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, 2000

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	35,545,666 shares
(Class)	(Outstanding at March 31, 2000)

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

ASSETS

	March 31, 2000 (Unaudited)	December 31, 1999 (Note)
Current assets:		
Cash and cash equivalents	$ 64,733	$ 35,296
Short-term investments	29,001	17,543
Contract revenue receivable	3,064	5,429
Prepaid expenses and other current assets	927	929
Total current assets	97,725	59,197
Property, plant and equipment, net	23,388	23,945
Patent costs, net	11,592	11,250
Deposits and other assets	1,647	1,724
Investment in joint ventures	17,492	6,991
	$ 151,844	$ 103,107

LIABILITIES AND STOCKHOLDERS' DEFICIT

	March 31, 2000	December 31, 1999
Current liabilities:		
Accounts payable	$ 1,302	$ 3,148
Accrued payroll and related expenses	1,706	1,215
Accrued liabilities	2,981	2,563
Deferred contract revenues	2,903	4,166
Current portion of long term debt and capital lease obligations	3,767	3,892
Total current liabilities	12,659	14,984
Long-term debt and capital lease obligations, less current portion	91,297	87,254
Stockholders' equity:		
Series A Convertible Exchangeable 5% Preferred stock, $.001 par value; 15,000,000 shares authorized, 120,150 shares issued and outstanding at March 31, 2000 and December 31, 1999, respectively	12,315	12,315
Accretion of series A Preferred stock dividends	274	120
Series B Convertible Exchangeable 5% Preferred stock, $.001 par value; 16,620 shares authorized, 12,015 shares and no shares issued and outstanding at March 31, 2000 and December 31, 1999, respectively	12,015	-
Accretion of series B Preferred stock dividends	127	-
Common stock, $.001 par value; 50,000,000 shares authorized, 35,546,000 shares and 31,613,000 shares issued and outstanding at March 31, 2000 and December 31, 1999, respectively	35	32
Additional paid-in capital	298,449	245,192
Unrealized gain (loss) on investments	42	(29)
Accumulated deficit	(275,370)	(256,761)
Total stockholders' equity	47,887	869
	$ 151,844	$ 103,107

Note: The balance sheet at December 31, 1999 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, 2000	Three months ended March 31, 1999
Revenue:		
Research and development revenues under collaborative agreements	$ 2,886	$ 6,576
Research and development revenues from joint ventures	1,168	-
Product Revenue	-	-
Total Revenue	4,054	6,576
Expenses:		
Research and development	13,239	14,316
General and administrative	1,824	2,815
Restructuring activities	1,608	-
Total Operating Expenses	16,671	17,131
(Loss) from operations	(12,617)	(10,555)
Equity in loss of joint ventures	(3,495)	-
Interest income	892	656
Interest expense	(3,107)	(2,705)
Net loss	(18,327)	(12,604)
Accretion of dividends on preferred stock	(281)	-
Net loss applicable to common stock	$(18,608)	$(12,604)
Basic and diluted net loss per share	$ (.56)	$ (.46)
Shares used in computing basic and diluted net loss per share	33,063	27,179

See accompanying notes.

See accompanying notes.

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

	Three months ended March 31, 2000	1999
Cash used in operations	$(11,053)	$(14,042)
Investing activities:		
Short-term investments	(11,387)	1,711
Property and equipment	(601)	(1,849)
Other assets	(453)	(598)
Investment in joint venture	(13,996)	-
Net cash used for investing activities	(26,437)	(736)
Financing activities:		
Net proceeds from issuance of equity securities	65,275	1,167
Proceeds from long-term borrowings	2,452	-
Principal payments on debt and capital lease obligations	(800)	(670)
Net cash provided from financing activities	66,297	497
Net increase (decrease) in cash and cash equivalents	29,437	(14,281)
Cash and cash equivalents at beginning of period	35,296	34,591
Cash and cash equivalents at end of period	$ 64,733	$ 20,310
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Interest paid	$ 308	$ 365
SUPPLEMENTAL DISCLOSURES OF NON-CASH INVESTING AND FINANCING ACTIVITIES:		
Additions to long-term debt obligations for acquisitions of property, plant and equipment	$-	$-

See accompanying notes.

ISIS PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS

1. BASIS OF PRESENTATION

The unaudited interim financial statements for the three month periods ended March 31, 2000 and 1999 have been prepared on the same basis as the Company's audited financial statements for the year ended December 31, 1999. 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, 1999 included in the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission.

