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): **February 27, 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 February 27, 2015, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter and fiscal year ended December 31, 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 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 February 27, 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: February 27, 2015

By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL
Chief Operating Officer

INDEX TO EXHIBITS

99.1	Press Release dated February 27, 2015.

Exhibit 99.1

ISIS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR 2014

- **Isis Outperforms 2014 Projections for Pro Forma Net Operating Loss and Year-end Cash**
- **Isis Achieves Profitable Fourth Quarter**
- **More than $230 Million in Payments from Partners Drives Significantly Improved Financial Results**
- **Conference Call Webcast Friday, February 27, 10:30 a.m. ET at www.isispharm.com**

CARLSBAD, Calif., February 27, 2015 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced it significantly outperformed both its pro forma net operating loss (NOL) guidance and its cash guidance ending the year in a strong financial position. Isis' significantly improved financial results were due in large part to the more than $230 million in payments the Company received from its partners. Isis' pro forma NOL of $16.3 million for 2014 was a nearly 60% improvement over its 2013 NOL of $40.2 million. On a GAAP basis, Isis reported income from operations of $10.1 million for the three months ended December 31, 2014 and a loss from operations for the year of $47.7 million, compared to a loss from operations of $19.9 million and $51.7 million for the same periods in 2013. Isis also reported GAAP net income of $31.1 million for the fourth quarter ended December 31, 2014, which was a significant improvement over the same period in 2013. Isis added more than $70 million of cash to its balance sheet in 2014, ending the year with $728.8 million, a more than $150 million increase over its cash guidance of $575 million. Isis' strong financial performance in 2014 was a result of the successful execution of its business strategy, its advancing pipeline and the demonstration that antisense is an efficient and effective drug discovery technology.

"2014 was another year of significant achievements for Isis with successes in every aspect of our business. We continued to advance our large pipeline of first-in-class or best-in- class drugs, including initiating Phase 3 programs for ISIS-APOCIII$_{Rx}$ and ISIS-SMN$_{Rx}$ and progressing the Phase 3 study of ISIS-TTR$_{Rx}$. Each of these drugs represents a potential near term commercial opportunity with Phase 3 data planned for the 2016/2017 timeframe. We and our partners reported clinical data from 18 studies in 2014. It is a reflection of the efficiency and effectiveness of our technology that 15 of these studies were positive. Of particular note, the clinical study results from two of our drugs, ISIS-APOCIII$_{Rx}$ and ISIS-FXI$_{Rx}$, were published in two separate papers in the New England Journal of Medicine. These publications illustrate the significant value of antisense technology to create novel therapies that effectively act through novel mechanisms to treat disease," said B. Lynne Parshall, chief operating officer at Isis Pharmaceuticals. "We continued to expand the reach of our technology as illustrated by the number and diversity of new drugs we have added to our pipeline in the last year, including generation 2.5 drugs, LICA conjugated drugs and drugs that target numerous organs and tissues beyond the liver. We added a new partnership with Janssen that expands the therapeutic application of our technology and we expanded existing partnerships."

"We took the next step in the evolution of our business strategy with the formation of our wholly owned subsidiary, Akcea Therapeutics. One of the most important contributions the Akcea team has made to date is the addition of a second ultra-rare indication for ISIS-APOCIII$_{Rx}$. This new indication is to treat patients with partial lipodystrophy. We believe this new indication could double the initial patient population for ISIS-APOCIII$_{Rx}$. We plan to initiate a Phase 3 study in patients with partial lipodystrophy rapidly, which should complete roughly in parallel with the Phase 3 FCS study. Both FCS and partial lipodystrophy are ultra-orphan indications with limited or no approved therapeutic options. With the Akcea team's commercial expertise, we believe we can develop a pricing and reimbursement strategy that supports the significant value ISIS-APOCIII$_{Rx}$ can potentially bring to these patients. All of these successes have established a strong base upon which to build in 2015," concluded Ms. Parshall.

