SECURITIES AND EXCHANGE COMMISSION

WASHINGTON, D.C. 20549

FORM 8-K

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

Date of Report (Date of earliest event reported): APRIL 20, 1999

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

DELAWARE
(State or other jurisdiction of incorporation)

000-19125	33-0336973
(Commission File No.)	(IRS Employer Identification No.)

2292 FARADAY AVENUE
CARLSBAD, CALIFORNIA 92008
(Address of principal executive offices and zip code)

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

ITEM 2. ACQUISITION OR DISPOSITION OF ASSETS.

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

In connection with the joint venture, Elan International Services, Ltd. ("EIS") purchased $15 million of Common Stock of Isis at a premium. Isis also issued a warrant to EIS to purchase 215,000 shares of Isis Common Stock at $24.00 per share. EIS also purchased $12 million of Preferred Stock of Isis, which bears a 5% dividend payable in Preferred Stock and is convertible into Isis Common Stock at a specified premium or exchangeable for 30.1% ownership of Orasense. Isis contributed a portion of the funding to Orasense to pay license fees to Elan for certain of the technology contributed to the joint venture.

Until March 31, 2002, EIS will, at Isis' request, purchase convertible debt of Isis in an amount equal to Isis' share of budgeted funding for Orasense. The convertible debt will have a term of six years, bear interest at the rate of 12% and be convertible into Isis Common Stock at a premium. Isis may prepay the convertible debt in cash or Isis Common Stock. Isis will use the proceeds of the sale of the convertible debt to provide additional development funding to Orasense.

EIS will have certain registration rights with respect to the Isis Common Stock and the Isis Common Stock issuable upon conversion of the Preferred Stock, the warrant and the convertible debt.

As part of the transaction, the parties entered into several agreements, including a Subscription, Joint Development and Operating Agreement, Securities Purchase Agreement, Convertible Promissory Note, Registration Rights Agreements, Warrant and License Agreements, a copy of each of which is attached hereto as an exhibit and incorporated herein by reference.

ITEM 7. FINANCIAL STATEMENTS AND EXHIBITS.

(a) Financial Statements of Businesses Acquired.

Not applicable.

(b) Pro Forma Financial Information.

Not applicable.

(c) Exhibits.

Exhibit No.	Description
10.1*	Subscription, Joint Development and Operating Agreement, dated April 20, 1999, by and among Registrant, Elan Corporation, plc ("Elan"), Elan International Services, Ltd. ("EIS"), and Orasense, Ltd. ("Orasense").
10.2	Securities Purchase Agreement, dated April 20, 1999, by and between Registrant and EIS.
10.3	Convertible Promissory Note, dated April 20, 1999, by and between Registrant and EIS.
10.4	Warrant to Purchase Shares of Common Stock, dated April 20, 1999, by and between Registrant and EIS.
10.5	Registration Rights Agreement, dated April 20, 1999, by and between Registrant and EIS.
10.6	Registration Rights Agreement, dated April 20, 1999, by and among Registrant, EIS and Orasense.
10.7*	License Agreement, dated April 20, 1999, by and between Elan and Orasense.
10.8*	License Agreement, dated April 20, 1999, by and between Registrant and Orasense.

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* Confidential treatment has been requested with respect to certain portions of this exhibit. Omitted portions have been filed separately with the Securities and Exchange Commission.

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:05/03/99 By: /s/ Stanley T. Crooke

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

Date:05/03/99 By: /s/ B. Lynne Parshall

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

INDEX TO EXHIBITS

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EXHIBIT 10.1

***TEXT OMITTED AND FILED SEPARATELY
CONFIDENTIAL TREATMENT REQUESTED
UNDER 17 C.F.R. SECTIONS 200.80(B)(4),
200.83 AND 240.24B-2

SUBSCRIPTION, JOINT DEVELOPMENT AND OPERATING AGREEMENT

ELAN CORPORATION, PLC

ELAN INTERNATIONAL SERVICES, LTD.

AND

ISIS PHARMACEUTICALS, INC.

AND

ORASENSE LTD.

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THIS SUBSCRIPTION, JOINT DEVELOPMENT AND OPERATING AGREEMENT made this 20th day of April, 1999,

AMONG:

(1) ELAN CORPORATION, PLC, a public limited company incorporated under the laws of Ireland, and having its registered office at Lincoln House, Lincoln Place, Dublin 2, Ireland ("ELAN");

(2) ELAN INTERNATIONAL SERVICES, LTD., a private limited company incorporated under the laws of Bermuda, and having its registered office at Clarendon House, 2 Church St., Hamilton, Bermuda ("EIS");

(3) ISIS PHARMACEUTICALS, INC., a corporation incorporated under the laws of Delaware and having its principal place of business at 2292 Faraday Avenue, Carlsbad, CA 92008, United States of America ("ISIS"); and

(4) ORASENSE LTD., a private limited company incorporated under the laws of Bermuda, and having its registered office at Clarendon House, 2 Church St., Hamilton, Bermuda ("NEWCO").

RECITALS:

A. Newco desires to issue and sell to the Participants (as defined below), and the Participants desire to purchase from Newco, for aggregate consideration of $15,000,000, apportioned between them as set forth herein, 12,000 shares of Newco's common stock, par value $1.00 per share (the "COMMON STOCK"), allocated 9,612 shares to Isis and 2,388 shares to EIS.

