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 5, 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 November 5, 2013, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended September 30, 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 November 5, 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: November 5, 2013

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

INDEX TO EXHIBITS

99.1	Press Release dated November 5, 2013.

ISIS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR THIRD QUARTER 2013

- **Improved 2013 financial guidance**
- **Conference Call Webcast Tuesday, November 5, 11:30 a.m. ET at www.isispharm.com**

CARLSBAD, Calif., November 5, 2013 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today reported a pro forma net operating loss (NOL) of $22.7 million and $23.5 million for the three and nine months ended September 30, 2013, respectively, compared to a pro forma NOL of $26.0 million and $36.0 million for the same periods in 2012. On a GAAP basis, Isis reported a loss from operations of $25.5 million and $31.8 million for the three and nine months ended September 30, 2013, respectively, compared to a loss from operations of $28.0 million and $42.8 million for the same periods in 2012. Isis increased its cash position during the first nine months of 2013, ending September with $671 million in cash compared to $374 million at December 31, 2012. The substantial increase in the Company's cash position was primarily due to the equity offering it completed in the second quarter and cash received from its partners in the first nine months of 2013, including the $100 million upfront payment Isis received from its recently announced strategic collaboration with Biogen Idec.

"Our increasingly strong financial performance is a result of meeting key milestones in our partnerships, adding new partners and expanding existing relationships. Our financial success is also driven by achievements from our expanding and maturing pipeline, as well as continuous improvements in our technology platform. We have completed key steps to move two important drugs, ISIS-APOCIII$_{Rx}$ and ISIS-SMN$_{Rx}$, into Phase 3 studies early next year. In addition, our Phase 2/3 study for ISIS-TTR$_{Rx}$ is enrolling on schedule, and we are pleased with the progress we and our partner, GlaxoSmithKline, are making to advance this drug towards the market," said B. Lynne Parshall, chief operating officer of Isis.

"The effective execution of our business strategy and the success of the drugs in our pipeline have contributed significantly to our financial performance this year. Already this year we have received $200 million from our partners," said Elizabeth L. Hougen, chief financial officer at Isis. "Because of our strong financial performance this year, we will substantially exceed our year-end cash guidance. We are now projecting to end the year with more than $625 million in cash. We are also reducing our projected pro forma NOL by more than 30 percent to a pro forma NOL in the mid $40 million range."

Upcoming Key Milestones

- Present the complete Phase 2 clinical data for ISIS-APOCIII$_{Rx}$ and Phase 1 clinical data for ISIS-APO(a)$_{Rx}$ at the American Heart Association.
- Report data from two clinical studies evaluating ISIS-SMN$_{Rx}$ in children and in infants with spinal muscular atrophy (SMA).
- Initiate Phase 3 programs on ISIS-APOCIII$_{Rx}$ and ISIS-SMN$_{Rx}$.

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, 2013 was $23.6 million and $105.0 million, respectively, compared to $11.6 million and $82.2 million for the same periods 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 earned more than $60 million in revenue from milestone and licensing payments in the first nine months of 2013 including:

- $25 million from Genzyme when the FDA approved the KYNAMRO™ NDA;
- $10 million when AstraZeneca added a second development candidate, ISIS-AR$_{Rx}$, to its collaboration;
- $16.5 million from GlaxoSmithKline because Isis initiated the Phase 2/3 study of ISIS-TTR$_{Rx}$ and advanced ISIS-GSK3$_{Rx}$ in development;
- $5.5 million from Biogen Idec because Isis advanced the Phase 2 study of ISIS-SMN$_{Rx}$ in infants; and
- $3.5 million when Xenon licensed XEN701.

Isis' revenue in the first nine months of 2013 also included more than $33 million in revenue Isis earned from its alliances with AstraZeneca, Biogen Idec, GlaxoSmithKline and Roche.

In September 2013, Isis and Biogen Idec entered into a new strategic neurology collaboration. As part of this collaboration, Isis received a $100 million upfront payment, which Isis will begin amortizing into revenue over six years starting in October 2013. In addition, in the fourth quarter of 2013, Isis has already earned $10 million in a milestone payment for advancing ISIS-DMPK$_{Rx}$ in development.

Operating Expenses

As projected, Isis' pro forma operating expenses of $46.3 million and $128.5 million for the three and nine months ended September 30, 2013, respectively, were moderately higher compared to $37.6 million and $118.2 million for the same periods in 2012 primarily due to higher development costs associated with the progression of several of the drugs in Isis' pipeline into later stage clinical trials.

On a GAAP basis, Isis' operating expenses for the three and nine months ended September 30, 2013 were $49.1 million and $136.8 million, respectively, compared to $39.6 million and $125.0 million for the same periods in 2012.

