SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(MARK ONE)

[X] QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the quarterly period ended March 31, 1999

OR

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

For the transition period from ____________ to ____________

Commission file number 0-19125

ISIS PHARMACEUTICALS, INC.
(Exact name of registrant as specified in its charter)

Delaware	33-0336973
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)

2292 Faraday Avenue, Carlsbad, CA 92008
(Address of principal executive offices, including zip code)

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

(Former name, former address and former fiscal year, if changed since last report)

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days.

(1) Yes [X] No [ ]   (2) Yes [X] No [ ]

Indicate the number of shares outstanding of each of the issuer's classes of common stock, as of the latest practicable date.

Common stock $.001 par value	28,241,989 shares
(Class)	(Outstanding at May 1, 1999)

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ISIS PHARMACEUTICALS, INC.
CONDENSED BALANCE SHEETS
(in thousands, except share data)

ASSETS

	March 31, 1999 (Unaudited)	December 31, 1998 (Note)
Current assets:		
Cash and cash equivalents	$ 20,310	$ 34,591
Short-term investments	22,547	24,258
Receivable from partners	5,256	3,466
Prepaid expenses and other current assets	739	872
Total current assets	48,852	63,187
Property, plant and equipment, net	22,374	21,542
Patent costs, net	9,467	9,113
Deposits and other assets	2,179	2,232
	$ 82,872	$ 96,074

LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT)

	March 31, 1999 (Unaudited)	December 31, 1998 (Note)
Current liabilities:		
Accounts payable	$ 2,729	$ 2,977
Accrued payroll and related expenses	1,708	3,088
Accrued liabilities	2,856	2,714
Deferred contract revenues	8,725	10,176
Current portion of long term debt and capital lease obligations	3,614	3,581
Total current liabilities	19,632	22,536
Long-term debt and capital lease obligations, less current portion	78,945	77,724
Stockholders' equity (deficit):		
Common stock, $.001 par value; 50,000,000 shares authorized, 27,329,445 shares and 27,053,000 shares issued and outstanding at March 31, 1999 and December 31, 1998, respectively	27	27
Additional paid-in capital	193,904	192,737
Unrealized gain on investments	84	166
Accumulated deficit	(209,720)	(197,116)
Total stockholders' equity (deficit)	(15,705)	(4,186)
	$ 82,872	$ 96,074

Note: The balance sheet at December 31, 1998 has been derived from the audited financial statements at that date.

See accompanying notes.

ISIS PHARMACEUTICALS, INC.
CONDENSED STATEMENTS OF OPERATIONS
(in thousands, except for per share amounts)
(UNAUDITED)

	Three months ended March 31, 1999	Three months ended March 31, 1998
Revenue:		
Research and development revenues under collaborative agreements	$ 6,576	$ 5,845
Expenses:		
Research and development	14,316	14,859
General and administrative	2,815	1,858
Total Operating Expense	17,131	16,717
Loss from operations	(10,555)	(10,877)
Interest income	656	1,050
Interest expense	2,705	1,704
Net loss	$(12,604)	$(11,526)
Basic and diluted net loss per share	$ (.46)	$ (.43)
Shares used in computing basic and diluted net loss per share	27,179	26,740

See accompanying notes.

ISIS PHARMACEUTICALS, INC.
CONDENSED STATEMENTS OF CASH FLOWS
(in thousands)
(UNAUDITED)

	Three months ended March 31, 1999	1998
Cash used in operations:	$(14,042)	$(16,279)
Investing activities:		
Short-term investments	1,711	6,938
Property and equipment	(1,849)	(1,071)
Other assets	(598)	(322)
Net cash provided from (used in) investing activities	(736)	5,545
Financing activities:		
Net proceeds from issuance of common stock	1,167	1,090
Proceeds from long-term borrowings	--	--
Principal payments on debt and capital lease obligations	(670)	(672)
Net cash provided from financing activities	497	418
Net decrease in cash and cash equivalents	(14,281)	(10,316)
Cash and cash equivalents at beginning of period	34,591	38,102
Cash and cash equivalents at end of period	$ 20,310	$ 27,786
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Interest paid	$ 365	$ 335

See accompanying notes.

