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): **August 6, 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 August 6, 2009, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended June 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 expense/benefit. These measures are provided as supplementary information and are not a substitute for financial measures calculated in accordance with GAAP. The Company reports these pro forma results to better enable financial statement users to assess 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. 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 August 6, 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: August 5, 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 August 6, 2009.

ISIS REPORTS STRONG FINANCIAL RESULTS AND HIGHLIGHTS FOR SECOND QUARTER OF 2009

- **Conference Call Webcast Thursday, August 6, 08:30 a.m. EDT at www.isispharm.com**

CARLSBAD, Calif., August 6, 2009 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced its financial results for the quarter ended June 30, 2009. During 2009 Isis has continued to successfully execute its business strategy and as a result reported $669,000 of pro forma net income for the quarter ended June 30, 2009, a significant improvement over the same period in 2008. Isis also reported a pro forma net operating loss of $1.3 million for the second quarter compared to pro forma net operating income of $4.6 million for the same period in 2008. Maintaining its strong cash position, Isis ended the quarter with $637.5 million of cash and remains on track to end 2009 with more than $550 million of cash. Isis also remains on track to meet its guidance of more than $145 million of pro forma net income and a pro forma net operating loss in the low to mid $20 million range, in both cases excluding non-cash stock compensation expense.

"Our strong financial performance is a direct result of the success of our technology platform and business strategy. We and our partners are advancing our large and growing pipeline of 19 drugs in development. Our partnership strategy not only allows our drugs to move forward effectively toward the market but also provides us with significant short and intermediate term financial benefits that enable us to continue to advance the technology and fill the pipeline with more exciting new drugs," said B. Lynne Parshall, COO and CFO of Isis.

Upcoming Key Milestones

- Report full data from a Phase 3 study evaluating mipomersen in homozygous Familial Hypercholesterolemia (FH) patients; positive top line data was reported in May 2009
- Report data from additional mipomersen studies in other patient populations
- Report data from a Phase 2 study evaluating ISIS 113715 in combination with sulfonylureas in patients with type 2 diabetes
- Begin clinical trials on at least one additional drug in 2009; clinical trials already initiated on three drugs this year
- Expand pipeline by moving at least two additional drugs into development in 2009; one new drug has already moved into development this year

Financial Results

On a GAAP basis, Isis reported a loss from operations of $4.8 million and $5.5 million for the three and six months ended June 30, 2009, respectively, compared to income from operations of $1.1 million and a loss from operations of $5.2 million for the three and six months ended June 30, 2008, respectively. Additionally, Isis reported a net loss of $2.9 million and net income of $168.9 million for the three and six months ended June 30, 2009, respectively, compared to its net loss of $3.7 million and $9.5 million for the same periods in 2008. Isis' financial 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. 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 six 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 six months ended June 30, 2009 was $31.0 million and $62.6 million compared to $29.7 million and $48.1 million in the same periods of 2008. The substantial increase in Isis' revenue is primarily due to an increase in revenue from the Company's collaboration with Genzyme because the three and six months ended June 30, 2008 only included one month of amortization of the $175 million license fee that Isis received in June 2008.

Isis' satellite companies also contributed to the increase in the Company's revenue:

- Regulus Therapeutics earned revenue from its strategic alliance with GlaxoSmithKline (GSK), including a $500,000 discovery milestone payment.
- Isis entered into a license agreement with Alnylam, which provided an $11 million license fee plus research funding. Isis began amortizing the license fee into revenue in the second quarter.
- Isis received a $375,000 milestone payment from Alnylam for initiation of clinical trials on ALN-VSP.
- Isis earned $1.4 million of revenue when Isis sold drug to OncoGenex Pharmaceuticals, Inc.

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, such as the bulleted items above. Assuming no new transactions, the Company's revenue will decrease when the $50 million upfront payment Isis received from Ortho-McNeil-Janssen in 2007 is fully amortized in the third quarter of this year.

