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, 2009**

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.)

1896 Rutherford Road
Carlsbad, CA 92008
(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, 2009, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended September 30, 2009. 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 stock options. The Company is presenting pro forma information excluding the effects of the non-cash compensation expense or benefit 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 November 5, 2009.

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 4, 2009

By: /s/ B. Lynne Parshall
B. LYNNE PARSHALL
Chief Operating Officer,
Chief Financial Officer and Director

INDEX TO EXHIBITS

99.1 Press Release dated November 5, 2009.

ISIS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR THIRD QUARTER OF 2009

- **Conference Call Webcast Thursday, November 5, 08:30 a.m. EST at www.isispharm.com**

CARLSBAD, Calif., November 5, 2009 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced its financial results for the third quarter ended September 30, 2009. For the quarter, Isis reported a net loss of $3.4 million and a net operating loss of $6.9 million. In addition, for the first nine months of 2009, Isis reported net income of $170.3 million and a net operating loss of $6.1 million. Isis is confident that it will meet its 2009 financial guidance of more than $145 million of net income and a net operating loss in the low to mid $20 million range. All amounts exclude non-cash stock compensation. Isis ended the third quarter with $607.8 million of cash, cash equivalents and short-term investments. Consistent with its guidance and based on its existing and committed cash, Isis expects that its 2009 year-end cash balance will be greater than $550 million.

"We are projecting to end 2009 in the strongest financial position in our history, maintaining our momentum of strong financial performance with our second year of profitability. And, we believe that our business model will enable us to sustain a strong financial position beyond this year. In addition to our financial success, we are performing in all other areas of our business. To date, we have reported positive top-line clinical data from our two most advanced programs, Phase 3 data on mipomersen in patients with homozygous familial hypercholesterolemia and most recently Phase 2 data on ISIS 113715 in patients with type 2 diabetes. Further, we and our partners have advanced a number of antisense drugs into development and into the clinic. As we approach the end of 2009, our financial position ensures that we can continue to advance our technology, discover and develop a significant number of promising new drugs, and capitalize on our technology to continue to build our financial strength," said B. Lynne Parshall, COO and CFO of Isis.

Upcoming Key Milestones

- Report full data at the upcoming American Heart Association (AHA) from a Phase 3 study evaluating mipomersen in homozygous FH patients; positive top line data was reported in May 2009
- Report data from additional mipomersen studies in other patient populations
- Isis will continue to expand its pipeline by moving at least three new drugs into development in 2009

Financial Results

On a GAAP basis, Isis reported a loss from operations of $10.4 million and $15.9 million for the three and nine months ended September 30, 2009, respectively, compared to income from operations of $176,000 and a loss from operations of $5.0 million for the three and nine months ended September 30, 2008, respectively. Isis' operating results in 2009 reflect higher expenses associated with the expansion of the Company's programs as discussed in more detail in the "Operating Expenses" section below, offset in part, by an increase in revenue recognized in 2009 from Isis' corporate partnerships compared to 2008. Additionally, Isis reported a net loss of $6.9 million and net income of $162.0 million for the three and nine months ended September 30, 2009, respectively, compared to net income of $1.6 million and a net loss of $7.9 million for the same periods in 2008. Also, Ibis' revenue and expense are included in Isis' 2008 financial results as discontinued operations and are not included in Isis' 2009 financial results. In addition, Isis' 2009 financial results reflect the sale of Ibis. Please refer to the reconciliation of pro forma and GAAP measures, which is explained later in this release.

As a result of selling Isis' diagnostic subsidiary, Ibis Biosciences, to Abbott Molecular Inc. (AMI) in the first quarter of 2009, Isis is reporting Ibis' financial results as discontinued operations. Accordingly, Isis has presented all periods of Ibis' operating results in Isis' financial statements separately as discontinued operations. The discontinued operations line in the first nine months of 2009 also includes the $171.8 million gain that Isis recognized on the sale, net of taxes. A reconciliation summarizing the adjustments made to reflect the changes to Isis' 2008 historical statement of operations appears later in this release.

