

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-Q

(MARK ONE)

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

For the quarterly period ended June 30, 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 33-0336973
(State or other jurisdiction of (I.R.S. Employer Identification No.)
incorporation or organization)

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 No (2) Yes 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 26,487,113 shares
(Class) (Outstanding at July 30, 1997)

EXHIBIT INDEX: Located at page number 12.

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ASSETS	June 30, 1997 ----- (Unaudited)	December 31, 1996 ----- (Note)
Current assets:		
Cash and cash equivalents	\$ 35,851	\$ 37,082
Short-term investments	34,745	40,542
Prepaid expenses and other current assets	1,975	1,732
	-----	-----
Total current assets	72,571	79,356
Property, plant and equipment, net	18,485	15,334
Patent costs, net	6,974	6,157
Deposits and other assets	1,027	458
	-----	-----
	\$ 99,057	\$ 101,305
	=====	=====
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	\$ 1,381	\$ 2,362
Accrued payroll and related expenses	1,251	1,489
Accrued liabilities	3,588	2,763
Deferred contract revenues	15,658	10,204
Current portion of long term debt and capital lease obligations	1,605	6,238
	-----	-----
Total current liabilities	23,483	23,056
Long-term debt and capital lease obligations, less current portion	33,526	19,864
Stockholders' equity:		
Common stock, \$.001 par value; 50,000,000 shares authorized, 26,446,000 shares and 26,201,000 shares issued and outstanding at June 30, 1997 and December 31, 1996, respectively	26	26
Additional paid-in capital	182,907	181,248
Unrealized gain on investments	162	178
Accumulated deficit	(141,047)	(123,067)
	-----	-----
Total stockholders' equity	42,048	58,385
	-----	-----
	\$ 99,057	\$ 101,305
	=====	=====

Note: The balance sheet at December 31, 1996 has been derived from the audited financial statements at that date.

See accompanying notes.

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

	Three months ended June 30,		Six months ended June 30,	
	----- 1997	----- 1996	----- 1997	----- 1996
Revenues:				
Research and development revenue under collaborative agreements	\$ 5,793	\$ 4,719	\$ 10,419	\$ 10,078
Interest income	766	1,011	1,713	2,061
	-----	-----	-----	-----
Total Revenues	6,559	5,730	12,132	12,139
Expenses:				
Research and development	13,374	11,212	25,160	21,028
General and administrative	2,054	1,601	3,761	2,999
Interest expense	557	238	1,191	486
	-----	-----	-----	-----

	15,985	13,051	30,112	24,513
	-----	-----	-----	-----
Net loss	\$ (9,426)	\$ (7,321)	\$ (17,980)	\$ (12,374)
	=====	=====	=====	=====
Net loss per share	\$ (.36)	\$ (.29)	\$ (.68)	\$ (.49)
	=====	=====	=====	=====
Weighted average common shares	26,381	25,459	26,330	25,404
	=====	=====	=====	=====

See accompanying notes.

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

	Six months ended June 30,	
	----- 1997 -----	----- 1996 -----
Cash used in operations:	\$ (11,698)	\$ (9,172)
Investing activities:		
Short-term investments	5,797	(12,107)
Property and equipment	(3,856)	(802)
Other assets	(1,492)	(18)
	-----	-----
Net cash provided from (used in) investing activities	449	(12,927)
	-----	-----
Financing activities:		
Net proceeds from issuance of common stock	1,659	2,316
Proceeds from long-term borrowings	11,378	--
Principal payments on debt and capital lease obligations	(3,019)	(1,160)
	-----	-----
Net cash provided from financing activities	10,018	1,156
	-----	-----
Net decrease in cash and cash equivalents	(1,231)	(20,943)
Cash and cash equivalents at beginning of period	37,082	46,463
	-----	-----
Cash and cash equivalents at end of period	\$ 35,851	\$ 25,520
	=====	=====
SUPPLEMENTAL DISCLOSURES OF CASH FLOW INFORMATION:		
Interest paid	\$ 1,080	\$ 486
SUPPLEMENTAL DISCLOSURES OF NON-CASH INVESTING AND FINANCING ACTIVITIES		
Additions to capital lease obligations for acquisitions of property, plant and equipment	\$ 670	\$ 1,294

See accompanying notes.

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ISIS PHARMACEUTICALS, INC.
NOTES TO FINANCIAL STATEMENTS

1. BASIS OF PRESENTATION

The unaudited interim financial statements for the three and six month periods ended June 30, 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 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, 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 July 1997, the Company entered into an agreement with CIBA Vision Corporation (a Novartis company) granting CIBA Vision exclusive worldwide distribution rights for fomivirsen (ISIS 2922). Under the terms of the agreement, the Company will receive \$20 million in a pre-commercial fee and milestones through the time of regulatory approval in the U.S. and Europe. In the third quarter of 1997, \$5 million of the pre-commercial fees and milestones will be received and recognized as revenue under collaborative agreements. The Company will manufacture and sell fomivirsen to CIBA Vision at a price that will allow the Company and CIBA Vision to share the commercial value of the product. CIBA Vision will market and sell fomivirsen worldwide and will be responsible for regulatory approvals outside of the U.S. and Europe. Once regulatory approvals are obtained, CIBA Vision will hold the registrations. Additionally, CIBA Vision receives the option to acquire the exclusive license to market and distribute a second generation antisense compound to treat CMV retinitis (ISIS 13312) which is currently in preclinical development by the Company.

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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, and the Company's relationships with its corporate partners. Such statements are subject to certain risks and uncertainties, particularly those inherent in both the process of discovering, developing and commercializing safe and effective drugs, 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 drug 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 \$5.8 million for the second quarter and \$10.4 million for the six month period ended June 30, 1997, compared with \$4.7 million and \$10.1 million, respectively, for the same periods in 1996. The revenue increase was primarily due to the growing scope of activities related to collaborative agreements with Novartis Pharma AG (formally Ciba-Geigy Limited) and Boehringer Ingelheim International GmbH. The Company also had interest income totaling \$0.8 million for the quarter and \$1.7 million for the six month period compared with \$1.0 million and \$2.1 million for the same periods in 1996. This decrease in interest income was primarily due to lower investment balances in the quarter ended June 30, 1997.

Research and development expenses increased to \$13.4 million for the three months and \$25.2 million for the six months ended June 30, 1997 from \$11.2 million and \$21.0 million for the same periods in 1996. This increase was attributable to an increase in preclinical and clinical development activities including compounds advancing into more expensive stages of clinical development. The Company expects that its development expenses will continue to increase as its current preclinical and clinical compounds advance and preclinical and clinical studies on additional compounds are undertaken.

General and administrative expenses increased to \$2.1 million for the quarter and \$3.8 million for the six months ended June 30, 1997, from \$1.6 million and \$3.0 million for the same periods 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 June 30, 1997, the Company recorded a net loss of \$9.4 million, or \$0.36 per share, compared with \$7.3 million, or \$0.29 per share, for the same period in 1996. During the six-month period ended June 30, 1997, the Company's net loss amounted to \$18.0 million, or \$0.68 per share, compared to \$12.4 million, or \$0.49 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.

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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 June 30, 1997, from the private and public sale of such securities. The Company has also financed a portion of its operations through contract research and development revenue, portions of which were paid in advance of work being performed, offsetting the Company's cash usage for operations.

As of June 30, 1997, the Company had cash, cash equivalents and short-term investments totaling \$70.6 million and working capital of \$49.1 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 resulted from the funding of operating losses, investments in capital equipment and principal payments on debt and capital lease obligations, offset in part, by an additional \$6.4 million advance under a line of credit made available to the Company by Boehringer Ingelheim.

The Company had long-term debt and capital lease obligations at June 30, 1997 totaling \$35.1 million, versus \$26.1 million at December 31, 1996. This increase, which was partially offset by principal repayments on existing obligations, was due to additional capital lease financing and a \$6.4 million borrowing under a line of credit with Boehringer Ingelheim. In addition, two new term loans totaling \$9.7 million were obtained from a bank to refinance \$6.5 million in existing notes secured by real property, and to fund facilities expansion. 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 terms thereof remain commercially attractive.

The Company expects to incur substantial additional research and development costs, including costs related to clinical trials, manufacturing, marketing and distribution and other capital expansion, 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 costs 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.

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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

(a) The Company held its Annual Meeting of Stockholders on June 6, 1997.

(b) Christopher F. O. Gabrieli, Alan C. Mendelson, J.D. and William R. Miller were elected to serve as directors for a three-year term and until their successors are duly elected and qualified.

Votes in Favor

Votes Withheld

Christopher F.O. Gabrieli	24,625,756	71,699
Alan C. Mendelson	24,624,244	73,211
William R. Miller	24,627,598	69,857

Other directors whose terms of office continued after the Annual Meeting were as follows: Stanley T. Crooke, M.D., Ph.D., Daniel L. Kisner, M.D., Mark B. Skaletsky, Larry Soll, Ph.D., Joseph H. Wender and Burkhard Blank, M.D.

(c) The following item was approved at the Annual Meeting:

The selection of Ernst & Young LLP as independent auditors of the Company for its fiscal year ending December 31, 1997.

Votes in favor:	24,632,561
Votes withheld:	37,868
Abstentions:	27,026

ITEM 5. OTHER INFORMATION

Not applicable.

ITEM 6. EXHIBITS AND REPORTS ON FORM 8-K

a. Exhibits

The following documents are exhibits to this 10-Q:

- 10.1 Revised form of Supplemental Stock Option Agreement under Registrant's 1992 Non-Employee Directors' Stock Option Plan.
- 10.2 Agreement between the Registrant and CIBA Vision Corporation dated July 10, 1997 (with certain confidential information deleted).

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- 10.3 Imperial Bank Note Secured by Deed of Trust dated March 24, 1997 in the amount of \$6,000,000; together with the related Deed of Trust and Assignment of Rents dated March 24, 1997.
- 10.4 Imperial Bank Note Secured by Deed of Trust dated March 24, 1997 in the amount of \$3,706,620; together with the related Deed of Trust and Assignment of Rents dated March 24, 1997.

b. Reports on Form 8-K

The Company filed no reports on Form 8-K the quarter ended June 30, 1997.

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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 12, 1997

By: /S/ STANLEY T. CROOKE

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

Date: August 12, 1997

By: /S/ B. LYNNE PARSHALL

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

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ISIS PHARMACEUTICALS, INC.
FORM 10-Q

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10.4	Imperial Bank Note Secured by Deed of Trust dated March 24, 1997 in the amount of \$3,706,620; together with the related Deed of Trust and Assignment of Rents dated March 24, 1997.	90

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EXHIBIT 10.1

Revised form of Supplemental Stock Option Agreement under Registrant's
1992 Non-Employee Directors' Stock Option Plan

Optionee: _____ Date: _____

ISIS PHARMACEUTICALS, INC.
SUPPLEMENTAL STOCK OPTION AGREEMENT

Isis Pharmaceuticals, Inc. (the "Company"), pursuant to its 1992 Non-Employee Directors' Stock Option Plan (the "Plan") has this day granted to the undersigned optionee, an option to purchase shares of the common stock of the Company ("Common Stock") as described herein. This option is not intended to qualify and will not be treated as an "incentive stock option" within the meaning of Section 422 of the Internal Revenue Code of 1986, as amended from time to time (the "Code"). This option is subject to all of the terms and conditions as set forth herein and on Attachment I hereto, which is incorporated herein in its entirety.

Number of Shares Subject to Option: _____

VESTING SCHEDULE:

Number of Shares (installment)	Date of Earliest Exercise (vesting)
_____	_____
_____	_____
_____	_____

Exercise Price Per Share: _____ 1 Expiration Date: _____ 2

Isis Pharmaceuticals, Inc.

By: _____ Optionee: _____

Duly authorized on behalf of
the Board of Directors Address:

OPTIONEE:

Acknowledges receipt of the option as described herein and the attachments referenced therein and understands that all rights and liabilities with respect to this option are set forth in the option and the Plan; and acknowledges that as of the date of grant of this option, it sets forth the entire understanding between the optionee and the Company regarding the acquisition of stock in the Company and supersedes all prior oral and written agreements on that subject.

- 1 Not less than 100% of the fair market value of the Common Stock on the date of grant of this option.
- 2 Less than 10 years from the date of grant of this option.

ATTACHMENT I

TERMS OF SUPPLEMENTAL STOCK OPTION

The details of your option are as follows:

- 1. The total number of shares of Common Stock subject to this option is set

forth on the first page of the Supplemental Stock Option Agreement. Subject to the limitations contained herein, this option shall be exercisable with respect to each installment indicated in the Vesting Schedule set forth on the first page of the Supplemental Stock Option Agreement on or after the date of vesting applicable to such installment.

2. (i) The Exercise Price of this option is set forth on the first page of Supplemental Stock Option Agreement.

(ii) Upon exercise of all or any part of each installment which has become exercisable by you, payment of the exercise price per share is due, in full, either (a) in cash (including check), or (b) by delivery of shares of Common Stock that have been held for the requisite period necessary to avoid a charge to the Company's reported earnings and valued at the fair market value on the date of exercise, or (c) by a combination of such methods of payment.

3. The minimum number of shares with respect to which this option may be exercised at any one time is 1,000, unless the number of shares available for exercise (that is, the remaining vested shares pursuant to paragraph 1) equals less than 1,000 shares, in which case the minimum number of shares exercised must equal the number of shares then vested.

4. Notwithstanding anything to the contrary contained herein, this option may not be exercised unless the shares issuable upon exercise of this option are then registered under the Securities Act of 1933, as amended (the "Act"), or, if such shares are not then so registered, the Company has determined that such exercise and issuance would be exempt from the registration requirements of the Act.

5. The term of this option commences on the date hereof and terminates on the Expiration Date (which date shall be no more than 10 years from the date this option is granted). This option will terminate prior to the expiration of its term as follows: 3 months after the termination of your service as a director with the Company or an affiliate of the Company (as defined in the Plan) for any reason or for no reason unless:

(a) such termination of service is due to your permanent and total disability (within the meaning of Section 422(c)(6) of the Code), in which event the option will terminate on the earlier of the Expiration Date or 1 year following such termination of service; or

(b) such termination of service is due to your death, in which event the option will terminate on the earlier of the Expiration Date or 18 months after your death; or

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(c) during any part of such 3 month period the option is not exercisable solely because of the condition set forth in paragraph 4 above, in which event the option will not terminate until the earlier of the Expiration Date or until it will have been exercisable for an aggregate period of 3 months after the termination of service; or

(d) exercise of the option within 3 months after termination of your service with the Company or an affiliate would result in liability under Section 16(b) of the Securities Exchange Act of 1934, in which case the option will terminate on the earlier of the Expiration Date, the 10th day after the last date upon which exercise would result in such liability or 6 months and 10 days after the termination of your service to the Company or an affiliate.

However, this option may be exercised following termination of your service as a non-employee director to the Company or an affiliate of the Company (as defined in the Plan) only as to that number of shares as to which it was exercisable on the date of termination under the provisions of paragraph 1 of this option.

6. (i) This option may be exercised, to the extent specified above, by delivering a notice of exercise (in a form designated by the Company) together with the exercise price to the Secretary of the Company, or to such other person as the Company may designate, during regular business hours, together with such additional documents as the Company may then require pursuant to subparagraph

6(f) of the Plan.

(ii) By exercising this option you agree that the Company may require you to enter an arrangement providing for the cash payment by you to the Company of any tax withholding obligation of the Company arising by reason of: the exercise of this option; the lapse of any substantial risk of forfeiture to which the shares are subject at the time of exercise; or the disposition of shares acquired upon such exercise.

7. This option is not transferable except by will or by the laws of descent and distribution, and is exercisable during your lifetime only by you; notwithstanding the foregoing, you may transfer part or all of this option to any of the following:

(i) your spouse, children (by birth or adoption), stepchildren, grandchildren, or parents;

(ii) a trust or other entity established solely for your benefit or the benefit of your spouse, children (by birth or adoption), stepchildren, grandchildren, or parents for estate planning purposes; or,

(iii) an organization which is exempt from taxation under Section 501(c)(3) of the Code or to which tax-deductible charitable contributions may be made under Section 170 of the Code.

Furthermore, you may, by delivering written notice to the Company, in a form satisfactory to the Company, designate a third party who, in the event of your death, will thereafter be entitled to exercise the option.

8. This option is not an employment contract and nothing in this option shall be deemed to create in any way whatsoever any obligation on your part to continue as a director of the Company.

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9. Any notices provided for in this option or the Plan shall be given in writing and shall be deemed effectively given upon receipt or, in the case of notices delivered by the Company to you, 5 days after deposit in the United States mail, postage prepaid, addressed to you at the address specified below or at such other address as you hereafter designate by written notice to the Company.

10. This option is subject to all the provisions of the Plan, a copy of which is attached hereto and its provisions are hereby made a part of this option, including without limitation the provisions of paragraph 6 of the Plan relating to option provisions, and is further subject to all interpretations, amendments, rules and regulations which may from time to time be promulgated and adopted pursuant to the Plan. In the event of any conflict between the provisions of this option and those of the Plan, the provisions of the Plan shall control.

Attachments:

1992 Non-Employee Directors' Stock Option Plan
Notice of Exercise

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EXHIBIT 10.2

Agreement between Registrant and CIBA Vision Corporation dated July 10, 1997
(with certain confidential information deleted).

CONFIDENTIAL TREATMENT REQUESTED UNDER 17 C.F.R. SECTIONS 200.80(b)(4), 200.83
AND 240.24b-2. * INDICATES OMITTED MATERIAL THAT IS THE SUBJECT OF A
CONFIDENTIAL TREATMENT REQUEST THAT IS FILED SEPARATELY WITH THE COMMISSION.

AGREEMENT

Between
ISIS PHARMACEUTICALS, INC.
and
CIBA VISION CORPORATION

JULY 10, 1997

AGREEMENT

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AGREEMENT

THIS AGREEMENT made effective as of July 10, 1997, by and between Isis Pharmaceuticals, Inc., a Delaware corporation having its principal offices at 2292 Faraday Avenue, Carlsbad, California 92008 ("Isis") and CIBA Vision Corporation, a Delaware corporation having its principal offices at 11460 Johns Creek Parkway, Duluth, Georgia 30097 ("CV").

