

---

---

# 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 2, 2006**

## ISIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

**Delaware**

(State or Other Jurisdiction of Incorporation)

**000-19125**

(Commission File No.)

**33-0336973**

(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:

- 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 November 2, 2006, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended September 30, 2006. 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 and costs associated with restructuring activities. The Company is presenting pro forma information excluding the effects of the restructuring activities and 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 2, 2006.

---

---

**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.

Dated: November 2, 2006

By: /s/ B. Lynne Parshall \_\_\_\_\_  
**B. LYNNE PARSHALL**  
Executive Vice President,  
Chief Financial Officer and Director

3

---

INDEX TO EXHIBITS

99.1 Press Release dated November 2, 2006.

4

---

**ISIS PHARMACEUTICALS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR  
THIRD QUARTER OF 2006**

- **Isis' Ibis Biosciences Division Achieves Key Commercial Milestones**
- **Release of New ISIS 301012 Data Planned for American Heart Association Meeting**
- **Conference Call Webcast Thursday, November 2, 10:00 am EST at [www.isispharm.com](http://www.isispharm.com)**

**CARLSBAD, Calif., November 2, 2006** - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS) today announced its financial results for the third quarter ended September 30, 2006. The Company's loss from operations for the three and nine months ended September 30, 2006 was \$18.3 million and \$51.4 million, respectively, compared to \$12.1 million and \$48.6 million for the same periods in 2005, according to GAAP. The Company's increase in loss from operations in the first nine months of 2006 compared to the same period in 2005 was principally a result of lower revenue in 2006 compared to 2005 offset by cost savings resulting from the Company's focus on its key programs. The cost savings achieved through the Company's reorganization in the first quarter of 2005 led to a decrease of \$7.1 million in R&D and SG&A expenses and \$7.8 million in restructuring activities for the first nine months of 2006 compared to the same period of 2005. These expense reductions were partially offset by compensation related to stock options for the first nine months of 2006 of \$4.2 million compared to \$613,000 of benefit related to the variable accounting of stock options that was included in the loss from operations for the same period of 2005.

The Company's pro forma loss from operations was \$17.1 million and \$47.6 million for the three and nine months ended September 30, 2006, respectively, compared to \$12.5 million and \$41.8 million for the same periods in 2005. The Company expects, consistent with previous guidance that its pro forma loss from operations will be in the high \$50 million range for 2006. 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 pro forma results excluding certain items primarily related to stock option expense/benefit, which are non-cash, and restructuring activities, which are not part of ongoing operations. 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. The adjustment from GAAP to pro forma loss from operations and expenses is illustrated in the Selected Financial Information included in this press release.

### Revenue

Total revenue for the three and nine months ended September 30, 2006 was \$3.3 million and \$12.6 million, respectively, compared to \$7.5 million and \$25.5 million for the same periods in 2005. The decrease in revenue for the three and nine months ended September 30, 2006 compared to the same periods in 2005 was primarily due to a decrease in revenue associated with Isis' collaboration with Eli Lilly and Company, which was extended in August 2005 to focus on a select number of targets. Isis' revenue fluctuates based on the timing of activities under contract, and as a result, it frequently includes non-recurring items. For example, in 2005, Isis earned non-recurring revenue in connection with milestones Isis achieved under its collaboration with Pfizer. In the third quarter of 2006, Isis earned revenue from Alnylam Pharmaceuticals, Inc. as a result of Alnylam's recently announced alliance with a major pharmaceutical company for the development of RNA interference (RNAi) therapeutics.

Isis' Ibis Biosciences™ division's (Ibis) revenue from government contracts fluctuates based on when the contracts are awarded, the period of performance for the contracts and the funding amount of the contracts. For example, in 2006, two large government contracts that were active in 2005 ended, resulting in reduced revenue in the first nine months of 2006 compared to the same period in 2005, offset by several new contracts. Additionally, Ibis recently announced that it has successfully completed the first phase of its Challenge Grant from the National Institute of Allergy and Infectious Diseases (NIAID), a part of the National Institutes of Health (NIH), and has been granted funding for subsequent phases that provide for the installation of an Ibis T5000 Biosensor System at Johns Hopkins University Medical Center. Isis expects that this additional funding, combined with extensions of other existing contracts and new contracts, will be the basis for Ibis' revenue from government contracts in the fourth quarter of 2006 and in 2007. A more detailed explanation follows below under Isis' Ibis Biosciences Division.