Operating Expenses

On a pro forma basis, operating expenses for the three and six months ended June 30, 2009 were $32.3 million and $61.8 million compared to $25.1 million and $46.4 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 six months ended June 30, 2009 were $35.8 million and $68.0 million compared to $28.6 million and $53.2 million for the same periods in 2008, including non-cash compensation expense related to stock options of $3.6 million and $6.3 million for the three and six months ended June 30, 2009 and $3.5 million and $6.8 million for the same periods in 2008. During the remainder of 2009, Isis' operating expenses will increase modestly as Isis continues its research and development activities described above.

Interest Expense

In 2009, Isis adopted FASB Staff Position No. APB 14-1 (FSP 14-1) 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. FSP 14-1 required retrospective application to all periods presented. Accordingly, the amount of interest expense Isis recorded in its statement of operations for the three and six months ended June 30, 2009 increased by $1.7 million and $3.3 million compared to an increase of $1.5 million and $3.0 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 $121.5 million and $118.0 million at June 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 second quarter of 2009 was $3.8 million compared to net income from continuing operations of $463,000 for the same period in 2008. For the six months ended June 30, 2009 and 2008, net loss from continuing operations was $4.6 million and $5.6 million, respectively.

Even though Isis finished the first six months of 2009 with a net loss from continuing operations, Isis had taxable income, which is primarily a result of 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 $656,000 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.

Isis' net loss from continuing operations also included a $2.5 million gain on investments that Isis recognized in the second quarter of 2009 when it sold the stock it held in OncoGenex. OncoGenex stock price increased significantly in the second quarter of 2009 after announcing encouraging data from its clinical studies of OGX-011 and OGX-427. This gain further demonstrates the value that Isis is recognizing from its satellite company strategy.

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 six 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 a net loss of $2.9 million for the three months ended June 30, 2009 and net income of $168.9 million for the six months ended June 30, 2009, compared to a net loss of $3.7 million and $9.5 million in the three and six months ended June 30, 2008. Basic and diluted net loss per share for the three months ended June 30, 2009 was $0.03 per share compared to $0.04 per share for the same period in 2008. Basic and diluted net income per share for the six months ended June 30, 2009 was $1.73 per share and $1.56 per share, respectively, compared to basic and diluted net loss per share of $0.10 for the same period in 2008. The improvement in Isis' net income and net income per share for the first half of 2009 over the same period in 2008 was primarily due to the gain Isis recognized when it sold Ibis to AMI.

Balance Sheet

As of June 30, 2009, Isis had cash, cash equivalents and short-term investments of $637.5 million compared to $491.0 million at December 31, 2008 and had consolidated working capital of $519.7 million at June 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. In addition, during the first half of 2009, Isis received more than $31 million in cash from its corporate partnerships, including the $11 million upfront license fee that Isis received from its recently announced licensing and collaboration agreement with Alnylam.

Regulus Therapeutics

Regulus' revenue for the three and six months ended June 30, 2009 was $1.1 million and $1.8 million compared to $656,000 and $748,000 for the same periods in 2008. The increase was primarily related to revenue from its collaboration with GSK, including the $500,000 discovery milestone payment that Regulus received from GSK for demonstrating a pharmacological effect in immune cells by specific microRNA inhibition.

Excluding non-cash compensation expense related to stock options, operating expenses for Regulus were $2.7 million and $5.5 million for the three and six months ended June 30, 2009 compared to $1.7 million and $2.8 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 $1.6 million and $3.8 million for the three and six months ended June 30, 2009 compared to $1.1 million and $2.1 million for the same periods in 2008.

Business Highlights

"During the last quarter, we and Genzyme made great progress regarding mipomersen on two important fronts, advancing the clinical development program and refining our regulatory strategy. We reported positive top-line results from a Phase 3 study of mipomersen in the largest, placebo-controlled Phase 3 study in homozygous FH patients. We reported that the study met its primary endpoint with a 25% reduction in LDL-C after 26 weeks of treatment with mipomersen versus 3% for placebo and all of its secondary endpoints in a highly statistically significant manner. We are very pleased with the performance of mipomersen in this study. These data are a significant milestone in the clinical development of mipomersen and support our efforts to make the drug available to patients in need," said Ms. Parshall.

