SECURITIES AND EXCHANGE COMMISSION WASHINGTON, DC 20549

FORM 10-Q/A (Amendment No. 1)

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For

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the	quarterly pe	riod ended	June	30,	2000					

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[] 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)

(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 38,448,777 SHARES (Class) (Outstanding at July 31, 2000)

ISIS PHARMACEUTICALS, INC. FORM 10-Q INDEX

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SIGNATURES

* N/A

Explanatory Note: This amendment to form 10-Q is filed solely to amend Part I, Item 1, Note 3 to Financial Statements, and Part II Item 6(a), Exhibits.

ISIS PHARMACEUTICALS, INC. CONDENSED BALANCE SHEETS (In Thousands)

ASSETS

Current assets: Cash and cash equivalents 62,043 35,296 Short-term investments 58,291 17,543 Contract revenue receivable 4,644 5,429 Prepald expenses and other current assets 1,219 929 Total current assets 16,188 59,197 Property, plant and equipment, net 22,596 23,945 Patent costs, net 11,886 11,259 East of the costs of		June 30, 2000	December 31, 1999
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Cash and cash equivalents 58,29 1,7,543 Short-term investments 58,29 1,7,543 Contract revenue receivable 4,644 5,429 Prepaid expenses and other current assets 1,210 929 Total current assets 126,188 59,197 Property, plant and equipment, net 22,596 23,945 Patent costs, net 11,886 11,250 Deposits and other assets 1,577 1,724 Investment in joint ventures 14,767 6,991 LIABILITIES AND STOCKHOLDERS' EQUITY Current liabilities: Accounts payable 1,134 3,148 Accounts payable and related expenses 2,344 1,215 Accounts payable and related expenses 2,344 1,215 Accounts payable and related expenses 2,344 1,215 Accurated liabilities 3,219 2,553 Deferred contract revenues 2,344 1,215 Current portion of long term debt and capital lease obligations, less current portion 94,504 87,254	Current assets:		
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Accretion of Series A Preferred stock dividends Series B Convertible Exchangeable 5% Preferred stock, \$.001 par value; 16,620 shares authorized, 12,015 shares and no shares issued and outstanding at June 30, 2000 and December 31, 1999, respectively Accretion of Series B Preferred stock dividends Common stock, \$.001 par value; 50,000,000 shares authorized, 38,375,438 shares and 31,613,000 shares issued and outstanding at June 30, 2000 and December 31, 1999, respectively 38 Additional paid-in capital Unrealized gain (loss) on investments (26) Accumulated deficit (289,978) (256,761) Total stockholders' equity 69,758 869	Series A Convertible Exchangeable 5% Preferred stock, \$.001 par value; 15,000,000 shares authorized, 120,150 shares issued		
outstanding at June 30, 2000 and December 31, 1999, respectively Accretion of Series B Preferred stock dividends Common stock, \$.001 par value; 50,000,000 shares authorized, 38,375,438 shares and 31,613,000 shares issued and outstanding at June 30, 2000 and December 31, 1999, respectively Additional paid-in capital Unrealized gain (loss) on investments Accumulated deficit Total stockholders' equity 12,015 277 277 277 278 277 279 277 279 277 28 28 29 20 20 20 20 20 20 20 20 20 20 20 20 20	Accretion of Series A Preferred stock dividends Series B Convertible Exchangeable 5% Preferred stock, \$.001 par	•	•
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Common stock, \$.001 par value; 50,000,000 shares authorized, 38,375,438 shares and 31,613,000 shares issued and outstanding at June 30, 2000 and December 31, 1999, respectively Additional paid-in capital Unrealized gain (loss) on investments Accumulated deficit Total stockholders' equity 38,375,438 shares 38 32 45,192 (26) (29) (29) (256,761)	· · · · · · · · · · · · · · · · · · ·	•	
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Additional paid-in capital 334,687 245,192 Unrealized gain (loss) on investments (26) (29) Accumulated deficit (289,978) (256,761) Total stockholders' equity 69,758 869		38	32
Unrealized gain (loss) on investments Accumulated deficit Total stockholders' equity (26) (29) (289,978) (256,761) 69,758 869	Additional paid-in capital	334,687	
Total stockholders' equity 69,758 869		(26)	
	Accumulated deficit	(289,978)	(256,761)
Total liabilities and stockholders' equity 177,024 103,107	Total stockholders' equity	69,758	869
	Total liabilities and stockholders' equity	177,024	103,107

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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 Per Share Data)

	Three months ended, June 30, 2000 1999		Six months June	ended, 30,
	2000	1999	June 2000	1999
Revenue: Research and development revenues under collaborative agreements	\$4,224		\$7,110	\$12.391
Research and development revenues from joint ventures	,	,	3,929	,
Total Revenue			11,039	
Expenses: Research and development General and administrative Restructuring activities	12,746 2,414 -	2,762	25,985 4,238 1,608	5,577
Total Operating Expenses	15,160	19,205	31,831	36,336
(Loss) from operations			(20,792)	(22,552)
Equity in loss of joint ventures Interest income Interest expense	(4,594) 1,596 (3,129)	(2,277) 551 (2,800)	(8,089) 2,488 (6,236)	(2,277) 1,207 (5,505)
Net loss			(32,629)	
Accretion of dividends on preferred stock	(306)	(117)	(587)	(117)
Net loss applicable to common stock	` ' '	` ' '	(33,216)	` ' '
Basic and diluted net loss per share	(' /	(\$0.59)	(' '	(\$1.06)
Shares used in computing basic and diluted net loss per share	36,979		35,021	

See accompanying notes.