### Expenses

Isis' operating expenses, according to GAAP, decreased significantly in the first nine months of 2006 compared to the same period in 2005 and were \$21.5 million and \$64.0 million for the three and nine months ended September 30, 2006, respectively, compared to \$19.6 million and \$74.1 million for the same periods in 2005. Isis' operating expenses on a pro forma basis for the three and nine months ended September 30, 2006 were \$20.4 million and \$60.2 million, respectively, compared to \$19.9 million and \$67.3 million for the same periods in 2005. These results represent a significant decrease of 11% in the Company's expenses for the first nine months of 2006 compared to the same period in 2005. The decrease in operating expenses on a pro forma basis for the nine months ended September 30, 2006 compared to the same period in 2005 reflects the impact of the Company's reorganization in the first quarter of 2005. As anticipated, Isis' pro forma operating expenses for the third quarter rose slightly in comparison to the average pro forma operating expenses for the first half of 2006. Isis expects pro forma operating expenses to continue to increase slightly during the fourth quarter of 2006 as the Company continues to expand its ISIS 301012 development program. The Company expects, consistent with previous guidance, that its 2006 pro forma operating expenses will be approximately equal to the annualized rate of the last two quarters of 2005, or approximately \$88 million.

As illustrated in the Selected Financial Information in this press release, Isis' pro forma operating expenses were adjusted from GAAP to exclude non-cash compensation related to stock options and costs associated with restructuring activities. Beginning in the first quarter of 2006, Isis included in its operating results non-cash compensation expense related to stock options as required by Statement of Financial Accounting Standards No. 123, Share-Based Payment (SFAS 123R), which, for the first nine months of 2006, was \$4.2 million. Prior to that, the Company's operating expenses included non-cash compensation benefit or expense as a result of variable accounting for stock options, which, for the first nine months of 2005, was a benefit of \$613,000. The adjustment to pro forma operating expenses for the nine months ended September 30, 2006 and 2005 also included a benefit of \$457,000 and expenses of \$7.4 million, respectively, associated with restructuring activities.

### Isis' Ibis Biosciences Division

To develop the Ibis T5000™ Biosensor System and related assay kits, Ibis receives contracts and grants from U.S. government agencies. To date, Ibis has delivered four systems to its government partners for use in biodefense and epidemiological surveillance. Ibis recently received its first commercial order for two Ibis T5000 Biosensor Systems from a U.S. government agency for human forensics applications. Ibis plans to install the first system under this order before the end of the year and the second system early in 2007. In addition, Ibis began earning commercial revenue from analyzing samples in its Assay

---

Services Laboratory. Ibis' recent achievements represent important steps in implementing its commercial plan.

In the third quarter of 2006, Ibis earned \$151,000 of commercial revenue from analyzing samples in its Assay Services Laboratory. In addition, Ibis generated revenue from its government contracts and grants of \$2.0 million and \$7.6 million for the three and nine months ended September 30, 2006, respectively, compared to revenue of \$3.4 million and \$8.7 million for the same periods in 2005. As discussed above, Ibis' revenue from government contracts fluctuates based on when the contracts are awarded, the period of performance for the contracts and the funding amount of the contracts. For example, in 2006, two large government contracts that were active in 2005 ended, resulting in reduced revenue in the first nine months of 2006 compared to the same period in 2005, offset by several new contracts. Additionally, Ibis recently announced that it has successfully completed the first phase of its Challenge Grant from the NIAID, a part of the NIH, and has been granted funding for subsequent phases that provide for the installation of an Ibis T5000 Biosensor System at Johns Hopkins University Medical Center. Ibis expects that this additional funding, combined with extensions of other existing contracts and new contracts, will be the basis for Ibis' revenue from government contracts in the fourth quarter of 2006 and in 2007.