ISIS PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS

1. BASIS OF PRESENTATION

The unaudited interim financial statements for the three months ended March 31, 1999 and 1998 have been prepared on the same basis as the Company's audited financial statements for the year ended December 31, 1998. The financial statements include all adjustments (consisting only of normal recurring adjustments) which the Company considers necessary for a fair presentation of the financial position at such dates and the operating results and cash flows for those periods. Results for the interim periods are not necessarily indicative of the results for the entire year. For more complete financial information, these financial statements, and notes thereto, should be read in conjunction with the audited financial statements for the year ended December 31, 1998 included in the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission.

2. SUBSEQUENT EVENTS

In April 1999, the Company established an agreement with Elan Pharmaceuticals, an Irish Company, to form a new subsidiary of Isis for purposes of developing a platform technology for the oral delivery of antisense drugs. The joint venture, Orasense Ltd. ("Orasense"), a Bermuda limited company, is initially owned 80.1% by Isis and 19.9% by Elan. In connection with the joint venture, Elan International Services Ltd. ("EIS") purchased $15 million of Common Stock of Isis at a premium. Isis also issued a warrant to EIS to purchase 215,000 shares of Isis Common Stock at $24.00 per share. EIS also purchased $12 million of Preferred Stock of Isis, which bears a 5% dividend payable in Preferred Stock and is convertible into Isis Common Stock at a specified premium or exchangeable for 30.1% ownership of Orasense. Isis contributed a portion of the funding to Orasense to pay license fees to Elan for certain of the technology contributed to the joint venture.

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

In addition to historical information contained in this Report, this Report contains forward-looking statements regarding Isis' business and products and their projected prospects and qualities as well as our relationships with our corporate partners. 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 the endeavor of building a business around such potential products. Actual results could differ materially from those discussed in this Form 10-Q. As a result, the reader should not place undue reliance on these forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in Isis' Annual Report on Form 10-K for the year ended December 31, 1998 which is on file with the U.S. Securities and Exchange Commission.

Since its inception in January 1989, almost all of Isis' resources have been devoted to our research, drug discovery and drug development programs. Isis is not yet profitable and expects to continue to have operating losses for the next several years. Our revenue comes from collaborative research and development agreements with pharmaceutical companies, research grants and interest income. The revenue from the collaboration increases the amount of research and development activity that Isis is able to fund and offsets a portion of its research and development costs. During the quarter ended September 30, 1998, Isis received approval from the U.S. Food and Drug Administration ("FDA") to begin marketing its first product, Vitravene(TM), a drug used to treat CMV retinitis.

RESULTS OF OPERATIONS

Isis' revenue from collaborative research and development agreements was $6.6 million for the quarter ended March 31, 1999, compared with $5.8 million for the same period in 1998, a 14% increase. The revenue increase was primarily due to revenue received from Zeneca Limited, Merck & Company and Abbott Laboratories Inc, partnerships established subsequent to March 31, 1998. The Company also had interest income totaling $.7 million for the quarter compared with $1.1 million for the same period in 1998. This decrease in interest income was primarily due to lower average investment balances in the quarter ended March 31, 1999.

Research and development expenses were $14.3 million for first quarter of 1999, consistent with $14.9 million for the same period in 1998. For both periods, research and development expenses were driven by the cost of preclinical and clinical activities to support forward progress of compounds in clinical trials. We expect that research and development expenses will continue to increase as compounds continue to advance in clinical development.

General and administrative expenses increased to $2.8 million for the quarter ended March 31, 1999, from $1.9 million for the same period in 1998. This increase in general and administrative expense is related to additional staffing in general and administrative functions and outside services required to support the growth in research and development. We expect that general and administrative expenses will continue to increase in the future to support our growing research and development efforts.

Interest expense increased to $2.7 million for the first quarter of 1999 from $1.7 million in the first quarter of 1998. This increase in interest expense is principally due to an additional $15 million follow-on private debt financing in the second quarter of 1998. This incremental $15 million brought the total borrowed under the private long-term debt arrangement to $40 million. Under the terms of the financing arrangements, payment of both principal and interest is deferred for the first five years. Therefore, of the $2.7 million interest expense in the first quarter 1999, $1.9 million was accrued under the long-term debt agreements and will not require current cash payment.