B. Elan is beneficially entitled to the use of certain patents which have been granted or are pending in relation to drug delivery including modification of the solubility, intrinsic dissolution, stability and/or permeability of an active agent, improved dosage form processing, modification of the surface of particles, and in vivo, in situ, and in vitro cell tissue and animal models for drug absorption.

C. Isis is beneficially entitled to the use of certain patents that have been granted or are pending in relation to metabolism and transport inhibitors and methods of identifying the same and in vivo, in situ, and in vitro cell tissue and animal models for drug absorption.

D. As of the date hereof, Elan Pharmaceutical Technologies, a division of Elan ("EPT"), has entered into a license agreement with Newco, and Isis has entered

into a license agreement with Newco, in connection with the license to Newco of the Elan Intellectual Property and the Isis Intellectual Property, respectively (each as defined below).

E. Elan and Isis have agreed to co-operate in the establishment and management of a business for the research, development and commercialization of the Products (as defined below) based on their respective technologies.

F. Elan and Isis have agreed to enter into this Agreement for the purpose of recording the terms and conditions of the joint venture and of regulating their relationship with each other and certain aspects of the affairs of and their dealings with Newco.

NOW IT IS HEREBY AGREED AS FOLLOWS:

CLAUSE 1

DEFINITIONS

1.1 In this Agreement, the following terms shall, where not inconsistent with the context, have the following meanings respectively.

"AFFILIATE" of any Person (in the case of a legal entity) shall mean any other Person controlling, controlled or under the common control of such first Person, as the case may be. For the purposes of this definition, "control" shall mean direct or indirect ownership of greater than fifty percent (50%) of the stock or shares entitled to vote for the election of directors or capital interests representing more than fifty percent (50%) of the equity thereof and "controlling" and "controlled" shall be construed accordingly. Notwithstanding the foregoing, Newco shall not be construed to be an Affiliate, as defined herein, of Elan or EIS.

"AGREEMENT" means this agreement (which expression shall be deemed to include the Recitals and the Schedules hereto).

"BUSINESS" means the business of Newco as described in Clause 2 and as more particularly specified in the Business Plan and such other business as the Participants may agree from time to time in writing (each in its sole discretion) should be carried on by Newco.

"BUSINESS PLAN" shall mean the business plan and program of development to be agreed by Elan and Isis within 60 days of the Closing Date, with respect to the research, development, and commercialization of the Products, which shall be reviewed and updated by Elan and Isis on an annual basis, upon mutual written agreement.

"CHANGE OF CONTROL" shall mean, with respect to a Party, the acquisition of [...***...] or more of its voting securities, the ability, by contract or otherwise, to control the board of directors or management of any such entity, or a sale of all or substantially all of the business of such Party to which the Transaction Documents relate, whether by merger, sale of stock, sale of assets or otherwise.

"CLOSING DATE" shall mean the date upon which the Transaction Documents are executed and delivered by the Parties and the transactions effected thereby are closed.

"COMMERCIALIZATION" shall mean the manufacture, promotion, distribution, marketing and sale of the Products and the Development Product.

"COMMON STOCK EQUIVALENTS" means any options, warrants, rights or any other securities convertible, exercisable or exchangeable, in whole or in part, for or into Common Stock.

"CONTROL" shall mean, with respect to a drug, the ability to grant a license or sublicense as contemplated herein without violating the terms of any agreement with any third party.

"CONVERTIBLE NOTE" means that certain convertible promissory note, of even date herewith, by and between Isis and EIS.

"DEVELOPMENT CANDIDATE" shall mean a [...***...] antisense inhibitor of TNF-(alpha), as more specifically detailed in the License Agreements.

"DEVELOPMENT PRODUCT" shall mean any product containing as an active ingredient the Development Candidate (or a Substituted Development Candidate) in an Oral formulation for humans.

"DIRECTORS" means, at any time, the directors of Newco.

"EIS DIRECTOR" has the meaning set forth in Clause 7.

"EIS EXCHANGE RIGHT" has the meaning assigned to such term in the Isis Securities Purchase Agreement.

"ELAN IMPROVEMENTS" has the meaning assigned thereto in the Elan License Agreement.

"ELAN INTELLECTUAL PROPERTY" has the meaning assigned thereto in the Elan License Agreement.

* CONFIDENTIAL TREATMENT REQUESTED

"ELAN KNOW-HOW" has the meaning assigned thereto in the Elan License Agreement.

"ELAN LICENSE" has the meaning assigned thereto in the Elan License Agreement.

"ELAN LICENSE AGREEMENT" means the license agreement between Elan and Newco, of even date herewith, attached hereto in Schedule 1.

"ELAN PATENT RIGHTS" has the meaning assigned thereto in the Elan License Agreement.

"ELAN PROGRAM TECHNOLOGY" shall mean all Program Technology solely conceived or made by Elan and/or its agents.

"ENCUMBRANCE" means any liens, charges, encumbrances, equities, claims, options, proxies, pledges, security interests, or other similar rights of any nature.

"EXCHANGE ACT" means the Securities Exchange Act of 1934, as amended.

"FIELD" shall mean the research, development and Commercialization of an Oral Platform for delivery of Oligonucleotide Drugs.

"FINANCIAL YEAR" means each year commencing on January 1 (or in the case of the first Financial Year, the date hereof) and expiring on December 31 of each year.

"FULLY DILUTED COMMON STOCK" means all of the issued and outstanding Common Stock, assuming the conversion, exercise or exchange of all outstanding Common Stock Equivalents.

"FUNDING AGREEMENT" shall mean the Funding Agreement, dated as of the date hereof, between Elan, EIS and Isis.