WHEREAS, Isis is developing an ophthalmic product containing fomivirsen sodium, and has the rights to certain related compounds; and

WHEREAS, CV desires to obtain, and Isis is willing to grant to CV, the exclusive worldwide right to market, sell and distribute such product and certain rights with respect to the related compounds, subject to and in accordance with the terms and conditions hereinafter set forth; and

WHEREAS, CV desires to obtain a supply of such product from Isis.

NOW THEREFORE, in consideration of the mutual covenants and obligations set forth herein, the parties hereto agree as follows:

1. Definitions

The following terms as used in this Agreement will have the meanings set forth in this Section:

- 1.1 "API" means the active pharmaceutical ingredient of the Product (as defined herein).
- 1.2 "Affiliate" will mean any person or entity that directly or indirectly controls or is controlled by or is under common control of a party to this Agreement. For purposes of this Agreement, "control" will be presumed where, directly or indirectly, a person or entity owns at least 50% of the common stock or voting ownership interests of the entity in question. For purposes of this Agreement, any reference to a party or to any Affiliate of a party will also include its employees, officers, agents and consultants.
- 1.3 "Agreement Period" will mean the period referred to in Section 25.1 hereof, and any mutually agreed upon extensions thereto.
- 1.4 "Effective Date" will mean the date first above written.
- 1.5 "European Approval" or "European Registration" will mean the approval of the Product (as hereinafter defined) for marketing by the European Commission

("EC"), or if the parties agree to seek approval through the mutual recognition process, then: (i) for purposes of Section 4 hereof, European Approval will mean approval by the Ministry of Health in Germany, France, or the UK; and (ii) for purposes of Section 3 hereof, European Approval will mean approval by the applicable governmental authority in Germany, France, the UK, Spain, Italy, the Netherlands and Portugal.

- 1.6 "FDCA" will mean the Federal Food, Drug and Cosmetics Act and all regulations and rules promulgated thereunder.

- 1.7 "FDA" will mean the United States Food and Drug Administration, and any successor entity thereto.
- 1.8 "Fill Facility" will mean the pharmaceutical production facility of [*] located in [*], or, if another production site is used, the facility where the API is processed into Product and filled into vials.
- 1.9 "IND" will be the Investigational New Drug application, as defined by the FDCA, covering the Product.
- 1.10 "GMPs" will mean current good manufacturing practices as defined from time to

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time in regulations promulgated under the FDCA or any successor laws or regulations governing the manufacture of the Product.

- 1.11 "Know-How" will mean any technology, formulae, trade secrets, technical data, pre-clinical and clinical data, and any other information or experience owned, controlled or possessed by Isis relating to, or useful in connection with, the development, manufacture, use or sale of the Product as well as any improvements or modifications to the Know-How developed by or for Isis during the Agreement Period.
- 1.12 "Net Average Sales Price" or "NASP" will mean [*].
- 1.13 "1984 Act" will mean the United States Drug Price Competition and Patent Term Restoration Act of 1984 (as amended), including 21 USC 355, 35 USC 155-156, 35 USC 271 and applicable regulations promulgated thereunder.

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- 1.14 "Non-Commercial Product" will mean Product ordered by CV for use as samples, in clinical trials, and for compassionate use, for which Product CV does not receive any compensation.
- 1.15 "Patents" will mean (i) United States Patent No. [*] and U.S. Patent No. [*]; (ii) any patents claiming priority to [*]; and (iii) any continuations, continuations-in-part, divisions, reexaminations, re-issues, extensions, or foreign equivalents of (i) or (ii) hereof, as of the Effective Date or arising during the Agreement Period. The foregoing definition is limited to claims of the Patents that read on the Product or on a method of using the Product.
- 1.16 "NDA" will mean the New Drug Application, as defined by the FDCA, covering the Product.
- 1.17 "Planned Indication" will be the indication for the Product for which FDA approval and European Approval is currently being sought, namely the treatment of "cytomegalovirus-related ("CMV") retinitis in patients with AIDS", without any proviso that the Product be used only after one or more other therapies have been utilized.

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- 1.18 "Product" will mean any ophthalmic product containing fomivirsen sodium (formerly known as the compound ISIS 2922) as an API.

- 1.19 "Project Team" will mean the Isis team responsible for overseeing the clinical development of the Product.
- 1.20 "Specifications" will mean the master formula, test methods/protocols, and other data and requirements used to manufacture, test, measure stability and store the Product, copies of which Specifications are attached as Exhibit A and which may be amended from time to time by the parties in accordance with the terms of this Agreement, or as required by the FDA.
- 1.21 "Territory" will mean all the countries in the world.
- 1.22 "Third Party Distributors" will mean any person or entity with whom CV or a CV Affiliate contracts to be responsible, in place of CV or such Affiliate, for the registration, marketing, selling and distribution of the Product.

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2. Grant of Rights.

- 2.1 Product Rights. Isis hereby grants to CV the exclusive worldwide right to market, sell and distribute the Product, and CV accepts such rights subject to the terms and conditions set forth herein.
- 2.2 Patent License. Subject to the terms and conditions of this Agreement and during the Agreement Period, Isis hereby grants to CV a worldwide, royalty-free, exclusive license under the Patents to make, have made, use and sell the Product and practice the Know-How, but only insofar as necessary to allow CV to take advantage of the provisions of Sections 12 and 16 hereof (the "License"). This License does not include the right to sublicense, unless necessary for the foregoing purpose. For any country in which CV has transferred its rights to the Product to Isis pursuant to Section 5.4, this License will then revert to Isis for such country.
- 2.3 Option for ISIS 13312. Isis hereby grants to CV an option to acquire an exclusive worldwide license to manufacture, have manufactured, use, distribute and sell ISIS 13312 on the following basic terms and conditions:
- (a) The option must be exercised by [*], whichever

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- is later. Isis will have given CV access to all information related to such compound during the period between the execution of this Agreement and the completion of such initial clinical trial as may be reasonably necessary for CV to review in order to decide whether to exercise the option.
- (b) If CV elects to exercise the option, the parties will negotiate in good faith for a period of at least three months, if necessary, to conclude a definitive agreement which will include provisions, inter alia, for [*], but will not include [*], except that CV's share of such [*]. If the parties cannot reach a good-faith agreement based on the foregoing within three months, Isis will thereafter be entitled to negotiate and enter into such an agreement with a third party, but not on terms more favorable to the third party than those last offered to CV.
- 2.4 Right of First Offer to Other Compounds. Isis hereby grants to CV a right of first offer to acquire the exclusive worldwide license (to the extent Isis has the right to grant such license) or right to manufacture, have manufactured, market, distribute and sell any antisense compound other than ISIS 13312 for the treatment of CMV

retinitis, on terms to be negotiated in good faith by the parties. Isis will keep CV informed about the status of development of, and any significant information

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relating to, such related compounds. CV may notify Isis of its interest in acquiring rights to any of such compounds by written notice within ninety (90) days after written notice by Isis that such compound has been identified by Isis for development and for the initiation of pre-IND toxicology studies. The parties will thereafter negotiate in good faith for a period of at least three months, if necessary, to conclude a definitive exclusive distribution or license agreement with respect to such compound. If the parties cannot reach a good-faith agreement within three months, Isis will thereafter be entitled to negotiate and enter into such an agreement with a third party, but not on terms more favorable to the third party than those last offered by CV.

3. Product Development and Regulatory Approvals

3.1 U.S. and Europe. Isis will diligently pursue completion of the clinical development of the Product for the Planned Indication, including obtaining FDA approval of the NDA and European Approval. Isis will bear the cost of all studies and user fees required to obtain such approvals, including any studies required to be performed post-approval by the applicable regulatory agency as a condition of initial approval, and including the cost of fulfilling any obligations to provide post-study drugs to study participants; provided that, if mutual recognition approval is sought in Europe, Isis' financial responsibility with respect to filing and user fees will be limited to the cost of a central EC filing at the time of submission in the first country. Clinical studies will be conducted in accordance with the protocols

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therefor and all applicable rules and regulations. CV will be kept informed of the status of the development, and will be invited to participate in all Project Team meetings. Isis will provide CV with all information concerning communications with the FDA or the relevant European regulatory agency, including, but not limited to, copies of correspondence, minutes of meetings, and teleconference reports. Isis will invite CV to participate in all meetings with the FDA and the European Regulatory authorities. While Isis will bear the primary responsibility for preparing and making the submissions for regulatory approvals in the United States and Europe, CV will (i) provide input into the regulatory strategy and (ii) will review drafts of all regulatory submissions as such drafts are prepared. Specifically, CV will have two weeks from receipt of a draft submission section to comment thereon, except that, with respect to the clinical trials section, CV agrees to review the draft of such section on-site at Isis' facility simultaneously with Isis' review thereof. The parties will endeavor to come to mutual agreement on the final submission. If Isis and CV are unable to reach agreement, Isis will make the final determination with respect to any such issues. In the event the parties agree that it is desirable or required that the application for European Approval be submitted and held in CV's name, the parties will cooperate to do so.

3.2 Registration Outside U.S. and Europe. CV will make commercially reasonable efforts, at its expense, to obtain regulatory approval to market the Product in jurisdictions other than the United States and Europe. Isis will reasonably cooperate and provide CV with all Know-How, copies of regulatory submissions,

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and other information necessary to assist CV in obtaining such approval; provided, any additional studies required will be conducted at CV's expense. CV will reimburse Isis for any out-of-pocket expenses related to Isis' assistance in obtaining such regulatory approvals.

- 3.3 Phase IV Studies and Supplemental Indications. CV will be responsible for conducting and bearing the cost of any studies or filings following regulatory approval in the United States and Europe for the Product for the Planned Indication, except for studies required to be performed post-approval in order to obtain the initial approval. In addition, CV will be responsible for the conduct and cost of additional studies required to support expanded labeling outside the indication or dosage administration instructions in the initial approved prescribing information. Isis will assist CV as reasonably requested in performing such studies, and CV will pay Isis' out-of-pocket expenses for such assistance. CV will be responsible for the cost of any change in presentation or packaging of the Product.
- 3.4 Site Approval. As part of obtaining regulatory approval to market the Product in the U.S. and in Europe, Isis will simultaneously be responsible for obtaining approval of its facility and the Fill Facility for the production of the Product for marketing. CV will have the option, but not the obligation, to participate in such site approval process at CV's expense.

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- 3.5 Launch Promotional Materials. CV will consult with Isis during CV's preparation of the launch promotional materials for the Product. CV will make the final determination as to any issues regarding such materials. Six weeks prior to the anticipated FDA approval of the registration of the Product, Isis will submit such materials to the FDA for approval. CV will have provided such materials to Isis at least two weeks prior to such FDA submission.
- 3.6 Transfer of Registrations. Within ten (10) days of obtaining U.S. and/or European Approval, Isis will request transfer of such registrations to CV including the IND and its European equivalents (unless, with respect to Europe, the registrations were submitted in CV's name). After transfer, CV will be responsible, and will bear the cost of, maintaining the registrations for the Product in the U.S. and Europe during the Agreement Period in compliance with all applicable laws, rules and regulations.

4. Payments

- 4.1 Payments. In consideration of the rights granted in Section 2 hereof, CV will pay Isis:

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- (a) Within ten (10) days of signing this Agreement, a non-refundable payment of [*] in consideration of the patent license granted in Section 2.2 and the Option for a license granted in Section 2.3 hereof (all "dollars" in this Agreement are U.S. dollars).
- (b) [*] within ten (10) days of [*].
- (c) [*] within ten (10) days of [*].
- (d) [*] within ten (10) days of [*].

4.2 Termination Option.

- (a) In the event Isis has not obtained such approval of the NDA in the United States by at least [*], then CV may, at its option,

terminate the Agreement by giving written notice to Isis no later than [*]. In the event of such termination: (i) Isis will repay to CV [*]; (ii) Isis will refund to CV any payments CV has made to Isis for Product ordered; and (iii) CV will return to Isis any inventory of Product which it has at the time of termination.

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- (b) If European Approval is not obtained by [*], then CV may, at its option terminate the Agreement with respect to Europe by giving written notice to Isis no later than [*]. In the event of such termination, Isis will refund any payments CV has made to Isis for Product ordered for Europe, unless such Product is reasonably saleable elsewhere, and CV will return to Isis any such Product which it has at the time of termination.
- (c) If the Agreement terminates pursuant to Section 4.2(a), then all of CV's rights under this Agreement will revert to Isis pursuant to Section 25.6 hereof. If the Agreement terminates with respect to Europe pursuant to Section 4.2(b), then CV's rights under this Agreement for Europe will revert to Isis pursuant to Section 25.6 hereof.

5. Marketing

- 5.1 CV Responsibilities. CV and its Affiliates will use commercially reasonable efforts to market, distribute and sell the Product worldwide, provided that, on a country-by-country basis, the Product has been granted a commercially reasonable regulatory approval (i.e., reasonable labeling or reasonable price in jurisdictions where price is set by regulatory authority). CV will provide Isis with a copy of its

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proposed marketing plans for the Product. Isis will be entitled to provide input to the marketing plans and the parties will endeavor to reach mutual agreement on such plans. If CV and Isis are unable to reach agreement, CV will make the final determination with respect to any marketing plan issues.

- 5.2 Compliance with Marketing Regulations. CV will comply with all applicable laws, rules and regulations with respect to its promotion of the Product. CV will provide Isis with post-launch promotional materials containing substantially new material for Isis' review and comment prior to finalizing such materials. CV will provide Isis with copies of all other promotional materials for the Product in North America and Europe. CV will also insure that any and all Third Party Distributors in North America and Europe comply with the material provisions of this Agreement, as well as with all applicable laws, rules and regulations with respect to the promotion of the Product, including but not limited to all applicable import/export laws and the U.S. Foreign Corrupt Practices Act. CV will also insure that all Third Party Distributors in North America and Europe have implemented a sales tracking system which could be relied upon in the unlikely event of a Product recall or need for patient notification.
- 5.3 Trademarks. The Product will be marketed by CV under a trademark chosen, owned and maintained by CV (the "Trademark"); provided such Trademark will be one to which Isis has no reasonable objection. If Isis has already registered a

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trademark for the Product, or has submitted a trademark for the Product to the FDA, Isis will assign such trademark to CV at CV's request.

- 5.4 Return of Rights. For any country in which CV, an Affiliate or Third Party Distributor: (i) fails to use commercially reasonable efforts to obtain regulatory approval; (ii) ceases to market the Product; (iii) fails to commercially reasonably market the Product where it has obtained a commercially reasonable regulatory approval; or (iv) substantially fails to market the Product in accordance with a commercially reasonable marketing plan, and the events in (i), (ii) (iii) and (iv) continue for a period of eighteen months if such events are due to a force majeure, then for such countries, CV will transfer the rights granted to it in Section 2 hereof and any applicable Product registration, filing and Know-How to Isis, and the parties will negotiate in good faith with respect to the transfer of the Trademark in such country.

6. Supply

- 6.1 During the Agreement Period, Isis will manufacture, or have manufactured, and supply to CV, subject to the terms and conditions hereinafter set forth, such amounts of bulk filled vials of the Product as CV may order, including performing the stability and release testing of the Product. (CV will be responsible for the labeling and packaging of the Product.) CV will be required to purchase its requirements of the Product from Isis during the Agreement Period, so long as Isis

is able to supply such Product to CV in compliance with the terms and conditions set forth herein.

7. Forecasts/Orders/Invoices

- 7.1 API. Isis will manufacture and test the API for the Product in accordance with the Specifications therefor and all applicable laws, rules and regulations, including current GMPs. Isis will maintain an inventory of API equal to the greater of 0.25 kg or the amount necessary to supply the next nine months of forecasted Product sales as set forth in the rolling forecast submitted to Isis pursuant to Section 7.2 hereof.
- 7.2 Rolling Forecast. Beginning in January, 1998, on or before the tenth day of each month during the Agreement Period, CV will provide Isis, with a copy to the Fill Facility, with a written eighteen month rolling forecast of the quantities of Product which CV expects to purchase during each of the next eighteen months. The forecast will be non-binding and for planning purposes only.
- 7.3 Purchase Orders. For deliveries to be made in 1998 and 1999, CV will provide Isis with purchase orders ("PO") at least nine (9) months in advance of the delivery

date set forth on the PO. Thereafter, orders will be placed six (6) months in advance of their requested delivery date. Orders will be for [*]; provided CV may, at its option, order [*] at an additional cost of [*] for the first two [*], and an additional [*] for any further [*]. Orders of [*] will be placed no more than twice in one calendar year. If demand exceeds expectations, Isis will make reasonable commercial efforts to supply additional Product within shorter lead times. All POs will set forth the quantity and delivery date. Within ten (10) days of receipt of a PO, Isis will return an acknowledgment copy of the PO either confirming the PO or stating any mutually agreed-upon changes to the PO.

7.4 Payment. For orders placed during 1997, 1998 and 1999, Isis will invoice CV for [*] upon acknowledging the order pursuant to Section 7.3 hereof. The remaining [*], will be invoiced simultaneously with such release. After January 1, 2000, CV will pay [*] upon placing the order, and the remaining [*], similarly adjusted, upon release thereof. Payment of undisputed invoiced amounts will be made within thirty (30) days of the date of the invoice.

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7.5 Launch Inventory. In the event CV obtains inventory in anticipation of a launch and such launch is delayed through no fault of CV, CV may return to Isis, for a full credit, any unsold units of such inventory when such units' shelf life has been reduced to eight (8) months.

8. Isis' Supply Price to CV

8.1 Definitions. As used in this Section:

- (a) The "Supply Price" will mean Isis' price to CV for the Product, except for Non-Commercial Product, [*]. The Supply Price for a particular order will be [*].
- (b) A "Delay" will be any time period equal to or exceeding one month in length, determined in rolling one-month intervals starting with the first full calendar month of delay.
- (c) "FDA Delay" will mean a Delay in the approval of the Product past [*], but will not include a Delay caused by an Isis Delay.

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- (d) "Isis Delay" will mean: (i) Isis' failure to file a complete NDA acceptable for filing by [*]; (ii) Isis' failure to timely respond to FDA inquiries and requests; or failure to supply Product for Launch in accordance with the terms of this Agreement, in the absence of a Force Majeure.
- (e) "CV Delay" will mean CV's failure to Launch the Product within [*] in the absence of any Isis Delay or Force Majeure.
- (f) "Launch" will mean the date on which CV makes its first shipment of Product to a third party customer.

