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 SECURITIES AND EXCHANGE COMMISSION  
 Washington, DC 20549  
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FORM 10-Q

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

For the quarterly period ended March 31, 1997

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  
 (State or other jurisdiction of  
 incorporation or organization)

33-0336973  
 (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)

NOT APPLICABLE  
 (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 of 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                      (2) YES X

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	26,353,117 shares
(Class)	(Outstanding at April 30, 1997)

EXHIBIT INDEX:        NO. 27 : FINANCIAL DATA SCHEDULE

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

ASSETS

	March 31, 1997 (Unaudited) -----	December 31, 1996 (Note) -----
Current assets:		
Cash and cash equivalents	\$ 26,249	\$ 37,082
Short-term investments	45,146	40,542
Prepaid expenses and other current assets	1,791	1,732
	-----	-----
Total current assets	73,186	79,356
Property, plant and equipment, net	17,791	15,334
Patent cost, net	6,393	6,157
Deposits and other assets	468	458
	-----	-----
	\$ 97,838	\$ 101,305
	=====	=====

LIABILITIES AND STOCKHOLDERS' EQUITY

Current liabilities:		
Accounts payable	\$ 2,434	\$ 2,362
Accrued payroll and related expenses	892	1,489
Accrued liabilities	3,908	2,763
Deferred contract revenues	13,837	10,204
Current portion of long-term debt and capital lease obligations	5,963	6,238
	-----	-----
Total current liabilities	27,034	23,056
Long-term debt and capital lease obligations, less current portion	19,817	19,864
Stockholders' equity:		
Common stock, \$.001 par value; 50,000,000 shares authorized, 26,336,000 shares and 26,201,000 shares issued and outstanding at March 31, 1997 and December 31, 1996, respectively	26	26
Additional paid-in capital	182,384	181,248
Unrealized gain on investments	198	178
Accumulated deficit	(131,621)	(123,067)
	-----	-----
Total stockholders' equity	50,987	58,385
	-----	-----
	\$ 97,838	\$ 101,305
	=====	=====

Note: The balance sheet at December 31, 1996 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,	
	1997	1996
	-----	-----
Revenue:		
Research and development revenue under collaborative agreements:	\$ 4,626	\$ 5,359
Interest Income	947	1,050
	-----	-----
	5,573	6,409
Expenses:		
Research and development	11,786	9,816
General and administrative	1,707	1,398
Interest expense	634	248
	-----	-----
	14,127	11,462
	-----	-----
Net Loss	\$ (8,554)	\$ (5,053)
	=====	=====
Net Loss per share	\$ (.33)	\$ (.20)
	=====	=====
Weighted average common shares	26,278	25,348
	=====	=====

See accompanying notes

ISIS PHARMACEUTICALS, INC.  
 CONDENSED STATEMENT OF CASH FLOWS  
 (in thousands)  
 (Unaudited)

	Three months ended	
	March 31,	
	1997	1996
	-----	-----
Cash used in operations:	\$ (3,711)	\$ (1,375)
Investing activities:		
Short-term investments	(4,604)	(21,994)
Property and equipment	(2,678)	(441)
Other assets	(268)	(242)
	-----	-----
Net cash used in investing activities	(7,550)	(22,677)
	-----	-----
Financing activities:		
Net proceeds from issuance of common stock	1,136	746
Principal payments on debt and capital lease obligations	(708)	(573)
	-----	-----
Net cash provided from financing activities	428	173
	-----	-----
Net decrease in cash and cash equivalents	(10,833)	(23,879)
Cash and cash equivalents at beginning of the period	37,082	46,463
	-----	-----
Cash and cash equivalents at end of period	\$ 26,249	\$ 22,584
	=====	=====
SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION:		
Interest paid	\$ 240	\$ 249
SUPPLEMENTAL DISCLOSURE OF NON-CASH INVESTING AND FINANCING ACTIVITIES:		
Additions to capital lease obligations for acquisitions of property, plant and equipment	\$ 386	\$ 1,238

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, 1997 and 1996 have been prepared on the same basis as the Company's audited financial statements for the year ended December 31, 1996. 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 of 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, 1996 included in the Company's Annual Report on Form 10-K filed with the Securities and Exchange Commission.

## 2. Accounting standard on earnings per share

In February 1997, the Financial Accounting Standards Board issued Statement No. 128, "Earnings per Share", which is required to be adopted on December 31, 1997. At that time, the Company will be required to change the method currently used to compute earnings per share and to restate all prior periods. Under the new requirements for calculating primary earnings per share, the dilutive effect of stock options will be excluded. The impact of Statement 128 on the calculation of earnings per share is not expected to be material.

## 3. Subsequent event

In April 1997, the Company entered into an agreement with a bank to borrow \$9.7 million. The proceeds of this loan were used to refinance the Company's existing real estate loans, which had an aggregate balance of \$6.6 million as of March 31, 1997, and provide funding for tenant improvements in a new 46,000 square foot building the Company began to occupy in the first quarter of 1997. The new loan bears interest at the prime rate plus 0.5 percent, will mature in March 2002 and requires payments of \$62,433 per month plus interest. The loan is secured by the real estate financed under this arrangement.

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 the Company's business and products and their projected prospects and qualities as well as the Company's relationship with its corporate partners. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that can be proven to be 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 projected in this Form 10-Q. As a result, the reader is cautioned not to 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, 1996 which is on file with the U.S. Securities and Exchange Commission, a copy of which is available from the Company.

Since its inception in January 1989, the Company has devoted substantially all of its resources to its research, drug discovery and development programs. The Company has been unprofitable since its inception and expects to incur additional operating losses for the next several years. The Company has entered into collaborative research and development agreements with pharmaceutical companies that generate revenue to augment the level of research and development activity and to offset portions of its research and development costs. To date, the Company has not received any significant revenue from the sale of products.