"INDEPENDENT THIRD PARTY" shall mean any person other than Newco, Isis, Elan or any of their respective Affiliates.

"ISIS DELIVERY KNOW-HOW" shall have the meaning given to such term in the Isis License Agreement.

"ISIS DELIVERY PATENTS" shall have the meaning given to such term in the Isis License Agreement.

"ISIS DELIVERY TECHNOLOGY" shall have the meaning given to such term in the Isis License Agreement.

"ISIS DEVELOPMENT CANDIDATE KNOW-HOW" shall have the meaning given to such term in the Isis License Agreement.

"ISIS DEVELOPMENT CANDIDATE PATENTS" shall have the meaning given to such term in the Isis License Agreement.

"ISIS DEVELOPMENT CANDIDATE TECHNOLOGY" shall have the meaning given to such term in the Isis License Agreement.

"ISIS DIRECTORS" has the meaning set forth in Clause 7.

"ISIS IMPROVEMENTS" shall have the meaning given to such term in the Isis License Agreement.

"ISIS INTELLECTUAL PROPERTY" shall have the meaning given to such term in the Isis License Agreement.

"ISIS LICENSE" shall have the meaning given to such term in the Isis License Agreement.

"ISIS LICENSE AGREEMENT" shall mean the license agreement between Isis and Newco, of even date herewith, attached hereto as Schedule 2

"ISIS OLIGONUCLEOTIDE DRUG" shall mean any Oligonucleotide Drug Controlled by Isis other than the Development Candidate.

"ISIS PRODUCTS" shall mean Products for Oral delivery based upon Isis Oligonucleotide Drugs that are made, designed, or otherwise created by or on behalf of Isis or any of its Affiliates after the date hereof pursuant to the Project using the Newco Technology and/or the Licensed Technologies.

"ISIS PROGRAM TECHNOLOGY" shall mean all Program Technology solely conceived or made by Isis and/or its agents.

"ISIS SECURITIES PURCHASE AGREEMENT" means that certain securities purchase agreement, of even date herewith, by and between Isis and EIS.

"LICENSE AGREEMENTS" means the Elan License Agreement and the Isis License Agreement.

"LICENSED TECHNOLOGIES" means, together, the Elan Intellectual Property and the Isis Intellectual Property.

"NEWCO MEMORANDUM OF ASSOCIATION AND BYE-LAWS" shall mean the Memorandum of Association and Bye-Laws of Newco.

"NEWCO PATENTS" shall mean any and all patents and patent applications Controlled by Newco, existing and/or pending as of the Effective Date or hereafter filed or obtained by Newco, other than Elan Patent Rights, Isis Delivery

Patent Rights and Isis Development Candidate License Rights. Newco Patent Rights shall also include all extensions, continuations, continuations-in-part, divisionals, patents-of-additions, re-examinations, re-issues, supplementary protection certificates and foreign counterparts of such patents and patent applications and any patents issuing thereon and extensions of any patents licensed hereunder.

"NEWCO PROGRAM TECHNOLOGY" shall mean all Program Technology other than Elan Program Technology and Isis Program Technology.

"NEWCO TECHNOLOGY" shall mean all Program Technology and all technology licensed or acquired by Newco or developed by Newco whether or not pursuant to the Research and Development Program, excluding, however, Isis Intellectual Property and Elan Intellectual Property.

"OLIGONUCLEOTIDE DRUG" shall mean any single stranded, [...***...] oligonucleotide including those [...***...] used as a human therapeutic and/or prophylactic compound containing between [...***...] nucleotides and/or nucleosides including oligonucleotide analogs which may include [...***...]. For purposes of this Agreement, Oligonucleotide Drug shall specifically exclude oligonucleotides used in gene therapy except [...***...] an oligonucleotide, oligonucleotides used as [...***...] or oligonucleotides used as adjuvants. Oligonucleotide Drug shall also specifically exclude polymers in which the linkages are amide based, such as peptides and proteins but shall not exclude [...***...]. Should Isis develop [...***...] oligonucleotides or should Elan independently discover drug delivery technology it believes to be potentially applicable to [...***...] oligonucleotides, then the Participants shall discuss in good faith whether such oligonucleotides can be formulated for Oral delivery using the Oral Platform, and whether such formulation appears feasible without requiring a significant further investment in developing or enhancing the Oral Platform; if such formulation appears feasible, the Participants shall discuss in good faith the inclusion of such oligonucleotides as Oligonucleotide Drugs.

"ORAL" shall mean administration by way of the mouth for the purpose of topical or systemic delivery by way of the alimentary canal.

"ORAL DELIVERY DEVICES" shall mean devices for delivering an active agent orally such as those employing [...***...] technologies.

*CONFIDENTIAL TREATMENT REQUESTED

"ORAL PLATFORM" shall mean formulation and excipient systems and technologies including [...***...] and further including the use of [...***...], which can be employed to develop dosage forms of Oligonucleotide Drugs, deliver said dosage forms to the alimentary canal and facilitate and/or promote the Oral systemic and topical delivery of Oligonucleotide Drugs.

"PARTICIPANT" means Isis or Elan, as the case may be, and "Participants" means both of the Participants together.

"PARTY" means Elan, Isis, or Newco, as the case may be, and "Parties" means all three together.

"PERSON" means an individual, partnership, corporation, limited liability company, business trust, joint stock company, trust, unincorporated association, joint venture, governmental entity or authority or other entity of whatever nature.