"In addition to reporting data from the first of our Phase 3 trials for mipomersen, we and Genzyme refined and communicated the regulatory path for mipomersen in the United States and Europe. While the strategy continues to evolve, Genzyme plans to file the first NDA for mipomersen in the U.S. for homozygous FH in the second half of 2010, with a similar filing in Europe shortly afterwards. Data from our Phase 3 study in severe hypercholesterolemia patients should be available at the time of these U.S. submissions and may provide the basis for a broader indication. A potential second filing in Europe will involve a broader patient population, namely heterozygous FH patients. This strategy ensures that mipomersen will reach the patients who need the drug the most first, and provide commercial experience with mipomersen as we broaden our indication to larger patient populations, such as heterozygous FH patients. We have now completed enrollment in the mipomersen Phase 3 study in heterozygous FH patients, the second of our four Phase 3 studies, and we expect to report the data from this study in the first half of 2010," continued Ms. Parshall.

"During the last quarter, we and our partners participated prominently in several scientific conferences, including ASCO and ADA, highlighting the versatility and broad applicability of antisense drugs to inhibit targets that could offer new avenues to treat disease, including cancer and type 2 diabetes. In addition to our clinical programs, we have active programs in many different therapeutic areas as well as established academic relationships with industry and academic leaders that expand our research capabilities. With the efficiency of our drug discovery technology we can broadly evaluate and conduct preliminary research on a vast array of new targets, so that we can add new drugs to our pipeline each year," added Ms. Parshall.

"In summary, it has been an eventful and promising first half of the year. Our financial position ensures that we can continue to invest our resources in filling the pipeline and continuing to move our drugs forward toward the market. We have the technology, the expertise and the momentum to realize the full potential of antisense as a drug discovery technology," concluded Ms. Parshall.

Drug Development Highlights

Mipomersen, the most advanced drug in Isis' cardiovascular pipeline, is being evaluated in a broad Phase 3 program in patients who cannot adequately control their cholesterol levels with current therapies and who need new treatment options.

- Isis and Genzyme reported positive top-line mipomersen Phase 3 data in patients with homozygous FH. The study met its primary endpoint, with a 25% reduction in LDL-C after 26 weeks of treatment, vs. 3% for placebo ($p<0.001$). The study also met each of its three secondary endpoints of reduction in apoB, total cholesterol and non-HDL-C.
- Genzyme continues to refine its European strategy for mipomersen.
- Isis and Genzyme completed enrollment in a Phase 3 study in heterozygous FH patients with coronary artery disease.

Isis' partnered pipeline continues to mature as antisense drugs that Isis' satellite companies are developing advance in clinical development.

- Altair reported a Phase 1 study that showed AIR645 was safe and well tolerated.
- Excaliard initiated a Phase 1 clinical study of EXC 001 for the local treatment of fibrosis.

Isis' collaborators presented new clinical data on drugs in Isis' partnered oncology franchise at this year's American Society of Clinical Oncology (ASCO) annual meeting.

- OncoGenex reported results of a randomized Phase 2 trial of OGX-011 in patients with advanced prostate cancer showing a median survival in patients treated with OGX-011 plus docetaxel of 23.8 months compared to 16.9 months for patients treated with docetaxel alone.
- OncoGenex reported that OGX-427 was well tolerated as a monotherapy in a Phase 1 study and demonstrated declines in circulating tumor cells and evidence of reduction in tumor markers.
- Eli Lilly and Company recently completed its Phase 1 study of LY2181308 and presented data confirming that LY2181308 penetrates tumor tissue and reduces survivin mRNA and protein levels in tumor cells.

Isis and its collaborators highlighted new antisense therapeutic programs and targets to treat metabolic diseases, including obesity, at the American Diabetes Association (ADA) scientific sessions.

- Isis presented new preclinical data on ISIS-SGLT2$_{Rx}$ showing robust and sustained reduction in SGLT2 levels that resulted in a significant reduction in blood glucose levels in multiple animal species.
- Isis and its collaborators presented data on a number of other promising new diabetes and anti-obesity targets demonstrating that reducing levels of these targets with antisense drugs can significantly lower blood glucose levels, increase the body's sensitivity to insulin, and reduce fat mass and body weight in animals.

