SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934

Date of report (Date of earliest event reported): **May 10, 2007**

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 May 10, 2007, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended March 31, 2007. 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 May 10, 2007.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ISIS PHARMACEUTICALS, INC.

Dated: May 9, 2007

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

INDEX TO EXHIBITS

99.1	Press Release dated May 10, 2007.

ISIS PHARMACEUTICALS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR FIRST QUARTER OF 2007

· **Conference Call Webcast Thursday, May 10, 10:00 am EDT at www.isispharm.com**

CARLSBAD, Calif., May 10, 2007 - Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), today announced its financial results for the quarter ended March 31, 2007. The Company's loss from operations for the quarter ended March 31, 2007 was $20.9 million compared to $16.0 million for the same period in 2006, according to GAAP. The Company's increase in loss from operations in the first quarter of 2007 compared to the same period in 2006 was a result of lower revenue in the first quarter of 2007 compared to the same period of 2006 along with higher expenses associated with the expanded development of its key programs. Also contributing to the increase in the loss from operations, according to GAAP, was an increase in non-cash compensation expense related to stock options, primarily reflecting an increase in Isis' stock price period to period. Isis remains on track to meet its guidance for a net operating loss, excluding non-cash compensation expense, in the mid to high $60 million range for 2007.

Isis' pro forma loss from operations was $18.5 million for the quarter ended March 31, 2007, compared to $14.6 million for the same period in 2006. The reasons for the Company's increase in its pro forma loss from operations in the first quarter of 2007 compared to the same period in 2006 were the same as those for the increase in the Company's loss from operations according to GAAP other than the effect of non-cash compensation expense related to stock options.

As illustrated in the Selected Financial Information in this press release, Isis' pro forma operating expenses and loss from operations were adjusted from GAAP to exclude non-cash compensation expense related to stock options and costs associated with restructuring activities. 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, which are non-cash, and restructuring activities, which are not part of ongoing operations. 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.

Revenue

Total revenue for the three months ended March 31, 2007 was $2.5 million compared to $5.0 million for the same period in 2006. Revenue was lower for the first quarter of 2007 compared to the same period in 2006 because of lower revenue from the Company's collaborations and differences in the timing of Ibis Biosciences, Inc.'s government contract revenue. 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, including those for drugs the Company manufactures

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for its partners. For example, in the first quarter of 2006, revenue included a one-time milestone of $750,000 that Isis received from Eli Lilly and Company.

Expenses

Even with the Company's increased costs associated with the expansion of its clinical development programs and with building the manufacturing, marketing and sales infrastructure required to successfully commercialize the Ibis T5000 Biosensor System, careful control of expenses in other areas resulted in operating expenses on a pro forma basis for the quarter ended March 31, 2007 of $21.0 million compared to $19.6 million for the same period in 2006. Isis' operating expenses for the three months ended March 31, 2007 were $23.4 million compared to $21.0 million for the same period in 2006, according to GAAP.

Beginning in 2006, Isis included in its operating results non-cash compensation expense related to stock options as required by Statement of Financial Accounting Standards No. 123R, *Share-Based Payment* (SFAS 123R). Non-cash compensation expense related to stock options increased from $1.4 million for the first quarter of 2006 to $2.4 million for the same period in 2007, primarily reflecting the increase in Isis' stock price from period to period. The adjustment to pro forma operating expenses for the first quarter of 2006 also included an expense of $36,000 associated with restructuring activities. There were no restructuring activities in the first quarter of 2007.

Ibis Biosciences, Inc.

Ibis' revenue for the three months ended March 31, 2007 was $1.6 million compared to $3.2 million for the same period in 2006. Ibis earned commercial revenue of $631,000 for the three months ended March 31, 2007, which consisted of the amortization of revenue for Ibis' first commercial instrument and assay kits, as well as revenue from Ibis' assay services business. Because Ibis provides a full year of support for each Ibis T5000™ Biosensor System following installation, Ibis is amortizing the revenue for each instrument sold over the period of this support obligation. Additionally, Ibis generated revenue from its government contracts and grants of $945,000 for the three months ended March 31, 2007 compared to $3.2 million for the same period in 2006. As Ibis has matured from research and development to commercial stage, some of its large government contracts that supported technology development have been successfully completed. New contracts supporting application development are being initiated, resulting in this transient decline in contract revenue. Isis expects that revenue from government contracts will continue to provide a solid revenue base going forward.

Excluding non-cash compensation expense related to stock options, operating expenses for Ibis were $4.3 million for the three months ended March 31, 2007 compared to $3.5 million for the same period in 2006. The increase in operating expenses primarily reflects an increase in sales, marketing and manufacturing costs necessary to support the early commercialization phase of the Ibis T5000 Biosensor System. Ibis generated a loss from operations of $3.1 million for the three months ended March 31, 2007 compared to $531,000 for the same period in 2006.