"PERMITTED TRANSFEREE" means any Affiliate or subsidiary of Elan, EIS or Isis, to whom this Agreement may be assigned, in whole or in part, pursuant to the terms hereof or in the case of Elan/EIS, an off-balance sheet special purpose entity created by Elan or EIS.

"PRIMARY TECHNOLOGICAL COMPETITOR OF ELAN" shall mean those entities listed on Schedule 2A to the Elan License Agreement.

"PRODUCT" shall mean any Oligonucleotide Drug under development or developed by or on behalf of Newco in an Oral formulation for administration to humans.

"PROGRAM TECHNOLOGY" shall mean all technology developed by or on behalf of Newco, whether by Elan, Isis, a third party or jointly by any combination thereof, pursuant to the Research and Development Program.

"PROJECT" shall mean all activity as undertaken by or on behalf of Newco in order to develop the Products in accordance with the Business Plan.

"REGISTRATION RIGHTS AGREEMENTS" means the Registration Rights Agreements of even date herewith relating to securities of Isis and Newco, respectively.

"REGULATORY APPLICATION" means any regulatory application or any other application for marketing approval for a Product, which Newco will file in any country of the Territory, including any supplements or amendments thereto.

"REGULATORY APPROVAL" means the final approval to market a Product in any country of the Territory, and any other approval which is required to launch the Product in the normal course of business.

*CONFIDENTIAL TREATMENT REQUESTED

"RESEARCH TERM" shall mean the period commencing on the Closing Date and continuing for a period of [...***...] thereafter, unless extended by the mutual written agreement of Elan and Isis; provided, however, that if a Participant shall be prevented by (i) events beyond the Participant's control, or (ii) by such Participant's delay or negligent act or omission, from performing its obligations under the Transaction Documents within said [...***...] period, then the other Participant at its option, may extend the duration of the Research Term by a term equal in length to the period during which the first Participant was unable to perform its obligations hereunder.

"RHA" means any relevant government health authority (or successor agency thereof) in any country of the Territory whose approval is necessary to market a Product in the relevant country of the Territory.

"SECURITIES ACT" means the Securities Act of 1933, as amended.

"SHARES" means the shares of Common Stock of Newco.

"STOCKHOLDER" means any of EIS, Isis, any Permitted Transferee or any other Person who subsequently becomes bound by this Agreement as a holder of the Shares, and "STOCKHOLDERS" means all of the Stockholders together.

"SUBSIDIARY" means any company that is a subsidiary of Newco within the meaning of applicable laws.

"SUBSTITUTED DEVELOPMENT CANDIDATE" shall mean an Isis Oligonucleotide Drug licensed to Newco by Isis for development by Newco in replacement of the Development Candidate pursuant to the Isis License Agreement.

"TECHNOLOGICAL COMPETITOR OF ELAN" shall mean any entity which has a significant program for the development of drug delivery systems and which is active in promoting and contracting the use of such drug delivery systems to third parties, a listing of which is contained on Schedule 2B to the Elan License Agreement, as the same shall be updated and revised on an annual basis by mutual consent of the Parties.

"TECHNOLOGICAL COMPETITOR OF ISIS" shall mean any entity which has a significant program for the discovery and development of antisense drugs, a listing of which is contained on Schedule 3 to the Elan License Agreement, as the same shall be updated and revised on an annual basis by mutual consent of the Parties.

"TERM" means the term of this Agreement.

"TERRITORY" means all of the countries of the world.

*CONFIDENTIAL TREATMENT REQUESTED

"THIRD PARTY OLIGONUCLEOTIDE DRUG" shall mean any Oligonucleotide Drugs Controlled by an Independent Third Party, other than an Isis Oligonucleotide Drug.

"THIRD PARTY PRODUCT" shall mean Products based upon Third Party Oligonucleotide Drug that are made, designed, or otherwise created by or on behalf of an Independent Third Party after the date hereof pursuant to the Project using the Newco Technology and/or the Licensed Technologies. For avoidance of doubt, any Product based upon an Oligonucleotide Drug jointly developed by an Independent Third Party and Isis other than pursuant of the Program shall be deemed to be an Isis Product.

"TRANSACTION DOCUMENTS" means this Agreement, the Funding Agreement, the Elan License Agreement, the Isis License Agreement, the Convertible Note, the Isis Securities Purchase Agreement, the Registration Rights Agreements and associated documentation of even date herewith, by and between Isis, Elan, EIS and Newco, as applicable.

"UNITED STATES DOLLAR" and "US$" and "$" means the lawful currency of the United States of America.

1.2 In addition, the following definitions have the meanings in the Clauses corresponding thereto, as set forth below.

DEFINITION	CLAUSE
"Buyout Option"	20.1
"Closing"	4.2
"Common Stock"	Recital
"Confidential Information"	22.1
"Co-sale Notice"	17.3
"Elan"	Recital
"Elan Valuation"	20.2
"EIS"	Recital
"EPT"	Recital
"Isis"	Recital
"Isis Valuation"	20.2
"Management Committee"	7.2.1
"Newco"	Recital
"Notice of Exercise"	17.2
"Notice of Intention"	17.2
"Offered Shares"	17.2
"Offering Price"	17.2
"Presiding Justice"	20.2
"Purchase Price"	20.2
"R&D Committee"	7.2.2
"Remaining Stockholders"	17.3

"Relevant Event"	21.2
"Research and Development Program"	9.1
"Selling Stockholder"	17.2
"Tag-Along Right"	17.3
"Transaction Proposal"	17.2
"Transfer"	17.1
"Transferee Terms"	17.3
"Transferring Stockholders"	17.3

1.3 Words importing the singular shall include the plural and vice versa.

1.4 Unless the context otherwise requires, reference to a recital, article, paragraph, provision, clause or schedule is to a recital, article, paragraph, provision, clause or schedule of or to this Agreement.