Isis partnered with non profit foundations to pursue new treatments for debilitating diseases, such as severe neurodegenerative diseases.

- Isis was awarded a grant from the Michael J. Fox Foundation's Therapeutic Development Initiative program for the discovery and development of an antisense drug for the treatment of Parkinson's Disease.

Isis benefits from its partners as they advance RNA-based technologies and develop drugs that incorporate Isis' technology resulting in financial benefits as these assets mature.

- Isis earned milestone payments from Archemix and Alnylam because each company advanced drugs that incorporate Isis' technology.
- Isis co-exclusively licensed its single-stranded RNA interference (ssRNAi) technology to Alnylam as part of a new strategic initiative to continue to develop the ssRNAi platform.
- Regulus achieved its first milestone in its inflammatory disease collaboration with GSK.

Conference Call

At 08:30 a.m. Eastern Time today, August 6, 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 866-788-0538 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, June 30,		Six months ended, June 30,	
	2009	2008(1)	2009	2008(1)
	(unaudited)		(unaudited)	
Revenue:				
Research and development revenue under collaborative agreements	$ 30,768	$ 23,556	$ 60,453	$ 41,262
Licensing and royalty revenue	224	6,147	2,115	6,815
Total revenue	30,992	29,703	62,568	48,077
Expenses:				
Research and development	32,146	25,288	60,688	47,071
General and administrative	3,673	3,334	7,350	6,165
Total operating expenses	35,819	28,622	68,038	53,236
Income (loss) from operations	(4,827)	1,081	(5,470)	(5,159)
Other income (expense):				
Investment income	1,678	2,302	3,812	5,336
Interest expense	(3,155)	(2,920)	(6,236)	(5,818)
Gain on investments, net	2,612	—	2,671	—
Income (loss) from continuing operations, before income tax benefit (expense)	(3,692)	463	(5,223)	(5,641)

Income tax benefit (expense)	(61)	—	656	—
Net income (loss) from continuing operations, net of income tax benefit (expense)	(3,753)	463	(4,567)	(5,641)
Discontinued Operations:				
Loss from discontinued operations	—	(5,165)	(29)	(5,729)
Gain on sale of Ibis Biosciences, Inc., net of tax	—	—	171,773	—
Net income (loss) from discontinued operations, net of tax	—	(5,165)	171,744	(5,729)
Net income (loss)	(3,753)	(4,702)	167,177	(11,370)
Net loss attributable to noncontrolling interest in Regulus Therapeutics Inc.	857	965	1,771	1,848
Net income (loss) attributable to Isis Pharmaceuticals, Inc. common stockholders	$ (2,896)	$ (3,737)	$ 168,948	$ (9,522)
Basic net income (loss) per share:				
Net income (loss) from continuing operations attributable to Isis Pharmaceuticals, Inc. common stockholders	$ (0.03)	$ 0.02	$ (0.03)	$ (0.04)
Net income (loss) from discontinued operations	—	(0.06)	1.76	(0.06)
Basic net income (loss)	$ (0.03)	$ (0.04)	$ 1.73	$ (0.10)
Shares used in computing basic net income (loss) per share	98,116	94,675	97,820	92,737
Diluted net income (loss) per share:				
Net income (loss) from continuing operations attributable to Isis Pharmaceuticals, Inc. common stockholders	$ (0.03)	$ 0.02	$ 0.02	$ (0.04)
Net income (loss) from discontinued operations	—	(0.06)	1.54	(0.06)
Diluted net income (loss)	$ (0.03)	$ (0.04)	$ 1.56	$ (0.10)
Shares used in computing diluted net income (loss) per share	98,116	94,675	111,608	92,737

(1) Adjusted for the required retrospective adoption of FSP 14-1 and SFAS 160.