ISIS PHARMACEUTICALS, INC. CONDENSED STATEMENTS OF CASH FLOWS (In Thousands) (Unaudited)

	Six Months June :	
	2000	1999
Cash used in operations	(19,385)	(28,351)
Investing activities: Short-term investments Property and equipment Other assets Investment in joint venture	(40,745) (924) (876) (15,865)	22,632 (894) (1,423) (12,015)
Net cash used for investing activities		8,300
Financing activities: Net proceeds from issuance of equity securities Proceeds from long-term borrowings Principal payments on debt and capital lease obligations	3,850 (1,411)	28,144 (1,338)
Net cash provided from financing activities	104,542	26,806
Net increase (decrease) in cash and cash equivalents	26,747	6,755
Cash and cash equivalents at beginning of period	35,296	27,618
Cash and cash equivalents at end of period		34,373
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION: Interest paid	530	1,654
SUPPLEMENTAL DISCLOSURES OF NON-CASH INVESTING AND FINANCING ACTIVITIES: Additions to long-term debt obligations for acquisitions of property, plant and equipment Conversion of preferred stock dividends into preferred stock	- 308	2,071 -

See accompanying notes.

ISIS PHARMACEUTICALS, INC.

NOTES TO FINANCIAL STATEMENTS

BASIS OF PRESENTATION

The unaudited interim financial statements for the six month periods ended June 30, 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 ISIS 104838, an antisense oligonucleotide to inhibit TNF-(alpha), 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 a portion of 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.

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 six month period ended June 30, 2000, Isis recognized \$2,490,566 in contract revenues for research and development activities performed for Orasense Ltd. This amount is included as research and development revenues from joint ventures for the related periods.

The results of operations of Orasense Ltd. for the six month period ended June 30, 2000 is as follows (in thousands):

	_	MONTHS END E 30, 2000	
Revenue Research and Development expense Net Loss	\$ \$ \$	6,151 6,151	

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-Registered Trademark- 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, Elan International Services, Ltd. ("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. During the six month period ended June 30, 2000, Isis recognized \$1,439,126 in contract revenues for research and development activities performed for HepaSense Ltd. This amount is included as research and development revenues from joint ventures for the related periods.

The results of operations of HepaSense Ltd. for the six month period ended June 30, 2000 is as follows (in thousands):

STX	MONTHS	ENDED
OIN	IIOIVIIIO	LIVELD

JUNE 30, 2000

Revenue Research and Development expense	\$ 3,939
Net Loss	\$ 3,939

AGOURON

In June 2000, Ibis Therapeutics ("Ibis"), a division of Isis Pharmaceuticals, Inc. and Agouron Pharmaceuticals, Inc., a Pfizer Company, entered into a collaboration for the discovery and development of small molecule drugs against certain RNA targets in an undisclosed therapeutic area. Using Ibis' proprietary technology and Agouron's expertise in small molecule drug discovery, the collaboration will focus on discovering drugs that bind to RNA. Agouron will fund collaborative research, pay an upfront technology access fee and make milestone payments totaling \$37 million for the first product. In addition, Agouron will develop and commercialize drugs discovered by the collaboration and will pay Isis royalties on the sales of drugs.

FINANCING

Over the six months ended June 30, 2000, Isis sold 2,939,460 shares of its common stock to institutional investors at negotiated prices of \$10.45 per share to \$27.25 per share. In addition, over the six months ended June 30, 2000 the company sold 1,997,879 shares of its common stock to Ridgeway Investment Limited at prices ranging from an average of \$7.57 per share to \$14.45 per share under the terms of the Common Stock Purchase Agreement filed as an exhibit to the prospectus dated December 6, 1999. The per share average purchase prices reflect the average trading prices of the common stock over a period of time less a discount from 4.5% to 5.875%.

