss per share for the three and nine months ended September 30, 2014 was $0.23 per share and $0.60 per share, respectively, compared to $0.21 per share and $0.33 per share for the same periods in 2013. Isis' net loss increased in the first nine months of 2014 primarily due to the planned increase in operating expenses associated with the Company's maturing pipeline of drugs offset in part by higher revenue.

Balance Sheet

As of September 30, 2014, Isis had cash, cash equivalents and short-term investments of $592.0 million compared to $656.8 million at December 31, 2013 and had working capital of $573.8 million at September 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 September 30, 2014 does not include approximately $23.5 million in payments that it recognized into revenue in the third quarter and received in the fourth quarter and $20.4 million of proceeds Isis received in November 2014 from participating in Regulus' recently completed equity offering.

Business Highlights

"We have made significant progress this year maturing our pipeline. Most notably, we have reported a substantial amount of clinical data from drugs to treat patients with a diverse range of diseases, including metabolic, cardiovascular and severe and rare diseases. We and our partners reported Phase 2 results from eight drugs, initiated Phase 3 studies on three drugs, began Phase 1 and 2 studies on six drugs and moved three drugs into development. The maturation of our pipeline ensures that we will have a continuous stream of clinical events to highlight," continued Ms. Parshall.

"As our pipeline of partnered drugs has matured, the potential milestone payments we can earn from our partners become more substantial. This year we have had numerous pipeline advances in many different partnered programs, which have resulted in significant payments from our partners this year. In addition to payments we receive as partnered drugs advance in development, we benefit from the successes of our satellite companies, which expand the application of our technology platform into areas of RNA therapeutics that are outside our core focus. The benefit of this strategy was most recently illustrated by the significant increase in the value of Regulus Therapeutics. We participated in Regulus' equity offering, which generated more than $20 million in cash for Isis. And since we continue to be a top shareholder in the company, our remaining equity position represents an even greater asset," concluded Ms. Parshall.

Corporate and Drug Development Highlights from the Third Quarter and Early Fourth Quarter

- Isis reported positive clinical results for ISIS-SMN$_{Rx}$ from two open-label Phase 2 studies in infants and children with spinal muscular atrophy. These data were presented at the World Muscle Society Congress.
  - Isis reported that the median event-free age of infants with SMA on September 2, 2014 compared favorably to that of infants with SMA in the PNCR natural history study.
  - Isis reported that time- and dose-dependent increases in muscle function scores were observed in both infants and children with SMA.
  - Isis presented clinical data showing that ISIS-SMN$_{Rx}$ is distributed throughout the spinal cord and neurons with greater amounts of full-length SMN2 mRNA and SMN protein in tissues from ISIS-SMN$_{Rx}$-treated infants compared to the amounts of full-length SMN2 mRNA and SMN protein in the tissues analyzed from untreated SMA infants.
- Isis' collaborators reported positive clinical results from three drugs in Isis' lipid franchise. These data were presented at the 2014 European Society of Cardiology Congress.
  - Dr. John Kastelein, M.D., Ph.D. presented data from a retrospective analysis of 104 patients with familial hypercholesterolemia treated for one year with KYNAMRO® (mipomersen sodium) injection in the long-term extension study showing that patients treated with KYNAMRO experienced a reduction in Major Adverse Cardiovascular Events (MACE) from 25.72/1000 months (in the two years prior to KYNAMRO treatment) to 4.85/1000 months.

- Dr. John Kastelein provided an overview of the Phase 2 program for ISIS-APOCIII$_{Rx}$ in which treatment with ISIS-APOCIII$_{Rx}$ produced consistent, robust and statistically significant reductions in triglycerides, apoC-III and non-HDL-Cholesterol and increases in HDL-Cholesterol in all patient populations evaluated.
- Dr. Sotirios Tsimikas, M.D. presented data from the Phase 1 study in which treatment with ISIS-APO(a)$_{Rx}$ produced dose-dependent and significant reductions in Lp(a) levels in healthy volunteers.

· Isis' partner, Regulus Therapeutics, reported positive interim results on RG-101, an anti-miR drug in development to treat patients with hepatitis C virus.
- Regulus reported a single dose of RG-101 demonstrated a substantial mean reduction in viral load in patients with varied hepatitis C virus (HCV) genotypes and treatment history.