Revenue

Revenue for the three and nine months ended September 30, 2009 was $26.8 million and $89.3 million compared to $29.5 million and $77.5 million in the same periods of 2008. Isis' revenue fluctuates based on the nature and timing of payments under agreements with the Company's partners, including license fees, milestone-related payments and other payments. In August 2009, Isis finished amortizing the revenue associated with the $50 million upfront payment Isis received from Ortho-McNeil-Janssen in 2007 resulting in less revenue in the third quarter of 2009 compared to the same period in 2008. The increase in Isis' revenue for the first nine months of 2009 increased compared to the same period in 2008 due primarily to an increase in revenue from the Company's collaboration with Genzyme.

Operating Expenses

On a pro forma basis, operating expenses for the three and nine months ended September 30, 2009 were $33.6 million and $95.4 million compared to $25.7 million and $72.1 million for the same periods in 2008. Consistent with Isis' guidance, the higher expenses in 2009 were primarily due to the expansion of the Company's clinical development programs, including additional expenses associated with the broad Phase 3 clinical program for mipomersen, the lead drug in Isis' cardiovascular franchise, expenses for Regulus as it builds its core team and expenses related to the Company's expansion of its drug discovery activities into new therapeutic areas. On a GAAP basis, Isis' operating expenses from continuing operations for the three and nine months ended September 30, 2009 were $37.2 million and $105.2 million compared to $29.3 million and $82.5 million for the same periods in 2008, including non-cash compensation expense related to stock options of $3.5 million and $9.8 million for the three and nine months ended September 30, 2009 and $3.6 million and $10.4 million for the same periods in 2008.

Interest Expense

In 2009, Isis adopted a new accounting standard for its 2 5/8% convertible notes, which required Isis to assign a value to its convertible debt without considering the conversion feature. As a result, Isis is recording its convertible debt at a discount, which Isis is amortizing over the expected life of the debt as additional non-cash interest expense. The new standard required retrospective application to all periods presented. Accordingly, the amount of interest expense Isis recorded in its statement of operations for the three and nine months ended September 30, 2009 increased by $1.7 million and $5.1 million compared to an increase of $1.6 million and $4.6 million for the same periods in 2008. This new standard did not impact Isis' cash, cash equivalents and

short-term investments but decreased the carrying value of Isis' $162.5 million convertible notes to $123.3 million and $118.0 million at September 30, 2009 and December 31, 2008, respectively, with corresponding increases to shareholders' equity. A reconciliation summarizing the adjustments made to reflect the changes to Isis' 2008 historical statement of operations appears later in this release.

Net Income (Loss) from Continuing Operations, Net of Income Tax Benefit

Net loss from continuing operations for the third quarter of 2009 was $12.0 million compared to net income from continuing operations of $560,000 for the same period in 2008. For the nine months ended September 30, 2009 and 2008, net loss from continuing operations was $17.3 million and $5.1 million, respectively.

Even though Isis finished the first nine months of 2009 with a net loss from continuing operations, Isis had taxable income primarily resulting from the significant upfront payments that the Company received from its strategic alliance with Genzyme in 2008 and the gain it recognized on the sale of Ibis to AMI earlier this year. Accounting rules require Isis to record an income tax benefit of $4.6 million on a line called "Income Tax Benefit" as part of its financial results from continuing operations because it will be using the tax benefits generated from its current year loss from continuing operations to offset a portion of its taxable income.

