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 5, 2015**

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 May 5, 2015, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended March 31, 2015. 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 related to equity awards. The Company is presenting pro forma information excluding the effects of the non-cash compensation because the Company believes it is useful for investors in assessing the Company's operating results compared to the prior year. 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 5, 2015.

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 5, 2015

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

INDEX TO EXHIBITS

99.1	Press Release dated May 5, 2015.

Exhibit 99.1

ISIS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR FIRST QUARTER 2015

- **Pro Forma Operating Income Driven by $46 Million in Partner Payments**
- **Conference Call Webcast Tuesday, May 5, 11:30 a.m. ET at www.isispharm.com**

CARLSBAD, Calif., May 5, 2015 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today reported pro forma operating income of $4.0 million for the three months ended March 31, 2015 compared to a pro forma net operating loss of $22.6 million for the same period in 2014. Isis' significantly improved financial results were due to higher revenue from milestone payments earned from its partners compared to the same quarter last year. On a GAAP basis, Isis reported a loss from operations of $9.3 million for the three months ended March 31, 2015 compared to $29.7 million for the same period in 2014. Isis maintained its strong cash position and ended the first quarter of 2015 with $695.1 million in cash compared to $728.8 million at December 31, 2014.

"Our successes in the first quarter enabled us to end the first quarter of 2015 in a strong financial position. We are continuing this momentum into the second quarter. Yesterday we achieved an important strategic objective for Isis when we licensed ISIS-FXI$_{Rx}$ to Bayer. Bayer is the optimal partner to develop and commercialize ISIS-FXI$_{Rx}$. Our goals for the ISIS-FXI$_{Rx}$ program were to maximize the value we derive from this program both in the near-term and in the long-term. We wanted a partner committed to investing to maximize the commercial value of the drug, and we wanted to retain substantial participation in the commercial value created. This partnership meets all of these goals. As a leader in the antithrombotic market, Bayer has the expertise, resources and commitment to broadly develop ISIS-FXI$_{Rx}$. They plan to conduct a robust development plan that represents a commitment to make a substantial investment in ISIS-FXI$_{Rx}$. Bayer's development plan combines near-term indications, which have the potential for early market entrance in patients with limited therapeutic options, with long-term indications in patients who are underserved by current antithrombotic treatments. In short, a development plan designed to take advantage of the profile of ISIS-FXI$_{Rx}$ and maximize its value. We are also pleased with the financial aspects of the transaction, which provide significant value upfront as well as a substantial royalty that enables us to participate in the long-term commercial success of ISIS-FXI$_{Rx}$," said B. Lynne Parshall, chief operating officer at Isis Pharmaceuticals.

"Subsequent to the first quarter, we licensed ISIS-FXI$_{Rx}$ to Bayer for a substantial upfront payment and significant milestone and other payments of up to $375 million plus tiered royalties in the low to high 20% range on gross margins of ISIS-FXI$_{Rx}$ achieving all of our financial objectives for the transaction. The financial terms of the transaction optimally balance near term value to us with our ability to participate in the commercial success of the drug. Importantly, Bayer plans to conduct a robust development plan, which represents a substantial investment in ISIS-FXI$_{Rx}$. Upon Hart-Scott-Rodino clearance, we expect to recognize approximately $85 million to $95 million of revenue from the Bayer upfront payment in 2015 and, of course the entire cash amount will augment our balance sheet," said Elizabeth L. Hougen, chief financial officer of Isis Pharmaceuticals. "We ended the first quarter in a strong financial position with pro forma operating income of $4 million and we were nearly break even with a pro forma net loss of $3 million. In addition, so far this year, we have generated more than $195 million in payments from our partners, including $100 million from Bayer, $42 million from Biogen, $35 million from Janssen and $17 million from GSK. This, together with continuing opportunities to earn additional milestone payments from our partners as we progress through the year, puts us on track to exceed our guidance of a pro forma net operating loss in the mid $50 million range and more than $630 million in cash."