Early Retirement of Debt

In January 2007, Isis issued $162.5 million of 2 ⅝% Convertible Subordinated Notes due 2027. Using a portion of the net proceeds from the issuance of these 2 ⅝% notes, Isis repurchased its 5 ½% Convertible Subordinated Notes due 2009. In January 2007, Isis repurchased approximately $44.2 million aggregate principal amount of the 5 ½% notes at a redemption price of $44.9 million plus accrued but unpaid interest, and in May 2007, Isis redeemed the remaining $80.8 million principal balance at a redemption price, including accrued but unpaid interest, of $82.2 million. The

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significantly lower interest rate of the 2 ⅝% notes reduces the Company's annual cash interest payments by approximately $2.6 million. In addition, the extended maturity date of the 2 ⅝% notes further strengthens Isis' financial position.

As a result of the early repayments of the 5 ½% notes, Isis recognized a primarily non-cash loss of $1.2 million on the early retirement of debt in the first quarter of 2007 related to the January repurchase and will recognize an additional primarily non-cash loss on the early retirement of debt of $2.0 million in the second quarter of 2007 related to the May redemption.

Net Loss

Isis' net loss applicable to common stock for the quarter ended March 31, 2007 was $13.0 million compared with a net loss applicable to common stock of $17.5 million for the same period in 2006. Isis recognized a benefit of $6.8 million for the three months ended March 31, 2007 in the loss attributed to 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 quarter of 2007 compared to the same period in 2006 offset by the increase in the Company's loss from operations. The decrease in the net loss applicable to common stock was also impacted by an increase in interest income, the loss on the early retirement of debt and a gain on investments. The gain on investments in the first quarter of 2007 was due to a gain of $1.5 million realized on the sale of a portion of the equity securities of Alnylam Pharmaceuticals, Inc. that Isis owned. In April 2007, Isis sold its remaining equity securities of Alnylam resulting in a realized gain of $2.0 million, which will be reflected in the Company's statement of operations in the second quarter of 2007.

Net Loss per Share

Isis' net loss per share for the three months ended March 31, 2007 was $0.16 per share compared to a net loss per share for the same period in 2006 of $0.24 per share. In the second half of 2006, Isis issued approximately 8.0 million shares of its common stock to Azimuth Opportunity Ltd. under an equity financing that raised proceeds of $75 million. In addition to the Azimuth shares, Isis issued approximately 1.4 million shares of its common stock in connection with the exercise of stock options and warrants, and the purchase of shares under its employee stock purchase plan. These additional shares, combined with the substantial decrease in net loss applicable to common stock, resulted in the significant decrease in net loss per share for the first quarter of 2007 compared to the same period in 2006.

Balance Sheet

As of March 31, 2007, Isis had cash, cash equivalents and short-term investments of $285.6 million, which included $49.6 million of cash and cash equivalents held by Symphony GenIsis, and had consolidated working capital of $194.1 million. At December 31, 2006, Isis had cash, cash equivalents and short-term investments of $193.3 million, which included $54.8 million of cash and cash equivalents held by Symphony GenIsis, and working capital of $181.1 million. Isis' significant increase in cash, cash equivalents and short-term investments primarily reflects the cash received from the issuance of the 2 ⅝% notes. Isis' cash and current liabilities will decline in the second quarter of 2007 by approximately $82.2 million as a result of Isis' repayment of its 5½% notes. Isis used $17.9 million of cash for operations in the first quarter ended March 31, 2007, which represents a decrease of approximately $1.1 million, or 6%, compared to $19.0 million used in the fourth quarter of 2006.

BUSINESS HIGHLIGHTS

"The first quarter culminated in our March presentation of new Phase 2 data for ISIS 301012 at the American College of Cardiology meeting," said B. Lynne Parshall, Executive Vice President and Chief Financial Officer at Isis. "In New Orleans, we reported results of three studies demonstrating ISIS 301012's potent and linear, dose-dependent, cholesterol-lowering activity in several settings: as monotherapy and in combination with statins in routine high cholesterol patients and in combination with maximally-tolerated lipid-lowering therapies in patients with the genetic disorder homozygous familial hypercholesterolemia, or FH. Furthermore, we reported that at doses as high as 400 mg/week, a dose that reduced apoB-100 to at or near undetectable levels, ISIS 301012 was well tolerated. We share our investigators' enthusiasm about ISIS 301012's potential to contribute meaningfully in the future management of cardiovascular disease, and we are actively preparing to take the next steps in the development path for ISIS 301012. In particular, we plan both to begin the pivotal FH program and a longer-term Phase 2 study in routine high cholesterol patients this year. At present, the draft designs for both of these trials call for simplified dosing regimens at 200 mg/week. We will be providing more detail as we finalize the protocols and initiate the studies.