8.2 Supply Price. The Supply Price for the [*] except as follows:

- (a) If FDA approval occurs [*] due to an FDA Delay, then for each month of such FDA Delay, there will be a corresponding [*] during the last of the [*] during which the Supply Price will be [*] instead of [*] (for example, a two-month FDA Delay would result in the Supply Price being [*] for [*] after the launch, and [*] for the next two months.)

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- (b) If there is an FDA Delay and also a CV Delay, then for each month of CV Delay, one month which would have been a [*] will be a [*].
- (c) If FDA approval occurs after [*], or Launch occurs after [*]

due to an Isis Delay, then for each month of such Isis Delay, one month which would have been a [*] month will be a [*] month (for example, if there is an Isis Delay for one month, there will be [*] and [*]). If there is an FDA Delay of one month and Isis Delay of one month, then there will be [*], [*] and [*].

(d) [*].

- 8.3 Subsequent Price. For [*] after the expiration of the [*], with the adjustments in Section 8.2 above, the Supply Price will be [*] . Thereafter, the Supply Price will be [*] .
- 8.4 Non-Commercial Product. Isis will provide CV, at its request as specified on purchase orders, with [*] units of Non-Commercial Product free of charge. The Supply Price for additional units of Non-Commercial Product will be [*] .

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8.5 Annual Adjustment.

- (a) For purposes of calculating the Supply Price to be paid for the initial order, CV will reasonably estimate its likely NASP for the Launch of the Product no later than ten (10) months prior to the expected Launch of the Product. Such estimate of the NASP shall be used for purposes of calculating payments due for Product until the end of the calendar year during which the Product is launched, subject to adjustment after the end of such year. Within forty-five (45) days of the end of such year and each calendar year thereafter, CV will prepare an accounting of: (i) the actual Supply Price for the Product based on the actual NASP during such year; (ii) the number of units used as Non-Commercial Product during such year; and (iii) the number of unsaleable units returned from customers during such year. CV will forward such accounting to Isis together with: (i) an additional payment if the initial Supply Price was less than such actual Supply Price or an invoice to Isis if the initial Supply Price was greater than the actual Supply Price; and (ii) an invoice for the difference between [*] and the actual Supply Price for such year times the number of Non-Commercial units used during such year in excess of such units which were provided to CV free of charge pursuant to Section 8.4 hereof. Payment will be made in U.S. dollars. At the same time, Isis will grant CV a credit

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for the unsaleable returns, to be applied to CV's next order, for up to one per cent of the total units sold during such year. The credit for each unit shall be equal to the actual Supply Price for such year less [*] . For each calendar year after the first year during which Product is sold, the Supply Price for the Product will be the actual Supply Price for the preceding calendar year, subject to adjustment on the same basis as the first initial Supply Price was adjusted under this Section 8.5.

- 8.6 Audits. CV will permit Isis, at Isis' expense, to have its books and records reflecting its calculation of: (i) the NASP for the Product; (ii) the number of units used as Non-Commercial Product; and (iii) unsaleable returns, examined by an independent certified public accountant retained by Isis and reasonably acceptable to CV during regular business hours, on reasonable advance notice. Such independent accountant will keep confidential any information obtained during such examination and will report to Isis only its opinion as to whether and

by how much the NASP was miscalculated. If thereafter CV and Isis cannot agree on the appropriate NASP, they will retain a second independent public accountant whose decision will be binding upon both parties. If CV's reported actual payments due Isis for the year ("Reported Payments") were incorrect by more than seven (7%), then CV will bear the expense of such second audit, if CV's Reported Payments were incorrect by less than two (2%) per cent, Isis will bear the expenses of such second audit, otherwise the parties will share such audit expenses equally.

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9. Quality

- 9.1 Compliance. The Product will be manufactured and tested by or for Isis in compliance with the NDA and foreign approvals, Specifications therefor, and all applicable federal, foreign, state and local laws, rules and regulations.
- 9.2 Testing. For each batch of Product manufactured, retention and stability samples will be drawn as required by the NDA and applicable laws and regulations. Isis will conduct, or have conducted, such other quality assurance tests and functions as may be required by the Specifications or applicable laws or regulations. Isis will retain, or will cause the Fill Facility to retain, all batch records for a period of one year after the expiration date of the applicable batch. CV will have access to all production and testing records related to the Product after release or rejection by Isis, including copies thereof, and any lot samples within seventy-two (72) hours of its request therefor. Isis will notify CV immediately of any media or sterility failures or problems related to the Product. Isis will provide CV with copies of annual stability data, stability reports and interim stability data. CV reserves the right to inspect and test any and all Product and batch records for Product shipped to CV hereunder. If CV rejects Product based on CV's own testing or inspection and the parties cannot agree on the disposition of such Product, they will retain a mutually agreeable third party to test such Product and will share the cost therefor. The decision of such party will be binding.

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- 9.3 Inspections. CV and its authorized representatives will have the right to inspect the production and quality assurance facilities where the API and the Product are produced, as well as the records related to such production, during normal business hours with reasonable advance notice. Isis will promptly notify CV of any governmental inspection of the facility, and, if possible, permit CV representatives to be present at the inspection, and will provide CV with copies of any FDA 483 or any similar reports related to the Product, the Fill Facility or the Isis facility where the active ingredient is produced.
- 9.4 Production Problems. Isis will promptly notify CV of any problems or unusual production situations which have the potential to adversely affect the production of the Product or its timely delivery to CV and will allow CV to participate in the resolution of any such problem or production situation.
- 9.5 Changes to Manufacturing Process and Specifications. As used in this Section 9.5, "Product Process" will mean the manufacturing process by which the API is made into finished Product and filled into vials, and "API Process" will mean the manufacturing process for producing bulk API. Either party may request changes to the manufacturing process or to the Specifications.

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- (a) Before Approval. Prior to FDA approval, Isis will not make any substantive changes to the Product Process or to Specifications until CV has had five business days from receipt of notification in writing thereof from Isis to object to such change. If CV fails to respond within such time period, CV will be deemed to have acquiesced to such change and Isis may proceed with the implementation of such change. In the event that CV does timely object to the change and the parties cannot reach mutual agreement, Isis will make the final determination as to such change. Non-substantive changes to the Specifications or to the Product Process, and changes to the API Process, may be implemented by Isis upon sending written notice to CV.
- (b) After Approval. After FDA approval, no substantive change to the Product Process or to the Specifications will be implemented by either party, whether requested by a party or requested or required by a governmental agency until the other party has had at least five business days from notice of such proposed change to object to the change or state that it believes prior FDA approval is required. If such party fails to respond within such time period, it will be deemed to have acquiesced to the change without FDA prior approval and the party responsible for the implementation of such change may proceed with such implementation. CV shall make the final determination after discussion by the parties, as to whether to go forward with any such change and as to whether to seek

prior FDA approval. With respect to substantive changes to the API Process, Isis will give CV at least five business days prior written notice of such change so that CV can make a determination, after consultation with Isis, as to whether prior FDA approval should be sought for such change. Isis will make the final determination as to whether or not to make any change in the API Process itself. Non-substantive changes to the Product Process, the API Process or to Specifications may be implemented by either party (where applicable) upon sending written notice of such change to the other party.

- 9.6 Costs of Changes. The cost associated with any changes made to the manufacturing process or the Specifications which are requested by Isis or required by any governmental agency in the U.S. or Europe will be borne by Isis. With respect to changes required by any governmental agency outside of the U.S. and Europe, the parties will mutually agree on how to respond to such requirement and on the allocation of the cost thereof. The costs associated with any change to the Specifications which are requested by CV will be borne by CV.
- 9.7 FDA Prior Approval. In the event Isis treats as non-substantive a change for which CV should have obtained FDA prior approval, and CV suffers damages or costs arising therefrom, Isis will indemnify CV for such losses and costs. In the event CV decides not to seek FDA prior approval for a change, and the FDA later

disagrees with that decision, CV will indemnify Isis from any damages or costs Isis sustains arising therefrom.

- 9.8 Alternative Fill Facility. In the event the parties agree to utilize a Fill Facility other than [*], the parties will share equally the cost and the benefits of moving to such new Fill Facility.

10. Release of Product

- 10.1 Upon determination by Isis that the Product meets the Specifications therefor, Isis will notify CV by facsimile that Product is ready for

release, along with a Certificate of Analysis and the Certificate of Release. Any objections by CV to the release of Product will be made within three (3) business days of receipt of the certificate of analysis and certificate of release, unless CV decides to test or inspect the batch records for such Product, in which case CV will make any objections within two (2) business days of receiving copies of the batch records or the results of the tests. If Isis disagrees with CV, the issue will be resolved by a third party in the same manner as set forth in Section 9.2 hereof.

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11. Labeling and Packaging

11.1 Artwork Approval. CV will supply Isis with the artwork for the initial labeling and packaging of the Product in sufficient time to allow Isis to have ten (10) business days to review and comment on the artwork prior to its submission to the FDA. Isis will submit the initial labeling and packaging to the FDA and other governmental agencies, as necessary, for approval. All necessary translations of the labeling and packaging will be the sole responsibility of CV.

11.2 Changes. The parties will cooperate and consult with each other with respect to any future labeling or packaging changes whether requested by one of the parties or by the FDA, but, as between the parties, CV will have the final responsibility for the decisions with respect to labeling and packaging. CV will bear the cost of any such changes, except that Isis will bear the cost of changes requested by Isis.

12. Second Source and Supply Failure

12.1 Optional Second Source. Upon mutual agreement, the parties will cooperate to qualify a second source to produce the API (if possible) and the finished Product, and will share equally the costs and benefits thereof. If Isis does not agree to qualify a second source, then CV may do so at its own expense and Isis will

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provide CV with all manufacturing processes and Know-How with respect to production of the Product.

12.2 Lost Profits Credit. In the event the Product is on backorder (CV cannot fill customers' orders) for a period of at least two months due to Isis' failure to supply Product in accordance with Section 7 hereof for reasons other than a Force Majeure, and provided CV had maintained at least three months' inventory prior to such supply failure, CV will be entitled to a credit for lost profits for such unfilled orders, which credit will be applied against future orders.

12.3 Supply Failure/Second Source.

(a) Intentional Failure. In the event Isis, or any successor to Isis, intentionally ceases to supply API or Product in breach of this Agreement, Isis will: (i) transfer its reserves of active ingredient to CV; (ii) acknowledge CV's license to the Patents and Know-How granted under Section 2.2 hereof; and (iii) assist CV in obtaining an NIH license required for the production of the API, all at Isis' cost, in order that CV will be able to qualify a second source for the production of the API and/or the Product. Thereafter, CV shall pay to Isis a royalty equal to the amount [*], or Isis will pay CV the amount [*]; provided CV has

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made reasonable commercial efforts to obtain a competitive third party supply price. Isis will be responsible for the costs of qualifying such second source or sources.

- (b) Unintentional Failure. In the event Isis ceases to supply API or Product by reason of its own negligence or a Force Majeure, Isis and CV will share the costs and benefits of qualifying a second source, and Isis will continue to supply Product to CV pursuant to this Agreement.

12.4 Supply Failure/Second Source Not Available.

- (a) Intentional Failure. In the event Isis intentionally ceases to supply the Product and the parties are unable, after good faith efforts, to secure a source for the Product within eighteen (18) months after such supply failure, then CV may terminate this Agreement and Isis will refund the payments made under Sections 4(b) through (d) less the amount of net profits, calculated in accordance with CV's standard accounting practices, earned by CV up to the time that CV is unable to obtain Product from Isis (the "Break-Even Amount").
- (b) Unintentional Failure. If no second source can be secured after good faith efforts in such eighteen (18) months, and the failure to supply is due to a Force Majeure or Isis' negligence, or the Product is withdrawn from the

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market through no fault of Isis, then CV may terminate this Agreement and Isis will refund one-half the Break-Even Amount to CV.

- (c) Termination. In the event of termination under this Section 12.4, CV will transfer all Product registrations to Isis, and the rights granted to CV under this Agreement will revert to Isis.

13. Manufacturing and Product Warranty

- 13.1 With respect to Product supplied to CV hereunder, Isis hereby warrants that the Product: (i) will have been manufactured in accordance and will be in compliance with the Specifications therefor and with all applicable requirements of the FDCA, similar foreign laws and regulations promulgated thereunder including, but not limited to, current GMPs, continuing compliance with stability requirements and any other applicable federal, foreign, state or local laws, rules or regulations; (ii) will not be adulterated or misbranded within the meaning of the FDCA or any applicable similar state, foreign or local laws in which the definition of adulteration or misbranding is substantially the same as in the FDCA; and (iii) will have at least twenty-one (21) months shelf-life remaining.

14. Post-Marketing Regulatory Matters

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- 14.1 Maintenance of Registrations. Isis will maintain the Product's registrations until such registrations are officially held by CV. Thereafter, CV will be responsible for maintaining such registrations.
- 14.2 Adverse Drug Reactions. ("ADRs"). CV will be responsible for the timely completion and submission of all ADR reports to the FDA and for communications with all ADR complainants. Isis will summarize and forward to CV any adverse reaction reports ("ADR") received by Isis within five (5) business days of receipt; provided Isis will forward any such complaints which involve death or life-threatening incidents to CV within twenty-four (24) hours of receipt. CV will investigate

all ADRs; provided, Isis will be responsible for all analytical testing of Product required by the investigation.

- 14.3 Technical Complaints. Physical or technical complaints relating to the Product which are received by CV or Isis will be investigated by Isis. CV will forward any Product sample to Isis for testing. Isis will promptly inform CV of any such test results. CV will be responsible for communicating with all such complainants and for all FDA notification and contact with respect to such complaints, but will keep Isis informed of such FDA contacts.
- 14.4 Field Alerts. The parties will exchange any information received by either party which may meet Field Alert Report criteria (21 CFR 314.81b1). Wherever possible the parties will discuss the necessity of filing a field alert report and collaborate in the submission thereof. CV will forward a copy of any such report

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to Isis and the parties will continue to discuss follow-up action on such field alert report after submission.

- 14.5 Product Recalls. The parties will immediately contact each other in the event that either party has any reason to believe that a recall of Product may be necessary. CV will, in consultation with Isis, resolve any issues with respect to the recall of any such Product including without limitation, the necessity of declaring the recall, the manner in which the recall should be conducted and the duration of the recall. Isis and CV will cooperate fully with respect to any such recall.
- 14.6 Other Information. Isis will cooperate and provide timely information to CV in order for CV to comply with any other regulatory requirements. With respect to annual reports, Isis will provide the required information to CV by the anniversary date of FDA approval each year.
- 14.7 Information Exchange. All information exchanged by the parties under this Section 14 will be forwarded to:

For CV in U.S.: Lawrence D. Mandt
Director, Regulatory & Medical Affairs
CIBA Vision Corporation
11460 Johns Creek Parkway
Duluth, Georgia 30155

For CV in Europe and rest of world:
Richard Bergstrom
Head, Central Drug Regulatory Affairs
CIBA Vision, A.G. Hettlingen
10 Grenstrasse
Buelach, SWITZERLAND

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For Isis: Mark W. Lotz
Executive Director, Regulatory Affairs
Isis Pharmaceuticals, Inc.
2292 Faraday Avenue
Carlsbad, California 92008

15. Patents

15.1 Prosecution and Maintenance.

- (a) Isis will undertake, diligently pursue, and bear all costs of the prosecution and maintenance of U.S. Patent No. [*] and the

foreign equivalents thereof in the countries listed on Exhibit B hereto, and U.S. Patent No. [*] in the U.S. Isis will keep CV fully and timely informed with respect to the course and conduct of patent application prosecution matters related to such Patents. CV will have the right but not the obligation to consult with Isis regarding such prosecution.

- (b) With respect to all Patents other than the U.S. Patents and the foreign equivalents [*] referred to in 15.1 (a) above, Isis will not terminate prosecution or maintenance of any Patent or claim which reads on the Product, or on a method of using the Product, without first giving CV forty-five (45) days prior written notice of its intention to do so. If CV

*CONFIDENTIAL TREATMENT REQUESTED

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does not wish Isis to terminate such Patent or claim, Isis will, at its option, transfer and assign such Patent or Patent application to CV, or allow CV to reimburse Isis for the cost of the further prosecution and maintenance of such Patent or Patent application.

- 15.2 Additional Filings. CV will have the right to request that Isis file, prosecute and maintain patents in jurisdictions other than those listed on Exhibit B. Upon CV's request, Isis will file, prosecute, and maintain such patents provided CV will be consulted with respect to the preparation and filing of such patents and will share the expenses therefor with CV paying [*] and Isis paying [*]. As used in this subsection, expenses will include outside consultant fees (i.e., legal) translation fees, and filing fees but will not include the internal costs of Isis or CV. Each party will bear its own internal costs with respect to the filing of the patents in such additional jurisdictions.

16. Infringement of Patent Rights

- 16.1 Notification. If either party will become aware of any infringement or threatened infringement of any Patents, including that contained in a notice provided under the 1984 Act by a party filing an ANDA or Paper NDA for this Product, or an equivalent action in any other country, then the party having such knowledge will

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give notice to the other within ten (10) days of becoming aware of such infringement or threatened infringement.

- 16.2 Action by Isis. Isis will have the right, but not the obligation, to take such action as it deems appropriate, whether by action, suit, proceeding or otherwise, at its own expense to prevent or eliminate the infringement of the Patents by others in the countries listed on Exhibit B and to collect damages. CV agrees to cooperate with Isis in any reasonable manner including, but not limited to, being named as a co-plaintiff in an action brought by Isis. Isis agrees to pay all reasonable out-of-pocket expense incurred by CV in the prosecution of any such action, suit or proceeding for infringement.

- 16.3 Action by CV. In the event that Isis does not take action for patent infringement to prevent or eliminate the infringement of Patents within one hundred twenty (120) days of receipt of notice of the infringement or threatened infringement thereof (or within thirty (30) days in the event such infringement is by Notice Under the 1984 Act), then within said one hundred twenty (120) days (or within said thirty (30) days if such infringement is under the 1984 Act) CV may, at its option, give notice to Isis that unless Isis undertakes such action,

CV will commence an action to terminate such infringement. If Isis fails to take such action within said one hundred twenty (120) days (or said thirty (30) days in the event such infringement is by Notice Under the 1984 Act) then Isis will grant CV an exclusive license to the applicable Patents so that CV will be able to take such

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action as it deems appropriate against any infringer of same. Such action by CV may be undertaken in the name of Isis, if necessary, and Isis agrees to cooperate with CV, and execute any necessary documents relating to such action.