Net Income (Loss) from Discontinued Operations

The net income (loss) from discontinued operations represents the operating results of Ibis that are presented separately in Isis' financial statements as a result of the sale of Ibis to AMI in January 2009. Net income from discontinued operations in the first nine months of 2009 primarily consists of the $202.5 million gain less income taxes. Accounting rules require Isis to allocate its 2009 tax expense between discontinued operations and continuing operations in its Consolidated Statement of Operations. Since the sale of Ibis to AMI was a discrete event that occurred in the first quarter of 2009, the accounting rules required Isis to record the total amount of its estimated income tax expense for discontinued operations in the first quarter of this year. Further, Isis was required to gross up this amount by the projected annual tax benefit it expects to record as part of its loss from continuing operations in 2009, which is described above. This means that in addition to the tax expense for the gain on the sale of Ibis, discontinued operations also includes the tax expense for other timing differences, which principally consists of the timing difference associated with the upfront funding Isis received from Genzyme. Accordingly, Isis recorded tax expense of $30.7 million in discontinued operations in the first quarter of 2009. A reconciliation summarizing the adjustments made to reflect the changes to Isis' 2008 historical statement of operations appears later in this release.

Net Income (Loss)

Isis reported net income of $162.0 million for the nine months ended September 30, 2009 compared to a net loss of $7.9 million for the same period in 2008. Basic and diluted net income per share for the nine months ended September 30, 2009 was $1.65 per share, compared to basic and diluted net loss per share of $0.08 for the same period in 2008. The improvement in Isis' net income and net income per share for the first nine months of 2009 over the same period in 2008 was primarily due to the gain Isis recognized when it sold Ibis to AMI. For the three months ended September 30, 2009, Isis reported a net loss of $6.9 million or $0.07 per share compared to net income of $1.6 million or $0.02 per share for the same period in 2008. In the third quarter of 2008, the discontinued operations line item included $4.1 million of income related to the call option that Isis granted to AMI in connection with the sale of Ibis. The call option income along with the decrease in revenue and increase in operating expenses discussed above contributed to the change in net income/loss from the third quarter of 2008 to the same period in 2009.

Balance Sheet

As of September 30, 2009, Isis had cash, cash equivalents and short-term investments of $607.8 million compared to $491.0 million at December 31, 2008 and had consolidated working capital of $504.5 million at September 30, 2009 compared to $393.7 million at December 31, 2008. Isis received $175 million from AMI in the first quarter of 2009 for its sale of Ibis, which resulted in the significant increases in both of these amounts. During the first nine months of 2009, Isis also received more than $34 million in cash from its corporate partnerships.

Regulus Therapeutics

Regulus' revenue for the three and nine months ended September 30, 2009 was $625,000 and $2.4 million compared to $681,000 and $1.4 million for the same periods in 2008. The increase was primarily related to revenue from its collaboration with GSK, including the discovery milestone payment that Regulus received from GSK.

Excluding non-cash compensation expense related to stock options, operating expenses for Regulus were $2.7 million and $8.3 million for the three and nine months ended September 30, 2009 compared to $2.0 million and $4.5 million for the same periods in 2008. The increase is primarily related to Regulus' continued efforts to build its team to support its internal microRNA programs and its GSK collaboration. Regulus generated a loss from operations, excluding non-cash compensation expense related to stock options, of $2.1 million and $5.9 million for the three and nine months ended September 30, 2009 compared to $1.3 million and $3.1 million for the same periods in 2008.

Business Highlights

"We had numerous significant accomplishments during the last quarter that demonstrate the productivity of our technology, the therapeutic potential of antisense drugs to a number of different disease targets and our continued commitment to lead the field of RNA-targeted therapeutics," said Ms. Parshall.

"Last month, we reported positive Phase 2 data for ISIS 113715 in patients with type 2 diabetes who are unable to control their glucose levels on existing sulfonylurea treatment. We demonstrated that treatment with ISIS 113715 showed consistent and statistically significant reductions in multiple short and intermediate measures of glucose control. In addition, ISIS 113715 caused statistically significant and clinically meaningful reductions in LDL cholesterol. Consistent with our preclinical data, we also observed a tendency toward weight loss even in this short-term study without strict dietary control. All of these observations combine to create a favorable drug profile, and we look forward to advancing this program."