2. STRATEGIC ALLIANCES

ORASENSE

On April 20, 1999, Isis Pharmaceuticals, Inc., a Delaware corporation ("Isis" or the "Company") and Elan Corporation, plc ("Elan") formed a joint venture to develop technology for the formulation of oral oligonucleotide drugs. The joint venture, Orasense Ltd. ("Orasense"), a Bermuda limited company, is initially owned 80.1% by the Company and 19.9% by Elan. Isis and Elan each contributed rights to certain oral drug delivery technology to the joint venture. In addition, Isis contributed rights to a proprietary oligonucleotide, which will be the first candidate for oral formulation by Orasense. Isis and Elan will provide development and manufacturing services to Orasense and will be entitled to royalties on milestone payments and royalties received by Orasense for development of orally formulated oligonucleotide drugs. If Isis enters into an agreement with Orasense for oral formulation of any Isis oligonucleotide drug, Isis will pay Orasense royalties and a portion of certain third party milestone payments with respect to the drug.

In conjunction with the joint venture, Elan International Services, Ltd. ("EIS") purchased 910,844 shares of Isis' Common Stock for $15,000,000 and 120,150 shares of Isis's Series A Convertible Preferred Stock for $12,015,000, which bears a 5% dividend payable in Preferred Stock. In conjunction with this transaction, Isis issued to EIS a five-year warrant to purchase up to 215,000 shares of Isis' Common Stock at $24 per share.

After March 31, 2002, the Series A Convertible Preferred Stock (including accrued dividends) will be convertible at EIS' option into shares of Isis' Common Stock at 125% of the 60-trading day average closing price of Isis' Common Stock ending two business days prior to March 31, 2002 (as adjusted for stock splits, stock dividends and the like). In the event of a liquidation of Isis or certain transactions involving a change of control of Isis, the agreement provides for automatic conversion of the Preferred Stock on terms similar to those set forth above.

Isis is not obligated to issue shares representing more than 19.99% of its then outstanding Common Stock upon conversion of the Series A Convertible Preferred Stock if it would result in a violation of the rules of any securities market or exchange upon which the Common Stock is traded.

At any time until June 30, 2002, the holders of the Series A Convertible Preferred Stock may exchange their Preferred Stock for common shares of Orasense held by Isis that represent 30.1% of the total outstanding capital stock of Orasense. The exchange right will terminate if the Preferred Stock is converted into Isis' Common Stock, unless such conversion occurs as a result of a liquidation or certain transactions involving a change of control of Isis.

Isis contributed $12,015,000 to Orasense, Ltd. as the purchase price for 9,612 shares of Common Stock of Orasense. Orasense will subcontract with other parties, including Isis and Elan, to perform research and development with respect to its oral drug delivery platform. Until March 31, 2002, EIS will, at Isis' request, purchase convertible debt of Isis in an amount equal to Isis' share of budgeted funding for Orasense. The convertible debt will have a term of six years, bear interest at the rate of 12% and be convertible into Isis' Common Stock at a premium. Isis may prepay the convertible debt in cash or in Isis' Common

Stock. Isis will use the proceeds of the sale of the convertible debt to provide additional development funding to Orasense.

While Isis owns 80.1% of the outstanding common stock of Orasense, Elan and its subsidiaries have retained significant minority investor rights that are considered "participating rights" as defined in EITF 96-16. Therefore, Isis does not consolidate the financial statements of Orasense, but instead accounts for its investment in Orasense under the equity method of accounting. During the three month period ended March 31, 2000, Isis recognized $1,168,000 in contract revenues for research and development activities performed for Orasense Ltd. This amount is included as research and development revenues from affiliate for the related periods.

The results of operations of Orasense Ltd. for the three month period ended March 31, 2000 is as follows (in thousands):

	Three months ended March 31, 2000
Revenue	0
Research and Development expense	$3,114
Net Loss	$3,114

HEPASENSE

On January 14, 2000, Isis and Elan Corporation formed a new joint venture to develop an antisense drug, ISIS 14803, to treat patients chronically infected with the Hepatitis C virus (HCV). The new joint venture is called HepaSense and plans to develop and commercialize this novel therapeutic for HCV while investigating delivery of the therapeutic with Elan's proprietary MEDIPAD(R) Drug Delivery System, a disposable subcutaneous infusion device. ISIS 14803 began Phase I clinical trials in early 2000. Isis and Elan have each licensed technology to HepaSense.