“Our financial performance in 2014 was a result of the successful execution of our business strategy, which ensures that we benefit from the achievements of the drugs in our pipeline and our continued innovation in developing RNA-targeted drugs. We received more than $230 million in payments from our partners, nearly half of which were milestone payments we earned as our partnered programs advanced. As such, we ended the year in a very strong financial position with nearly $730 million in cash, significantly higher than our projection of more than $575 million. In addition, we outperformed our NOL guidance by ending the year with a pro forma NOL of $16.3 million compared to our pro forma NOL guidance of low $50 million range. We also reported net income on both a pro forma and GAAP basis for our fourth quarter primarily resulting from nearly $70 million in milestone payments and more than $30 million related to our ownership in Regulus. Further, we took advantage of favorable market conditions and the increase in our stock price to refinance the majority of our outstanding convertible debt, obtaining a very favorable interest rate while reducing the potential dilution from the convertible notes,” said Elizabeth L. Hougen, chief financial officer of Isis Pharmaceuticals.

“We are carrying this momentum into 2015. We plan to continue to progress the drugs we have in pivotal Phase 3 studies, initiate additional Phase 3 studies, and advance our drugs that are in or entering early and mid-stage development. We also plan to expand our pipeline and continue to invest in advancing our technology. Although our clinical programs are increasing in size and cost, we are projecting a pro forma NOL in the mid $50 million range, which is very similar to our 2014 guidance. We are able to keep our projections in line with last year's projections because of the many opportunities we have to earn significant revenue as our partnered programs continue to advance. Already this year, we have earned $27 million in milestone payments from our partners. We are also projecting to end the year with more than $630 million in cash, which represents net cash outflows of only $100 million to move forward our large and growing pipeline of drugs," concluded Ms. Hougen.

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 twelve months ended December 31, 2014 was $84.9 million and $214.2 million, respectively, compared to $42.2 million and $147.3 million for the same periods in 2013. Isis’ revenue fluctuates based on the nature and timing of payments under agreements with its partners, including license fees, milestone-related payments and other payments. For example, nearly two-thirds of Isis’ revenue in 2014 was from milestone payments the Company earned from the success of its drugs and partnerships. Isis’ revenue from milestone payments in 2014 was primarily comprised of:

- $80 million from Biogen Idec for advancing ISIS-SMN$_{Rx}$, including initiating two Phase 3 studies, initiating a Phase 1 study of ISIS-DMPK-2.5$_{Rx}$, validating two undisclosed targets to treat neurological disorders under its neurology collaborations, and advancing a third drug into development;
- $29 million from GSK for advancing the Phase 2/3 study of ISIS-TTR$_{Rx}$ and further advancing ISIS-HBV$_{Rx}$, ISIS-GSK4-L$_{Rx}$, and ISIS-RHO-2.5$_{Rx}$ (formerly ISIS-GSK5-2.5$_{Rx}$);
- $22 million from AstraZeneca for initiating a Phase 1 clinical study of ISIS-AR-2.5$_{Rx}$ and advancing ISIS-STAT3-2.5$_{Rx}$; and
- $4 million from Achaogen when Achaogen initiated a Phase 3 study of plazomicin.

Isis' revenue in 2014 also included nearly $70 million in revenue from the amortization of upfront fees and manufacturing services performed for its partners and $9.9 million in revenue from its relationship with Alnylam.

Operating Expenses

As projected, Isis' pro forma operating expenses of $66.3 million and $230.5 million for the three and twelve months ended December 31, 2014, respectively, were higher compared to $59.0 million and $187.5 million for the same periods in 2013. The expected increase in operating expenses was primarily due to higher costs associated with its Phase 3 programs for ISIS-TTR$_{Rx}$, ISIS-SMN$_{Rx}$ and ISIS-APOCIII$_{Rx}$. As drugs move forward to more advanced stages of development, including into longer and larger 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 were ongoing in 2014, and advanced numerous drugs into clinical development in 2014.

On a GAAP basis, Isis' operating expenses for the three and twelve months ended December 31, 2014 were $74.8 million and $261.9 million, respectively, compared to $62.1 million and $199.0 million for the same periods in 2013.

Loss on Retirement of Debt

In November 2014, Isis refinanced the majority of its outstanding convertible debt by issuing $500 million of 1% convertible senior notes due 2021 (1% Notes) and used a substantial portion of the net proceeds from the issuance of these notes to repurchase $140 million principal amount of the Company's 2¾% convertible senior notes due 2019 (2¾% Notes), which were trading at a significant premium due to almost a four-fold increase in the Company's stock price since the notes were issued in 2012. As a result of the early repurchase of the 2¾% Notes, Isis recognized an $8.3 million non-cash loss.