During the quarter ended March 31, 1999, Isis recorded a net loss of $12.6 million, or $.46 per share, compared with $11.5 million, or $.43 per share, for the same period in 1998. We expect that operating losses will increase for several more years as research and development activities grow. Operating losses may fluctuate from quarter to quarter because of differences in the timing of revenue and expense recognition.

Isis believes that inflation and changing prices have not had a material effect on its operations to date.

LIQUIDITY AND CAPITAL RESOURCES

We have financed our operations with revenue from contract research and development, through the sale of equity securities and the issuance of long-term debt. From Isis' inception through March 31, 1999, Isis has earned approximately $152 million in revenue from contract research and development. Isis has also raised net proceeds of approximately $185 million from the sale of equity securities since it was founded. We have borrowed approximately $80 million under long-term debt arrangements to finance a portion of its operations.

As of March 31, 1999, Isis had cash, cash equivalents and short-term investments totaling $42.9 million and working capital of $29.2 million. In comparison, we had cash, cash equivalents and short-term investments of $58.8 million and working capital of $40.7 million as of December 31, 1998. The decreases in cash and working capital during the quarter resulted from the funding of operating losses, investments in capital equipment and principal payments on debt and capital lease obligations.

The agreement with Boehringer Ingelheim provides us with a $40 million line of credit. This line of credit is to be used to support the collaboration cell adhesion programs. Restrictions on the credit line are based on the anticipated collaboration costs, the amount of funds available to us, and our average stock price over specified periods. As of March 31, 1999 this line of credit was not available. We believe that it will be available before the end of 1999. As of March 31, 1999, the outstanding balance under this line of was $22.6 million.

In 1997 and 1998, Isis borrowed a total of $40 million in a private transaction. The loans bear interest at 14% per annum and must be repaid on November 1, 2007. No payments of either principal or interest are required during the first five years of the loans. After the first five years, interest must be paid quarterly. No principal payments are required until November 1, 2007. In conjunction with these transactions, Isis issued warrants to purchase 800,000 shares of common stock at a price of $25 per share. The warrants issued in connection with both of these financings expire on November 1, 2004. Because interest is deferred during the first five years, the balance of these borrowings will accrue to a total of $78 million on November 1, 2002. The debt under these arrangements is carried on the balance sheet net of the amortized amount allocated to the warrants and including accrued interest. The combined carrying amount of these notes at March 31, 1999 was $43.2 million.

As of March 31, 1999, our long-term obligations totaled $82.6 million, versus $81.3 million at December 31, 1998. This increase was due to the accrual of interest on the ten-year notes described above, partially offset by principal repayments on existing obligations. We expect that capital lease obligations will increase over time to fund capital equipment acquisitions required for Isis' growing business. We will continue to use lease financing as long as the terms remain commercially attractive. We believe that our existing cash, cash equivalents and short-term investments, combined with interest income and contract revenue will be sufficient to meet its anticipated requirements at least until the end of 2000.

YEAR 2000 COMPUTER ISSUES

Until recently many computer programs were written to store only two digits of date-related information. Thus the programs were unable to distinguish between the year 1900 and the year 2000. As a result, many computer experts have significant concerns regarding how those programs will function after December 31, 1999. This is frequently referred to as the "Year 2000 Problem." Because Isis was founded in 1989, our computer systems and equipment are relatively new and generally not subject to the date and time issues that create the Year 2000 problems.

A team of Isis employees is conducting our Year 2000 initiative. The team's activities are designed to ensure that there is no adverse effect on our core business operations and that transactions with customers, suppliers, corporate partners and financial institutions are fully supported. Our Year 2000 plan includes the following phases: inventorying critical business systems and vendors, assessment of the probability of Year 2000 non-compliance, remediation activities including repairing or replacing identified systems, testing, and developing contingency plans.