Excluding non-cash compensation expense related to stock options under SFAS 123R, operating expenses for Ibis were \$3.5 million and \$10.7 million for the three and nine months ended September 30, 2006, respectively, compared to \$3.5 million and \$10.3 million for the same periods in 2005. The increase in operating expenses primarily reflects an increase in sales, marketing and manufacturing costs necessary to move from the development of the Ibis Biosensor System to commercialization, offset by a decrease in costs associated with equipment purchased under government contracts. Ibis generated a loss from operations of \$1.7 million and \$3.7 million for the three and nine months ended September 30, 2006, respectively, compared to \$97,000 and \$1.6 million for the same periods in 2005.

#### **Net Loss**

Isis' net loss applicable to common stock for the three and nine months ended September 30, 2006 was \$12.1 million and \$31.8 million, respectively, compared with a net loss applicable to common stock of \$15.2 million and \$64.5 million, for the same periods in 2005. Isis recognized a benefit of \$6.7 million and \$20.3 million for the three and nine months ended September 30, 2006, respectively, in the Noncontrolling Interest in Symphony GenIsis Inc., resulting from Isis' collaboration with Symphony GenIsis. This benefit was a significant reason for the improvement in Isis' net loss applicable to common stock in the first nine months of 2006 compared to 2005. The decrease in the net loss applicable to common stock was also impacted by a net gain on investments and a decrease in interest expense, offset by an increase in Isis' loss from operations. The net gain on investments in the first nine months of 2006 over the same period in 2005 was due to a gain of \$2.7 million realized on the sale of a portion of the equity securities of Alnylam that Isis owns offset by a non-cash loss on investment of \$465,000 related to the impairment of the Company's equity investment in Antisense Therapeutics Ltd. (ATL). The impairment reflects the decrease in the market value of ATL's stock. The decrease in interest expense was primarily due to the effect of a lower debt balance during the first nine months of 2006 compared to the same period in 2005 resulting from the conversion of the Company's \$100 million Lilly loan in the third quarter of 2005.

#### **Net Loss per Share**

Isis' net loss per share for the three and nine months ended September 30, 2006 was \$0.16 and \$0.44 per share, respectively, compared to a net loss per share for the same periods in 2005 of \$0.24 and \$1.08 per share. In August 2005, Isis issued 12 million shares of common stock in a private placement that raised net proceeds of \$48 million. Also in August 2005, Isis issued 2.5 million shares to Lilly in connection

---

with the conversion of the Company's \$100 million Lilly loan. These additional shares, combined with the substantial decrease in net loss applicable to common stock, explain the significant decrease in net loss per share for the first nine months of 2006 compared to the same period in 2005.

#### **Balance Sheet**

In 2006, Isis completed two very important transactions that continued its successful efforts to strengthen its balance sheet. First, in April 2006, Isis entered into a \$75 million collaboration with Symphony GenIsis, Inc. to fund development of ISIS 301012 and two new diabetes drugs. Additionally, in May 2006, Isis obtained a \$75 million equity financing commitment from Azimuth Opportunity Ltd. Under this arrangement, Isis may at its discretion, from time to time, sell registered shares of its common stock at a small discount to the market price to Azimuth. There are no up-front fees or warrants related to the transaction. To date, Isis has drawn \$20.0 million under the Azimuth equity line by issuing approximately 2.7 million shares of its common stock. The Company's third quarter balance sheet reflects \$5 million of these draws. The Symphony GenIsis collaboration and the Azimuth Opportunity transaction provide Isis with the financial strength to continue to successfully execute its goals.

Isis ended the third quarter of 2006 with cash, cash equivalents and short-term investments of \$126.9 million, which included \$58.6 million of cash and cash equivalents held by Symphony GenIsis. Isis had consolidated working capital of \$117.5 million at September 30, 2006. At December 31, 2005, Isis had cash, cash equivalents and short-term investments of \$94.4 million and working capital of \$82.1 million. The significant increase in cash, cash equivalents and short-term investments primarily reflects the consolidation of the cash and cash equivalents held by Symphony GenIsis along with proceeds of \$5.0 million that Isis received from the initial drawdown under the Azimuth equity financing, \$4.4 million that Isis received from the sale of a portion of its Alnylam equity securities, and amounts received from contracts and stock option exercises, offset by cash used in operations. Operating cash usage for the third quarter of 2006 was \$15.5 million, which represents a slight increase compared to \$15.0 million in the third quarter of 2005.