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, 2015 was $62.6 million compared to $28.2 million for the same period in 2014. Isis earned $46 million in revenue from milestone payments from its partners in the first quarter of 2015, which consisted of:

- $31 million from Biogen including the following:
  - $10 million for initiating investigational new drug supporting studies for ISIS-BIIB4$_{Rx}$;
  - $9 million for advancing CHERISH, the Phase 3 study for ISIS-SMN$_{Rx}$ in infants with SMA;
  - $7 million for advancing the Phase 2 open-label extension study for ISIS-SMN$_{Rx}$ in children with SMA; and
  - $5 million for validating an undisclosed target to treat a neurological disorder.
- $15 million from GSK for advancing the Phase 3 study of ISIS-TTR$_{Rx}$.

Isis' revenue in the first quarter of 2015 also included $16.6 million in revenue from the amortization of upfront fees and manufacturing services performed for its partners, including revenue from the amortization of the $35 million upfront payment Isis received from Janssen for the companies' new collaboration. Isis' revenue in the first quarter of 2014 included $19.5 million in revenue from the amortization of upfront fees and manufacturing services and $7.7 million in revenue from Alnylam.

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.

Operating Expenses

Isis is conducting more later-stage clinical trials in 2015 than it did in 2014, including the continuation of its Phase 3 programs for ISIS-TTR$_{Rx}$, ISIS-SMN$_{Rx}$ and ISIS-APOCIII$_{Rx}$. As such, Isis' pro forma operating expenses of $58.6 million for the three months ended March 31, 2015 were higher compared to $50.8 million for the same period in 2014. As drugs move forward to more advanced stages of development, including into longer and larger clinical studies, the costs of development increase. On a GAAP basis, Isis' operating expenses for the three months ended March 31, 2015 were $71.9 million compared to $57.8 million for the same period in 2014. Isis' operating expenses on a GAAP basis included non-cash compensation expense related to equity awards, which increased for the three months ended March 31, 2015 compared to the same period in 2014 due to an increase in Isis' stock price from 2014 to 2015.

Income Tax Benefit

Isis recognized a net tax benefit of $0.8 million for the three months ended March 31, 2015 compared to a tax benefit of $2.3 million for the same period in 2014. Isis' tax benefit in both the first quarter of 2015 and 2014 was primarily the result of unrealized gains on its equity investment in Regulus, which reflected the significant increase in Regulus' stock price. As of March 31, 2015, Isis' investment in Regulus was valued at more than $90 million.

Net Loss

Isis reported a net loss of $16.7 million for the three months ended March 31, 2015 compared to $31.3 million for the same period in 2014. Basic and diluted net loss per share for the three months ended March 31, 2015 was $0.14 per share compared to $0.27 per share for the same period in 2014. Isis' net loss decreased in the first quarter of 2015 primarily due to an increase in revenue from milestone payments.

Balance Sheet

As of March 31, 2015, Isis had cash, cash equivalents and short-term investments of $695.1 million compared to $728.8 million at December 31, 2014 and had working capital of $735.1 million at March 31, 2015 compared to $721.3 million at December 31, 2014. Isis' working capital increased in the first quarter of 2015 primarily due to the increase in the carrying value of its investment in Regulus, slightly offset by the decrease in cash. Isis' cash balance at March 31, 2015 did not include $124 million, which is comprised of $24 million in payments Isis has received from its partners since the end of the first quarter plus the $100 million upfront payment Isis is eligible to receive from Bayer.

Business Highlights

"Bayer is the second new partner we added this year. Earlier in the year, we added Janssen as our partner in the discovery and development of antisense drugs to treat autoimmune disorders of the GI tract. Our Janssen collaboration expands our technology to a new area, the oral administration of antisense drugs for the local treatment of autoimmune diseases in the gastrointestinal tract," continued Ms. Parshall.