Gain on Investment in Regulus Therapeutics Inc.

In November 2014, Regulus Therapeutics, Inc., a company Isis co-founded, completed a public offering in which the Company participated as a selling shareholder. As a result of the shares Isis sold in the offering and other shares it sold throughout the year, Isis received nearly $23 million of cash and recorded a $19.9 million gain. Isis now owns approximately 5.5 million shares, or approximately 11%, of Regulus' common stock.

Isis' total proceeds from sales of stock in its satellite companies were more than $25 million during 2014, including sales of its shares in Regulus.

Income Tax Benefit

Isis recognized a net tax benefit of $15.4 million for the year ended December 31, 2014 compared to a tax benefit of $5.9 million in 2013. Isis' tax benefit increased in 2014 compared to 2013 primarily because of the substantial increase in the value of Isis' investment in Regulus and the resulting unrealized gain.

Net Income (Loss)

Isis reported net income of $31.1 million and a net loss of $39.0 million for the three and twelve months ended December 31, 2014, respectively, compared to a net loss of $24.3 million and $60.6 million for the same periods in 2013. Basic and diluted net income per share for the three months ended December 31, 2014 was $0.26 per share and $0.25 per share, respectively, while basic and diluted net loss per share was $0.33 per share for the year ended December 31, 2014. In comparison, basic and diluted net loss per share for the three and twelve months ended December 31, 2013 was $0.21 per share and $0.55 per share, respectively. Isis' net loss for the year ended December 31, 2014 decreased significantly compared to 2013 primarily due to a decrease in Isis' net operating loss, the gain from its investment in Regulus, and the tax benefit the company recorded in 2014 offset, in part, by the non-cash loss on Isis' early retirement of a large portion of its 2 ¾% Notes.

Balance Sheet

As of December 31, 2014, Isis had cash, cash equivalents and short-term investments of $728.8 million compared to $656.8 million at December 31, 2013 and working capital of $721.3 million at December 31, 2014 compared to $637.7 million at December 31, 2013. Isis' working capital increased significantly in 2014 primarily due to the more than $230 million in cash Isis received from its partners, demonstrating Isis' successful execution of its business strategy. Isis' working capital also increased due to the increase in the carrying value of Isis' investment in Regulus.

In November 2014, Isis successfully refinanced a majority of its 2¾% Notes. In the refinancing, Isis reduced the interest rate to 1%, reduced the potential dilution from its convertible notes and extended the maturity to November 2021. Consistent with accounting rules, Isis' balance sheet at December 31, 2014 included $327.5 million of the $500 million principal amount of the notes in the liabilities section and the remainder in stockholders' equity.

Drug Development Highlights in 2014 and early 2015

- Isis and its partners reported data from 20 clinical studies of which 17 were positive, including:
  - A retrospective analysis from a Phase 3 long-term extension study in which patients with familial hypercholesterolemia treated with KYNAMRO (mipomersen sodium) injection for a mean of one or two years had a significant reduction in major adverse cardiovascular events (MACE) compared to two years prior to therapy.
  - Four data presentations from Phase 2 studies in which patients with high to extremely high triglyceride levels treated with ISIS-APOCIII$_{Rx}$ experienced significant reductions in triglycerides, and patients with elevated triglycerides and type 2 diabetes treated with ISIS-APOCIII$_{Rx}$ experienced significant reductions in both triglycerides and HbA1c.
  - Phase 2 data from two open-label studies in which infants and children with SMA treated with ISIS-SMN$_{Rx}$ experienced time- and dose-dependent increases in muscle function. In addition, the median event-free age of ISIS-SMN$_{Rx}$ - treated infants with SMA compared favorably to that of infants with SMA in a PNCR natural history study.
  - Phase 2 data in which ISIS-FXI$_{Rx}$-treated patients undergoing total knee replacement surgery experienced a seven-fold lower incidence of venous thromboembolism and numerically fewer bleeding events compared to patients treated with enoxaparin.
  - Phase 2 data in which ISIS-GCGR$_{Rx}$-treated 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 treatment with ISIS-GCGR$_{Rx}$.
  - Phase 2 top line data in which ISIS-PTP1B$_{Rx}$-treated patients with type 2 diabetes who were uncontrolled on metformin with or without sulfonylurea experienced statistically significant mean reductions in body weight and HbA1c (0.7 percentage point) at 36 weeks.
  - Phase 1/2 data in which ISIS-STAT3-2.5$_{Rx}$-treated patients with cancer experienced preliminary evidence of antitumor activity.
  - Phase 1 data in which ISIS-APO(a)$_{Rx}$ treatment produced dose-dependent and significant reductions in Lp(a) levels in normal volunteers.
  - Phase 2 data in which ISIS-PKK$_{Rx}$ treatment produced significant, dose-dependent reductions of prekallikrein, or PKK, of up to 95 percent in healthy volunteers.
- ISIS-DMPK-2.5$_{Rx}$ was granted orphan drug status for the treatment of myotonic dystrophy Type 1 by the U.S Food and Drug Administration.
- Isis, together with its partners, continued to advance its pipeline of drugs, initiating 12 clinical studies, including four Phase 3 studies and four Phase 2 studies.
- Isis added 12 drugs to its pipeline.

