# 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 8, 2003**

# 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.) |

**2292 Faraday Avenue**
**Carlsbad, CA 92008**
(Address of Principal Executive Offices and Zip Code)

Registrant's telephone number, including area code: **(760) 931-9200**

**Item 7. Financial Statements and Exhibits.**

(c) Exhibits.

99.1 Press Release dated May 8, 2003.

**Item 9. Regulation FD Disclosure.**

On May 8, 2003, Isis Pharmaceuticals, Inc. (the "Company") issued a press release announcing the Company's financial results for the quarter ended March 31, 2003. 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 that exclude certain adjustments associated with non-cash compensation expense/benefit, as applicable. The Company is presenting pro forma information excluding the effects of the non-cash compensation expense/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 12. 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.

## 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 8, 2003

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 8, 2003. |

Contact: Elizabeth Hougen, Vice President, Finance
Karen Lundstedt, Vice President, Corporate Communications
Isis Pharmaceuticals, 760-931-9200
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**ISIS PHARMACEUTICALS REPORTS FINANCIAL RESULTS AND HIGHLIGHTS FOR THE FIRST QUARTER 2003**

**CARLSBAD, CA May 8, 2003** — Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), today announced its financial results for the first quarter of 2003. Total revenue for the three months ended March 31, 2003 totaled $14.0 million, compared with $18.0 million for the same period in 2002. Operating expenses for the quarters ended March 31, 2003 and 2002 were $32.9 million and $27.7 million, respectively. As a result, the company's loss from operations was $18.9 million for the first quarter 2003 according to both generally accepted accounting principles (GAAP) and on a proforma basis, excluding a nominal non-cash compensation expense. This compared to a $9.7 million loss from operations for the same period in 2002 on a GAAP basis and an $11.3 million loss on a proforma basis, which excludes $1.5 million in non-cash compensation benefit.

In 2002, Isis reacquired product rights to ISIS 14803 for hepatitis C and the oral formulation of ISIS 104838 as a result of Elan Corporation plc.'s conclusion of its participation in the HepaSense™ and Orasense™ collaborations. As a result, Isis no longer earned revenue from these affiliates in 2003. This was the primary reason for the $4.0 million decrease in total revenue in the first quarter of 2003 compared to the same period of 2002.

The first quarter of 2003 benefited from transactions that provided new sources of revenue not present in the same period of 2002, including:

- the addition of new GeneTroveä partnerships with atugen AG, GlaxoSmithKline, Pfizer Inc. and Pharmacia Corporation in late 2002 and early 2003
- the addition of a new contract with the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID), in April 2002, to advance the company's small molecule antibacterial drug discovery program
- the achievement of a second milestone in February 2003 in the company's antisense drug discovery collaboration with Amgen

The company continued to invest in the development of its large product pipeline during the first quarter of 2003. As a result, total operating expenses increased by $5.2 million over that reported for the same period of 2002. The increase was primarily due to costs for the Phase III trial of Affinitak™ for non-small cell lung cancer (NSCLC), two Phase III trials of alicaforsen (ISIS 2302) for Crohn's disease, Phase II trials of alicaforsen for ulcerative colitis, ISIS 14803 in hepatitis C and ISIS 104838 in rheumatoid arthritis. Also contributing to the increase were costs associated with increased gene functionalization

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and target validation activities in support of the company's numerous GeneTrove collaborations and costs related to the company's $100 million, multi-year research collaboration with Eli Lilly and Company.

Total operating expenses for the first quarter 2003 included approximately $9,000 in non-cash compensation expense related to stock options granted to consultants. In the same period of the previous year the company incurred $1.5 million in non-cash compensation benefit associated primarily with an option exchange program offered to non-officer employees in January 2000, which were accounted for as variable options. All remaining options in this program were either exercised or cancelled in December 2002.