"We have a pipeline of novel antisense drugs that could provide significant value in the near-term with six drugs in Phase 3 development including, ISIS-SMN_{Rx}, ISIS-TTR_{Rx} and ISIS-$APOCIII_{Rx}$. Enrollment for both of the Phase 3 studies of ISIS-SMN_{Rx} is on track, and we plan to share data on these studies in the 2016/2017 timeframe. We are pleased that Biogen is expanding the Phase 3 program for ISIS-SMN_{Rx} by conducting two additional studies of ISIS-SMN_{Rx} including a study evaluating ISIS-SMN_{Rx}, in newborns screened at birth and shown to have SMA, but who are presymptomatic. We presented positive data on ISIS-TTR_{Rx} in patients with FAP at the American Academy of Neurology. We are also pleased that GSK is planning to expand the clinical program for ISIS-TTR_{Rx} by initiating two additional Phase 3 studies, one in patients with TTR-related cardiomyopathy and one in Japan in patients with FAP. And of course, our wholly owned subsidiary, Akcea Therapeutics, is off to a great start, and we look forward to sharing more about this with you next month when we host an Akcea webcast call," concluded Ms. Parshall.

Drug Development Highlights (*2015 first quarter and subsequent activities*)

- Isis and its partners reported positive data on six drugs in Isis' pipeline, including:
  - Isis reported positive results from an ongoing open-label extension study of ISIS-TTR_{Rx} in patients with FAP. In the open-label study after thirteen weeks of treatment with ISIS-TTR_{Rx}, TTR protein was reduced up to 92 percent with a median reduction of 78 percent in patients with FAP compared to their baseline TTR levels at entry into the Phase 3 study.
  - AstraZeneca reported clinical and preclinical data on ISIS-STAT3-2.5_{Rx} demonstrating evidence of antitumor activity in patients with cancer including advanced/metastatic hepatocellular carcinoma and diffuse large B cell lymphoma. Additionally, AstraZeneca reported that, in preclinical studies, co-treatment of ISIS-STAT3-2.5_{Rx} and MEDI4736, an immune checkpoint inhibitor, showed significantly greater antitumor activity than when either drug was administered alone. AstraZeneca plans to initiate two clinical studies evaluating ISIS-STAT3-2.5_{Rx} in combination with MEDI4736 this year.
  - Isis reported top-line Phase 2 data on ISIS-$PTP1B_{Rx}$ demonstrating that patients with type 2 diabetes experienced statistically significant mean reductions in body weight and HbA1c (0.7 percentage point) at 36 weeks.

- Regulus reported clinical data on RG-101 showing that patients with hepatitis C virus achieved sustained viral suppression after only a single dose of RG-101, and that some patients remained below the level of detection for hepatitis C virus 20 weeks after a single dose.
- Isis reported Phase 1 results showing that ISIS-ANGPTL3$_{Rx}$ produced significant reductions of up to 93 percent in ANGPTL3, up to 63 percent in triglycerides and up to 46 percent in total cholesterol in healthy volunteers.
- Isis reported Phase 1 results showing that ISIS-PKK$_{Rx}$ produced significant, dose-dependent reductions of PKK of up to 95 percent in healthy volunteers.

Corporate Highlights (*2015 first quarter and subsequent activities*)

- Isis licensed ISIS-FXI$_{Rx}$ to Bayer HealthCare to develop and commercialize ISIS-FXI$_{Rx}$ for the prevention of thrombosis.
  - Isis is eligible to receive up to $375 million in payments, including a $100 million upfront payment and a $55 million milestone payment upon advancement of the program following completion of the planned Phase 2 study.
  - Isis is eligible to receive tiered royalties in the low to high 20 percent range on gross margins of ISIS-FXI$_{Rx}$.
  - This transaction is subject to clearances under the Hart-Scott Rodino Antitrust Improvements Act.
- Isis formed an alliance with Janssen to discover and develop antisense drugs to treat autoimmune disorders of the GI tract.
  - Isis received $35 million in upfront payments and is eligible to receive nearly $800 million in development, regulatory and sales milestone payments and license fees for the programs under this alliance.
  - Isis will also receive tiered royalties that on average are double digits on sales of drugs successfully commercialized.
- Isis formed a wholly owned subsidiary, Akcea Therapeutics, to develop and commercialize its lipid drugs, ISIS-APOCIII$_{Rx}$, ISIS-APO(a)$_{Rx}$, ISIS-ANGPTL3$_{Rx}$ and the follow on drugs for these programs.
- Isis and Alnylam formed a new agreement that includes a cross-license of intellectual property, providing each company rights to certain of each other's technology advances.
  - The new agreement also provides each company with exclusive RNA therapeutic license rights for two programs.
- Isis generated more than $195 million in payments from partners, including the following:
  - $100 million from Bayer
  - $42 million from Biogen
  - $35 million from Janssen
  - $17 million from GSK