"We're very pleased with our progress in the third quarter, particularly the multiple commercial milestones achieved by our Ibis Biosciences division," said B. Lynne Parshall, Executive Vice President and Chief Financial Officer at Isis. "Our instrument alliance with Bruker Daltonics is already providing increased international visibility for the Ibis T5000 Biosensor System as a result of our recent European introduction. We're excited to have secured our first commercial order for Ibis T5000 systems, and we expect to carry the recent momentum of Ibis achievements through the end of the year and beyond as we establish this business and increase revenue by addressing significant market opportunities such as hospital-acquired infection surveillance.

"While much of our third quarter news involved Ibis, we have aggressively advanced development of our antisense drugs, particularly ISIS 301012, which is one of our key assets. Our first study evaluating ISIS 301012 in combination with statin therapy is ongoing, and blinded safety analyses have prompted us to both extend the treatment durations and increase doses much earlier than we had originally planned. We look forward to sharing the first of these data, for five weeks of treatment at doses up through 300 mg/week as an add-on to stable statin therapy, at the AHA meeting later this month. Also at AHA, we plan to present results from the 300 mg/week dose cohort of the monotherapy trial treating patients with ISIS 301012 for three months – this is the continuation of the trial for which we presented lower-dose cohorts in May.

---

“Financially,” Ms. Parshall added, “Isis is in a strong position with \$126.9 million in cash and short-term investments. During the quarter, we reported our first commercial revenues from Ibis and extended key government R&D contracts that include future funding for an instrument placement at Johns Hopkins. We also earned \$750,000 from Alnylam related to its alliance with Biogen Idec and, following the quarter’s close, we received an \$8 million partial payment for the monetization of Isis’ royalty rights in Macugen®. These latter two events show how Isis is benefiting from our licensing and partnership agreements, and underscore that our strategy of leveraging our intellectual property portfolio is providing ongoing and growing financial value. Finally, we have been able to further strengthen Isis’ balance sheet by negotiating agreements such as our Azimuth equity line, from which we have drawn down \$20 million to date.

“Overall, we remain on track to meet our net operating loss guidance in the high \$50 million range, and we believe we have sufficient resources to meet our anticipated cash requirements through at least the end of 2008,” Ms. Parshall concluded.

### 2006 Third Quarter Highlights and Upcoming Activities

#### **Isis Commercializes Ibis T5000 Biosensor System**

*Isis’ Ibis Biosciences division made significant commercial progress during the quarter, securing key contracts and expanding its intellectual property portfolio.*

- Ibis received a purchase order from a U.S. government agency for the commercial sale of two Ibis T5000 Biosensor Systems. The systems will be used for forensics research.
- Ibis received a contract, valued at up to \$1.9 million, from a U.S. government agency to perform analysis of up to 10,000 samples in its Ibis T5000 Assay Services Laboratory.
- Ibis was awarded a patent that broadly covers the method employed by the Ibis T5000 Biosensor System for identification and characterization of bacterial pathogens.
- Isis’ manufacturing partner, Bruker Daltonics, introduced the Ibis T5000 Biosensor System into the European market. This followed the earlier signing of a collaboration agreement under which Bruker will be responsible for instrument manufacturing and installation, order processing and support services for the Ibis T5000 Biosensor System.
- Isis successfully completed the first phase of its Challenge Grant from the National Institute of Allergy and Infectious Diseases, a part of the National Institutes of Health, and has been granted funding for subsequent phases that provide for the installation of an Ibis T5000 Biosensor System at Johns Hopkins University Medical Center.

#### **ISIS 301012 Activities**

The Phase 2 development program for ISIS 301012, which targets apoB-100 for the treatment of high cholesterol, is progressing in multiple studies, and the drug continues to exhibit strong safety and efficacy profiles. In fact, the product’s safety profile in combination with statins in blinded, in-progress trials has been sufficiently encouraging to prompt acceleration of plans to increase and extend dosing.