1.5 Reference to a statute or statutory provision includes a reference to it as from time to time amended, extended or re-enacted.

1.6 The headings in this Agreement are inserted for convenience only and do not affect its construction.

1.7 Unless the context or subject otherwise requires, references to words in one gender include references to the other genders.

1.8 Capitalized terms used but not defined herein shall have the meanings ascribed in the Transaction Documents, if defined therein.

CLAUSE 2

NEWCO'S BUSINESS

2.1 The primary objective of Newco and any Subsidiaries is to carry on the business of the development, testing, registration, manufacture, commercialization and licensing of Products in the Territory and to achieve the objectives set out in this Agreement. The focus of the collaborative venture will be to develop the Products using the Elan Intellectual Property, the Isis Intellectual Property and the Newco Technology to agreed-upon specifications and timelines.

2.2 Except as the Participants otherwise agree in writing and except as may be provided in this Agreement, the Business Plan or the License Agreements, the Participants shall exercise their respective powers in relation to Newco so as to ensure that the Business is carried on in a proper and prudent manner.

2.3 Each Participant shall use all commercially reasonable and proper means at its disposal and within its power to maintain, extend and improve the Business of

Newco, within the limits of this Agreement, and to further the reputation and interests of Newco.

2.4 The central management and control of Newco shall be exercised in Bermuda and shall be vested in the Directors and such Persons as they may delegate the exercise of their powers in accordance with the Newco Memorandum of Association and Bye-Laws. The Participants shall use their best endeavors to ensure that to the extent required pursuant to the laws of Bermuda, and to ensure the sole residence of Newco in Bermuda, all meetings of the Directors are held in Bermuda or other jurisdictions outside the United States and generally to ensure that Newco is treated as resident for taxation purposes in Bermuda.

CLAUSE 3

REPRESENTATIONS AND WARRANTIES

3.1 REPRESENTATIONS AND WARRANTIES OF NEWCO: Newco hereby represents and warrants to each of the Stockholders as follows, as of the date hereof:

3.1.1 ORGANIZATION: Newco is an exempted company duly organized, validly existing and in good standing under the laws of Bermuda, and has all the requisite corporate power and authority to own and lease its properties, to carry on its business as presently conducted and as proposed to be conducted, to execute this Agreement, which has been duly authorized and is enforceable against Newco in accordance with its terms, and to carry out the transactions contemplated hereby.

3.1.2 CAPITALIZATION: As of the date hereof, the authorized capital stock of Newco consists of 12,000 shares of Common Stock. Prior to the date hereof, no shares of capital stock of Newco have been issued.

3.1.3 AUTHORIZATION: The execution, delivery and performance by Newco of this Agreement, including the issuance of the Shares, have been duly authorized by all requisite corporate actions; this Agreement has been duly executed and delivered by Newco and is the valid and binding obligation of Newco, enforceable against it in accordance with its terms, except as limited by applicable bankruptcy, insolvency, reorganization, moratorium and other laws of general application affecting the enforcement of creditors' rights generally, and by general equity principles and limitations on the availability of equitable relief, including specific performance. The Shares, when issued as contemplated hereby, will be validly issued and outstanding, fully paid and non-assessable and not subject to preemptive or any other similar rights of the Stockholders or others.

3.1.4 NO CONFLICTS: The execution, delivery and performance by Newco of this Agreement, the issuance, sale and delivery of the Shares, and compliance with the provisions hereof by Newco, will not:

(i) violate any provision of applicable law, statute, rule or regulation applicable to Newco or any ruling, writ, injunction, order, judgment or decree of any court, arbitrator, administrative agency or other governmental body applicable to Newco or any of its properties or assets;

(ii) conflict with or result in any breach of any of the terms, conditions or provisions of, or constitute (with notice or lapse of time or both) a default (or give rise to any right of termination, cancellation or acceleration) under its charter or organizational documents or any material contract to which Newco is a party, except where such violation, conflict or breach would not, individually or in the aggregate, have a material adverse effect on Newco; or

(iii) result in the creation of, any Encumbrance upon any of the properties or assets of Newco, except as contemplated by the Transaction Documents.

3.1.5 APPROVALS: As of the date hereof, no permit, authorization, consent or approval of or by, or any notification of or filing with, any Person is required in connection with the execution, delivery or performance of this Agreement by Newco. Newco has full authority to conduct its business as contemplated in the Business Plan and the Transaction Documents.

3.1.6 DISCLOSURE: This Agreement does not contain any untrue statement of a material fact or omit to state any material fact necessary to make the statements contained herein not misleading. Newco is not aware of any material contingency, event or circumstance relating to its business or prospects, which could have a material adverse effect thereon, in order for the disclosure herein relating to Newco not to be misleading in any material respect.

3.1.7 NO BUSINESS; NO LIABILITIES: Newco has not conducted any business or incurred any liabilities or obligations prior to the date hereof, except solely in connection with its organization and formation.