RESULTS OF OPERATIONS

The Company had contract revenue of \$4.6 million for the first quarter ended March 31, 1997, compared with \$5.4 million for the same period in 1996. The revenue decrease was primarily due to the fact that in the quarter ended March 31, 1996, concurrent with the execution of an expanded collaborative agreement with Novartis Limited, the Company recognized contract revenue totaling approximately \$1.9 million for work performed in 1995 under the terms of the expanded agreement. This decrease was partially offset by an increase in revenue from a collaborative agreement with Boehringer Ingelheim GmbH. The Company also had an interest income totaling \$0.9 million for the quarter compared with \$1.1 million for the same period in 1996. This decrease in interest income was primarily due to lower investment balances in the quarter ended March 31, 1997.

Research and development expenses increased 20 percent to \$11.8 million for the three months ended March 31, 1997 from \$9.8 million for the same period in 1996. This increase was attributable to an increase in preclinical and clinical development activities including the progression of compounds into more advanced and more expensive stages of clinical development. The Company expects that its development expenses will continue to increase as its current preclinical and clinical activities advance and additional preclinical and clinical studies are undertaken.

General and administrative expenses increased to \$1.7 million for the quarter ended March 31, 1997, from \$1.4 million for the same period in 1996. The Company expects that its general and administrative expenses will increase in the future in support of its expanding operations.

During the quarter ended March 31, 1997, the Company recorded a net loss of \$8.6 million, or \$.33 per share, compared with \$5.1 million, or \$.20 per share, for the same period in 1996. The Company expects that its operating losses will increase for the remainder of the fiscal year and beyond as its activities grow, and may fluctuate from quarter to quarter as a result of differences in the timing and composition of revenue earned and expenses incurred.

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

#### LIQUIDITY AND CAPITAL RESOURCES

Since its inception, the Company has financed its operations primarily through the sale of equity securities, raising net proceeds aggregating approximately \$180 million, as of March 31, 1997, from the private and public sale of such securities. The Company has also financed a portion of its operations through contract research revenue, portions of which are paid in advance of work being performed, offsetting the Company's cash usage for operations.

As of March 31, 1997, the Company had cash, cash equivalents and short-term investments totaling \$71.4 million and working capital of \$46.2 million. In comparison, the Company had cash, cash equivalents and short-term investments of \$77.6 million and working capital of \$56.3 million as of December 31, 1996. 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 Company had long-term debt and capital lease obligations at March 31, 1997 totaling \$25.8 million, versus \$26.1 million at December 31, 1996. The decrease was due to principal repayments on existing obligations, partially offset by additional capital lease financing. The Company expects that its capital lease obligations will increase over time to fund capital equipment acquisitions required for its expanding business. Lease lines will continue to be used by the Company to the extent that the terms thereof remain commercially attractive.

The Company expects to incur substantial additional research and development costs, including costs related to clinical trials, manufacturing costs, and marketing and distribution expenses, and expects losses to continue to increase as the Company's preclinical testing and clinical trial efforts expand. It is the Company's intention to seek additional collaborative research and development relationships with suitable potential corporate partners. There can be no assurance that any agreements resulting from these discussions will successfully reduce the Company's funding requirements, and arrangements with collaborative partners or others may require the Company to relinquish rights to certain of its technologies, product candidates or products. Additional equity or debt financings will be required, and there can be no assurance that these funds will be available on favorable terms,

if at all. If additional funds are raised by issuing equity securities, further dilution to then existing stockholders may result.

The Company anticipates that its existing available cash, cash equivalents and short-term investments, combined with anticipated interest income and contract revenues, will be adequate to satisfy its anticipated capital requirements for approximately two years. The Company's future capital requirements will depend on many factors, including continued scientific progress in its research, drug discovery and development programs; the magnitude of these programs and progress with preclinical and clinical trials; the time and costs involved in obtaining regulatory approvals; the cost involved in filing, prosecuting and enforcing patent claims; competing technological and market developments; changes in the existing collaborative research and development relationships and the ability of the Company to establish additional research and development arrangements; and the cost of manufacturing scale-up and effective commercialization activities and arrangements. If adequate funds are not available, the Company may be required to significantly curtail one or more of its research, drug discovery or development programs.

Uncertainties associated with the length and expense of preclinical and clinical testing of any of the Company's products could greatly increase the cost of development of such product and affect the timing of anticipated revenue from product sales, and failure by the Company to obtain regulatory approval for any product will preclude its commercialization. In addition, the failure by the Company to obtain patent protection for its products may make certain of its products commercially unattractive.

## 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

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None.

## b. Reports on Form 8-K

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The Company filed no reports on Form 8-K during the quarter ended March 31, 1997.

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.

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(Registrant)

Date: May 7, 1997

By: /S/ STANLEY T. CROOKE

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

Date: May 7, 1997

By: /S/ B. LYNNE PARSHALL

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

EXHIBIT INDEX

Exhibit No.  
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Description  
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Financial Data Schedule

This schedule contains summary financial information derived from the Company's Condensed Balance Sheet as of March 31, 1997 (Unaudited) and Condensed Statements of Operations for the Three Months Ended March 31, 1997(Unaudited) and is qualified in its entirety by the reference to such financial statements.

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3-MOS		
	DEC-31-1996	
	JAN-01-1997	
	MAR-31-1997	
		26,249
	45,146	
	0	
	0	
	73,186	
		17,791
	0	
	97,838	
27,034		
		19,817
0		
		0
		26
	50,961	
97,838		
		0
	5,573	
		0
	0	
	13,493	
	0	
	634	
	(8,554)	
		0
(8,554)		
	0	
	0	
		0
	(8,554)	
	(.33)	
	(.33)	