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

	Historical Isis Pharmaceuticals, Inc. Six months ended June 30, 2008(1)	Discontinued Operations (2)	FSP 14-1(3)	Adjusted six months ended June 30, 2008
		(unaudited)		
Revenue:				
Research and development revenue under collaborative agreements	$ 47,499	$ (6,237)	$ —	$ 41,262
Licensing and royalty revenue	6,815	—	—	6,815
Total revenue	54,314	(6,237)	—	48,077
Expenses:				
Research and development	57,642	(10,571)	—	47,071
General and administrative	8,635	(2,470)	—	6,165
Total operating expenses	66,277	(13,041)	—	53,236
Income (loss) from operations	(11,963)	6,804	—	(5,159)
Other income (expense):				
Investment income	5,515	(179)	—	5,336
Interest expense	(2,788)	—	(3,030)	(5,818)
Net income (loss) from continuing operations	(9,236)	6,625	(3,030)	(5,641)
Net loss from discontinued operations	—	—	—	(5,729)
Net income (loss)	(9,236)	6,625	(3,030)	(11,370)
Net loss attributable to noncontrolling interest in Regulus Therapeutics Inc.	1,848	—	—	1,848
Net loss attributable to noncontrolling interest in Ibis Biosciences, Inc.	896	(896)	—	—
Net income (loss) attributable to Isis Pharmaceuticals, Inc. common stockholders	$ (6,492)	$ 5,729	$ (3,030)	$ (9,522)
Basic and diluted net income (loss) per share:				
Net income (loss) from continuing operations attributable to Isis Pharmaceuticals, Inc. common stockholders	$ (0.07)			$ (0.04)
Net income (loss) from discontinued operations	—			(0.06)
Basic and diluted net income (loss)	$ (0.07)			$ (0.10)
Shares used in computing basic and diluted net income (loss) per share	92,737			92,737

(1) The historical condensed consolidated statement of operations reflects the required retrospective adoption of SFAS 160.

(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 FSP 14-1.

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, June 30,		Six months ended, June 30,	
	2009	2008	2009	2008
	(unaudited)		(unaudited)	
As reported operating expenses according to GAAP	$ 35,819	$ 28,622	$ 68,038	$ 53,236
Excluding compensation expense related to stock options pursuant to SFAS 123(R)	(3,565)	(3,540)	(6,268)	(6,823)
Pro forma operating expenses	$ 32,254	$ 25,082	$ 61,770	$ 46,413
As reported income (loss) from operations according to GAAP	$ (4,827)	$ 1,081	$ (5,470)	$ (5,159)
Excluding compensation expense related to stock options pursuant to SFAS 123(R)	(3,565)	(3,540)	(6,268)	(6,823)
Pro forma income (loss) from operations	$ (1,262)	$ 4,621	$ 798	$ 1,664
As reported net income (loss) according to GAAP	$ (2,896)	$ (3,737)	$ 168,948	$ (9,522)
Excluding compensation expense related to stock options pursuant to SFAS 123(R)	(3,565)	(4,006)	(4,710)	(7,765)
Pro forma net income (loss)	$ 669	$ 269	$ 173,658	$ (1,757)

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, June 30,		Six months ended, June 30,	
	2009	2008	2009	2008
	(unaudited)		(unaudited)	
Revenue:				
Research and development revenue under collaborative agreements	$ 1,125	$ 656	$ 1,763	$ 748
Total revenue	1,125	656	1,763	748
Expenses:				
Research and development	2,214	1,606	4,057	2,918
General and administrative	611	917	1,270	1,132
Total operating expenses	2,825	2,523	5,327	4,050
Loss from operations	$ (1,700)	$ (1,867)	$ (3,564)	$ (3,302)

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

	June 30, 2009	December 31, 2008(1)
	(unaudited)	

Assets:				
Cash, cash equivalents and short-term investments	$	637,511	$	490,998
Other current assets		10,001		27,386
Property, plant and equipment, net		26,636		17,371
Other assets		35,013		37,021
Total assets	$	709,161	$	572,776
Liabilities and stockholders' equity:				
Other current liabilities	$	45,769	$	32,037
Current portion of deferred contract revenue		82,092		92,662
2 5/8% convertible subordinated notes		121,464		117,993
Long-term obligations, less current portion		10,643		9,938
Long-term deferred contract revenue		143,376		172,766
Stockholders' equity		305,817		147,380
Total liabilities and stockholders' equity	$	709,161	$	572,776

(1) Adjusted for the required retrospective adoption of FSP 14-1 and SFAS 160.

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