"We are experiencing strong interest from the pharmaceutical industry in licensing ISIS 301012, along with broader interest in all of our antisense programs. The transaction we completed last year with Symphony Capital supports the development of ISIS 301012 and allows us to be strategic in partnering this key asset. We are initiating the process through which we will evaluate the potential licensees and select the most strategically attractive partner.

"Our PCSK9-focused cardiovascular drug discovery and development collaboration with Bristol-Myers Squibb underscores the industry's confidence in the use of antisense drugs for the treatment of chronic diseases. We are pleased with the nearly $200 million potential deal value for this research-stage program, which we believe reflects the size of the opportunity for developing an antisense drug that inhibits a well-validated target for cardiovascular disease treatment. The financial impact of the deal for us, not including milestone or manufacturing revenue, results in about $8 million in revenue annually for the three years of the collaboration since we will amortize the $15 million upfront payment, and receive research funding of approximately $3 million per year.

"We are pleased with the progress we are making with commercialization of the Ibis T5000 Biosensor System. We are on target to meet our projected placements of 8-15 instruments in 2007. We expect that existing and new government contracts will provide a solid revenue base going forward, to which we will add increasing commercial revenues from instrument and kit sales and assay services.

“We are looking forward to carrying the momentum of our recent accomplishments forward in 2007. With our current cash position and based on reasonable assumptions for new sources of revenue and cash, we believe we have sufficient resources to meet our anticipated funding requirements through at least the middle of 2010,” Ms. Parshall concluded.

Cardiovascular Program Highlights

ISIS 301012 – Phase 2 Data at ACC

ISIS 301012 inhibits production of apoB-100 to reduce low-density lipoprotein (LDL) cholesterol and other atherogenic lipids and triglycerides. Isis is developing ISIS 301012 to reduce LDL-cholesterol in the significant and growing number of patients who are unable to achieve recommended LDL-cholesterol levels. At the American College of Cardiology meeting at the end of March, Isis reported

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new data from three Phase 2 studies. Collectively, the key conclusions from the Phase 2 studies are that treatment with ISIS 301012:

- Resulted in highly consistent and predictable linear, dose-dependent, prolonged reductions of apoB and related atherogenic lipids including LDL-cholesterol and triglycerides in patients with polygenic hypercholesterolemia (routine high cholesterol) and in patients with homozygous FH.
- Was similarly effective when administered as a single agent, when coadministered with moderately-dosed statins and when added to maximally-tolerated lipid-lowering therapies.
- Was well tolerated in all Phase 2 trials.

Development of ISIS 301012 is continuing in three ongoing studies in which it is being coadministered with statins for three months in polygenic hypercholesterolemic patients, and with maximally-tolerated lipid-lowering therapies in homozygous and heterozygous FH patients. Isis expects results from these studies later in the year. Additionally, Isis plans to start its pivotal FH trials this year, as well as to initiate a longer-term dosing study in coadministration with statins in patients with routine high cholesterol.

PCSK9 – Bristol-Myers Squibb Partnership

Yesterday, Isis announced a strategic partnership with Bristol-Myers Squibb (BMS) with a potential value of approximately $200 million for the discovery and development of antisense drugs targeting PCSK9, which helps regulate the amount of cholesterol in the bloodstream.

Under the collaboration, Isis will license to BMS exclusive access to its PCSK9 research program. While BMS will fund all activities under the collaboration, both companies will be responsible for preclinical development. BMS will be responsible for clinical development, regulatory, and commercialization activities. In addition, BMS will work with Isis to leverage Isis’ extensive oligonucleotide medicinal chemistry expertise for identification of follow-on PCSK9 antisense drugs with advanced antisense chemistries that may offer even greater potency and oral bioavailability.

BMS will pay Isis a $15 million upfront licensing fee, and will provide Isis with at least $9 million in research funding over a period of three years. Isis will also receive up to $168 million for the achievement of pre-specified development and regulatory milestones for the first drug in the collaboration, as well as additional milestones associated with development of follow-on compounds. BMS will also pay Isis royalties on sales of products resulting from the collaboration.

ISIS 353512 – Agreement with KIT for Preclinical Studies

During the quarter, Isis signed an agreement with the Korea Institute of Technology (KIT) under which KIT will conduct IND-enabling studies to support preclinical development of ISIS 353512, targeting C-reactive protein, in exchange for a nominal royalty.

Other Highlights

Ibis Biosciences, Inc. – Commercial Progress

2006 marked the transition of Ibis Biosciences from research and development to commercial stage. During the first quarter of 2007, Isis made the division a wholly owned subsidiary called Ibis Biosciences, Inc.

- In the first quarter, Ibis shipped the second of two commercial Ibis T5000 Biosensor Systems to a U.S. Government customer for human forensics applications.
- Ibis is shipping a number of types of assay kits including kits for detection of influenza.
- Ibis expects to begin manufacturing assay kits in its newly-constructed manufacturing facility later this quarter.