16.4 Apportionment of Damages and Expenses. Any damages recovered by the party bringing the action for patent infringement will be used first to compensate that party for its out-of-pocket expenses in the prosecution of any such action, suit or proceeding for infringement. Any remaining damages recovered by that party will be apportioned between CV and Isis in proportion to the damage incurred by each party as a result of the infringement [*]. With respect to an action brought under the 1984 Act, the parties will share the expenses equally, except that if CV brings such an action after Isis has declined to do so, and CV loses such action, CV will bear [*] of the expenses and Isis will bear [*].

16.5 Invalidity. In the event the claims reading on the Product contained in the Patents are declared invalid or unenforceable by a judgment, decree or decision of a court, tribunal or other authority of competent jurisdiction such that patent protection in the U.S. or Europe is thereby vitiated and a competitive product enters the market, the applicable Supply Price of the Product set forth in Section 8 hereof shall be reduced as follows:

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- (a) If patent protection in both the U.S. and Europe is vitiated within the first seven years after Launch (as defined in Section 8) of the Product, the Supply Price shall be reduced by [*] until the end of the third year after Launch, by [*] for the fourth and fifth year and by [*] for the sixth and seventh year. Thereafter, there will be no Supply Price reduction under this Section 16.5.
- (b) If patent protection is vitiated only in the U.S., then the provisions of subsection (a) above will apply except that the Supply Price reduction will be [*].
- (c) If patent protection is vitiated only in Europe, then the provisions of subsection (a) above will apply except that the Supply Price reduction will be [*].

17. Third Party Rights

17.1 Notification. If either party will become aware of any action, or suit, or threat of action or suit, by a third party alleging that the manufacture, use or sale or offer for sale of the Product or the practice of Know-How infringes a patent, or violates any other proprietary rights of any third party, the party aware will promptly notify the other party of the same and fully disclose the basis therefor.

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- 17.2 Isis Obligations. Isis agrees to use diligent efforts to defend any such action. Isis agrees to cooperate and consult with CV during the course of such defense and to keep CV fully informed with respect to all significant aspects of such action. CV agrees to assist Isis by providing information in the possession and control of CV and to provide such fact witnesses as may be reasonably necessary to such defense.
- 17.3 Third Party License. If, by the terms of any settlement or if by a judgment, decree or decision of a court, tribunal or other authority of competent jurisdiction, CV is required to obtain a license from a third party in order to market, sell and distribute Product (hereinafter "Third Party License") and/or to compensate or pay damages to such third party and/or pay royalties under such a license, then, (i) in the US and Europe, Isis will pay all such damages or royalties, and (ii) in the rest of the world, the parties will share [*] the payment of such damages or royalties in the country to which such settlement, judgment, decree or decision directly relates, so long as the reason for such settlement, etc. does not arise from (i) CV's failure to appropriately acquire regulatory approval in such jurisdiction or from (ii) any other action or inaction on the part of CV, its Affiliates or Third Party Distributor in such jurisdiction.
- 17.4 Injunction. If, by the terms of any settlement or of a judgment, decree or decision of a court, tribunal or other authority of competent jurisdiction, CV is enjoined

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entirely from selling the Product in the U.S. and Europe, Isis will immediately reimburse CV for one-half of the amounts paid to Isis under Section 4 hereof, less net profits already earned by CV from sales of the Product. In addition, Isis will indemnify CV for any direct or consequential damages and costs that are payable as the result of any such settlement or judgment.

18. Patent Term Extension

- 18.1 Within sixty (60) days after approval of an NDA for the Product, and at CV's request, Isis will file and prosecute, at its own cost and expense, an application for an extension of the Patent. Isis will also file any similar applications in Europe. CV will also list the appropriate Patents in the "Orange Book".

19. License Agreements

- 19.1 Isis will maintain its license from [*] for so long as such license is required to manufacture, use or sell the Product. Isis will maintain its license agreement with [*] so long as such license is required to manufacture, use or sell the Product. Isis will be responsible for paying all royalties owed to [*] or any other third party in connection with the manufacture, use or sale of the Product.

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20. Warranties

- 20.1 Isis Warranties. In addition to the Warranty set forth in Section 13 hereof, Isis warrants and represents that: (a) it is the owner of the Patents and Know-How and has the right to grant the rights granted to CV under Section 2 hereof free and clear of any encumbrance; (b) it has not assigned or conveyed any interest in the Patents or Know-How which may be inconsistent with the rights granted to CV hereunder; (c) to the best of its knowledge and after a diligent search, the practice of the Patents and Know-How in the United States and Europe does not

infringe any rights of third parties; (d) it is not aware of any third party infringing the Patents in the Territory; (e) it has prosecuted all patent applications within the Patents in good faith and has no reason to believe any patent included in the Patents would be invalid or would be held to be unenforceable by a court of competent jurisdiction; and (f) it is a corporation duly incorporated and in good standing in its state of incorporation and has all requisite power to enter into and perform this Agreement, and, upon execution by the parties hereto, this Agreement will constitute a valid and legally-binding obligation of Isis enforceable in accordance with its terms.

20.2 CV Warranties. CV warrants and represents that it is a corporation duly incorporated and in good standing in its state of incorporation and has all requisite power to enter into and perform this Agreement, and, upon execution by the

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parties hereto, this Agreement will constitute a valid and legally binding obligation of CV, enforceable in accordance with its terms.

21. Compliance with Law

The parties, their Affiliates, and Third Party Distributors will at all times comply with any and all applicable federal, foreign, state and local laws and regulations with respect to their obligations and activities under this Agreement. In the event a governmental agency forces the cessation of the manufacture or distribution of the Product due to any actual or alleged violation or acts of non-compliance with laws or regulations by Isis, Isis will use its best efforts to resume operations as soon as possible. It is expressly understood that such governmental action will not be considered an event of force majeure under Section 26 hereof.

22. Indemnification

22.1 Isis to CV. Isis will indemnify and hold harmless CV, its Affiliates and their officers, agents and employees against any claim, loss, damage, penalty, assessment, or expense including reasonable attorneys' fees and the cost of any recall ("Claim") arising directly or indirectly from any breach of any of Isis' warranties under Sections 13 or 20 hereof, or breach of the other obligations or covenants under this Agreement, or for any governmental action taken as a result of any such breach.

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22.2 CV to Isis. CV will indemnify and hold harmless Isis, its Affiliates and their officers, directors, agents and employees against any Claim arising directly or indirectly from (a) any breach by CV, its Affiliates, or Third Party Distributors of (i) the warranty under Section 20 hereof or (ii) the other obligations or covenants under this Agreement, or (b) any negligence, omission, or intentional wrongdoing by CV, its Affiliates or Third Party Distributors in connection with the sale and distribution of the Product, or (c) for any governmental action taken as a result of any such breach or any such act of negligence, omission or intentional wrongdoing.

22.3 Procedure. In the event that an indemnified party receives notice of, or becomes aware of, a Claim in respect of which indemnity may be sought hereunder, and the indemnified party intends to seek indemnity hereunder, the indemnified party will promptly provide the indemnifying party with notice of such Claim and the intention to seek indemnity. The indemnifying party will have the right, at its option and its own expense, to be represented by counsel of its own choice and to defend against, negotiate, settle or otherwise deal with any such Claim, provided that the indemnifying party will not enter into any settlement or compromise of any such Claim which could lead to liability or create any financial or other obligation on the part of

the indemnified party without the indemnified party's prior written consent. The indemnified party may participate in the defense of any Claim with counsel of its own choice and at its own expense. The parties agree to cooperate fully with each other in connection with the defense, negotiation or settlement of

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any such Claims. In the event that the indemnifying party does not undertake the defense, compromise or settlement of a Claim the indemnified party will have the right to control the defense or settlement of such Claim with counsel of its choosing provided, however, that the indemnified party will not settle or compromise any such claim without the indemnifying party's prior written consent, which consent will not be unreasonably withheld.

23. Scientific Publications.

23.1 Submission and Approval. Any scientific publication or presentation by either party with respect to the Product, including publications relating to clinical studies, will be approved by the other party prior to publication or presentation, such approval not to be unreasonably delayed or withheld. Due regard will be given to each party's legitimate interests, i.e., protection of confidential information, commercialization of the Product, etc. Any proposed publications which are to make public any findings, data or results of the studies relating to the Product will be provided to the other party at least thirty (30) days prior to submission for publication for the other party's approval, except that abstracts may be provided seven (7) days prior to submission for publication.

23.2 Patent Considerations. If a party, in its reasonable judgment, needs additional time to seek patent or other appropriate protection (the "Patenting Party") for any of the information to be published or presented by the other party (the "Publishing

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Party"), the Patenting Party will promptly notify the Publishing Party of such need in writing, and the Publishing Party will defer such publication or presentation until such time as the Publishing Party is notified by the Patenting Party that such patent or other appropriate protection has been applied for.

24. Proprietary Information and Announcements

24.1 "Proprietary Information." As used herein, "Proprietary Information" will mean all technical, sales or other confidential business information, including the Know-How, related to the subject matter of this Agreement disclosed by one party to the other at any time prior to or during the Agreement Period and identified as confidential, together with all records generated or maintained Isis relating to Product produced for CV. Proprietary Information will not include information which, as demonstrated by competent evidence: (i) was known to the receiving party prior to the disclosure; (ii) was generally available to the public at the time of disclosure or becomes available to the public after disclosure other than through any act or omission of the receiving party in breach of this Agreement; (iii) becomes known to the receiving party as the result of disclosure from a third party under no obligation of secrecy to the other party; or (iv) is required to be disclosed by law or pursuant to the disclosure requirements of a governmental agency, provided that the party ordered to disclose the Proprietary Information notifies the party which owns or supplied the Proprietary Information sought to be disclosed

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pursuant to such request, requirement or order in sufficient time to allow the owner/supplying party to oppose such request, requirement or order.

24.2 Confidentiality Obligations. During the Agreement Period and for a period of five (5) years after the expiration or earlier termination of this Agreement, neither party will: (i) disclose, publish or make available any Proprietary Information disclosed to it by the other party: (a) to any third party, except to Affiliates which will be bound by the same obligation of confidentiality; or (b) to any employees who do not need to know or have access to such Proprietary Information; or (ii) sell, transfer or otherwise use, except for the purposes herein, any such Proprietary Information. After expiration or earlier termination of this Agreement, each party will return the Proprietary Information of the other party and will destroy all copies thereof, other than records which must be retained as a matter of law.

24.3 Publicity. During the Agreement Period, neither party will make any press release or other public announcement relating to this Agreement, or otherwise disclose the terms of this Agreement to any third party other than an Affiliate, without the prior written consent of the other party except as required by a court of competent jurisdiction or pursuant to the disclosure requirements of a governmental agency.

25. Term and Termination

25.1 Agreement Period. The term of this Agreement will commence as of the Effective Date and will expire fifteen (15) years thereafter, unless previously terminated and notwithstanding any suspension due to a force majeure event under Section 26 hereof. If, at the time of such expiration, CV is continuing to make commercially

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reasonable efforts to market the Product, it may extend the Agreement for an additional five years, on six months' prior written notice, unless Isis has a reasonable objection thereto.

25.2 Material Breach. This Agreement may be canceled by either party upon written notice in the event the other party fails to perform a material obligation under this Agreement within thirty (30) days after receiving notice of such failure. If the nature of the failure is such that it cannot be cured within the thirty-day period, no termination will occur provided the defaulting party will have commenced to cure such breach within thirty days and thereafter diligently proceeds to effect and complete such cure within ninety (90) days from the date of the original notice.

25.3 CV's Option. This Agreement may be terminated by CV pursuant to the provisions of Section 4.2 hereof.

25.4 Bankruptcy. Either party may terminate this Agreement upon written notice in the event that the other party will file for protection in bankruptcy or will be adjudicated as bankrupt or will make an assignment for the benefit of creditors or will have a receiver, whether appointed by private instrument or court offices, appointed for its property.

25.5 Survival. Termination or expiration of this Agreement will not relieve either party from the liabilities and obligations approved prior to the Effective Date of

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termination or expiration, and the provisions of Sections 13, 17, 20, 22 and 24 hereof will survive any termination or expiration of this Agreement.

25.6 Post-Termination. All rights to the Patents, Know-How, Product

Registrations, and Isis trademarks granted to CV under this Agreement will revert to Isis upon expiration or termination of this Agreement. After the expiration or termination of this Agreement, so long as the termination of the Agreement is not the result of a material breach on the part of CV, its Affiliates and Third Party Distributors, then CV, its Affiliates and Third Party Distributors will have the right to sell all Products released for distribution before such date as well as the right to sell all such Products in the process of manufacture on such date, provided that CV will pay the applicable Supply Price and render reports to Isis with respect to such Product in the manner required hereunder.

26. Force Majeure

26.1 Neither party will be liable to the other for loss or damages, or, except as expressly provided in this Agreement, have any right to terminate this Agreement for any default or delay attributable to any cause beyond the reasonable control of that party, including but not limited to, an act of God, flood, fire, explosion, strike, lockout, earthquake, labor dispute, war, revolution, civil commotion, act of a public enemy, blockade, embargo, or governmental action other than one resulting from the act, omission or negligence of a party. In the event such a default or

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delay occurs, the party affected will notify the other party and will exercise diligent efforts to resume performance of its obligations as soon as possible.

27. Miscellaneous

27.1 No Waiver. Failure of either party to insist upon strict observance of or compliance with any of the terms of this Agreement in one or more instances will not be deemed to be a waiver of its right to insist upon such observance or compliance with those or other terms of this Agreement with respect to subsequent breaches of any of the terms of this Agreement.

27.2 Notices. All notices and demands required or permitted hereunder will be in writing and given by certified or registered mail, postage prepaid or by a nationally recognized express mail service, or hand delivered at the following addresses:

If to CV: CIBA Vision Corporation, U.S. Ophthalmics
11460 Johns Creek Parkway
Duluth, Georgia 30155
Attn: President

cc: General Counsel
CIBA Vision Corporation
11460 Johns Creek Parkway
Duluth, Georgia 30155

If to Isis: Isis Pharmaceuticals, Inc.
2292 Faraday Avenue
Carlsbad, California 92008
Attn: President

cc: General Counsel
Isis Pharmaceuticals, Inc.
2292 Faraday Avenue
Carlsbad, California 92008

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or to such other address as to which either party may notify the other. Notice will be deemed to be effective three (3) days after mailing, or upon receipt if hand delivered or sent by express mail

service.

- 27.3 Assignment. This Agreement will be binding upon and inure to the benefit of the parties, their successors and permitted assigns. Neither party may assign this Agreement without the prior written consent of the non-assigning party, which consent will not be unreasonably withheld.
- 27.4 Governing Law. This Agreement is governed by the laws of the State of New York that are applicable to contracts negotiated, executed and performed within that state.
- 27.5 Severability. In the event any one or more of the provisions of this Agreement should for any reason be held by any court of authority having jurisdiction over either the parties or this Agreement to be invalid, illegal or unenforceable, such provision or provisions will be validly reformed so as to nearly approximate the intent of the parties as possible or, if unreformable, will be divisible and deleted in such jurisdiction; otherwise, this Agreement will continue in full force effect.
- 27.6 Independent Contractors. Nothing in this Agreement is intended or will be deemed to constitute a partnership, agency, employer-employee or joint venture relationship between the parties. All activities by the parties hereunder will be

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performed by them as independent contractors. Neither party will incur any debts or make any commitments for the other party, except to the extent specifically provided herein.

- 27.7 Entire Agreement/Modification. The terms of this Agreement represent the entire agreement of the parties with respect to the subject matter herein and will not be modified or supplemented except in a written document duly executed by the parties, which document will state that it is an amendment or modification to this Agreement. This Agreement will prevail in the event of any inconsistencies between it and the terms of any purchase order, acknowledgment, invoice or other form utilized by the parties.

IN WITNESS WHEREOF, the parties have caused this Agreement to be executed by their duly authorized representatives as of the day and year indicated below.

CIBA VISION CORPORATION

ISIS PHARMACEUTICALS, INC.

By: Stephen M. Martin
Title: President
Date: July 10, 1997

By: B. Lynne Parshall
Title: Executive Vice President
Date: July 10, 1997

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Attachment for Ciba Vision - Isis Agreement
Exhibit A

[*CONFIDENTIAL TREATMENT REQUESTED FOR
ENTIRE CONTENTS OF EXHIBIT A]

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Exhibit B

[*CONFIDENTIAL TREATMENT REQUESTED FOR
ENTIRE CONTENTS OF EXHIBIT B]

EXHIBIT 10.3

Imperial Bank Note Secured By Deed of Trust dated March 24, 1997
in the amount of \$6,000,000; Deed of Trust and Assignment of Rents
dated March 24, 1997.

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DO NOT DESTROY THIS NOTE:

WHEN PAID, THIS NOTE, WITH THE DEED OF TRUST SECURING SAME, MUST BE SURRENDERED
TO THE TRUSTEE FOR CANCELLATION BEFORE RECONVEYANCE WILL BE MADE.

[LOGO]

IMPERIAL BANK
Member FDIC
NOTE SECURED BY DEED OF TRUST

\$6,000,000.00

Menlo Park, California,

MARCH 24, 1997

On JULY 1, 2002, and as hereinafter provided, for value received, the undersigned promises to pay to IMPERIAL BANK ("Bank"), a California banking corporation, or order, at its Special Markets Group office, the principal sum of \$ SIX MILLION AND NO/100 or such sums up to the maximum if so stated, as the Bank may now or hereafter advance to or for the benefit of the undersigned in accordance with the terms hereof, together with interest from date of disbursement or n/a, whichever is later, on the unpaid principal balance [] at the rate of % per year [X] at the rate of .50% per year in excess of the rate of interest which Bank has announced as its prime lending rate (the "Prime Rate"), which shall vary concurrently with any change in such Prime Rate, or \$250.00, whichever is greater. Interest shall be computed at the above rate on the basis of the actual number of days during which the principal balance is outstanding, divided by 360, which shall, for interest computation purposes, be considered one year.