3.2 REPRESENTATIONS AND WARRANTIES OF THE STOCKHOLDERS: Each of the Stockholders hereby severally represents and warrants to Newco as follows as of the date hereof:

3.2.1 ORGANIZATION: Such Stockholder is a corporation duly organized and validly existing under the laws of its jurisdiction of organization and has

all the requisite corporate power and authority to own and lease its respective properties, to carry on its respective business as presently conducted and as proposed to be conducted and to carry out the transactions contemplated hereby.

3.2.2 AUTHORITY: Such Stockholder has full corporate power and authority to enter into this Agreement and to perform its obligations hereunder, which have been duly authorized by all requisite corporate action of such Stockholder. This Agreement is the valid and binding obligation of such Stockholder, enforceable against it in accordance with its terms, except as limited by applicable bankruptcy, insolvency, reorganization, moratorium and other laws of general application affecting the enforcement of creditors' rights generally, and by general equity principles and limitations on the availability of equitable relief, including specific performance.

3.2.3 NO CONFLICTS: The execution, delivery and performance by such Stockholder of this Agreement, purchase of the Shares, and compliance with the provisions hereof by such Stockholder will not:

(i) violate any provision of applicable law, statute, rule or regulation known by and applicable to such Stockholder or any ruling, writ, injunction, order, judgment or decree of any court, arbitrator, administrative agency or other governmental body applicable to such Stockholder or any of its properties or assets;

(ii) conflict with or result in any breach of any of the terms, conditions or provisions of, or constitute (with notice or lapse of time or both) a default (or give rise to any right of termination, cancellation or acceleration) under the charter or organizational documents of such Stockholder or any material contract to which such Stockholder is a party, except where such violation, conflict or breach would not, individually or in the aggregate, have a material adverse effect on such Stockholder; or

(iii) result in the creation of, any Encumbrance upon any of the properties or assets of such Stockholder, except as contemplated by the Transaction Documents.

3.2.4 APPROVALS: As of the date hereof, no material permit, authorization, consent or approval of or by, or any notification of or filing with, any Person is required in connection with the execution, delivery or performance of this Agreement by such Stockholder.

3.2.5 INVESTMENT REPRESENTATIONS: Such Stockholder is capable of evaluating the merits and risks of its investment in Newco. Such Stockholder has not been formed solely for the purpose of making this investment and such

Stockholder is acquiring the Common Stock for investment for its own account, not as a nominee or agent, and not with the view to, or for resale in connection with, any distribution of any part thereof. Such Stockholder understands that the Shares have not been registered under the Securities Act or applicable state and foreign securities laws by reason of a specific exemption from the registration provisions of the Securities Act and applicable state and foreign securities laws, the availability of which depends upon, among other things, the bona fide nature of the investment intent and the accuracy of such Stockholders' representations as expressed herein. Such Stockholder understands that no public market now exists for any of the Shares and that there is no assurance that a public market will ever exist for such Shares.

3.3 SURVIVAL: The representations and warranties in this Clause 3 shall survive for a period of two years from and after the date hereof.

CLAUSE 4

AUTHORIZATION AND CLOSING

4.1 Newco has authorized the issuance to (i) EIS of 2,388 shares of Common Stock and (ii) Isis of 9,612 shares of Common Stock, issuable as provided in Clause 4.3 hereof.

4.2 The closing (the "CLOSING") shall take place at the offices of Brock Silverstein LLC at 153 East 53rd Street, New York, New York 10022 on the date hereof or such other place if any, as the Parties may agree and shall occur contemporaneously with the closing under the Isis Securities Purchase Agreement.

4.3 At the Closing,

4.3.1 Newco shall issue and sell to EIS, and EIS shall purchase from Newco, upon the terms and subject to the conditions set forth herein, 2,388 shares of Common Stock for an aggregate purchase price of $2,985,000. Newco shall issue and sell to Isis, and Isis shall purchase from Newco, upon the terms and conditions set forth herein, 9,612 shares of Common Stock for an aggregate purchase price of $12,015,000.

4.3.2 The Parties shall execute and deliver to each other, as applicable, certificates in respect of the Common Stock described above and any other certificates, resolutions or documents which the Parties shall reasonably require.

4.4 EXEMPTION FROM REGISTRATION:

The Shares will be issued under an exemption or exemptions from registration under the Securities Act. Accordingly, the certificates evidencing the Shares shall, upon issuance, contain the following legend:

THE SECURITIES REPRESENTED HEREBY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND MAY NOT UNDER ANY CIRCUMSTANCES BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF WITHOUT AN EFFECTIVE REGISTRATION STATEMENT FOR SUCH SECURITIES UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND ANY APPLICABLE STATE SECURITIES LAWS OR AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY THAT REGISTRATION IS NOT REQUIRED UNDER SUCH ACT OR APPLICABLE STATE SECURITIES LAWS.

THE TRANSFER OF THE SECURITIES REPRESENTED BY THIS CERTIFICATE IS ALSO SUBJECT TO THE RESTRICTIONS CONTAINED IN THAT CERTAIN SUBSCRIPTION, JOINT DEVELOPMENT AND OPERATING AGREEMENT, DATED APRIL 20, 1999, BY AND AMONG ELAN CORPORATION, PLC, ELAN INTERNATIONAL SERVICES, INC., ISIS PHARMACEUTICALS, INC. AND ORASENSE LTD.

CLAUSE 5

CERTAIN ASSIGNMENT RIGHTS

5.1 At any time after exercise of the EIS Exchange Right and upon 1 month's prior notice in writing from Elan to Newco and Isis, Newco shall assign the Newco Intellectual Property from Newco to a wholly-owned subsidiary of Newco to be incorporated in Ireland, which company shall be newly incorporated by Elan to facilitate such assignment.