In April 2003, Isis implemented an employee stock option exchange program to ensure that the company maintains one of its key assets, its employee base. The program allows employees to surrender certain higher-priced options in exchange for a lesser number of lower-priced options. The replacement options will be treated as variable options and thus may subject Isis to non-cash compensation charges beginning in the second quarter of 2003. Variable stock options can result in significant non-cash increases and decreases in compensation expense as a result of the variability in the company's stock price.

The company's net loss applicable to common stock for the first quarter 2003 was $24.5 million, or $0.44 per share, compared with a net loss applicable to common stock of $18.3 million, or $0.34 per share, for the same period last year. The net loss applicable to common stock for the quarter ended March 31, 2003 included a non-cash loss on investments of $2.4 million related to the impairment of certain equity investments in biotech companies. This charge reflects the current market climate and is associated with the decline in market value of the equity investments from their initial valuations.

Isis maintained a strong balance sheet by ending the quarter with $269.5 million in cash and short-term investments and working capital of $227.5 million. At December 31, 2002, Isis had cash and short-term investments of $289.4 million and working capital of $244.2 million. Cash and short-term investments and working capital decreased primarily as a result of operating activities.

"To date in 2003, we have expanded our preclinical development portfolio of products, continued to advance our large development pipeline and added new partners to our extensive list of GeneTrove customers," said B. Lynne Parshall, Isis' Executive Vice President and CFO. "In response to disappointing results from the first Phase III trial of Affinitak, we initiated a restructuring of the company in April 2003. The associated restructuring charges will be recorded in our second quarter financials. The operating plan we have implemented enables us to continue aggressive development of products in our pipeline that provide multiple opportunities for success, while preserving our cash."



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## Isis' First Quarter 2003 and Recent Highlights

*Clinical Development Progress*

- Announced, with Lilly, results of a Phase III trial that evaluated the antisense agent Affinitak when combined with chemotherapy in patients with advanced NSCLC. No difference was observed in a primary log-rank analysis of the overall survival of the two groups. Other key findings from the trial

included the observation that those patients who completed the prescribed course of therapy appeared to survive longer than patients receiving chemotherapy alone. Additionally, based on a stratified log-rank statistical analysis of all 616 patients that considered predefined variables, including duration of treatment, survival of the Affinitak treated patients was greater than that of the patients in the control arm.

Lilly is continuing to follow patients currently enrolled in its second Phase III study and is not enrolling additional patients in studies of Affinitak. Isis and Lilly will make decisions about the development of Affinitak upon review of the results of the second Phase III trial.

- Initiated a Phase II clinical trial of alicaforsen in people with active ulcerative colitis (UC). The study will compare the safety and efficacy of different dosing regimens of the enema formulation of alicaforsen to placebo.

*Drug Discovery Progress*

- Achieved a significant milestone in the development of the anticancer second-generation antisense compound, ISIS 23722, as part of the company's broad antisense drug discovery collaboration with Lilly. ISIS 23722 targets survivin, a molecule that allows the survival of cells that would normally undergo programmed cell death, and is the first compound from the partnership to be selected for clinical development by Lilly. As a result of the achievement, Isis will receive a $1.5 million payment from Lilly.

- Added the company's first cardiovascular drug candidate, ISIS 301012, an antisense inhibitor of ApoB-100, to its development pipeline.

*GeneTrove Business Activity*

- Entered into a target validation agreement with Pfizer. Under this agreement, Pfizer will obtain access to Isis' antisense inhibitors and acquire a license to specific patents within Isis' intellectual property estate for use in its internal antisense-based functional genomics program.

- Licensed specific functional genomics patents to atugen AG. atugen supplements its existing intellectual property position by gaining rights to practice Isis' antisense-based functional genomics technology, and to use antisense for discovery and validation of targets and for small molecule drug discovery research in its in-house programs and for its customers.



Isis will conduct a live webcast conference call to discuss this earnings release on Thursday, May 8 at 10:00 am Eastern time. To participate over the Internet go to http://www.isispharm.com . A replay of the webcast will be available at this address for up to 30 days.