Interest shall be payable [X] monthly [] quarterly [] included with principal [X] in addition to principal [] beginning MAY 1, 1997, and if not so paid shall become a part of the principal. All payments shall be applied first to interest, and the remainder, if any, on principal. [X] (If checked), Principal shall be payable in installments of \$*, or more, each installment on the day of each , beginning .

Any partial prepayment shall be applied to the installments, if any, in inverse order of maturity. Should default be made in the payment of principal or interest when due, or in the performance or observance, when due, of any item, covenant or condition of any deed of trust, security agreement or other agreement (including amendments or extensions thereof) securing or pertaining to this note, at the option of the holder hereof and without notice or demand, the entire balance of principal and accrued interest then remaining unpaid shall (a) become immediately due and payable, and (b) thereafter bear interest, until paid in full, at the increased rate of 5% per year in excess of the rate provided for above, as it may vary from time to time.

Defaults shall include, but not be limited to, the failure of the maker(s) to pay principal or interest when due; the filing as to each person obligated hereon, whether as maker, co-maker, endorser or guarantor (individually or collectively referred to as the "Obligor") of a voluntary or involuntary petition under the provisions of the Federal Bankruptcy Act; the issuance of any attachment or execution against any asset of any Obligor; the death of any Obligor; or any deterioration of the financial condition of any Obligor which results in the holder hereof considering itself, in good faith, insecure.

[X] If any installment payment or principal balance payment due hereunder is delinquent ten or more days, Obligor agrees to pay a late charge in the amount of 5% of the payment so due and unpaid, in addition to the payment; but nothing in this paragraph is to be construed as any obligation on the part of the holder of this note to accept payment of any installment past due or less than the total unpaid principal balance after maturity.

If this note is not paid when due, each Obligor promises to pay all costs and expenses of collection and reasonable attorney's fees incurred by the holder hereof on account of such collection, plus interest at the rate applicable to principal, whether or not suit is filed hereon. Each Obligor shall be jointly and severally liable hereon and consents to renewals, replacements and extensions of time for payment hereof, before, at, or after maturity; consents to the acceptance, release or substitution of security for this note; and waives demand and protest and the right to assert any statute of limitations. Any married person who signs this note agrees that recourse may be had against separate property for any obligations hereunder. The Indebtedness evidenced hereby shall be payable in lawful money of the United States. In any action brought under or arising out of this note, each Obligor, including successor(s) or assign(s) hereby consents to the application of California law, to the jurisdiction of any competent court within the State of California, and to service of process by any means authorized by California law.

This note is secured by a deed of trust, dated MARCH 24, 1997, to IMPERIAL BANCORP as Trustee which contains the following provisions: "In the event the herein described property or any part thereof, or any interest therein is sold, agreed to be sold, conveyed, transferred, disposed of, further encumbered, or alienated by trustor or by the operation of law or otherwise, without the written consent of beneficiary first obtained, all obligations secured by this instrument, irrespective of the maturity dates expressed therein, at the option of the holder beneficiary, and without demand or notice shall immediately become due and payable. Consent to one such transaction shall not be deemed to be a waiver of the right to require such consent to future or successive transactions."

No single or partial exercise of any power hereunder, or under any deed of trust, security agreement or other agreement in connection herewith shall preclude other or further exercises thereof or the exercise of any other such power. The holder hereof shall at all times have the right to proceed against any portion of the security for this note in such order and in such manner as such holder may consider appropriate, without waiving any rights with respect to any of the security. Any delay or omission on the part of the holder hereof in exercising any right hereunder, or under any deed of trust, security agreement or other agreement, shall not operate as a waiver of such right, or of any other right, under this note or any deed of trust, security agreement or other agreement in connection herewith.

* See Addendum attached hereto and made a part hereof by this reference.

ISIS PHARMACEUTICALS, INC.,

a Delaware corporation

By: /s/ GARY J. G. ATKINSON

Vice President, Finance

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ADDENDUM ATTACHED TO THAT CERTAIN NOTE SECURED BY DEED OF TRUST DATED MARCH 24, 1997 EXECUTED BY ISIS PHARMACEUTICALS, INC.

ADDENDUM

1. Advances under the note shall be available through December 31, 1997. On June 30, 1997, the outstanding balance of the advances under the Note shall be converted to an amortizing loan payable in 60 equal monthly payments of principal plus accrued interest commencing August 1, 1997.

All principal and accrued but unpaid interest shall in any event be due and payable on July 1, 2002.

2. The following Reference Provision is by this reference incorporated in the Note:

REFERENCE PROVISION

1. Other than (i) non-judicial foreclosure and all matters in connection therewith regarding security interests in real or personal property; or (ii) the appointment of a receiver, or the exercise of other provisional remedies (any and all of which may be initiated pursuant to applicable law), each controversy, dispute or claim between the parties arising out of or relating to this Note "Agreement"), which controversy, dispute or claim is not settled in writing within thirty (30) days after the "Claim Date" (defined as the date on which a party subject to the Agreement gives written notice to all other parties that a controversy, dispute or claim exists), will be settled by a reference proceeding in California in accordance with the provisions of Section 638 et seq. of the California Code of Civil Procedure ("CCP"), or their successor section, which shall constitute the exclusive remedy for the settlement of any controversy, dispute or claim concerning this Agreement, including whether such controversy, dispute or claim is subject to the reference proceeding and except as set forth above, the parties waive their rights to initiate any legal proceedings against each other in any court or jurisdiction other than the Superior Court in the County where the Real Property, if any, is located or Los Angeles County if none (the "Court"). The referee shall be a retired Judge of the Court selected by mutual agreement of the parties, and if they cannot so agree within forty-five (45) days after the Claim Date, the referee shall be promptly selected by the Presiding Judge of the Court (or his representative). The referee shall be appointed to sit as a temporary judge, with all of the powers of a temporary judge, as authorized by law, and upon selection should take and subscribe to the oath of office as provided for in Rule 244 of the California Rules of Court (or any subsequently enacted Rule). Each party shall have one peremptory challenge pursuant to CCP Section 170.6. The referee shall (a) be requested to set the matter for hearing within sixty (60) days after the Claim Date and (b) try any and all issues of law or fact and report a statement of decision upon them, if possible, within ninety (90) days of the Claim Date. Any decision rendered by the referee will be final, binding and conclusive and

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judgment shall be entered pursuant to CCP Section 644 in any court in the State of California having jurisdiction. Any party may apply for a reference proceeding at any time after thirty (30) days following the notice to any other party of the nature of the controversy, dispute or claim, by filing a petition for a hearing and/or trial. All discovery permitted by this Agreement shall be completed no later than fifteen (15) days before the first hearing date established by the referee. The referee may extend such period in the event of a party's refusal to provide requested discovery for any reason whatsoever, including, without limitation, legal objections raised to such discovery or unavailability of a witness due to absence or illness. No party shall be entitled to "priority" in conducting discovery. Depositions may be taken by either party upon seven (7) days written notice, and request for production or inspection of documents shall be responded to within ten (10) days after service. All disputes relating to discovery which cannot be resolved by the

parties shall be submitted to the referee whose decision shall be final and binding upon the parties. Pending appointment of the referee as provided herein, the Court is empowered to issue temporary and/or provisional remedies, as appropriate.

2. Except as expressly set forth in this Agreement, the referee shall determine the manner in which the reference proceeding is conducted including the time and place of all hearings, the order of presentation of evidence, and all other questions that arise with respect to the course of the reference proceeding. All proceedings and hearings conducted before the referee, except for trial, shall be conducted without a court reporter, except that when any party so requests, a court reporter will be used at any hearing conducted before the referee. The party making such a request shall have the obligation to arrange for and pay for the court reporter. The costs of the court reporter at the trial shall be borne equally by the parties.

3. The referee shall be required to determine all issues in accordance with existing case law and the statutory laws of the State of California. The rules of evidence applicable to proceedings at law in the State of California will be applicable to the reference proceeding. The referee shall be empowered to enter equitable as well as legal relief, to provide all temporary and/or provisional remedies and to enter equitable orders that will be binding upon the parties. The referee shall issue a single judgment at the close of the reference proceeding which shall dispose of all of the claims of the parties that are the subject of the reference. The parties hereto expressly reserve the right to contest or appeal from the final judgment or any appealable order or appealable judgment entered by the referee. The parties hereto expressly reserve the right to findings of fact, conclusions of law, a written statement of decision, and the right to move for a new trial or a different judgment, which new trial, if granted, is also to be a reference proceeding under this provision.

4. In the event that the enabling legislation which provides for appointment of a referee is repealed (and no successor statute is enacted), any dispute between the parties that would otherwise be determined by the reference procedure herein described will be resolved and determined by arbitration. The arbitration will be conducted by a retired judge of the Court, in accordance with the California Arbitration Act, Section 1280 through Section 1294.2 of the CCP as amended from time to time. The limitations with respect to discovery as set forth hereinabove shall apply to any such arbitration proceeding.

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RECORDING REQUESTED BY
IMPERIAL BANK

WHEN RECORDED MAIL TO

IMPERIAL BANK
9920 SO LA CIENEGA BLVD
INGLEWOOD CA 90301
Attn Lending Services

INDEX AS DEED OF TRUST AND ASSIGNMENT OF RENTS
SPACE ABOVE THIS LINE FOR RECORDER'S USE

Real Estate Loan
Short Form

DEED OF TRUST AND ASSIGNMENT OF RENTS

BY THIS DEED OF TRUST, made on MARCH 24, 1997

by ISIS PHARMACEUTICALS, INC., a Delaware corporation
whose address is 2280 Faraday Drive

(herein called "Trustor"),

(Number and Street)

Carlsbad

(City)

California

(State)

92008

(zip code)

to IMPERIAL BANCORP, a California corporation as Trustee, for the benefit of
IMPERIAL BANK, a California corporation, as Beneficiary, Trustor irrevocably

GRANTS, TRANSFERS AND ASSIGNS TO TRUSTEE IN TRUST, WITH POWER OF SALE, all that property in the City of Carlsbad, County of San Diego, State of California, described as:

SEE EXHIBIT "A" ATTACHED HERETO AND MADE A PART HEREOF BY THIS REFERENCE

SEE EXHIBIT "B" FOR HAZARDOUS MATERIALS PROVISIONS AND CROSS DEFAULT PROVISIONS ATTACHED HERETO AND MADE A PART HEREOF BY THIS REFERENCE

and commonly known as 2280, 2282 and 2292 Faraday Avenue, Carlsbad, California 92008

INCLUDING (a) all appurtenances and easements and rights of way used in connection therewith or as a means of access thereto; (b) all buildings, improvements and fixtures now or hereafter placed thereon, it being understood and agreed that all classes of property attached or unattached used in connection therewith shall be deemed fixtures; and (c) any water rights and/or the stock of any water company which rights and/or stock are appurtenant or pertain to said property.

TOGETHER WITH the rents, issues and profits thereof, SUBJECT, HOWEVER, to the right, power and authority hereinafter given to and conferred upon Trustor to collect and retain such rents, issues and profits prior to any default hereunder.

FOR THE PURPOSE OF SECURING: (1) Payment of the indebtedness with interest thereon evidenced by two Promissory Notes in the principal sum of (i) \$6,000,000.00 and (ii) \$3,706,620.00, both executed by Trustor, both dated March 24, 1997, both payable to Beneficiary or order, and all modifications, extensions or renewals thereof; (2) Payment of such additional sums with interest thereon as the then record owner of said property may hereafter borrow from Beneficiary, when evidenced by a note (or notes) or any agreement reciting that it is so secured; (3) Performance of each agreement of Trustor and Borrower incorporated herein by reference or contained herein; and (4) Performance of each agreement of Trustor contained in any and all agreements executed by Trustor for the purpose of further securing any obligations secured hereby.

In the event the herein described property, or any part thereof, or any interest therein, is sold, agreed to be sold, conveyed, transferred, disposed of, further encumbered, or alienated by Trustor or by the operation of law or otherwise without the

written consent of beneficiary first obtained, all obligations secured by this instrument, irrespective of the maturity dates expressed therein, at the option of the holder beneficiary, and without demand or notice, shall immediately become due and payable. Consent to one such transaction shall not be deemed to be a waiver of the right to require such consent to future or successive transactions.

TO PROTECT THE SECURITY OF THIS DEED OF TRUST, TRUSTOR AGREES: By the execution and delivery of this Deed of Trust and the obligation(s) secured hereby, that provisions (1) to (30), inclusive, of the Fictitious Deed of Trust recorded in Los Angeles, Riverside, San Francisco, Solano, Sonoma, Monterey, Contra Costa, San Bernardino, San Diego, Ventura, Santa Clara, Sacramento, Marin and Alameda Counties February 29, 1980, and in Orange, San Mateo and Santa Barbara Counties March 4, 1980, in the Book and at the Page or as the document number of Official Records in the office of the County Recorder of the County where said property is located as set forth and noted below opposite the name of such County, viz:

COUNTY			COUNTY		
Los Angeles	Document 80-206967		San Bernardino	Document 80-052391	
Orange	Book 13522	Page 522	San Diego	Book 1980	Page 80-070516
Riverside	Book 1980	Page 40216	Ventura	Book 5605	Page 585
San Francisco	Book C953	Page 187	Santa Clara	F 168	Page 720
San Mateo	Reel 7942	Image 117	Sacramento	Book 8002-29	Page 3
Solano	Book 1980	Page 15924	Santa Barbara	Document 80-8831	
Sonoma	Document 80-11977		Marin	Book 3684	Page 09
Monterey	Reel 1392	Page 1128	Alameda	Document 80-036324	
Contra Costa	Book 9752	Page 322			

hereby are adopted and incorporated herein and made a part hereof as fully as though set forth herein at length; that Trustor will observe said provisions; and that the references to property, obligations, and parties in said provisions shall be construed to refer to the property, obligations, and parties set forth in this Deed of Trust.

TRUSTOR REQUESTS that a copy of any notice of default and of any notice of sale hereunder shall be mailed to Trustor at the address hereinabove set forth.

The following portions of provisions (1) to (30) of the Fictitious Deed of Trust incorporated into this Deed of Trust are amended as follows:

a) In paragraphs 7, 15 and 21, wherever "Prime Rate charged by Imperial Bank" appears, "Default rate as charged by Imperial Bank as set forth in the obligation secured hereby" is hereby substituted. b) The first two full sentences in paragraph 20 are deleted in their entirety and are replaced by the following provisions; Trustor hereby absolutely and unconditionally assigns and transfers to Beneficiary all the leases (including all security deposits, guarantees and other security at any time given as security for the performance of the obligations of the tenants thereunder), income, rents, issues, deposits, profits and proceeds of the property to which Trustor may be entitled, whether now due, past due or to become due, and hereby gives to and confers upon Beneficiary the right, power and authority to collect such income, rents, issues, deposits, profits and proceeds. This assignment of the leases, income, rents, issues, deposits, profits and proceeds constitutes an irrevocable direction and authorization of all tenants under the leases to pay all rent, income and profits to Beneficiary upon demand and without further consent or other action by Trustor. This is an absolute assignment, not an assignment for security only, and Beneficiary's right to rents, issues and profits is not contingent on Beneficiary's possession of all or any portion of the property. Trustor irrevocably appoints Beneficiary its true and lawful attorney-in-fact, at the option of Beneficiary at any time, to demand, receive and enforce payment, to give receipts, releases and satisfactions, and to sue, either in the name of Trustor or in the name of the Beneficiary, for all such income, rents, issues, deposits, profits and proceeds and apply the same to the indebtedness secured hereby. It is understood and agreed that neither the foregoing assignment of leases, income, rents, issues, deposits, profits and proceeds to Beneficiary nor the exercise by Beneficiary of any of its rights or remedies under this Section or under any similar provision of the Deed of Trust shall be deemed to make Beneficiary a "mortgagee-in-possession" or otherwise obligated, responsible or liable in any manner with respect to the property or the use, occupancy, enjoyment or operation of all or any portion thereof. Notwithstanding anything to the contrary contained herein or in the obligation secured hereby, so long as no event which is, or with notice or passage of time or both would constitute, an event of default shall have occurred, Trustor shall have a license to collect all income, rents, issues, profits and proceeds from the property as trustee for the benefit of Beneficiary and Trustor, and Trustor shall apply the funds so collected first to the payment of the indebtedness secured hereby which are then due and payable in such manner as Beneficiary elects and thereafter to the account of Trustor, Upon the occurrence of such event, such license shall be deemed revoked and any rents received thereafter by Trustor shall be held by Trustor in trust for the benefit of Beneficiary and shall be delivered in kind to Beneficiary immediately upon receipt thereof by Trustor. Upon the occurrence of such event, Trustor agrees to deliver the original copies of all leases to Beneficiary. Trustor hereby irrevocably constitutes and appoints Beneficiary its true and lawful attorney-in-fact to enforce, in Trustor's name or

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in Beneficiary's name or otherwise, all rights of Trustor in the instruments, including without limitation, checks and money orders, tendered as payments of rents and to do any and all things necessary and proper to carry out the purposes hereof.

SIGNATURE OF TRUSTOR

ISIS PHARMACEUTICALS, INC., a Delaware

corporation

By: /s/ GARY J.G. ATKINSON

VICE PRESIDENT, FINANCE

SIGNATURES MUST BE ACKNOWLEDGED BEFORE A NOTARY PUBLIC

REQUEST FOR FULL RECONVEYANCE

To Be Used Only When Note Has Been Paid

A reconveyance will be issued upon presentation to Imperial Bancorp of this request properly signed and accompanied by the reconveyance fee, the Deed of Trust, the original note or notes secured by said Deed of Trust and any receipt or document evidencing any other indebtedness secured thereby.

To IMPERIAL BANCORP, Trustee

Dated: _____

The undersigned is the legal owner of the note or notes and of all other indebtedness secured by the within Deed of Trust. Said note or notes, together with all other indebtedness secured by said Deed of Trust, have been fully paid and satisfied and you are hereby requested and directed on payment to you of any sums owing to you under the terms of said Deed of Trust to cancel said note or notes and all other evidences of indebtedness delivered to you herewith and said Deed of Trust and to reconvey without warranty to the parties designated by the terms of said Deed of Trust all the estate now held by you thereunder.