Income Tax Benefit

Isis recognized a tax benefit of $5.2 million and $6.4 million for the three and nine months ended September 30, 2013, respectively, compared to $706,000 and $704,000 for the same periods in 2012. Isis' tax benefit in 2013 is primarily related to an increase in the Company's unrealized gain on its investment in Regulus, which reflects the increase in Regulus' stock price this year.

Net Loss

Isis reported a net loss of $24.6 million and $36.4 million for the three and nine months ended September 30, 2013, respectively, compared to $37.6 million and $62.8 million for the same periods in 2012. Basic and diluted net loss per share for the three and nine months ended September 30, 2013 were $0.21 per share and $0.33 per share, respectively, compared to $0.37 per share and $0.63 per share for the same periods in 2012. Isis' net loss for the nine months ended September 30, 2013 decreased compared to 2012 primarily due to the increase in the amount of revenue Isis earned from its partners in the first nine months of 2013, offset in part, by a moderate increase in operating expenses. In addition, Isis' income tax benefit in 2013 increased by $5.7 million compared to 2012. Also contributing to the decrease in Isis' net loss was a $4.8 million loss on the early retirement of its 2 $^{5}/_{8}$% convertible subordinated notes the Company recorded in 2012 when it successfully refinanced its convertible debt.

Balance Sheet

As of September 30, 2013, Isis had cash, cash equivalents and short-term investments of $670.9 million compared to $374.4 million at December 31, 2012 and working capital of $660 million at September 30, 2013 compared to $349.1 million at December 31, 2012. Contributing to the substantial increase in the Company's cash in the first nine months of 2013 was the approximately $210 million from the issuance of its common stock and nearly $200 million in payments from its partners, including the $100 million upfront payment Isis received from its recently announced strategic collaboration with Biogen Idec. Isis' working capital increased in 2013 primarily due to the increase in cash and the increase in the value of Isis' ownership in Regulus. At September 30, 2013, the carrying value of Isis' investment in Regulus increased to $65.0 million compared to $33.6 million at December 31, 2012. This increase demonstrates the value that Isis is realizing from its satellite company strategy.

Business Highlights

"So far in 2013, we have had a number of successes in our pipeline. We have announced multiple sets of positive clinical data for both ISIS-APOCIII$_{Rx}$ and ISIS-SMN$_{Rx}$. And our Phase 3 program for ISIS-TTR$_{Rx}$ is on track to complete enrollment next year. Beyond these late-stage assets, we have added new drugs into our pipeline, including ISIS-DMPK$_{Rx}$ to treat patients with myotonic dystrophy and ISIS-ANGPTL3$_{Rx}$ to treat patients with hyperlipidemia. We have initiated new clinical studies on six drugs, including Phase 2 studies for two of our drugs to treat type 2 diabetes in our metabolic franchise. This maturing group of assets represents the next set of commercial opportunities beyond our current late-stage drugs," continued Ms. Parshall.

"The maturation of our pipeline and successes of our antisense technology have allowed us to expand existing partnerships as well as add new partners. These relationships allow us to broaden our therapeutic efforts into disease areas that are outside of our internal expertise. For example, our broad strategic alliance with Biogen Idec couples Biogen Idec's extensive resources and expertise in neurological diseases with our antisense technology. Together we plan to create a franchise of novel treatments for neurological disorders. The benefits Biogen Idec brings to our efforts in neurological diseases are evident in our SMA program, which we partnered with Biogen Idec early last year. In less than two years, this program is poised to begin Phase 3 early next year," continued Ms. Parshall.

"We expect the pipeline momentum we have created in 2013 to continue as we advance our pipeline. The progress of our partnered programs should continue to provide us with a steady stream of milestone payments as these programs mature and as we add new partnered programs to the pipeline," concluded Ms. Parshall.

Drug Development Highlights

- Isis reported encouraging Phase 1 and Phase 2 data on a number of antisense drugs, demonstrating good safety and tolerability profiles with encouraging results in measures of efficacy in multiple disease settings.
    - Isis reported multiple Phase 2 data sets on ISIS-APOCIII$_{Rx}$ demonstrating that ISIS-APOCIII$_{Rx}$ works in patients with high to severely high triglycerides, including patients with FCS. Treatment with ISIS-APOCIII$_{Rx}$ resulted in significant reductions of apoC-III and triglycerides, and significant increases in HDL-C.
    - Dr. Kathy Swoboda presented follow up data from a single-dose open-label Phase 1 study of ISIS-SMN$_{Rx}$ in children with SMA at the International Congress of the World Muscle Society. In this study, data suggest that children from the two highest doses continued to show improvements in muscle function tests up to 14 months after a single injection of ISIS-SMN$_{Rx}$.
    - Isis reported Phase 2 data on ISIS-CRP$_{Rx}$ in patients with rheumatoid arthritis (RA).