a. Exhibits

- 3.1 Amended and Restated Certificate of Incorporation.(1)
- 3.2 Bylaws.(1)
- 3.3 Certificate of Designation of the Series A Convertible Preferred Stock.(2)
- 3.4 Certificate of Designation of the Series B Convertible Preferred Stock.(3)
- 4.1 Reference is made to Exhibits 3.1, 3.2, 3.3 and 3.4.
- 4.2 Specimen Common Stock Certificate.(1)
- 4.3 Specimen Series A Preferred Stock Certificate.
- 4.4 Specimen Series B Preferred Stock Certificate.
- 4.5 Purchase Agreement for 14% Senior Subordinated Discount Notes due November 1, 2001 and Warrants for Common Stock dated October 24, 1997 (with certain confidential information deleted).(4)
- 4.6 First Supplement to Purchase Agreement for 14% Senior Subordinated Discount Notes due November 1, 2001 and Warrants for Common Stock dated May 1, 1998 (with certain confidential information deleted).(5)
- 4.7 Registration Rights Agreement dated April 20, 1999 among Registrant, Elan International Services, Ltd., and Orasense, Ltd.(6)
- 4.8 Registration Rights Agreement dated January 14, 2000 among Registrant, Elan International Services, Ltd., and Hapasense, Ltd.(7)
- 4.9 Voting Rights Agreement among the Registrant, Novartis and Dr. Cooke, dated November 9, 1990.(1)
- 10.33 Agreement between Registrant and Agouron Pharmaceuticals dated June 9, 2000 (with certain confidential information deleted).*
- 27.1 Financial Data Schedules*
- (1) Filed as an exhibit to the Registrant's Registration Statement on Form S-1 (No. 33-39640) or amendments thereto and incorporated herein by reference.
- (2) Filed as an exhibit to the Registrant's Registration Statement on Form S-3 (No. 333-71911) or amendments thereto and incorporated herein by reference.
- (3) Filed as an exhibit to the Registrant's 8-K dated as of January 8, 2000 and incorporated herein by reference.
- (4) Filed as an exhibit to the Registrant's Annual Report on Form 10-K for the year ended December 31, 1997, and incorporated herein by reference.
- (5) Filed as an exhibit to the Registrant's Quarterly Report on Form 10-Q for the quarter ended June 30, 1998 and incorporated herein by reference.
- (6) Filed as an exhibit to the Registrant's report on Form 8-K dated April 20, 1999 and incorporated herein by reference.
- (7) Filed as an exhibit to the Registrant's report on Form 8-K dated January 28, 2000 and incorporated herein by reference.
- * Previously filed.
 - b. Reports on Form 8-K

Not applicable

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: August 29, 2000

By: /S/ B. LYNNE PARSHALL

B. Lynne Parshall Executive Vice President and Chief Financial Officer (Duly Authorized Officer and Principal Financial and Accounting Officer) FRONT

NUMBER *SHARES*

INCORPORATED UNDER THE LAWS OF THE STATE OF DELAWARE On March 25, 1991

ISIS PHARMACEUTICALS, INC. Series A Convertible Preferred Stock, par value \$.001

	is the record holder of) Shares of the Series
A Convertible Preferred Stock, par value \$.001, of transferable only on the books of the Corporation person or by duly authorized attorney, upon surreproperly endorsed or assigned.	of ISIS PHARMACEUTICALS, INC. n by the holder hereof, in
A statement of the rights, preferences, privilege to or imposed upon the respective classes or serior corporation and upon holders thereof as establish incorporation or by any Certificate of Designation number of shares constituting each series and the be obtained by any stockholder upon request and a principal office of the Corporation.	ies of shares of stock of the hed by the Certificate of on of Preferences, and the e designations thereof, may
IN WITNESS WHEREOF, the Corporation has caused the by its duly authorized officers this day	
SECRETARY	PRESIDENT

BACK

FOR VALUE RECEIVED,	hereby sell, assign and
transfer unto	
the within named Corporation, represented in the control of the co	Shares of the Preferred Stock of ented by the within Certificate and do
	of said Preferred Stock on the books of e provisions of the By-Laws thereof, with remises.
Dated	A.D
In Presence of:	

Notice: The signature to this assignment must strictly correspond with the name as written upon the face of the Certificate in every particular and without alteration or enlargement or any change whatever.

FRONT

NUMBER *SHARES*

INCORPORATED UNDER THE LAWS OF THE STATE OF DELAWARE On March 25, 1991

ISIS PHARMACEUTICALS, INC. Series B Convertible Preferred Stock, par value \$.001

THIS CERTIFIES THAT	_ is the record holder of
) Shares of the Series
B Convertible Preferred Stock, par value \$.001, of I transferable only on the books of the Corporation by person or by duly authorized attorney, upon surrended properly endorsed or assigned.	ISIS PHARMACEUTICALS, INC. y the holder hereof, in
A statement of the rights, preferences, privileges at or imposed upon the respective classes or series Corporation and upon holders thereof as established Incorporation or by any Certificate of Designation on number of shares constituting each series and the debe obtained by any stockholder upon request and with principal office of the Corporation.	of shares of stock of the by the Certificate of of Preferences, and the esignations thereof, may
IN WITNESS WHEREOF, the Corporation has caused this by its duly authorized officers this day of	
SECRETARY	PRESIDENT

BACK

FOR VALUE RECEIVED,	hereby sell, assign and	
transfer unto		
	_ Shares of the Preferred Stock of	
the within named Corporation, represented by hereby irrevocably constitute and appoint		
Attorney to transfer the said shares of said the said Corporation, pursuant to the provis full powers of substitution in the premises.	sions of the By-Laws thereof, with	
Dated	A.D	
		_
In Presence of:		

Notice: The signature to this assignment must strictly correspond with the name as written upon the face of the Certificate in every particular and without alteration or enlargement or any change whatever.