Do not lose or destroy this Deed of Trust OR THE NOTE which it secures. Both must be delivered to the Trustee for cancellation before reconveyance will be made.

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State of California)
) SS
County of San Diego)

On May 5, 1997, before me, the undersigned, Notary Public in and for said State, personally appeared Gary Atkinson, personally known to me (or proved to me on the basis of satisfactory evidence) to be the person(s) whose name(s) is/are subscribed to the within instrument and acknowledged to me that he/she/they executed the same in his/her/their authorized capacity(ies), and that by his/her/their signature(s) on the instrument the person(s), or the entity upon behalf of which the person(s) acted, executed this instrument.

WITNESS my hand and official seal.

ANGIE STROOT
COMM. #1080447
NOTARY PUBLIC-CALIFORNIA

EXHIBIT 'B' ATTACHED TO THAT CERTAIN DEED OF TRUST AND ASSIGNMENT OF RENTS
EXECUTED BY ISIS PHARMACEUTICALS, INC., DATED MARCH 24, 1997

HAZARDOUS MATERIALS INDEMNITY AGREEMENT

1. Trustor hereby represents to Beneficiary that neither Trustor nor, to the best of its knowledge, after having made reasonable and appropriate inquiry, any current or previous owner, tenant, occupant or user of the real property secured hereby ("Property"), has used, generated, released, discharged, stored, installed or disposed of any Hazardous Material (as defined below) on, under, in, about or near the Property, nor have any of them transported Hazardous Material to, from or across the Property. In addition, Trustor covenants as follows:

(a) Trustor will not, nor will Trustor permit or suffer any of its partners, officers, employees, agents, tenants, or any other licensee or invitee or trespasser to cause or permit any Hazardous Materials to be brought upon, kept, or used or disposed of on, under, in or about the Property, except for Hazardous Materials used in the normal course of Trustor's business, provided that Trustor complies with all city, county, federal and all other regulations, laws and restrictions relating to Hazardous Materials.

(b) If Trustor breaches the representations, covenants, or obligations stated in this paragraph 1, or if by any other cause whatsoever the presence of Hazardous Materials on, under, in, about or near the Property results in the contamination of the Property or other properties by Hazardous Materials, then, in addition to other remedies available to Beneficiary, Trustor shall, at its sole cost and expense, indemnify, defend and hold Beneficiary and its officers, employees, agents, affiliates and successors-in-interest harmless from any and all losses, obligations, claims, judgements, damages, penalties, fines, costs, liabilities, expenses, including actual attorneys' fees and costs, and the costs of any clean-up, and any other losses which may arise at any time as a result of such contamination, or allegation thereof by a governmental agency, or the determination by any court or governmental agency, or by Beneficiary or its successor-in-interest, that the uses of the Property must be limited or that the Hazardous Materials should be removed and the damage to the Property and its environs restored.

(c) The indemnifications of Beneficiary, and its officers, employees, agents, affiliates and successors-in-interest by Trustor contained in this paragraph 1 includes, without limitations costs incurred in connection with any investigation of site conditions, or any cleanup, remedial removal or restoration where required by any Federal, state or local governmental agency or political subdivision, or by any insurance company, or by Beneficiary or its successor-in-interest in the exercise of its reasonable discretion, because of Hazardous Material present in the soil, ground, water, air, any improvements ("Improvements") located on the Property, or otherwise in, on, under, about or near the Property.

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(d) Without limiting the foregoing, if the presence of any Hazardous Material in, on, under, about or near the Property is caused or permitted by Trustor, its tenants, or either of their successors-in-interest, officers, employees, agents, licensees or invitees, or by trespassers, and results in any contamination of the Property or other properties, Trustor shall take all actions at its sole cost and expense as are necessary to return the Property to the condition existing prior to the introduction of any such Hazardous Materials to the Property; provided that the Beneficiary's approval of such an action shall be first obtained, which approval shall not be unreasonably

withheld as long as such actions would not potentially have an adverse material long-term or short-term effect on the Property.

(e) The foregoing clean-up and indemnification obligations shall survive the reconveyance or foreclosure of this Deed of Trust securing Trustor's obligations under the Loan.

(f) Trustor also agrees: (i) to provide Beneficiary with copies of any communications outside the normal course of Trustor's business, between Trustor, or its tenant, officers, employees, agents or predecessors or successors-in-interest, licensees or invitees and any third parties, including but not limited to, governmental authorities relative to any Hazardous Material on, under, in, about or near or affecting the Property; and (ii) that nondisclosure of any such communication prior to recordation of this Deed of Trust shall be deemed an affirmative representation that no such communication has been received by or is known to Trustor, its officers, employees or agents; and (iii) the Beneficiary is hereby granted the right (but not the obligation) to participate in any proceeding with any governmental agency or court relative to any Hazardous Materials on, in, under, about, near or affecting the Property.

(g) As used herein the term "Hazardous Materials" means any hazardous, toxic or infectious substance, material, gas or waste which is or becomes regulated by any governmental authority, or the United States Government, or any of their agencies, or which has been identified as a toxic, cancer causing or otherwise hazardous substance. The term "Hazardous Materials" includes, without limitation, any material or substance which is: (i) defined as a "hazardous waste," "extremely hazardous waste" or "restricted hazardous waste" under Sections 25115, 25117 or 25122.7, or is listed pursuant to Section 25140, of the California Health and Safety Code, Division 20, Chapter 6.5, as it may from time to time be amended (the "Hazardous Waste Control Law"); (ii) defined as a "hazardous substance" under Section 25316 of the California Health and Safety Code, Division 20, Chapter 6.8 as now existing or hereinafter amended (the "Carpenter-Presley-Tanner Hazardous Substance Account Act"); (iii) defined as a "hazardous material," "hazardous substance" or "hazardous waste" under Section 25501 of the California Health and Safety Code, Division 20, Chapter 6.95 as presently existing or hereinafter amended (the "Hazardous Materials Release Response Plans and Inventory"); (iv) defined as a "hazardous substance" under Section 25281 of the California Health and Safety Code, Division 20, Chapter 6.7 as presently existing or hereinafter amended (the "Underground Storage of Hazardous Substances Act"), (v) petroleum; (vi) polychlorinated biphenyls (PCB); (vii) asbestos; (viii) listed under Article 9 or defined as "hazardous" or "extremely hazardous" pursuant to Article 11 of Title 22 of the California Administrative Code, Division 4, Chapter 20, as now existing or hereinafter amended; (ix) designated as a "hazardous substance" pursuant to Section 307 of the Federal Water Pollution Control Act (33 U.S.C. 1317), as presently existing or

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hereinafter amended or designated as a "hazardous substance" pursuant to Section 311 of the Clean Water Act, 33 U.S.C. 1251 et seq. (33 U.S.C. 1321); (x) defined as a "hazardous waste" pursuant to Section 1004 of the Federal Resource Conservation and Recovery Act, 42 U.S.C. 69012 et seq. (42 U.S.C. 6903), as presently existing or hereinafter amended; or (xi) defined as a "hazardous substance" pursuant to Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act, 42 U.S.C. 9601 et seq. (42 U.S.C. 9601), as presently existing or hereafter amended.

(h) Trustor also represents that the Property is not a "hazardous waste property" or within a "border zone" as defined in California Health and Safety Code 25117.3 and 25117.4 nor is the Property subject to the requirements for notice to the California Department of Health Services, as such notice requirement is defined in California Health and Safety Code 25221(a) as presently existing.

(i) Trustor also represents that the Property and its intended use complies with all applicable laws and governmental regulation including, without limitation, all applicable Federal, state and local laws pertaining to air and

water quality, waste disposal and other environmental matters, including but not limited to, the clean water, clean air, federal water pollution control, solid waste disposal, resource conservation recovery and comprehensive environmental response compensation and liability acts enacted by the U.S. Congress, and the California Environmental Quality Act and all regulations adopted by the State of California pursuant thereto, and the rules and regulations and ordinances of the County of San Diego and the City of Carlsbad, concerning air and water quality, waste disposal and other environmental matters, and the rules and regulations of the California Department of Health Services, the regional Water Quality Control Board, the regional Air Quality Management District, the California State Water Resources Control Board, the U.S. Environmental Protection Agency, and all other applicable Federal, state and local agencies and bureaus.

(j) Trustor acknowledges that this is an environmental provision as described in California Code of Civil Procedure, Section 736.

The breach by Trustor of any representation or covenant contained in this paragraph 1 shall constitute an immediate event of default hereunder, affording to Beneficiary any and all remedies for said default available hereunder or under applicable law.

2. Upon a default hereunder by Trustor, Beneficiary shall have each of the following remedies, in addition to any other remedies, hereunder or under applicable law, which Beneficiary may otherwise have for said default:

(a) Beneficiary or its employees, acting by themselves or through a court-appointed receiver, may: (i) enter upon, possess, manage, operate, dispose of, and contract to dispose of the Property or any part thereof; (ii) take custody of all accounts; (iii) negotiate with governmental authorities with respect to the Property's environmental compliance and remedial measures; (iv) take any action necessary to enforce compliance with environmental provisions,

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including but not limited to spending rents to abate the problem; (v) make, terminate, enforce or modify leases of the Property upon such terms and conditions as Beneficiary deems proper; (vi) contract for goods and services, hire agents, employees, and counsel, make repairs, alterations, and improvements to the Property necessary, in Beneficiary's judgement, to protect or enhance the security hereof; (vii) incur the risks and obligations ordinarily incurred by owners of property (without any personal obligation on the part of the receiver); and/or (viii) take any and all other actions which may be necessary or desirable to comply with Trustor's obligations hereunder and under any other documents (collectively "Loan Documents") executed by Trustor in connection therewith. All sums realized by Beneficiary under this subparagraph, less all costs and expenses incurred by it under this subparagraph including attorney fees, and less such sums as Beneficiary deems appropriate as a reserve to meet future expenses under this subparagraph, shall be applied on any indebtedness secured hereby in such order as Beneficiary shall determine. Neither application of said sums to said indebtedness, nor any other action taken by Beneficiary under this subparagraph shall cure or waive any event of default or notice of default hereunder, or nullify the effect of any such notice of default. Beneficiary, or any employee or agent of Beneficiary, or a receiver appointed by a court of competent jurisdiction, may take any action or proceeding hereunder without regard to: (A) the adequacy of the security for the indebtedness secured hereunder; (B) the existence of a declaration that the indebtedness secured hereby has been declared immediately due and payable; or (C) the filing of a notice of default.

(b) With or without notice, and without releasing Trustor from any obligation hereunder, to cure any default of Trustor and, in connection therewith, Beneficiary or its agents, acting by themselves or through a court appointed receiver, may enter upon the Property or any part thereof and perform such acts and things as Beneficiary deems necessary or desirable to inspect, investigate, assess, and protect the security hereof, including without limitation of any of its other rights: (i) to obtain a court order to enforce Beneficiary's right to enter and inspect the Property under California Civil Code Section 2929.5, to which the decision of Beneficiary as to whether there

exists a release or threatened release of a Hazardous Material onto the Property shall be deemed reasonable and conclusive as between the parties hereto; and (ii) to have a receiver appointed under California Code of Civil Procedure Section 564 to enforce Beneficiary's right to enter and inspect the Property for Hazardous Materials. All costs and expenses incurred by Beneficiary with respect to the audits, tests, inspections, and examinations which Beneficiary or its agents or employees may conduct, including the fees of the engineers, laboratories, contractors, consultants, and attorneys, shall be paid by Trustor immediately upon demand by Beneficiary. All costs and expenses incurred by Trustee and Beneficiary pursuant to this subparagraph (including without limitation court costs, consultant fees and attorney fees, whether incurred in litigation or not and whether before or after judgement) shall bear interest at the default rate of interest ("Default Rate") set forth in the promissory note ("Note") secured hereby, from the date they are incurred until said sums have been paid.

(c) To seek a judgement that Trustor has breached its covenants, representations and/or warranties with respect to the Hazardous Materials, as set forth in paragraph I above, by commencing and maintaining an action or actions in any court of competent jurisdiction for breach of contract pursuant to California Code of Civil Procedure

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Section 736, whether commenced prior to foreclosure of the Property or after foreclosure of the Property, and to seek the recovery of any and all costs, damages, expenses, fees, penalties, fines, judgements, indemnification payments to third parties, and other out-of-pocket costs or expenses actually incurred by Beneficiary (collectively, the "Environmental Costs") incurred or advanced by Beneficiary relating to the cleanup, remediation or other response action required by applicable law or to which Beneficiary believes necessary to protect the Property, it being conclusively presumed between Beneficiary and Trustor that all such Environmental Costs incurred or advanced by Beneficiary relating to the cleanup, remediation or other response action of or to the Property were made by Beneficiary in good faith. All Environmental Costs incurred by Beneficiary under this subparagraph (including without limitation court costs, consultant fees and attorney fees, whether incurred in litigation or not and whether before or after judgement) shall bear interest at the Default Rate from the date of expenditure until said sums have been paid. Beneficiary shall be entitled to bid, at any foreclosure sale of the Property, the amount of said costs, expenses and interest in addition to the amount of the other obligations hereby secured as a credit bid, the equivalent of cash. Trustor acknowledges and agrees that notwithstanding any term or provision contained herein or in the Loan Documents: (i) the Environmental Costs shall be exceptions to any nonrecourse or exculpatory provision of the Loan Documents; (ii) Trustor shall be fully and personally liable for the Environmental Costs hereunder; (iii) such liability shall not be limited to the original principal amount of the obligations secured by this Deed of Trust; and (iv) Trustor's obligations shall survive the foreclosure, deed in lieu of foreclosure, release, reconveyance, or any other transfer of the Property or this Deed of Trust. For the purposes of any action brought under this subparagraph, Trustor hereby waives the defense of laches, and any applicable statute of limitations.

(d) To waive its lien against the Property or any portion thereof, whether fixtures or personal property, to the extent such property is found to be environmentally impaired in accordance with California Code of Civil Procedure Section 726.5 and to exercise any and all rights and remedies of an unsecured creditor against Trustor and all of Trustor's assets and property for the recovery of any deficiency and Environmental Costs, including, but not limited to, seeking an attachment order under California Code of Civil Procedure Section 483.010. As between Beneficiary and Trustor, for purposes of California Code of Civil Procedure Section 726.5, Trustor shall have the burden of proving that Trustor or any related party (or any affiliate or agent of Trustor or any related party) was not in any way negligent in permitting the release or threatening release of the Hazardous Material. Trustor acknowledges and agrees that notwithstanding any term or provision contained herein or in the Loan Documents, all judgements and awards entered against Trustor shall be exceptions to any nonrecourse or exculpatory provision of the Loan Documents, and Trustor shall be fully and personally liable for all judgements and awards entered

against Trustor hereunder and such liability shall not be limited to the original principal amount of the obligations secured by this Deed of Trust and Trustor's obligations shall survive the foreclosure, deed in lieu of foreclosure, release, reconveyance, or any other transfer of the Property or this Deed of Trust. For the purpose of any action brought under this subparagraph, Trustor hereby waives the defense of laches and any applicable statute of limitations.

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Exhibit "B" to Deed of Trust
ISIS PHARMACEUTICALS, INC.
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(e) All rights and remedies of Beneficiary hereunder are cumulative and in addition to all rights and remedies provided in the Loan Documents or by applicable law.

CROSS DEFAULT

Default in the performance or observance of any of the terms and provisions: (i) of any documents, including without limitation this Deed of Trust, ("Loan Documents") executed by Trustor or any entity guaranteeing any of Trustor's obligations to Beneficiary ("Guarantor") in connection with the obligations secured hereby; or (ii) of any documents executed by Trustor or Guarantor in connection with any other obligations of Trustor or any Guarantor to Beneficiary, including but not limited to Beneficiary Loan Number 00700002641 and 00700002724 (collectively, "Other Documents"), shall constitute a default under the terms of each of the Loan Documents and the Other Documents at Beneficiary's option, thereby making available to Beneficiary any and all of the remedies set forth therein.

EXHIBIT 10.4

Imperial Bank Note Secured By Deed of Trust dated March 24, 1997
in the amount of \$3,706,620; Deed of Trust and Assignment of Rents
dated March 24, 1997.

DO NOT DESTROY THIS NOTE:

WHEN PAID, THIS NOTE, WITH THE DEED OF TRUST SECURING SAME, MUST BE SURRENDERED
TO THE TRUSTEE FOR CANCELLATION BEFORE RECONVEYANCE WILL BE MADE.

[LOGO]

IMPERIAL BANK
Member FDIC
NOTE SECURED BY DEED OF TRUST

\$3,706,620.00 San Diego, California, MARCH 24, 1997

On April 1, 2002, and as hereinafter provided, for value received, the undersigned promises to pay to IMPERIAL BANK ("Bank"), a California banking corporation, or order, at its San Diego Regional office, the principal sum of \$3,706,620.00 or such sums up to the maximum if so stated, as the Bank may now or hereafter advance to or for the benefit of the undersigned in accordance with the terms hereof, together with interest from date of disbursement or n/a, whichever is later, on the unpaid principal balance [] at the rate of n/a% per year [X] at the rate of 0.50% per year in excess of the rate of interest which Bank has announced as its prime lending rate (the "Prime Rate"), which shall vary concurrently with any change in such Prime Rate, or \$250.00, whichever is greater. Interest shall be computed at the above rate on the basis of the actual number of days during which the principal balance is outstanding, divided by 360, which shall, for interest computation purposes, be considered one year.

Interest shall be payable [X] monthly [] quarterly [] included with principal [X] in addition to principal [] beginning May 1, 1997, and if not so paid shall become a part of the principal. All payments shall be applied first to interest, and the remainder, if any, on principal. [X] (If checked), Principal shall be payable in installments of \$12,433.00, or more, each installment on the 1st day of each month, beginning May 1, 1997.

Any partial prepayment shall be applied to the installments, if any, in

inverse order of maturity. Should default be made in the payment of principal or interest when due, or in the performance or observance, when due, of any item, covenant or condition of any deed of trust, security agreement or other agreement (including amendments or extensions thereof) securing or pertaining to this note, at the option of the holder hereof and without notice or demand, the entire balance of principal and accrued interest then remaining unpaid shall (a) become immediately due and payable, and (b) thereafter bear interest, until paid in full, at the increased rate of 5% per year in excess of the rate provided for above, as it may vary from time to time.