In conjunction with the formation of HepaSense, EIS purchased 12,015 shares of Isis' Series B Preferred stock for $12,015,000. In April 2000, EIS purchased an additional 298,000 shares of Isis' common stock for $7,500,000. EIS will purchase an additional $7.5 million of common stock at a premium to Isis' market price upon completion of a mutually agreed milestone.

After June 30, 2002, the preferred stock (including accrued dividends) will be convertible at EIS' option, into shares of Isis' common stock at 125% of the 60-trading day average closing price of Isis' common stock ending two business days prior to June 30, 2002 (as adjusted for stock splits, stock dividends and the like). In the event of a liquidation of Isis or certain transactions involving a change of control of Isis, the agreement provides for automatic conversion of the preferred stock on terms similar to those set forth above.

Isis is not obligated to issue shares representing more than 19.99% of its then outstanding Common Stock upon conversion of the Preferred Stock if it would result in a violation of the rules of any securities market or exchange upon which the Common Stock is traded.

At any time until June 30, 2002, the holders of preferred stock may exchange their preferred stock with Isis for preferred shares of HepaSense, Ltd. held by Isis that represent 60.2% of the total outstanding preferred stock of HepaSense. The exchange right will terminate if the Isis Series B Convertible Preferred stock is converted into Isis' common stock, unless such conversion occurs as a result of a liquidation or certain transactions involving a change of control of Isis.

Isis contributed $12,015,000 to HepaSense as the purchase price for 6,001 shares of common stock of HepaSense and 3,612 shares of HepaSense preferred stock. Until July 14, 2002, EIS will, at Isis' request, purchase convertible debt of Isis in an amount equal to Isis' share of budgeted funding for HepaSense. The convertible debt will have a term of six years, bear interest at the rate of 12% and be convertible into Isis' common stock at a premium. Isis may prepay the convertible debt in cash or Isis' common stock. Isis will use the proceeds of the sale of the convertible debt to provide additional development funding to HepaSense.

While Isis owns 80.1% of the outstanding common stock of HepaSense, Elan and its subsidiaries have retained significant minority investor rights that are considered "participating rights" as defined in EITF 96-16. Therefore, Isis does not consolidate the financial statements of HepaSense, but instead accounts for its investment in HepaSense under the equity method of accounting.

The results of operations of HepaSense Ltd. for the three month period ended March 31, 2000 is as follows (in thousands):

	Three months ended March 31, 2000
Revenue	$ 0
Research and Development expense	$1,250
Net Loss	$1,250

3. FINANCING

On March 8, 2000, Isis sold 1,000,000 shares of our common stock to an institutional investor at a negotiated price of $27.25 per share. In addition, during the first quarter of 2000 we sold 1,551,614 shares of our common stock to Ridgeway Investment Limited at an average purchase price of $9.67 per share under the terms of the Common Stock Purchase Agreement filed as an exhibit to the prospectus dated December 6, 1999. The $9.67 per share average purchase price reflects the average trading prices of the common stock on the Nasdaq National Market during the respective drawdown periods.

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, 1999 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 few years. Our revenue comes from collaborative research and development agreements with pharmaceutical companies, research grants and interest income. The revenue from the collaborations increased the amount of research and development activity that Isis is able to fund and offset a portion of our research and development costs. During January 2000, Isis entered into an agreement with Elan Pharmaceuticals, an Irish Company, to form a joint venture to develop an antisense drug, ISIS 14803, to treat patients chronically infected with the Hepatitis C virus (HCV).

RESULTS OF OPERATIONS

Isis' revenue from collaborative research and development agreements was $4.1 million for the three months ended March 31, 2000, compared with $6.6 million for the same period in 1999. The revenue decrease was due primarily to the conclusion of development funding at December 1999 by Novartis for the cancer drugs ISIS 5132 and ISIS 3521 and Boehringer Ingelheim for ISIS 2302. The Company also had interest income totaling $0.9 million for the three months ended March 31, 2000, compared with $0.7 million for the same period in 1999. This increase in interest income was due primarily to higher average cash and investment balances and, in part to higher interest rates.

Research and development expenses were $13.2 million for the three months ended March 31, 2000, compared with $14.3 million for the same period in 1999. For both periods, research and development expenses were driven by the cost of preclinical and clinical activities to support the progress of drugs in clinical trials. The decrease in research and development expenses is directly related to the implementation of our restructuring plan.