- Isis continued to mature its pipeline by advancing drugs in development and initiating new clinical studies.
    - Isis advanced the Phase 2/3 study of ISIS-TTR$_{Rx}$, a drug to treat patients with familial amyloid polyneuropathy. As a result, Isis earned $2 million from GlaxoSmithKline.
    - Isis advanced the Phase 2 study of ISIS-SMN$_{Rx}$ in infants with SMA. As a result, Isis earned a $2 million milestone payment from Biogen Idec.
    - Isis initiated Phase 2 studies on ISIS-GCGR$_{Rx}$ and ISIS-PTP1B$_{Rx}$, antisense drugs designed to control glucose in patients with type 2 diabetes.
- Isis and its partners continued to add new drugs to the development pipeline.

- Isis and Biogen Idec selected a development candidate, ISIS-DMPK$_{Rx}$, for the treatment of patients with myotonic dystrophy type I. Upon initiation of IND-enabling studies, Isis earned a $10 million milestone payment from Biogen Idec.
- GlaxoSmithKline added a development candidate, ISIS-GSK3$_{Rx}$ to its collaboration with Isis. Isis earned $7 million in milestone payments from GlaxoSmithKline as a result.
- Regulus nominated a development candidate, RG-101, to move forward in development for the treatment of patients with hepatitis C virus. This is the first drug targeting a microRNA that Regulus has moved into development.

Corporate Highlights

- Isis formed a broad strategic alliance with Biogen Idec to discover and develop antisense drugs to treat neurological disorders.

- Isis received a $100 million upfront payment from Biogen Idec as part of the collaboration that combines Biogen Idec's expertise in neurology with Isis' leadership in antisense technology to develop novel therapies to treat neurological diseases. Isis is eligible to receive substantial milestone payments, license fees and royalty payments for all treatments developed through this collaboration.

Conference Call

At 11:30 a.m. Eastern Time today, November 5, 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 866-652-5200, 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 30 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 for the treatment of patients with HoFH. 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, 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.

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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,	
	2013	2012	2013	2012
	(unaudited)		(unaudited)	
Revenue:				
Research and development revenue under collaborative agreements	$ 23,383	$ 11,127	$ 102,918	$ 80,085
Licensing and royalty revenue	202	474	2,118	2,091
Total revenue	$ 23,585	11,601	105,036	82,176

Expenses:				
Research, development and patent expenses	45,660	36,551	126,603	115,700
General and administrative	3,430	3,096	10,241	9,281
Total operating expenses	49,090	39,647	136,844	124,981
Loss from operations	(25,505)	(28,046)	(31,808)	(42,805)
Other income (expense):				
Equity in net loss of Regulus Therapeutics Inc.	—	—	—	(1,139)
Investment income	434	408	1,400	1,485
Interest expense	(4,867)	(5,937)	(14,470)	(16,335)
Gain on investments, net	175	—	2,073	19
Loss on early retirement of debt	—	(4,770)	—	(4,770)
Loss before income tax benefit	(29,763)	(38,345)	(42,805)	(63,545)
Income tax benefit	5,193	706	6,437	704
Net loss	$ (24,570)	$ (37,639)	$ (36,368)	$ (62,841)
Basic and diluted net loss per share	$ (0.21)	$ (0.37)	$ (0.33)	$ (0.63)
Shares used in computing basic and diluted net loss per share	115,263	100,680	108,608	100,351

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

	Three months ended, September 30,		Nine months ended, September 30,	
	2013	2012	2013	2012
	(unaudited)		(unaudited)	
As reported operating expenses according to GAAP	$ 49,090	$ 39,647	$ 136,844	$ 124,981
Excluding compensation expense related to equity awards	(2,812)	(2,034)	(8,318)	(6,761)
Pro forma operating expenses	$ 46,278	$ 37,613	$ 128,526	$ 118,220
As reported loss from operations according to GAAP	$ (25,505)	$ (28,046)	$ (31,808)	$ (42,805)
Excluding compensation expense related to equity awards	(2,812)	(2,034)	(8,318)	(6,761)
Pro forma loss from operations	$ (22,693)	$ (26,012)	$ (23,490)	$ (36,044)

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 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, 2013	December 31, 2012
	(unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	$ 670,898	$ 374,446
Investment in Regulus Therapeutics Inc.	65,004	33,622
Other current assets	27,402	15,370
Property, plant and equipment, net	87,273	91,084
Other assets	31,339	31,164
Total assets	$ 881,916	$ 545,686
Liabilities and stockholders' equity:		
Other current liabilities	$ 47,301	$ 38,397
Current portion of deferred contract revenue	55,977	35,925

2 3/4% convertible senior notes	148,705	143,990
Long-term obligations, less current portion	77,481	77,952
Long-term deferred contract revenue	151,006	66,656
Stockholders' equity	401,446	182,766
Total liabilities and stockholders' equity	$ 881,916	$ 545,686

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