Conference Call

At 11:30 a.m. Eastern Time today, May 5, 2015, 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 RNA-targeted technology to discover and develop novel drugs for its product pipeline and for its partners. Isis' broad pipeline consists of 38 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/rare diseases and cardiovascular diseases. These include ISIS-APOCIII$_{Rx}$, a drug Isis is developing and plans to commercialize through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with familial chylomicronemia syndrome and partial lipodystrophy; ISIS-TTR$_{Rx}$, a drug Isis is developing with GSK to treat patients with the polyneuropathy and cardiomyopathy forms of TTR amyloidosis; and ISIS-SMN$_{Rx}$, a drug Isis is developing with Biogen 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, including KYNAMRO, ISIS-APOCIII$_{Rx}$, ISIS-SMN$_{Rx}$ and ISIS-TTR$_{Rx}$, 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, 2014, which is on file with the SEC. Copies of this 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, March 31,	
	2015	2014
Revenue:	(unaudited)	
Research and development revenue under collaborative agreements	$ 61,892	$ 19,550
Licensing and royalty revenue	691	8,611
Total revenue	62,583	28,161
Expenses:		
Research, development and patent expenses	64,447	53,448
General and administrative	7,466	4,380
Total operating expenses	71,913	57,828
Income (loss) from operations	(9,330)	(29,667)
Other income (expense):		
Investment income	845	657
Interest expense	(9,021)	(4,943)
Gain on investments, net	-	397
Loss before income tax benefit	$ (17,506)	$ (33,556)
Income tax benefit	789	2,276
Net loss	$ (16,717)	$ (31,280)
Basic and diluted net loss per share	$ (0.14)	$ (0.27)
Shares used in computing basic and diluted net loss per share	118,948	117,128

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

	Three months ended, March 31,	
	2015	2014
	(unaudited)	
As reported operating expenses according to GAAP	$ 71,913	$ 57,828
Excluding compensation expense related to equity awards	(13,305)	(7,069)
Pro forma operating expenses	$ 58,608	$ 50,759
As reported income (loss) from operations according to GAAP	$ (9,330)	$ (29,667)
Excluding compensation expense related to equity awards	(13,305)	(7,069)
Pro forma income (loss) from operations	$ 3,975	$ (22,598)
As reported net loss according to GAAP	$ (16,717)	$ (31,280)
Excluding compensation expense related to equity awards	(13,305)	(7,069)
Pro forma net loss	$ (3,412)	$ (24,211)

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, 2015 (unaudited)	December 31, 2014
Assets:		
Cash, cash equivalents and short-term investments	$ 695,054	$ 728,832
Investment in Regulus Therapeutics Inc.	93,446	81,881
Other current assets	46,927	25,884
Property, plant and equipment, net	89,047	88,958
Other assets	30,959	30,254
Total assets	$ 955,433	$ 955,809
Liabilities and stockholders' equity:		
Other current liabilities	$ 47,702	$ 63,619
Current portion of deferred contract revenue	52,586	51,713
1% convertible senior notes	332,274	327,486
2 3/4% convertible senior notes	48,579	48,014
Long-term obligations, less current portion	79,358	79,400
Long-term deferred contract revenue	119,083	127,797
Stockholders' equity	275,851	257,780
Total liabilities and stockholders' equity	$ 955,433	$ 955,809

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