"An important component of our business strategy is to encourage innovation and support the advancement of antisense drugs, including those drugs our satellite company partners are developing. We are now in a financial position to make strategic investments in some of our satellite companies, which guarantees that our partners have the resources to advance the development of existing antisense drugs and add new antisense drugs into development. Consistent with our strategy, we have invested in Regulus Therapeutics to ensure that it has the capital to continue to explore the therapeutic opportunities of

targeting microRNAs. This year we also invested in iCo Therapeutics to support the clinical development of iCo-007, an antisense drug currently in Phase 1 studies for the treatment of ocular disease. And most recently, we participated in Altair Therapeutics' financing. This financing will fund Altair's Phase 2 development of AIR645, an antisense drug discovered by us and licensed to Altair, as well as move additional antisense asthma drugs toward development," continued Ms. Parshall.

"Finally, we are delighted to announce that we have been selected for two podium presentations at the upcoming AHA meeting, the premier cardiovascular symposium. In these presentations, mipomersen investigators will present detailed information from our first Phase 3 study on the performance of mipomersen, including the effect of mipomersen on important cardiovascular parameters such as LDL-C and Lp(a), which are generally accepted risk factors for cardiovascular disease. In May of this year, we reported the top-line data from this study, which met its primary endpoint with a 25 percent reduction in LDL-C in patients with homozygous familial hypercholesterolemia. The study also met each of its secondary endpoints of reductions in apolipoprotein B, total cholesterol and non-HDL cholesterol. We are very pleased with the performance of mipomersen in this first of three studies, and we look forward to reporting the complete data at the AHA. During the next year, we and our partner Genzyme will be completing and reporting on the remaining Phase 3 and Phase 2 studies on mipomersen as Genzyme prepares for the first NDA filing for mipomersen," concluded Ms. Parshall.

Quarterly Highlights

Isis reported positive top-line Phase 2 data on ISIS 113715 in patients with type 2 diabetes on stable doses of sulfonylurea.

- Treatment with 200 mg per week of ISIS 113715 for 13 weeks showed consistent and statistically significant reductions in multiple short and intermediate measures of glucose control.
- ISIS 113715 also showed statistically significant and clinically meaningful reductions in LDL-C and a tendency toward weight loss.
- The safety profile of the drug remains positive with no exacerbation of sulfonylurea-induced hypoglycemia or other clinically significant adverse effects.

Isis' pipeline matures as antisense drugs continue to advance in development and show promise in clinical studies.

- Altair reported the successful completion of a Phase 1 study that showed AIR645 was safe and well tolerated. Altair intends on initiating Phase 2 studies on AIR645 soon.
- OncoGenex initiated a Phase 1 study evaluating OGX-427 in patients with bladder cancer.
- Achaogen reported the successful completion of a Phase 1 study on ACHN-490.

Isis supports its dominant patent estate and maintains an extensive and broad intellectual property position.

- Isis received a notice of allowance that expands the scope of Isis' Crooke patents and Isis, Alnylam and Regulus were granted a key microRNA patent in Japan.

Conference Call

At 08:30 a.m. Eastern Time today, November 5, 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 866-783-2145 and refer to passcode "ISIS2009," 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 expertise in RNA to discover and develop novel drugs for its product pipeline and for its partners. The Company has successfully commercialized the world's first antisense drug and has 19 drugs in development. Isis' drug development programs are focused on treating cardiovascular, metabolic and severe neurodegenerative diseases and cancer. Isis' partners are developing antisense drugs invented by Isis to treat a wide variety of diseases. Isis and Alnylam Pharmaceuticals are joint owners of Regulus Therapeutics Inc., a company focused on the discovery, development and commercialization of microRNA therapeutics. Isis also has made significant innovations beyond human therapeutics resulting in products that other companies, including Abbott, are commercializing. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of over 1,600 issued patents worldwide. Additional information about Isis is available at www.isispharm.com.

This press release includes forward-looking statements regarding Isis Pharmaceuticals' business, the financial position and outlook for Isis as well as Regulus, its majority-owned subsidiary, and the therapeutic and commercial potential of the Company's 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 products. 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, 2008, 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, including Regulus Therapeutics Inc.