Defaults shall include, but not be limited to, the failure of the maker(s) to pay principal or interest when due; the filing as to each person obligated hereon, whether as maker, co-maker, endorser or guarantor (individually or collectively referred to as the "Obligor") of a voluntary or involuntary petition under the provisions of the Federal Bankruptcy Act; the issuance of any attachment or execution against any asset of any Obligor; the death of any Obligor; or any deterioration of the financial condition of any Obligor which results in the holder hereof considering itself, in good faith, insecure.

[X] If any installment payment or principal balance payment due hereunder is delinquent ten or more days, Obligor agrees to pay a late charge in the amount of 5% of the payment so due and unpaid, in addition to the payment; but nothing in this paragraph is to be construed as any obligation on the part of the holder of this note to accept payment of any installment past due or less than the total unpaid principal balance after maturity.

If this note is not paid when due, each Obligor promises to pay all costs and expenses of collection and reasonable attorney's fees incurred by the holder hereof on account of such collection, plus interest at the rate applicable to principal, whether or not suit is filed hereon. Each Obligor shall be jointly and severally liable hereon and consents to renewals, replacements and extensions of time for payment hereof, before, at, or after maturity; consents to the acceptance, release or substitution of security for this note; and waives demand and protest and the right to assert any statute of limitations. Any married person who signs this note agrees that recourse may be had against separate property for any obligations hereunder. The indebtedness evidenced hereby shall be payable in lawful money of the United States. In any action brought under or arising out of this note, each Obligor, including successor(s) or assign(s) hereby consents to the application of California law, to the jurisdiction of any competent court within the State of California, and to service of process by any means authorized by California law.

This note is secured by a deed of trust, dated MARCH 24, 1997, to IMPERIAL BANCORP as Trustee which contains the following provisions: "In the event the herein described property or any part thereof, or any interest therein is sold, agreed to be sold, conveyed, transferred, disposed of, further encumbered, or alienated by trustor or by the operation of law or otherwise, without the written consent of beneficiary first obtained, all obligations secured by this instrument, irrespective of the maturity dates expressed therein, at the option of the holder beneficiary, and without demand or notice shall immediately become due and payable. Consent to one such transaction shall not be deemed to be a waiver of the right to require such consent to future or successive transactions."

No single or partial exercise of any power hereunder, or under any deed of trust, security agreement or other agreement in connection herewith shall preclude other or further exercises thereof or the exercise of any other such power. The holder hereof shall at all times have the right to proceed against any portion of the security for this note in such order and in such manner as such holder may consider appropriate, without waiving any rights with respect to any of the security. Any delay or omission on the part of the holder hereof in exercising any right hereunder, or under any deed of trust, security agreement or other agreement, shall not operate as a waiver of such right, or of any other right, under this note or any deed of trust, security agreement or other agreement in connection herewith.

* See Addendum attached hereto and made a part hereof by this reference.

ISIS PHARMACEUTICALS, INC.

a Delaware corporation

By: /s/ GARY J. G. ATKINSON

Vice President, Finance

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ATTACHED TO THAT CERTAIN NOTE SECURED BY DEED OF TRUST DATED MARCH 24, 1997
EXECUTED BY ISIS PHARMACEUTICALS, INC.

ADDENDUM

The following Reference Provision is by this reference incorporated in the Note:

REFERENCE PROVISION

1. Other than (i) non-judicial foreclosure and all matters in connection therewith regarding security interests in real or personal property; or (ii) the appointment of a receiver, or the exercise of other provisional remedies (any and all of which may be initiated pursuant to applicable law), each controversy, dispute or claim between the parties arising out of or relating to this Note ("Agreement"), which controversy, dispute or claim is not settled in writing within thirty (30) days after the "Claim Date" (defined as the date on which a party subject to the Agreement gives written notice to all other parties that a controversy, dispute or claim exists), will be settled by a reference proceeding in California in accordance with the provisions of Section 638 et seq. of the California Code of Civil Procedure ("CCP"), or their successor section, which shall constitute the exclusive remedy for the settlement of any controversy, dispute or claim concerning this Agreement, including whether such controversy, dispute or claim is subject to the reference proceeding and except as set forth above, the parties waive their rights to initiate any legal proceedings against each other in any court or jurisdiction other than the Superior Court in the County where the Real Property, if any, is located or Los Angeles County if none (the "Court"). The referee shall be a retired Judge of the Court selected by mutual agreement of the parties, and if they cannot so agree within forty-five (45) days after the Claim Date, the referee shall be promptly selected by the Presiding Judge of the Court (or his representative). The referee shall be appointed to sit as a temporary judge, with all of the powers of a temporary judge, as authorized by law, and upon selection should take and subscribe to the oath of office as provided for in Rule 244 of the California Rules of Court (or any subsequently enacted Rule). Each party shall have one peremptory challenge pursuant to CCP Section 170.6. The referee shall (a) be requested to set the matter for hearing within sixty (60) days after the Claim Date and (b) try any and all issues of law or fact and report a statement of decision upon them, if possible, within ninety (90) days of the Claim Date. Any decision rendered by the referee will be final, binding and conclusive and judgment shall be entered pursuant to CCP Section 644 in any court in the State of California having jurisdiction. Any party may apply for a reference proceeding at any time after thirty (30) days following the notice to any other party of the nature of the controversy, dispute or claim, by filing a petition for a hearing and/or trial. All discovery permitted by this Agreement shall be completed no later than fifteen (15)

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days before the first hearing date established by the referee. The referee may extend such period in the event of a party's refusal to provide requested discovery for any reason whatsoever, including, without limitation, legal objections raised to such discovery or unavailability of a witness due to absence or illness. No party shall be entitled to "priority" in conducting discovery. Depositions may be taken by either party upon seven (7) days written notice, and request for production or inspection of documents shall be responded to within ten (10) days after service. All disputes relating to discovery which cannot be resolved by the parties shall be submitted to the referee whose decision shall be final and binding upon the parties. Pending appointment of the referee as provided herein, the Court is empowered to issue temporary and/or provisional remedies, as appropriate.

2. Except as expressly set forth in this Agreement, the referee shall determine the manner in which the reference proceeding is conducted including the time and place of all hearings, the order of presentation of evidence, and all other questions that arise with respect to the course of the reference proceeding. All proceedings and hearings conducted before the referee, except

for trial, shall be conducted without a court reporter, except that when any party so requests, a court reporter will be used at any hearing conducted before the referee. The party making such a request shall have the obligation to arrange for and pay for the court reporter. The costs of the court reporter at the trial shall be borne equally by the parties.

3. The referee shall be required to determine all issues in accordance with existing case law and the statutory laws of the State of California. The rules of evidence applicable to proceedings at law in the State of California will be applicable to the reference proceeding. The referee shall be empowered to enter equitable as well as legal relief, to provide all temporary and/or provisional remedies and to enter equitable orders that will be binding upon the parties. The referee shall issue a single judgment at the close of the reference proceeding which shall dispose of all of the claims of the parties that are the subject of the reference. The parties hereto expressly reserve the right to contest or appeal from the final judgment or any appealable order or appealable judgment entered by the referee. The parties hereto expressly reserve the right to findings of fact, conclusions of law, a written statement of decision, and the right to move for a new trial or a different judgment, which new trial, if granted, is also to be a reference proceeding under this provision.

4. In the event that the enabling legislation which provides for appointment of a referee is repealed (and no successor statute is enacted), any dispute between the parties that would otherwise be determined by the reference procedure herein described will be resolved and determined by arbitration. The arbitration will be conducted by a retired judge of the Court, in accordance with the California Arbitration Act, Section 1280 through Section 1294.2 of the CCP as amended from time to time. The limitations with respect to discovery as set forth hereinabove shall apply to any such arbitration proceeding.

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RECORDING REQUESTED BY
IMPERIAL BANK

WHEN RECORDED MAIL TO

IMPERIAL BANK
9920 SO LA CIENEGA BLVD
INGLEWOOD CA 90301
Attn Lending Services

INDEX AS DEED OF TRUST AND ASSIGNMENT OF RENTS
SPACE ABOVE THIS LINE FOR RECORDER'S USE

Real Estate Loan
Short Form

DEED OF TRUST AND ASSIGNMENT OF RENTS

BY THIS DEED OF TRUST, made on MARCH 24, 1997

by ISIS PHARMACEUTICALS, INC., a Delaware corporation (herein called "Trustor"),
whose address is 2280 Faraday Drive

(Number and Street)

Carlsbad
(City)

California
(State)

92008
(Zip Code)

to IMPERIAL BANCORP, a California corporation as Trustee, for the benefit of IMPERIAL BANK, a California corporation, as Beneficiary, Trustor irrevocably GRANTS, TRANSFERS AND ASSIGNS TO TRUSTEE IN TRUST, WITH POWER OF SALE, all that property in the City of Carlsbad, County of San Diego, State of California, described as:

SEE EXHIBIT "A" ATTACHED HERETO AND MADE A PART HEREOF BY THIS REFERENCE

SEE EXHIBIT "B" FOR HAZARDOUS MATERIALS PROVISIONS AND CROSS DEFAULT PROVISIONS ATTACHED HERETO AND MADE A PART HEREOF BY THIS REFERENCE

and commonly known as 2280, 2282 and 2292 Faraday Avenue, Carlsbad, California 92008

INCLUDING (a) all appurtenances and easements and rights of way used in

connection therewith or as a means of access thereto; (b) all buildings, improvements and fixtures now or hereafter placed thereon, it being understood and agreed that all classes of property attached or unattached used in connection therewith shall be deemed fixtures; and (c) any water rights and/or the stock of any water company which rights and/or stock are appurtenant or pertain to said property.

TOGETHER WITH the rents, issues and profits thereof, SUBJECT, HOWEVER, to the right, power and authority hereinafter given to and conferred upon Trustor to collect and retain such rents, issues and profits prior to any default hereunder.

FOR THE PURPOSE OF SECURING: (1) Payment of the indebtedness with interest thereon evidenced by two Promissory Notes in the principal sum of (i) \$6,000,000.00 and (ii) \$3,706,620.00, both executed by Trustor, both dated March 24, 1997 both payable to Beneficiary or order, and all modifications, extensions or renewals thereof; (2) Payment of such additional sums with interest thereon as the then record owner of said property may hereafter borrow from Beneficiary, when evidenced by a note (or notes) or any agreement reciting that it is so secured; (3) Performance of each agreement of Trustor and Borrower incorporated herein by reference or contained herein; and (4) Performance of each agreement of Trustor contained in any and all agreements executed by Trustor for the purpose of further securing any obligations secured hereby.

In the event the herein described property, or any part thereof, or any interest therein, is sold, agreed to be sold, conveyed, transferred, disposed of, further encumbered, or alienated by Trustor or by the operation of law or otherwise without the

written consent of beneficiary first obtained, all obligations secured by this instrument, irrespective of the maturity dates expressed therein, at the option of the holder beneficiary, and without demand or notice, shall immediately become due and payable. Consent to one such transaction shall not be deemed to be a waiver of the right to require such consent to future or successive transactions.

TO PROTECT THE SECURITY OF THIS DEED OF TRUST, TRUSTOR AGREES: By the execution and delivery of this Deed of Trust and the obligation(s) secured hereby, that provisions (1) to (30), inclusive, of the Fictitious Deed of Trust recorded in Los Angeles, Riverside, San Francisco, Solano, Sonoma, Monterey, Contra Costa, San Bernardino, San Diego, Ventura, Santa Clara, Sacramento, Marin and Alameda Counties February 29, 1980, and in Orange, San Mateo and Santa Barbara Counties March 4, 1980, in the Book and at the Page or as the document number of Official Records in the office of the County Recorder of the County where said property is located as set forth and noted below opposite the name of such County, viz:

COUNTY		COUNTY	
Los Angeles	Document 80-206967	San Bernardino	Document 80-052391
Orange	Book 13522 Page 522	San Diego	Book 1980 Page 80-070516
Riverside	Book 1980 Page 40216	Ventura	Book 5605 Page 585
San Francisco	Book C953 Page 187	Santa Clara	F 168 Page 720
San Mateo	Reel 7942 Image 117	Sacramento	Book 8002-29 Page 3
Solano	Book 1980 Page 15924	Santa Barbara	Document 80-8831
Sonoma	Document 80-11977	Marin	Book 3684 Page 09
Monterey	Reel 1392 Page 1128	Alameda	Document 80-036324
Contra Costa	Book 9752 Page 322		

hereby are adopted and incorporated herein and made a part hereof as fully as though set forth herein at length; that Trustor will observe said provisions; and that the references to property, obligations, and parties in said provisions shall be construed to refer to the property, obligations, and parties set forth in this Deed of Trust.

TRUSTOR REQUESTS that a copy of any notice of default and of any notice of sale hereunder shall be mailed to Trustor at the address hereinabove set forth.

The following portions of provisions (1) to (30) of the Fictitious Deed of Trust incorporated into this Deed of Trust are amended as follows:

a) In paragraphs 7, 15 and 21, wherever "Prime Rate charged by Imperial Bank" appears, "Default rate as charged by Imperial Bank as set forth in the obligation secured hereby" is hereby substituted. b) The first two full sentences in paragraph 20 are deleted in their entirety and are replaced by the following provisions: Trustor hereby absolutely and unconditionally assigns and transfers to Beneficiary all the leases (including all security deposits, guarantees and other security at any time given as security for the performance of the obligations of the tenants thereunder), income, rents, issues, deposits, profits and proceeds of the property to which Trustor may be entitled, whether now due, past due or to become due, and hereby gives to and confers upon Beneficiary the right, power and authority to collect such income, rents, issues, deposits, profits and proceeds. This assignment of the leases, income, rents, issues, deposits, profits and proceeds constitutes an irrevocable direction and authorization of all tenants under the leases to pay all rent, income and profits to Beneficiary upon demand and without further consent or other action by Trustor. This is an absolute assignment, not an assignment for security only, and Beneficiary's right to rents, issues and profits is not contingent on Beneficiary's possession of all or any portion of the property. Trustor irrevocably appoints Beneficiary its true and lawful attorney-in-fact, at the option of Beneficiary at any time, to demand, receive and enforce payment, to give receipts, releases and satisfactions, and to sue, either in the name of Trustor or in the name of the Beneficiary, for all such income, rents, issues, deposits, profits and proceeds and apply the same to the indebtedness secured hereby. It is understood and agreed that neither the foregoing assignment of leases, income, rents, issues, deposits, profits and proceeds to Beneficiary nor the exercise by Beneficiary of any of its rights or remedies under this Section or under any similar provision of the Deed of Trust shall be deemed to make Beneficiary a "mortgagee-in-possession" or otherwise obligated, responsible or liable in any manner with respect to the property or the use, occupancy, enjoyment or operation of all or any portion thereof. Notwithstanding anything to the contrary contained herein or in the obligation secured hereby, so long as no event which is, or with notice or passage of time or both would constitute, an event of default shall have occurred, Trustor shall have a license to collect all income, rents, issues, profits and proceeds from the property as trustee for the benefit of Beneficiary and Trustor, and Trustor shall apply the funds so collected first to the payment of the indebtedness secured hereby which are then due and payable in such manner as Beneficiary elects and thereafter to the account of Trustor. Upon the occurrence of such event, such license shall be deemed revoked and any rents received thereafter by Trustor shall be held by Trustor in trust for the benefit of Beneficiary and shall be delivered in kind to Beneficiary immediately upon receipt thereof by Trustor. Upon the occurrence of such event, Trustor agrees to deliver the original copies of all leases to Beneficiary. Trustor hereby irrevocably constitutes and appoints Beneficiary its true and lawful attorney-in-fact to enforce in Trustor's name or

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in Beneficiary's name or otherwise, all rights of Trustor in the instruments, including without limitation, checks and money orders, tendered as payments of rents and to do any and all things necessary and proper to carry out the purposes hereof.

SIGNATURE OF TRUSTOR

ISIS PHARMACEUTICALS, INC., a Delaware corporation

By: /s/ GARY J. G. ATKINSON

VICE PRESIDENT, FINANCE

SIGNATURES MUST BE ACKNOWLEDGED BEFORE A NOTARY PUBLIC

REQUEST FOR FULL RECONVEYANCE
To Be Used Only When Note Has Been Paid

A reconveyance will be issued upon presentation to Imperial Bancorp of this request properly signed and accompanied by the reconveyance fee, the Deed of Trust, the original note or notes secured by said Deed of Trust and any receipt or document evidencing any other indebtedness secured thereby.

To IMPERIAL BANCORP, Trustee

Dated: -----

The undersigned is the legal owner of the note or notes and of all other indebtedness secured by the within Deed of Trust. Said note or notes, together with all other indebtedness secured by said Deed of Trust, have been fully paid and satisfied and you are hereby requested and directed on payment to you of any sums owing to you under the terms of said Deed of Trust to cancel said note or notes and all other evidences of indebtedness delivered to you herewith and said Deed of Trust and to reconvey without warranty to the parties designated by the terms of said Deed of Trust all the estate now held by you thereunder.

Do not lose or destroy this Deed of Trust OR THE NOTE which it secures. Both must be delivered to the Trustee for cancellation before reconveyance will be made.

State of California)
)Ss
County of San Diego)

On May 5, 1997, before me, the undersigned, Notary Public in and for said State, personally appeared Gary Atkinson personally known to me (or proved to me on the basis of satisfactory evidence) to be the person(s) whose name(s) is/are subscribed to the within instrument and acknowledged to me that he/she/they executed the same in his/her/their authorized capacity(ies), and that by his/her/their signature(s) on the instrument the person(s), or the entity upon behalf of which the person(s) acted, executed this instrument.

WITNESS my hand and official seal.

ANGIE STROOT
Comm. #1080447
NOTARY PUBLIC - CALIFORNIA
SAN DIEGO COUNTY
Comm. Exp. Dec. 11, 1999

/s/ Angie Stroot

Notary Seal

State of California)
)Ss
County of)

On _____, before me, the undersigned, Notary Public in and for said State, personally appeared _____, personally known to me (or proved to me on the basis of satisfactory evidence) to be the person(s) whose name(s) is/are subscribed to the within instrument and acknowledged to me that he/she/they executed the same in his/her/their authorized capacity(ies), and that by his/her/their signature(s) on the instrument the person(s), or the entity upon behalf of which the person(s) acted, executed this instrument.