General and administrative expenses decreased to $1.8 million for the quarter ended March 31, 2000, from $2.8 million for the same period in 1999. This decrease in general and administrative expense is primarily related to our restructuring activities.

The total cost of restructuring was recorded this quarter and totaled $1.6 million. This expense is comprised primarily of labor costs for our reduction in work force.

Interest expense was $3.1 million for the first quarter compared with $2.7 million for the same quarter last year. The increase is due primarily to accruing interest on our $40 million debt financing that was completed in 1997 and 1998. In this financing, payment of interest accrues for the first five years and no principal payments are due for 10 years. The increase in interest expense is also due to borrowings by Isis during 1999 and 2000 under a debt facility from Elan related to the OraSense joint venture to fund Isis' share of OraSense expenses. Of the $3.1 million of interest expense recognized in the first quarter of 2000, $2.3 million was accrued under the long-term debt agreements because it does not require current cash payment.

During the quarter ended March 31, 2000, Isis recorded a net loss applicable to common stock of $18.6 million, or $.56 per share, compared with $12.6 million, or $.46 per share, for the same period in 1999. The first quarter 2000 loss includes $1.2

million in joint venture revenue together with $3.5 million for Isis' equity in the loss of Orasense and HepaSense, the joint ventures. Isis' loss from operations was $12.6 million for the first quarter of 2000, compared to $10.6 million for the same period in 1999. The loss from operations in the first quarter of 2000 includes the $1.6 million restructuring costs described above. The increase in loss from operations is also related to the decrease in revenue during the first quarter 2000 as compared to the first quarter 1999. 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, 2000, Isis has earned approximately $180 million in revenue from contract research and development. Isis has also raised net proceeds of approximately $320 million from the sale of equity securities since it was founded. We have borrowed approximately $85 million under long-term debt arrangements to finance a portion of our operations.

As of March 31, 2000, Isis had cash, cash equivalents and short-term investments totaling $93.7 million and working capital of $85.0 million. In comparison, we had cash, cash equivalents and short-term investments of $52.8 million and working capital of $44.2 million as of December 31, 1999. The increases in cash and working capital are due primarily to the sale of 2.6 million shares of common stock to institutional investors and 1.4 million shares sold to employees under the company's stock option and stock purchase plans.

Isis' collaborative agreement with Boehringer Ingelheim provided a line of credit which was used to support the collaboration cell adhesion programs. As of March 31, 2000, the outstanding balance of this obligation was $22.6 million. In 1999 Isis reacquired the rights to Isis 2302 from Boehringer Ingelheim. Therefore, there will be no further draws against this line.

In 1997 and 1998, Isis borrowed a total of $40 million in private transactions. The loans bear interest at 14% per annum and must be repaid on November 1, 2007. The interest accrues 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 accrued 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, 2000 was $51.2 million.

As of March 31, 2000, our long-term obligations totaled $91.3 million, versus $87.3 million at December 31, 1999. The increase was due to the accrual of interest on the ten-year notes described above and the addition of $2.5 million in loans related to partnership agreements, including the Orasense joint venture. This increase was 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 our anticipated requirements for at least the next 24-36 months.

QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The Company is exposed to changes in interest rates primarily from its long-term debt arrangements and, secondarily, its investments in certain short-term investments. The Company invests its excess cash in highly liquid short-term investments that are typically held for the duration of the term of the respective instrument. The Company does not utilize derivative financial instruments, derivative commodity instruments or other market risk sensitive instruments, positions or transactions to manage exposure to interest rate changes. Accordingly, the Company believes that, while the securities the Company holds are subject to changes in the financial standing of the issuer of such securities, the Company is not subject to any material risks arising from changes in interest rates, foreign currency exchange rates, commodity prices, equity prices or other market changes that affect market risk sensitive instruments.

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

27.1 Financial Data Schedules

b. Reports on Form 8-K

On January 28, 2000, the Registrant filed the following report on Form 8-K:

Report dated January 14, 2000 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 exhibits 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 11, 2000	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 11, 2000	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, 2000 (Unaudited) and Condensed
Statements of Operations for the Three Months Ended March 31, 2000 (Unaudited)
and is qualified in its entirety by reference to such financial statements.

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3-MOS
DEC-31-2000
JAN-01-2000
MAR-31-2000
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