Isis plans to present new data from two ongoing studies at the American Heart Association Annual Scientific Sessions: the first involves five weeks of therapy with a range of dosage cohorts (30, 100, 200, 300 mg/wk) in combination with statin therapy; the second involves twelve weeks of single-agent therapy at 300 mg/wk which is the continuation of the monotherapy trial on which Isis presented data for the

---

lower-dose cohorts in May of 2006. The new data on ISIS 301012 will be presented on Sunday, November 12, at a Cardiovascular Seminar Session in Chicago. On Monday morning, November 13, the day after the scientific presentation, Isis plans to webcast a special presentation to discuss these new data and the ISIS 301012 program with the investment community. The special webcast presentation can be accessed by visiting the Isis home page at [www.isispharm.com](http://www.isispharm.com).

#### **Conference Call**

Isis will conduct a live webcast conference call to discuss this earnings release and financial projections for its Ibis Biosciences division today, Thursday, November 2 at 10:00 am EST. To participate over the Internet go to [www.isispharm.com](http://www.isispharm.com). A replay of the webcast will be available for a limited time.

#### **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 14 drugs in development. Isis’ drug development programs are aimed at treating cardiovascular, metabolic and inflammatory diseases. Isis’ partners are focused in disease areas such as ocular, viral and neurodegenerative diseases, and cancer. In its Ibis division, Isis is developing and commercializing the Ibis T5000 Biosensor System, a revolutionary system to identify infectious organisms. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of approximately 1,500 issued patents worldwide. Additional information about Isis is available at [www.isispharm.com](http://www.isispharm.com).

This press release includes forward-looking statements regarding Isis Pharmaceuticals’ business, the financial position of Isis, and the therapeutic and commercial potential of the Company’s technologies and products in development. Any statement describing Isis’ goals, expectations, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis’ goals. 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, in developing and commercializing systems to identify infectious organisms that are effective and commercially attractive, 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, 2005, and its quarterly report on Form 10-Q for the quarter ended June 30, 2006, which are on file with the SEC. Copies of these and other documents are available from the Company.

Macugen® is a registered trademark of (OSI) Eyetech  
Ibis Biosciences™ is a trademark of Isis Pharmaceuticals, Inc.  
Ibis T5000™ is a trademark of Isis Pharmaceuticals, Inc.

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

	Three months ended September 30,		Nine months ended September 30,	
	2006 (unaudited)	2005	2006 (unaudited)	2005 (unaudited)
<b>Revenue:</b>				
Research and development revenue under collaborative agreements	\$ 2,469	\$ 7,122	\$ 11,260	\$ 24,695
Licensing and royalty revenue	784	336	1,327	797 31
<b>Total revenue</b>	<b>3,253</b>	<b>7,458</b>	<b>12,587</b>	<b>25,492</b>
<b>Operating expenses:</b>				
Research and development	18,973	18,212	56,327	61,523
Selling, general and administrative	2,823	1,724	8,099	5,771
Compensation expense/(benefit) related to variable accounting of stock options	—	15	—	(613)
Restructuring activities	(279)	(349)	(457)	7,385
<b>Total operating expenses</b>	<b>21,517</b>	<b>19,602</b>	<b>63,969</b>	<b>74,066</b>
<b>Loss from operations</b>	<b>(18,264)</b>	<b>(12,144)</b>	<b>(51,382)</b>	<b>(48,574)</b>
<b>Other income (expenses):</b>				
Investment income	1,682	1,241	3,837	2,095
Interest expense	(2,256)	(4,269)	(6,816)	(18,009)
Gain on investments, net	—	—	2,263	—
<b>Net loss before noncontrolling interest in Symphony GenIsis, Inc.</b>	<b>(18,838)</b>	<b>(15,172)</b>	<b>(52,098)</b>	<b>(64,488)</b>
<b>Loss attributed to noncontrolling interest in Symphony GenIsis, Inc.</b>	<b>6,733</b>	<b>—</b>	<b>20,341</b>	<b>—</b>
<b>Net loss applicable to common stock</b>	<b>\$ (12,105)</b>	<b>\$ (15,172)</b>	<b>\$ (31,757)</b>	<b>\$ (64,488)</b>
<b>Basic and diluted net loss per share</b>	<b>\$ (0.16)</b>	<b>\$ (0.24)</b>	<b>\$ (0.44)</b>	<b>\$ (1.08)</b>
<b>Shares used in computing basic and diluted net loss per share</b>	<b>73,588</b>	<b>64,086</b>	<b>72,934</b>	<b>59,734</b>