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, September 30,		Nine months ended, September 30,	
	2009	2008(1)	2009	2008(1)
	(unaudited)		(unaudited)	
Revenue:				
Research and development revenue under collaborative agreements	$ 25,962	$ 28,488	$ 86,415	$ 69,750
Licensing and royalty revenue	809	975	2,923	7,790
Total revenue	26,771	29,463	89,338	77,540
Expenses:				
Research and development	33,832	26,024	94,520	73,096
General and administrative	3,335	3,263	10,685	9,428
Total operating expenses	37,167	29,287	105,205	82,524
Income (loss) from operations	(10,396)	176	(15,867)	(4,984)
Other income (expense):				
Investment income	1,430	3,468	5,243	8,804
Interest expense	(3,185)	(3,084)	(9,422)	(8,902)
Gain on investments, net	123	—	2,794	—
Income (loss) from continuing operations, before income tax benefit	(12,028)	560	(17,252)	(5,082)
Income tax benefit	3,968	—	4,625	—
Net income (loss) from continuing operations, net of income tax benefit	(8,060)	560	(12,627)	(5,082)
Discontinued Operations:				
Loss from discontinued operations	—	(155)	(29)	(5,884)
Gain on sale of Ibis Biosciences, Inc., net of tax	—	—	171,773	—
Net income (loss) from discontinued operations, net of tax	—	(155)	171,744	(5,884)
Net income (loss)	(8,060)	405	159,117	(10,966)
Net loss attributable to noncontrolling interest in Regulus Therapeutics Inc.	1,136	1,208	2 ,907	3,056
Net income (loss) attributable to Isis Pharmaceuticals, Inc. common stockholders	$ (6,924)	$ 1,613	$ 162,024	$ (7,910)
Basic and diluted net income (loss) per share:				
Net income (loss) from continuing operations attributable to Isis Pharmaceuticals, Inc. common stockholders	$ (0.07)	$ 0.02	$ (0.10)	$ (0.02)
Net income (loss) from discontinued operations	—	—	1.75	(0.06)
Basic and diluted net income (loss)	$ (0.07)	$ 0.02	$ 1.65	$ (0.08)
Shares used in computing basic net income (loss) per share	98,320	95,863	97,988	93,786
Shares used in computing diluted net income (loss) per share	98,320	100,181	97,988	93,786

(1) Adjusted for the required retrospective adoption of the accounting standard for debt that became effective in 2009.

Isis Pharmaceuticals, Inc.
Reconciliation of Isis' 2008 Historical Statement of Operations
(In Thousands, Except Per Share Data)

	Historical Isis Pharmaceuticals, Inc. Nine months ended September 30, 2008(1)	Discontinued Operations (2)	New Accounting Standard for Debt(3)	Adjusted nine months ended September 30, 2008
		(unaudited)		
Revenue:				
Research and development revenue under collaborative agreements	$ 78,739	$ (8,989)	$ —	$ 69,750
Licensing and royalty revenue	7,790	—	—	7,790
Total revenue	86,529	(8,989)	—	77,540
Expenses:				
Research and development	89,611	(16,515)	—	73,096
General and administrative	13,206	(3,778)	—	9,428
Total operating expenses	102,817	(20,293)	—	82,524
Income (loss) from operations	(16,288)	11,304	—	(4,984)
Other income (expense):				
Investment income	13,061	(4,257)	—	8,804
Interest expense	(4,297)	—	(4,605)	(8,902)
Net income (loss) from continuing operations	(7,524)	7,047	(4,605)	(5,082)
Net loss from discontinued operations	—	—	—	(5,884)
Net income (loss)	(7,524)	7,047	(4,605)	(10,966)
Net loss attributable to noncontrolling interest in Regulus Therapeutics Inc.	3,056	—	—	3,056
Net loss attributable to noncontrolling interest in Ibis Biosciences, Inc.	1,163	(1,163)	—	—