Corporate Highlights in 2014 and early 2015

- Isis formed a wholly owned subsidiary, Akcea Therapeutics Inc., to develop and commercialize its lipid drugs, ISIS-APOCIII$_{Rx}$, ISIS-APO(a)$_{Rx}$, ISIS-ANGPTL3$_{Rx}$ and any follow-on drugs for these programs.
- Isis formed an alliance with Janssen to discover and develop antisense drugs to treat autoimmune disorders of the gastrointestinal tract.
- Isis formed an alliance with AstraZeneca to discover and develop novel delivery methods for antisense oligonucleotides.
- Isis and Alnylam formed a new agreement that included a cross-license of intellectual property on four disease targets, providing each company with exclusive RNA therapeutic license rights for two programs.
- Isis generated more than $250 million in payments from its partners and received proceeds of more than $25 million through the sale of stock it owned in its satellite company partners.
- Isis and its partners were recognized by the drug development community for their innovative and collaborative alliances and their 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 for the development and approval of KYNAMRO.
  - Isis' innovative collaboration with Biogen Idec was voted breakthrough alliance of 2014 by Thomson Reuters Recap.
- Isis' senior vice president of research, Frank Bennett, Ph.D., was awarded the Commitment to a Cure Award by the ALS Association for his research and commitment to develop a treatment for amyotrophic lateral sclerosis.
- Isis' founder, CEO and chairman of the board of directors, Stanley T. Crooke, M.D., Ph.D., was recognized with several awards.
  - The prestigious SCRIP Lifetime Achievement Award.
  - The SMA Breakthrough Award by CURE SMA.

2015 Goals

In 2015, Isis plans to achieve the following goals itself and with its partners:

- Advance the pipeline:
  - Report clinical data on eight or more drugs, including:
    - An update on the Phase 2 open-label study for ISIS-SMN$_{Rx}$ in infants with SMA
    - Phase 2 data for ISIS-PTP1B$_{Rx}$ and ISIS-GCCR$_{Rx}$ in patients with type 2 diabetes
    - Phase 2 data for ISIS-STAT3-2.5$_{Rx}$ (AZD9150) in patients with lymphoma
    - Phase 1/2 data for ISIS-AR-2.5$_{Rx}$ (AZD5312) in patients with androgen receptor tumors, such as prostate cancer
    - Phase 3 FOCUS FH study data for KYNAMRO
    - Phase 2 data on ISIS-APO(a)$_{Rx}$ in patients with high Lp(a)
    - Phase 2 data on ISIS-DMPK-2.5$_{Rx}$ in patients with myotonic dystrophy type 1
    - A number of Phase 1 data readouts
  - Initiate up to 13 clinical studies, including a Phase 3 study on ISIS-APOCIII$_{Rx}$ in patients with partial lipodystrophy and numerous Phase 2 studies, including:
    - ISIS-FGFR4$_{Rx}$ in obese patients
    - ISIS-FXI$_{Rx}$ in patients with renal disease
    - ISIS-GCGR$_{Rx}$ in patients with type 2 diabetes (dose optimization)
    - ISIS-HBV$_{Rx}$ in patients with hepatitis B viral infection
    - ISIS-HTT$_{Rx}$ in patients with Huntington's Disease
    - ISIS-PKK$_{Rx}$ in patients with hereditary angioedema
- Broaden the pipeline by adding up to five new drugs in both partnered and unpartnered programs.
- Continue to successfully execute the business strategy to generate revenue and cash.