CLAUSE 6

NON-COMPETITION

6.1 The Parties acknowledge and agree to be bound by the provisions of Clause 11 of the Elan License Agreement and the provisions of Clause 11 of the Isis License Agreement which set forth the agreement between the parties thereto in relation to the non-competition obligations of Elan and Isis, respectively.

CLAUSE 7

DIRECTORS; MANAGEMENT AND R&D COMMITTEES

7.1. DIRECTORS:

Prior to the exercise of the EIS Exchange Right, the Board of Directors of Newco shall be composed of four Directors. Isis shall have the right to nominate three directors of Newco ("ISIS DIRECTORS"), provided that one such director is a resident of Bermuda, and EIS shall have the right to nominate one Director of Newco ("EIS DIRECTOR"). Isis may appoint one of the Isis Directors to be the chairman of Newco. Each Participant agrees to vote its shares of Common Stock in favor of the election of the nominees of the other Participant to the Board of Directors.

7.1.1 If the chairman is unable to attend any meeting of the Board, the Isis Directors shall be entitled to appoint another Director to act as chairman in his place at the meeting.

7.1.2 If EIS removes the EIS Director, or Isis removes any of the Isis Directors, EIS or Isis, as the case may be, shall indemnify the other Stockholder against any claim by such removed Director arising from such removal.

7.1.3 The Directors shall meet not less than three times in each Financial Year and all Directors' meetings shall be held in Bermuda to the extent required pursuant to the laws of Bermuda or to ensure the sole residence of Newco in Bermuda.

7.1.4 At any such meeting, the presence of the EIS Director and one of the Isis Directors shall be required to constitute a quorum and, subject to Clause 18 hereof, the affirmative vote of a majority of the Directors present at a meeting at which such a quorum is present shall constitute an action of the Directors. In the event of any meeting being inquorate, the meeting shall be adjourned for a period of seven days. A notice shall be sent to the EIS Director and the Isis Directors specifying the date, time and place where such adjourned meeting is to be held and reconvened.

7.1.5 The chairman of Newco shall hold office until the first meeting of the Directors after the exercise by EIS of the EIS Exchange Right. In the event that the EIS Exchange Right is exercised at any time by EIS, each of Isis, and EIS shall cause the board of Directors of Newco to be reconfigured so that an equal number of Directors are designated by EIS and Isis. Thereafter, each of EIS and Isis, beginning with EIS, shall have the right, exercisable alternatively, of nominating one Director to be chairman of Newco for a term of one year. If the chairman of Newco is unable to attend any meeting of the Directors, the Directors shall be

entitled to appoint another Director to act as chairman of Newco in his place at the meeting.

7.1.6 In case of an equality of votes at a meeting of the board of Directors of Newco, the chairman of Newco shall not be entitled to a second or casting vote. In the event of continued deadlock, the board of Directors shall resolve the deadlock pursuant to the provisions set forth in Clause 19.

7.2 MANAGEMENT AND R&D COMMITTEES:

7.2.1 The Directors shall appoint a management committee (the "MANAGEMENT COMMITTEE") to perform certain operational functions, such delegation to be consistent with the Directors' right to delegate powers pursuant to the Newco Memorandum of Association of Bye-Laws. The Management Committee shall initially consist of four members, two of whom will be nominated by EIS and two of whom will be nominated by Isis, and each of whom shall be entitled to one vote, whether or not present at any Management Committee meeting during which such operational functions are discussed. Except as otherwise provided herein or in the License Agreements, decisions of the Management Committee shall require approval by at least one EIS nominee on the Management Committee and one Isis nominee on the Management Committee. Each of EIS and Isis shall be entitled to remove any of their nominees to the Management Committee and appoint a replacement in place of any nominees so removed.

7.2.2 The Management Committee shall appoint a research and development committee (the "R&D COMMITTEE") which shall initially be comprised of four members, two of whom will be nominated by Elan and two of whom will be nominated by Isis, and each of whom shall have one vote, whether or not present at an R&D Committee meeting during which research and development issues are discussed. Decisions of the R&D Committee shall require approval by at least one Elan nominee on the R&D Committee and one Isis nominee on the R&D Committee. Each of Elan and Isis shall be entitled to remove any of their nominees to the R&D Committee and appoint a replacement in place of any nominees so removed.

7.2.3 The Management Committee shall be responsible for, inter alia, devising, implementing and reviewing strategy for the business of Newco, and the operation of Newco, and in particular, devising Newco's strategy for research and development and to monitor and supervise the implementation of Newco's strategy for research and development.

7.2.4 The R&D Committee shall be responsible for:

7.2.4.1 designing that portion of the Business Plan that relates to the Project for consideration by the Management Committee;

7.2.4.2 establishing a joint Project team consisting of an equal number of team members from Elan and Isis, including one Project leader from each of Elan and Isis; and

7.2.4.3 implementing such portion of the Business Plan that relates to the Project, as approved by the Management Committee.

7.2.5 In the event of any dispute amongst the R&D Committee, the R&D Committee shall refer such dispute to the Management Committee whose decision on the dispute shall be binding on the R&D Committee. If the Management Committee cannot resolve the matter, the dispute will be referred to the President of EPT and the Chief Executive Officer of Isis pursuant to Clause 19 hereof.