Net income (loss) attributable to Isis Pharmaceuticals, Inc. common stockholders	$ (3,305)	$ 5,884	$ (4,605)	$ (7,910)
Basic and diluted net income (loss) per share:				
Net income (loss) from continuing operations attributable to Isis Pharmaceuticals, Inc. common stockholders	$ (0.04)			$ (0.02)
Net income (loss) from discontinued operations	—			(0.06)
Basic and diluted net income (loss)	$ (0.04)			$ (0.08)
Shares used in computing basic and diluted net income (loss) per share	93,786			93,786

(1) The historical condensed consolidated statement of operations reflects the required retrospective adoption of the accounting standard for non-controlling interests that became effective in January 2009.

(2) As a result of selling Ibis to AMI, Isis removed Ibis' operating results from its continuing operations and reclassified them as discontinued operations.

(3) Adjustment to reflect the required retrospective adoption of the accounting standard for debt that became effective in 2009.

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, September 30,		Nine months ended, September 30,	
	2009	2008	2009	2008
	(unaudited)		(unaudited)	
As reported operating expenses according to GAAP	$ 37,167	$ 29,287	$ 105,205	$ 82,524
Excluding compensation expense related to stock options pursuant to SFAS 123(R)	(3,546)	(3,612)	(9,814)	(10,434)
Pro forma operating expenses	$ 33,621	$ 25,675	$ 95,391	$ 72,090
As reported income (loss) from operations according to GAAP	$ (10,396)	$ 176	$ (15,867)	$ (4,984)
Excluding compensation expense related to stock options pursuant to SFAS 123(R)	(3,546)	(3,612)	(9,814)	(10,434)
Pro forma income (loss) from operations	$ (6,850)	$ 3,788	$ (6,053)	$ 5,450
As reported net income (loss) according to GAAP	$ (6,924)	$ 1,613	$ 162,024	$ (7,910)
Excluding compensation expense related to stock options pursuant to SFAS 123(R)	(3,546)	(4,050)	(8,256)	(11,815)
Pro forma net income (loss)	$ (3,378)	$ 5,663	$ 170,280	$ 3,905

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 stock options, which are non-cash. Isis has regularly reported non-GAAP measures for operating expenses and loss from operations 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.

Regulus Therapeutics Inc.
Statements of Operations
(In Thousands)

	Three months ended, September 30,		Nine months ended, September 30,	
	2009	2008	2009	2008
	(unaudited)		(unaudited)	
Revenue:				
Research and development revenue under collaborative agreements	$ 625	$ 681	$ 2,388	$ 1,429
Total revenue				

	625	681	2,388	1,429
Expenses:				
Research and development	2,225	2,374	6,282	5,292
General and administrative	712	517	1,982	1,328
Total operating expenses	2,937	2,891	8,264	6,620
Loss from operations	$ (2,312)	$ (2,210)	$ (5,876)	$ (5,191)

Isis Pharmaceuticals, Inc.
Condensed Consolidated Balance Sheets
(In Thousands)

	September 30, 2009 (unaudited)	December 31, 2008(1)
Assets:		
Cash, cash equivalents and short-term investments	$ 607,840	$ 490,998
Other current assets	11,407	27,386
Property, plant and equipment, net	26,911	17,371
Other assets	34,420	37,021
Total assets	$ 680,578	$ 572,776
Liabilities and stockholders' equity:		
Other current liabilities	$ 37,778	$ 32,037
Current portion of deferred contract revenue	76,941	92,662
2 5/8% convertible subordinated notes	123,265	117,993
Long-term obligations, less current portion	12,532	9,938
Long-term deferred contract revenue	125,237	172,766
Stockholders' equity	304,825	147,380
Total liabilities and stockholders' equity	$ 680,578	$ 572,776

(1) Adjusted for the required retrospective adoption of the accounting standards for debt and non-controlling interests that became effective in January 2009.

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