**Ibis Biosciences Division Statements of Operations**  
(In Thousands)

	Three months ended September 30,		Nine months ended September 30,	
	2006 (unaudited)	2005	2006 (unaudited)	2005 (unaudited)
<b>Revenue:</b>				
Assay services revenue (1)	\$ 151	\$ —	\$ 151	\$ —
Research and development revenue under collaborative agreements	1,988	3,429	7,596	8,651
<b>Total revenue</b>	<b>2,139</b>	<b>3,429</b>	<b>7,747</b>	<b>8,651</b>
<b>Operating expenses:</b>				
Cost of assay services (2)	65	—	65	—
Research and development	2,992	3,293	9,547	9,472
Selling, general and administrative	736	233	1,789	783
<b>Total operating expenses</b>	<b>3,793</b>	<b>3,526</b>	<b>11,401</b>	<b>10,255</b>
<b>Loss from operations</b>	<b>\$ (1,654)</b>	<b>\$ (97)</b>	<b>\$ (3,654)</b>	<b>\$ (1,604)</b>

(1) Ibis' assay services revenue has been classified as research and development revenue under collaborative agreements on Isis' condensed consolidated statement of operations.

(2) Ibis' cost of assay services has been classified as research and development expenses on Isis' condensed consolidated statement of operations.

**Reconciliation of GAAP to Proforma Basis:  
Consolidated Operating Expenses and Loss From Operations  
(In Thousands)**

	Three months ended September 30,		Nine months ended September 30,	
	2006	2005	2006	2005
	(unaudited)		(unaudited)	
<b>As reported operating expenses according to GAAP</b>	\$ 21,517	\$ 19,602	\$ 63,969	\$ 74,066
Excluding compensation (expense)/benefit related to variable accounting of stock options	—	(15)	—	613
Excluding compensation expense related to stock options pursuant to SFAS 123R	(1,417)	—	(4,190)	—
Excluding restructuring activities	279	349	457	(7,385)
<b>Proforma operating expenses</b>	<u>\$ 20,379</u>	<u>\$ 19,936</u>	<u>\$ 60,236</u>	<u>\$ 67,294</u>
<b>As reported loss from operations according to GAAP</b>	\$ (18,264)	\$ (12,144)	\$ (51,382)	\$ (48,574)
Excluding compensation (expense)/benefit related to variable accounting of stock options	—	(15)	—	613
Excluding compensation expense related to stock options pursuant to SFAS 123R	(1,417)	—	(4,190)	—
Excluding restructuring activities	279	349	457	(7,385)
<b>Proforma loss from operations</b>	<u>\$ (17,126)</u>	<u>\$ (12,478)</u>	<u>\$ (47,649)</u>	<u>\$ (41,802)</u>

**Condensed Consolidated Balance Sheets  
(In Thousands)**

	September 30, 2006 (unaudited)	December 31, 2005
<b>Assets:</b>		
Cash, cash equivalents and short-term investments	\$ 126,871	\$ 94,389
Other current assets	10,052	11,469
Property, plant and equipment, net	7,227	9,130
Other assets	43,618	51,385
Total assets	<u>\$ 187,768</u>	<u>\$ 166,373</u>
<b>Liabilities and stockholders' equity:</b>		
Current liabilities	\$ 19,436	\$ 23,793
5.5% convertible subordinated notes	125,000	125,000
Long-term obligations, net of current portion	9,736	14,915
Noncontrolling interest in Symphony GenIsis, Inc.	32,019	—
Stockholders' equity	1,577	2,665
Total liabilities, noncontrolling interest and stockholders' equity	<u>\$ 187,768</u>	<u>\$ 166,373</u>

###

**Contacts**

Elizabeth Hougen, Vice President, Finance  
Kate Corcoran, Ph.D., Vice President, Corporate Development  
Isis Pharmaceuticals, 760-603-2331  
<http://www.isispharm.com>