Financing and Other Corporate Activity

- Isis used proceeds from its 2 ⅝% Convertible Subordinated Notes issued in January 2007 to complete the redemption and repurchase of all existing 5 ½% Convertible Subordinated Notes, resulting in approximately $2.6 million per year in interest savings and strengthening its balance sheet by extending the maturity on the debt.
- Jeffrey M. Jonas, M.D., joined Isis as Executive Vice President. Dr. Jonas leads Clinical Development, Preclinical Development, Regulatory Affairs, and Quality Assurance and Compliance at Isis.
- During the quarter, Isis was awarded 24 new patents worldwide, of which seven were U.S. patents.

Conference Call

At 10:00 a.m. Eastern Time today, May 10, Isis will conduct a live webcast conference call to discuss this earnings release and related activities. Interested parties may access the webcast at www.isispharm.com or listen to the call by dialing 913-312-1229. A 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 17 drugs in development. Isis' drug development programs are focused on treating cardiovascular and metabolic diseases. Isis' partners are developing drugs for cancer, and inflammatory and other diseases. Ibis Biosciences, Inc., Isis' wholly owned subsidiary, 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 over 1,500 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 outlook for Isis and its Ibis Biosciences subsidiary, and the therapeutic and commercial potential of Isis' 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, including those statements that are described as Isis' goals or projections. 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, 2006, which is on file with the SEC. Copies of this and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Isis," "Company," "we," "our," and "us" means Isis Pharmaceuticals and its subsidiaries.

ISIS PHARMACEUTICALS, INC.
SELECTED FINANCIAL INFORMATION

Condensed Consolidated Statements of Operations
(In Thousands, Except Per Share Data)

	Three months ended, March 31,	
	2007	2006
Revenue:		
Research and development revenue under collaborative agreements	$ 2,002	$ 4,468
Licensing and royalty revenue	448	490
Total revenue	2,450	4,958
Expenses:		
Research and development	19,949	18,372
Selling, general and administrative	3,402	2,566
Restructuring activities	—	36
Total operating expenses	23,351	20,974
Loss from operations	(20,901)	(16,016)
Other income (expense):		
Investment income	3,401	811
Interest expense	(2,628)	(2,275)
Gain on investments	1,521	—
Loss on early retirement of debt	(1,219)	—
Net loss before noncontrolling interest in Symphony GenIsis, Inc.	(19,826)	(17,480)
Loss attributed to noncontrolling interest in Symphony GenIsis, Inc.	6,806	—
Net loss applicable to common stock	$ (13,020)	$ (17,480)
Basic and diluted net loss per share	$ (0.16)	$ (0.24)
Shares used in computing basic and diluted net loss per share	82,456	72,377

Ibis Biosciences, Inc.
Statements of Operations

(In Thousands)

	Three months ended, March 31,	
	2007	2006
	(unaudited)	
Revenue:		
Commercial revenue (1)	$ 631	$ —
Research and development revenue under collaborative agreements	945	3,198
Total revenue	1,576	3,198
Expenses:		
Cost of commercial revenue (2)	718	—
Research and development	3,005	3,280
Selling, general and administrative	988	449
Total operating expenses	4,711	3,729
Loss from operations	$ (3,135)	$ (531)

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

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

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

	Three months ended, March 31,	
	2007	2006
	(unaudited)	
As reported operating expenses according to GAAP	$ 23,351	$ 20,974
Excluding compensation expense related to stock options pursuant to SFAS 123(R)	(2,364)	(1,374)
Excluding restructuring activities	—	(36)
Proforma operating expenses	$ 20,987	$ 19,564
As reported loss from operations according to GAAP	$ (20,901)	$ (16,016)
Excluding compensation expense related to stock options pursuant to SFAS 123(R)	(2,364)	(1,374)
Excluding restructuring activities	—	(36)
Proforma loss from operations	$ (18,537)	$ (14,606)

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

	March 31, 2007	December 31, 2006
	(Unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	$ 285,554	$ 193,333
Other current assets	10,513	12,870
Property, plant and equipment, net	7,042	7,157
Other assets	46,795	42,547
Total assets	$ 349,904	$ 255,907
Liabilities, noncontrolling interest and stockholders' equity:		
Current portion of 5 ½% convertible subordinated notes	$ 80,825	$ —
Other current liabilities	21,116	25,139
Long-term portion of 5 ½% convertible subordinated notes	—	125,000
2 5/8% convertible subordinated notes	162,500	—
Long-term obligations, net of current portion	6,032	7,866
Noncontrolling interest in Symphony GenIsis, Inc.	22,533	29,339
Stockholders' equity	56,898	68,563
Total liabilities, noncontrolling interest and stockholders' equity	$ 349,904	$ 255,907

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