An inventory of all computer equipment, operating systems and applications including other equipment that uses embedded microprocessors has been completed. Compliance assessment has been completed for all critical or important systems and equipment. Remediation activities have been completed for all but five systems or pieces of equipment. We estimate that all required remediation and validation will be completed by the third quarter of 1999. Testing of our critical and important systems and applications is ongoing and is scheduled to be completed by the third quarter of 1999. Contingency planning will begin in the second quarter of 1999. Based on the work completed to date, we believe that with the completed remediation work, the Year 2000 issue will not pose significant operational problems for our computer systems and equipment.

We have also requested information from our significant suppliers, corporate partners and financial institutions to ensure that those parties are addressing Year 2000 issues where their systems could impact our operations. We are assessing the extent to which our operations are vulnerable should those organizations fail to properly modify their computer systems. The failure of systems maintained by our vendors, corporate partners or financial institutions could affect our ability to process transactions, conduct research and development projects, manufacture products, or engage in other normal business activities. We have received responses from all but one of the critical or important third parties and are in the process of evaluating those responses to identify areas of exposure. We are also in the process of identifying alternate sources for products or services in the event that any of our present primary or secondary vendors are not successful in resolving their Year 2000 issues. We will continue to monitor the progress of critical and important third parties throughout 1999 to ascertain that they achieve their Year 2000 objectives.

Our most likely exposure to Year 2000 problems is related to our high dependence on commercial utilities such as water and power. If the providers of these utilities are not able to maintain service due to Year 2000 noncompliance it could result in temporarily halting research and development activities until the service is restored or until suitable alternate facilities in a different geographic area could be obtained. It is not possible to precisely estimate the length of delays in research and development projects in those circumstances, but it could range from three to six months.

While we believe our planning and preparations will be adequate to address our internal Year 2000 concerns, we cannot guarantee that the systems of other companies, on which our systems and operations rely, will be converted on a timely basis and will not have a material effect on us. The total cost of the Year 2000 risk assessment and remediation is funded through operating cash flows, and we are expensing these costs as they are incurred. Based on information obtained to date, the cost of identifying and remediating exposures to the Year 2000 Problem is not expected to be material to our results of operations or financial position. The estimated total cost of our Year 2000 assessment and remediation is not expected to exceed $500,000.

PART II - OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

The Company is not party to any legal proceedings.

ITEM 2. CHANGES IN SECURITIES

Not applicable.

ITEM 3. DEFAULT UPON SENIOR SECURITIES

Not applicable.

ITEM 4. SUBMISSION OF MATTERS TO A VOTE OF SECURITY HOLDERS

Not applicable.

ITEM 5. OTHER INFORMATION

Not applicable.

ITEM 6. EXHIBITS AND REPORTS ON FORM 8-K

a. Exhibits

None.

b. Reports on Form 8-K

On April 30, 1999, the Company filed the following report on form 8-K:

> Report dated April 20, 1999 which described the joint venture the Registrant entered into with Elan Corporation, plc. No financial statements were filed with this report on Form 8-K. Eight documents, including the Subscription, Joint Development and Operating Agreement, security and warrant purchase agreements and related license agreements (with certain confidential information deleted) were filed as an exhibit to the report.

ISIS PHARMACEUTICALS, INC.

SIGNATURES

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

ISIS PHARMACEUTICALS, INC.
(Registrant)

Date: May 8, 1998   By: /s/ STANLEY T. CROOKE

Stanley T. Crooke, M.D., Ph.D.
Chairman of the Board and Chief Executive Officer
(Principal Executive Officer)

Date: May 8, 1998   By: /s/ B. LYNNE PARSHALL

B. Lynne Parshall
Executive Vice President and Chief Financial Officer
(Principal Financial Officer)

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THIS SCHEDULE CONTAINS SUMMARY FINANCIAL INFORMATION DERIVED FROM THE COMPANY'S CONDENSED BALANCE SHEET AS OF MARCH 31, 1999 (UNAUDITED) AND CONDENSED STATEMENTS OF OPERATIONS FOR THE THREE MONTHS ENDED MARCH 31, 1999 (UNAUDITED) AND IS QUALIFIED IN ITS ENTIRETY BY REFERENCE TO SUCH FINANCIAL STATEMENTS.

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3-MOS
DEC-31-1999
JAN-01-1999
MAR-31-1999
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