· Together with its partners, Isis continued to advance its pipeline of drugs.
- Isis initiated ENDEAR, the Phase 3 study evaluating ISIS-SMN$_{Rx}$ in infants with SMA.
- Isis initiated APPROACH, the Phase 3 study evaluating ISIS-APOCIII$_{Rx}$ in patients with familial chylomicronemia syndrome.
- Achaogen initiated a Phase 3 study of plazomicin in patients with serious multi-drug resistant, gram-negative bacterial infections.
- Isis added a new drug, ISIS-BIIB3$_{Rx}$, to its pipeline. ISIS-BIIB3$_{Rx}$ is part of Isis' strategic neurology alliance with Biogen Idec and is in development to treat an undisclosed neurodegenerative disease.
- Isis added a new drug, ISIS-GSK5$_{Rx}$, to its pipeline. ISIS-GSK5$_{Rx}$ is part of Isis' alliance with GSK and is in development to treat an undisclosed ocular disease
- 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.

Conference Call

At 11:30 a.m. Eastern Time today, November 7, 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 34 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 has numerous drugs in Phase 3 development in severe and rare and cardiovascular diseases. These include a novel triglyceride lowering drug, ISIS-APOCIII$_{Rx}$, for patients with familial chylomicronemia syndrome; ISIS-TTR$_{Rx}$, which Isis is developing with GSK to treat patients with the polyneuropathy form of TTR amyloidosis; and, ISIS-SMN$_{Rx}$, which Isis is developing with Biogen Idec to treat infants and children with spinal muscular atrophy, a severe and rare neuromuscular disease. 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, September 30,		Nine months ended, September 30,	
	2014	2013	2014	2013
Revenue:	(unaudited)		(unaudited)	
Research and development revenue under collaborative agreements	$ 43,798	$ 23,258	$ 119,975	$ 102,543
Licensing and royalty revenue	265	327	9,325	2,493
Total revenue	44,063	23,585	129,300	105,036
Expenses:				
Research, development and patent expenses	61,086	45,660	173,798	126,603
General and administrative	4,470	3,430	13,313	10,241
Total operating expenses	65,556	49,090	187,111	136,844
Loss from operations	(21,493)	(25,505)	(57,811)	(31,808)
Other income (expense):				
Investment income	675	434	2,003	1,400
Interest expense	(4,998)	(4,867)	(14,902)	(14,470)
Gain on investments, net	538	175	675	2,073
Loss before income tax (expense) benefit	(25,278)	(29,763)	(70,035)	(42,805)
Income tax (expense) benefit	(1,398)	5,193	(2)	6,437
Net loss	$ (26,676)	$ (24,570)	$ (70,037)	$ (36,368)
Basic and diluted net loss per share	$ (0.23)	$ (0.21)	$ (0.60)	$ (0.33)
Shares used in computing basic and diluted net loss per share	117,811	115,263	117,511	108,608

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, September 30,		Nine months ended, September 30,	
	2014	2013	2014	2013
	(unaudited)		(unaudited)	
As reported operating expenses according to GAAP	$ 65,556	$ 49,090	$ 187,111	$ 136,844
Excluding compensation expense related to equity awards	(8,118)	(2,812)	(22,894)	(8,318)
Pro forma operating expenses	$ 57,438	$ 46,278	$ 164,217	$ 128,526
As reported loss from operations according to GAAP	$ (21,493)	$ (25,505)	$ (57,811)	$ (31,808)
Excluding compensation expense related to equity awards	(8,118)	(2,812)	(22,894)	(8,318)
Pro forma income (loss) from operations	$ (13,375)	$ (22,693)	$ (34,917)	$ (23,490)
As reported net loss according to GAAP	$ (26,676)	$ (24,570)	$ (70,037)	$ (36,368)
Excluding compensation expense related to equity awards	(8,118)	(2,812)	(22,894)	(8,318)
Pro forma net loss	$ (18,558)	$ (21,758)	$ (47,143)	$ (28,050)

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)

	September 30, 2014 (unaudited)	December 31, 2013
Assets:		
Cash, cash equivalents and short-term investments	$ 591,986	$ 656,761
Investment in Regulus Therapeutics Inc.	47,426	52,096
Other current assets	41,751	26,653
Property, plant and equipment, net	88,068	86,198
Other assets	24,572	25,448
Total assets	$ 793,803	$ 847,156
Liabilities and stockholders' equity:		
Other current liabilities	$ 55,598	$ 49,677
Current portion of deferred contract revenue	51,727	48,135
2 3/4% convertible senior notes	155,437	150,334
Long-term obligations, less current portion	75,655	77,830
Long-term deferred contract revenue	110,614	142,790
Stockholders' equity	344,772	378,390
Total liabilities and stockholders' equity	793,803	$ 847,156

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