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs. The company has commercialized its first product, Vitravene(R) (fomivirsen), to treat CMV-induced retinitis in AIDS patients. In addition, Isis has 13 antisense products in its development pipeline, with two in late-stage development and five in Phase II human clinical trials. Affinitak(TM) (formerly called LY900003 and ISIS 3521), an inhibitor of PKC-alpha, is in Phase III development for non-small cell lung cancer, and alicaforsen (ISIS 2302), an ICAM-1 inhibitor, is in Phase III human clinical trials for Crohn's disease. Isis has a broad patent estate, as the owner or exclusive licensee of nearly 1,200 issued patents worldwide. Isis' GeneTrove(TM) division uses antisense to assist pharmaceutical industry partners in validating and prioritizing potential gene targets through customized services. Ibis Therapeutics(TM) is a division focused on the diagnosis of infectious organisms and the discovery of small molecule drugs that bind to RNA. Additional information about Isis is available at www.isispharm.com .

This press release contains forward-looking statements concerning the financial position and clinical goals of Isis Pharmaceuticals, Inc., the planned development activities and therapeutic potential for our products in our pipeline, and the potential value of the company's functional genomics and drug discovery technology platform. Any statement describing a goal, expectation, intention or belief of the company 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 financing such activities. Actual results could differ materially from those projected in this release. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' research and development programs are described in additional detail in the company's Annual Report on Form 10-K, for the year ended December 31, 2002, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.



- Financial Data to Follow —



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

| | Three months ended, March 31, | |
|---|---|---|
| | 2003 | 2002 |
| | (unaudited) | |
| Revenue: | | |
| Research and development revenues under collaborative agreements | $ 13,780 | $ 14,714 |
| Research and development revenues from affiliates | — | 3,034 |

| | | |
|---|---|---|
| Licensing revenues | 200 | 211 |
| Total revenue | 13,980 | 17,959 |
| | | |
| Expenses: | | |
| Research and development | 30,261 | 26,983 |
| General and administrative | 2,622 | 2,226 |
| Compensation (benefit) related to stock options | 9 | (1,532) |
| Total operating expenses | 32,892 | 27,677 |
| | | |
| Loss from operations | (18,912) | (9,718) |
| | | |
| Equity in loss of affiliates | — | (5,767) |
| Investment and other income | 1,636 | 2,144 |
| Interest expense | (4,608) | (4,631) |
| Loss on investments | (2,438) | — |
| | | |
| Net loss | (24,322) | (17,972) |
| | | |
| Accretion of dividends on preferred stock | (171) | (335) |
| | | |
| Net loss applicable to common stock | $ (24,493) | $ (18,307) |
| | | |
| Basic and diluted net loss per share | $ (0.44) | $ (0.34) |
| | | |
| Shares used in computing basic and diluted net loss per share | 55,375 | 53,923 |

**Reconciliation of GAAP to Proforma Basis: Loss From Operations**
**(In Thousands)**

| | Three months ended, March 31, | |
|---|---|---|
| | 2003 | 2002 |
| | (unaudited) | |
| **As reported loss from operations according to GAAP** | **$ (18,912)** | **$ (9,718)** |
| Excluding compensation expense/(benefit) related to stock options | 9 | (1,532) |
| **Proforma loss from operations** | **$ (18,903)** | **$ (11,250)** |



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

| | March 31, 2003 | December 31, 2002 |
|---|---|---|
| | (unaudited) | |
| Assets: | | |
| Current assets | $ 294,663 | $ 320,180 |
| Property, plant and equipment, net | 60,797 | 59,094 |
| Other assets | 59,635 | 59,409 |
| Total assets | $ 415,095 | $ 438,683 |
| Liabilities and stockholders' equity: | | |
| Current liabilities | $ 67,159 | $ 75,950 |
| 5.5% Convertible subordinated notes | 125,000 | 125,000 |
| Long-term obligations, net of current portion | 74,951 | 67,893 |
| Long-term deferred revenue, net of current portion | 13,710 | 14,363 |
| Stockholders' equity | 134,275 | 155,477 |
| Total liabilities and stockholders' equity | $ 415,095 | $ 438,683 |