Conference Call

At 10:30 a.m. Eastern Time today, February 27, 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 through its wholly owned subsidiary, Akcea Therapeutics, to treat patients with severely high triglycerides, such as patients with familial chylomicronemia syndrome; ISIS-TTR$_{Rx}$, a drug Isis is developing with GSK to treat patients with the polyneuropathy form of TTR amyloidosis; and, ISIS-SMN$_{Rx}$, a drug 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, 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, 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.

Isis Pharmaceuticals' Contacts:

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

	Three months ended, December 31,		Years ended, December 31,	
	2014	2013	2014	2013
Revenue:	(unaudited)			
Research and development revenue under collaborative agreements	$ 82,539	$ 41,275	$ 202,514	$ 144,194
Licensing and royalty revenue	2,322	973	11,647	3,091
Total revenue	84,861	42,248	214,161	147,285
Expenses:				
Research, development and patent expenses	67,953	57,430	241,751	184,033
General and administrative	6,828	4,676	20,140	14,918
Total operating expenses	74,781	62,106	261,891	198,951
Income (loss) from operations	10,080	(19,858)	(47,730)	(51,666)
Other income (expense):				
Investment income	679	686	2,682	2,085
Interest expense	(7,305)	(4,885)	(22,209)	(19,355)
Gain on investments, net	1,116	305	1,256	2,378
Gain on investment in Regulus Therapeutics, Inc.	19,366	-	19,902	-
Loss on early retirement of debt	(8,292)	-	(8,292)	-
Income (loss) before income tax benefit	15,644	(23,752)	(54,391)	(66,558)
Income tax benefit	15,409	(524)	15,407	5,914
Net income (loss)	$ 31,053	$ (24,276)	(38,984)	$ (60,644)
Basic net income (loss) per share	$ 0.26	$ (0.21)	$ (0.33)	$ (0.55)
Diluted net income (loss) per share	$ 0.25	$ (0.21)	$ (0.33)	$ (0.55)
Shares used in computing basic net income (loss) per share	118,223	116,122	117,691	110,502
Shares used in computing diluted net income (loss) per share	122,839	116,122	117,691	110,502

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, December 31,		Years ended, December 31,	
	2014	2013	2014	2013
	(unaudited)		(unaudited)	
As reported operating expenses according to GAAP	$ 74,781	$ 62,106	$ 261,891	$ 198,951
Excluding compensation expense related to equity awards	(8,488)	(3,101)	(31,383)	(11,418)
Pro forma operating expenses	$ 66,293	$ 59,005	$ 230,508	$ 187,533
As reported income (loss) from operations according to GAAP	$ 10,080	$ (19,858)	$ (47,730)	$ (51,666)
Excluding compensation expense related to equity awards	(8,488)	(3,101)	(31,383)	(11,418)
Pro forma income (loss) from operations	$ 18,568	$ (16,757)	$ (16,347)	$ (40,248)
As reported net income (loss) according to GAAP	$ 31,053	$ (24,276)	$ (38,984)	$ (60,644)
Excluding compensation expense related to equity awards	(8,488)	(3,101)	(31,383)	(11,418)
Pro forma net income (loss)	$ 39,541	$ (21,175)	$ (7,601)	$ (49,226)

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 pro forma 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)

	December 31, 2014	December 31, 2013
Assets:		
Cash, cash equivalents and short-term investments	$ 728,832	$ 656,761
Investment in Regulus Therapeutics Inc.	81,881	52,096
Other current assets	25,884	26,653
Property, plant and equipment, net	88,958	86,198
Other assets	30,254	25,448
Total assets	$ 955,809	$ 847,156
Liabilities and stockholders' equity:		
Other current liabilities	$ 60,737	$ 49,677
Current portion of deferred contract revenue	54,595	48,135
1% convertible senior notes	327,486	-
2¾% convertible senior notes	48,014	150,334
Long-term obligations, less current portion	79,400	77,830
Long-term deferred contract revenue	127,797	142,790
Stockholders' equity	257,780	378,390
Total liabilities and stockholders' equity	$ 955,809	$ 847,156

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