WITNESS my hand and official seal.

Notary Seal

EXHIBIT "A" ATTACHED TO THAT CERTAIN DEED OF TRUST AND ASSIGNMENT OF RENTS DATED MARCH 24, 1997 EXECUTED BY ISIS PHARMACEUTICALS, INC.

EXHIBIT "A"

LEGAL DESCRIPTION:

PARCEL A:

LOTS 5, 6 AND 7 OF CARLSBAD TRACT NO. 84-91 IN THE CITY OF CARLSBAD, COUNTY OF SAN DIEGO, STATE OF CALIFORNIA, ACCORDING TO MAP THEREOF NO. 11230, FILED IN THE OFFICE OF THE COUNTY RECORDER OF SAN DIEGO COUNTY, MAY 10, 1985.

PARCEL B:

A NON-EXCLUSIVE EASEMENT ON, OVER AND UNDER THE COMMON AREA AS DEFINED AND SHOWN ON THOSE CERTAIN AMENDED AND RESTATED DECLARATION OF ESTABLISHMENT OF COVENANTS, CONDITIONS AND RESTRICTIONS, AND RESERVATION OF EASEMENTS (THE "DECLARATIONS"), DATED JUNE 28, 1988 AND RECORDED AUGUST 8, 1988 AS FILE 89-387705 OF OFFICIAL RECORDS, FOR THE PURPOSES OF INGRESS AND EGRESS, PARKING, THE CONSTRUCTION, INSTALLATION, MAINTENANCE, REMOVAL, REPLACEMENTS, OPERATION AND USE OF UTILITIES, INCLUDING BUT NOT LIMITED TO SEWERS, WATER AND GAS PIPES, DRAINAGE LINES AND SYSTEMS, ELECTRIC POWER, CONDUIT LINES AND WIRING, TELEPHONE, CONDUITS, LINES AND WIRES AND OTHER UTILITIES, PUBLIC OR PRIVATE, BENEATH THE GROUND SURFACE (EXCEPT VAULTS, VENTS, ACCESS, STRUCTURES AND OTHER FACILITIES REQUIRED TO BE ABOVE GROUND), SUBJECT TO THE TERMS, AS MORE PARTICULARLY SET FORTH IN THE DECLARATION.

A.P.N.'s: 212-061-31-00 and 212-061-32-00 and 212-061-33-00

Properties also known as: 2292 Faraday Avenue (Lot 5), 2280 Faraday Avenue (Lot 6) and 2282 Faraday Avenue (Lot 7), Carlsbad, California 92008

EXHIBIT 'B' ATTACHED TO THAT CERTAIN DEED OF TRUST AND ASSIGNMENT OF RENTS EXECUTED BY ISIS PHARMACEUTICALS, INC., DATED MARCH 24, 1997

1. Trustor hereby represents to Beneficiary that neither Trustor nor, to the best of its knowledge, after having made reasonable and appropriate inquiry, any current or previous owner, tenant, occupant or user of the real property secured hereby ("Property"), has used, generated, released, discharged, stored, installed or disposed of any Hazardous Material (as defined below) on, under, in, about or near the Property, nor have any of them transported Hazardous Material to, from or across the Property. In addition, Trustor covenants as follows:

(a) Trustor will not, nor will Trustor permit or suffer any of its partners, officers, employees, agents, tenants, or any other licensee or invitee or trespasser to cause or permit any Hazardous Materials to be brought upon, kept, or used or disposed of on, under, in or about the Property, except for Hazardous Materials used in the normal course of Trustor's business, provided that Trustor complies with all city, county, federal and all other regulations, laws and restrictions relating to Hazardous Materials.

(b) If Trustor breaches the representations, covenants, or obligations stated in this paragraph 1, or if by any other cause whatsoever the presence of Hazardous Materials on, under, in, about or near the Property results in the contamination of the Property or other properties by Hazardous Materials, then, in addition to other remedies available to Beneficiary, Trustor shall, at its sole cost and expense, indemnify, defend and hold Beneficiary and its officers, employees, agents, affiliates and successors-in-interest harmless from any and all losses, obligations, claims, judgments, damages, penalties, fines, costs, liabilities, expenses, including actual attorneys' fees and costs, and the costs of any clean-up, and any other losses which may arise at any time as a result of such contamination, or allegation thereof by a governmental agency, or the determination by any court or governmental agency, or by Beneficiary or its successor-in-interest, that the uses of the Property must be limited or that the Hazardous Materials should be removed and the damage to the Property and its environs restored.

(c) The indemnifications of Beneficiary, and its officers, employees, agents, affiliates and successors-in-interest by Trustor contained in this paragraph 1 includes, without limitation, costs incurred in connection with any investigation of site conditions, or any cleanup, remedial removal or restoration where required by any Federal, state or local governmental agency or political subdivision, or by any insurance company, or by Beneficiary or its successor-in-interest in the exercise of its reasonable discretion because of Hazardous Material present in the soil, ground, water, air, any improvements ("Improvements") located on the Property, or otherwise in, on, under, about or near the Property.

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Exhibit "B" to Deed of Trust
ISIS PHARMACEUTICALS, INC.
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(d) Without limiting the foregoing, if the presence of any Hazardous Material in, on, under, about or near the Property is caused or permitted by Trustor, its tenants, or either of their successors-in-interest, officers, employees, agents, licensees or invitees, or by trespassers, and results in any contamination of the Property or other properties, Trustor shall take all actions at its sole cost and expense as are necessary to return the Property to the condition existing prior to the introduction of any such Hazardous Materials to the Property; provided that the Beneficiary's approval of such an action shall be first obtained, which approval shall not be unreasonably withheld as long as such actions would not potentially have an adverse material long-term or short-term effect on the Property.

(e) The foregoing clean-up and indemnification obligations shall survive the reconveyance or foreclosure of this Deed of Trust securing Trustor's obligations under the Loan.

(f) Trustor also agrees: (i) to provide Beneficiary with copies of any communications outside the normal course of Trustor's business, between Trustor, or its tenant, officers, employees, agents or predecessors or

successors-in-interest, licensees or invitees and any third parties, including but not limited to, governmental authorities relative to any Hazardous Material on, under, in, about or near or affecting the Property; and (ii) that nondisclosure of any such communication prior to recordation of this Deed of Trust shall be deemed an affirmative representation that no such communication has been received by or is known to Trustor, its officers, employees or agents; and (iii) the Beneficiary is hereby granted the right (but not the obligation) to participate in any proceeding with any governmental agency or court relative to any Hazardous Materials on, in, under, about, near or affecting the Property.

(g) As used herein the term "Hazardous Materials" means any hazardous, toxic or infectious substance, material, gas or waste which is or becomes regulated by any governmental authority, or the United States Government, or any of their agencies, or which has been identified as a toxic, cancer causing or otherwise hazardous substance. The term "Hazardous Materials" includes, without limitations any material or substance which is: (i) defined as a "hazardous waste," "extremely hazardous waste" or "restricted hazardous waste" under Sections 25115, 25117 or 25122.7, or is listed pursuant to Section 25140, of the California Health and Safety Code, Division 20, Chapter 6.5, as it may from time to time be amended (the "Hazardous Waste Control Law"); (ii) defined as a "hazardous substance" under Section 25316 of the California Health and Safety Code, Division 20, Chapter 6.8 as now existing or hereinafter amended (the "Carpenter-Presley-Tanner Hazardous Substance Account Act"); (iii) defined as a "hazardous material," "hazardous substance" or "hazardous waste" under Section 25501 of the California Health and Safety Code, Division 20, Chapter 6.95 as presently existing or hereinafter amended (the "Hazardous Materials Release Response Plans and Inventory"); (iv) defined as a "hazardous substance" under Section 25281 of the California Health and Safety Code, Division 20, Chapter 6.7 as presently existing or hereinafter amended (the "Underground Storage of Hazardous Substances Act"); (v) petroleum; (vi) polychlorinated biphenyls (PCB); (vii) asbestos; (viii) listed under Article 9 or defined as "hazardous" or "extremely hazardous" pursuant to Article 11 of Title 22 of the California Administrative Code, Division 4, Chapter 20, as now existing or hereinafter amended; (ix) designated as a "hazardous substance" pursuant to Section 307 of the Federal Water Pollution Control Act (33 U.S.C. 1317), as presently existing or

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hereinafter amended or designated as a "hazardous substance" pursuant to Section 311 of the Clean Water Act, 33 U.S.C. 1251 et seq. (33 U.S.C. 1321); (x) defined as a "hazardous waste" pursuant to Section 1004 of the Federal Resource Conservation and Recovery Act, 42 U.S.C. 69012 et seq. (42 U.S. C. 6903), as presently existing or hereinafter amended; or (xi) defined as a "hazardous substance" pursuant to Section 101 of the Comprehensive Environmental Response, Compensation and Liability Act, 42 U.S.C. 9601 et seq. (42 U.S.C. 9601), as presently existing or hereafter amended.

(h) Trustor also represents that the Property is not a "hazardous waste property" or within a "border zone" as defined in California Health and Safety Code 25117.3 and 25117.4 nor is the Property subject to the requirements for notice to the California Department of Health Services, as such notice requirement is defined in California Health and Safety Code 25221(a) as presently existing.

(i) Trustor also represents that the Property and its intended use complies with all applicable laws and governmental regulation including, without limitation, all applicable Federal, state and local laws pertaining to air and water quality, waste disposal and other environmental matters, including but not limited to, the clean water, clean air, federal water pollution control, solid waste disposal, resource conservation recovery and comprehensive environmental response compensation and liability acts enacted by the U.S. Congress, and the California Environmental Quality Act and all regulations adopted by the State of California pursuant thereto, and the rules and regulations and ordinances of the County of San Diego and the City of Carlsbad, concerning air and water quality, waste disposal and other environmental matters, and the rules and regulations of

the California Department of Health Services, the regional Water Quality Control Board, the regional Air Quality Management District, the California State Water Resources Control Board, the U.S. Environmental Protection Agency, and all other applicable Federal, state and local agencies and bureaus.

(j) Trustor acknowledges that this is an environmental provision as described in California Code of Civil Procedure, Section 736.

The breach by Trustor of any representation or covenant contained in this paragraph 1 shall constitute an immediate event of default hereunder, affording to Beneficiary any and all remedies for said default available hereunder or under applicable law.

2. Upon a default hereunder by Trustor, Beneficiary shall have each of the following remedies, in addition to any other remedies, hereunder or under applicable law, which Beneficiary may otherwise have for said default:

(a) Beneficiary or its employees, acting by themselves or through a court-appointed receiver, may: (i) enter upon, possess, manage, operate, dispose of, and contract to dispose of the Property or any part thereof, (ii) take custody of all accounts; (iii) negotiate with governmental authorities with respect to the Property's environmental compliance and remedial measures; (iv) take any action necessary to enforce compliance with environmental provisions,

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including but not limited to spending rents to abate the problem; (v) make, terminate, enforce or modify leases of the Property upon such terms and conditions as Beneficiary deems proper; (vi) contract for goods and services, hire agents, employees, and counsel, make repairs, alterations, and improvements to the Property necessary, in Beneficiary's judgement, to protect or enhance the security hereof, (vii) incur the risks and obligations ordinarily incurred by owners of property (without any personal obligation on the part of the receiver); and/or (viii) take any and all other actions which may be necessary or desirable to comply with Trustor's obligations hereunder and under any other documents (collectively "Loan Documents") executed by Trustor in connection therewith. All sums realized by Beneficiary under this subparagraph, less all costs and expenses incurred by it under this subparagraph, including attorney fees, and less such sums as Beneficiary deems appropriate as a reserve to meet future expenses under this subparagraph, shall be applied on any indebtedness secured hereby in such order as Beneficiary shall determine. Neither application of said sums to said indebtedness, nor any other action taken by Beneficiary under this subparagraph shall cure or waive any event of default or notice of default hereunder, or nullify the effect of any such notice of default. Beneficiary, or any employee or agent of Beneficiary, or a receiver appointed by a court of competent jurisdiction, may take any action or proceeding hereunder without regard to: (A) the adequacy of the security for the indebtedness secured hereunder; (B) the existence of a declaration that the indebtedness secured hereby has been declared immediately due and payable; or (C) the filing of a notice of default.

(b) With or without notice, and without releasing Trustor from any obligation hereunder, to cure any default of Trustor and, in connection therewith, Beneficiary or its agents, acting by themselves or through a court appointed receiver, may enter upon the Property or any part thereof and perform such acts and things as Beneficiary deems necessary or desirable to inspect, investigate, assess, and protect the security hereof, including without limitation of any of its other rights: (i) to obtain a court order to enforce Beneficiary's right to enter and inspect the Property under California Civil Code Section 2929.5, to which the decision of Beneficiary as to whether there exists a release or threatened release of a Hazardous Material onto the Property shall be deemed reasonable and conclusive as between the parties hereto; and (ii) to have a receiver appointed under California Code of Civil Procedure Section 564 to enforce Beneficiary's right to enter and inspect the Property for Hazardous Materials. All costs and expenses incurred by Beneficiary with respect

to the audits, tests, inspections, and examinations which Beneficiary or its agents or employees may conduct, including the fees of the engineers, laboratories, contractors, consultants, and attorneys, shall be paid by Trustor immediately upon demand by Beneficiary. All costs and expenses incurred by Trustee and Beneficiary pursuant to this subparagraph (including without limitation court costs, consultant fees and attorney fees, whether incurred in litigation or not and whether before or after judgement) shall bear interest at the default rate of interest ("Default Rate") set forth in the promissory note ("Note") secured hereby, from the date they are incurred until said sums have been paid.

(c) To seek a judgement that Trustor has breached its covenants, representations and/or warranties with respect to the Hazardous Materials, as set forth in paragraph I above, by commencing and maintaining an action or actions in any court of competent jurisdiction for breach of contract pursuant to California Code of Civil Procedure

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Section 736, whether commenced prior to foreclosure of the Property or after foreclosure of the Property, and to seek the recovery of any and all costs, damages, expenses, fees, penalties, fines, judgements, indemnification payments to third parties, and other out-of-pocket costs or expenses actually incurred by Beneficiary (collectively, the "Environmental Costs") incurred or advanced by Beneficiary relating to the cleanup, remediation or other response action required by applicable law or to which Beneficiary believes necessary to protect the Property, it being conclusively presumed between Beneficiary and Trustor that all such Environmental Costs incurred or advanced by Beneficiary relating to the cleanup, remediation or other response action of or to the Property were made by Beneficiary in good faith. All Environmental Costs incurred by Beneficiary under this subparagraph (including without limitation court costs, consultant fees and attorney fees, whether incurred in litigation or not and whether before or after judgement) shall bear interest at the Default Rate from the date of expenditure until said sums have been paid. Beneficiary shall be entitled to bid, at any foreclosure sale of the Property, the amount of said costs, expenses and interest in addition to the amount of the other obligations hereby secured as a credit bid, the equivalent of cash. Trustor acknowledges and agrees that notwithstanding any term or provision contained herein or in the Loan Documents: (i) the Environmental Costs shall be exceptions to any nonrecourse or exculpatory provision of the Loan Documents; (ii) Trustor shall be fully and personally liable for the Environmental Costs hereunder; (iii) such liability shall not be limited to the original principal amount of the obligations secured by this Deed of Trust; and (iv) Trustor's obligations shall survive the foreclosure, deed in lieu of foreclosure, release, reconveyance, or any other transfer of the Property or this Deed of Trust. For the purposes of any, action brought under this subparagraph, Trustor hereby waives the defense of [aches, and any applicable statute of limitations.

(d) To waive its lien against the Property or any portion thereof, whether fixtures or personal property, to the extent such property is found to be environmentally impaired in accordance with California Code of Civil Procedure Section 726.5 and to exercise any and all rights and remedies of an unsecured creditor against Trustor and all of Trustor's assets and property for the recovery of any deficiency and Environmental Costs, including, but not limited to, seeking an attachment order under California Code of Civil Procedure Section 483.010. As between Beneficiary and Trustor, for purposes of California Code of Civil Procedure Section 726.5, Trustor shall have the burden of proving that Trustor or any related party (or any affiliate or agent of Trustor or any related party) was not in any way negligent in permitting the release or threatening release of the Hazardous Material. Trustor acknowledges and agrees that notwithstanding any term or provision contained herein or in the Loan Documents, all judgements and awards entered against Trustor shall be exceptions to any nonrecourse or exculpatory provision of the Loan Documents, and Trustor shall be fully and personally liable for all judgements and awards entered against Trustor hereunder and such liability shall not be limited to the original principal amount of the obligations secured by this Deed of Trust and

Trustor's obligations shall survive the foreclosure, deed in lieu of foreclosure, release, reconveyance, or any other transfer of the Property or this Deed of Trust. For the purpose of any action brought under this subparagraph, Trustor hereby waives the defense of laches and any applicable statute of limitations.

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(e) All rights and remedies of Beneficiary hereunder are cumulative and in addition to all rights and remedies provided in the Loan Documents or by applicable law.

CROSS DEFAULT

Default in the performance or observance of any of the terms and provisions: (i) of any documents, including without limitation this Deed of Trust, ("Loan Documents") executed by Trustor or any entity guaranteeing any of Trustor's obligations to Beneficiary ("Guarantor") in connection with the obligations secured hereby; or (ii) of any documents executed by Trustor or Guarantor in connection with any other obligations of Trustor or any Guarantor to Beneficiary, including but not limited to Beneficiary Loan Number 00700002641 and 00700002724 (Collectively, "Other Documents"), shall constitute a default under the terms of each of the Loan Documents and the Other Documents at Beneficiary's option. thereby making available to Beneficiary any and all of the remedies set forth therein.

<ARTICLE> 5

<LEGEND>

THIS SCHEDULE CONTAINS SUMMARY FINANCIAL INFORMATION DERIVED FROM THE COMPANY'S CONDENSED BALANCE SHEET AS OF JUNE 30, 1997 (UNAUDITED) AND CONDENSED STATEMENTS OF OPERATIONS FOR THE SIX MONTHS ENDED JUNE 30, 1997 (UNAUDITED) AND IS QUALIFIED IN ITS ENTIRETY BY REFERENCE TO SUCH FINANCIAL STATEMENTS.

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