7.2.6 On not more than two times in each Financial Year, Elan and Isis shall permit Newco or its duly authorized representative on reasonable notice and at any reasonable time during normal business hours to have access to inspect and audit the accounts and records of Elan or Isis and any other book, record, voucher, receipt or invoice relating to the calculation or the cost of the Research and Development Program and to the accuracy of the reports which accompanied them. Any such inspection of Elan's or Isis's records, as the case may be, shall be at the expense of Newco, except that if such inspection reveals an overpayment in the amount paid to Elan or Isis, as the case may be, for the Research and Development Program hereunder in any Financial Year of 5% or more of the amount due to Elan or Isis, as the case may be, then the expense of such inspection shall be borne solely by Elan or Isis, as the case may be, instead of by Newco. Any surplus over the sum properly payable by Newco to Elan or Isis, as the case may be, shall be paid promptly by Elan or Isis, as the case may be, to Newco. If such inspection reveals a deficit in the amount of the sum properly payable to Elan or Isis, as the case may be, by Newco, Newco shall pay the deficit to Elan or Isis, as the case may be.

CLAUSE 8

THE BUSINESS PLAN AND REVIEWS

8.1 The Directors shall meet as soon as reasonably practicable after the Closing Date hereof and shall agree upon and approve the Business Plan for the current Financial Year within 60 days of the date hereof. The research and development budget contained in the Business Plan shall provide for the supply of the Development Candidate and the [...***...] and [...***...] compounds by Isis to Newco at [...***...]. In subsequent Financial Years, the Directors shall meet prior to the accounting reference date specified in Clause 15 and agree upon and approve the Business Plan for

*CONFIDENTIAL TREATMENT REQUESTED

the following Financial Year, or any amendment or modification to the Business Plan.

8.2 The Participants agree that the Management Committee shall submit to the Directors on February 15th, May 15th, August 15th, and November 15th or as soon as reasonably practicable thereafter in each Financial Year a report on the performance of the Business and research and development activities of Newco, and the Directors shall hold such meeting as may be necessary to review the performance of Newco against the Business Plan for the relevant year.

CLAUSE 9

RESEARCH AND DEVELOPMENT WORK

9.1 During the Research Term, Newco will diligently pursue the research and development of the Elan Intellectual Property, Isis Intellectual Property and Newco Technology in accordance with the Research and Development Program. The "RESEARCH AND DEVELOPMENT PROGRAM" will be the program for (a) the development of the Oral Platform, and (b) the development of the Development Product in the Field, including without limitation, screening, in-vitro pharmacology, toxicology, stability, prototype dosage form development, formulation, optimization, clinical and regulatory activities. Such work shall be agreed to and conducted by Elan and/or Isis under contract with Newco as provided in the Business Plan.

9.2 Isis and Elan shall provide such research and development services as may be reasonably required by Newco in accordance with the provisions in the License Agreements. Newco shall pay Isis and Elan for any research and development work carried out by them on behalf of Newco at the end of each month during the Research and Development Program, subject to the proper vouching of research and development work and expenses. An invoice shall be issued to Newco by Isis or Elan, as applicable, by the 15th day of the month following the month in which work was performed. The payments by Newco to Isis or Elan, as the case may be, shall be at the rates prescribed in the respective License Agreement. Research and development activities that are outsourced to third party providers shall be charged to Newco at [...***...].

9.3 In the event the Management Committee, by unanimous vote of its members, shall determine that preclinical toxicology or pharmacology studies indicate that clinical trials of the Development Candidate should not be undertaken, or the Management Committee determines that development of the Development Candidate is not economically viable, Isis in good faith shall offer, and the Management Committee, by unanimous vote of its members shall approve, an Isis Oligonucleotide Drug in pre-clinical development that it deems economically viable as a Substituted Development Candidate, subject to the agreement of the

*CONFIDENTIAL TREATMENT REQUESTED

Participants, negotiating in good faith, to changes concerning the budget, Business Plan and funding of Newco.

9.4 Except as otherwise provided herein and as provided in the Isis License Agreement, upon designation of an Isis Oligonucleotide as a Substituted Development Candidate, (i) all rights to the Development Candidate shall revert to Isis and (ii) all provisions contained herein and in the Isis License Agreement other than in the preceding clause (i) relating to the Development Candidate shall be deemed to apply to the Substituted Development Candidate as if it were the Development Candidate.

CLAUSE 10

INTELLECTUAL PROPERTY RIGHTS

10.1 Title and all other ownership rights, including patent rights, relating to the Elan Intellectual Property shall belong to Elan. Title and all other ownership rights, including patent rights relating to the Isis Intellectual Property shall belong to Isis. Title and all other ownership rights, including patent rights, relating to the Newco Technology shall belong to Newco.

10.2 The Participants shall discuss in good faith all material issues relating to filing, prosecution and maintenance of Elan Patents, Isis Development Candidate Patents and Isis Delivery Patents insofar as such patent rights are of relevance to the License Agreements and any patentable inventions and discoveries within the Elan Intellectual Property, Isis Intellectual Property and Newco Technology that relate to the License Agreements and any patentable improvements thereto. Subject to mutual agreement to the contrary by Isis and Elan the following provisions shall apply:

10.2.1 Elan, at its expense, shall make a good faith effort (i) to secure the grant of any material patent applications within the Elan Patents that relate to the Field; (ii) to file and prosecute patent applications on material patentable inventions and discoveries within the Elan Improvements that relate to the Field; (iii) to defend all such applications against third party oppositions; and (iv) to maintain in force any material issued letters patent within the Elan Patents that relate to the Field (including any letters patent that may issue covering any such Elan Improvements that relate to the Field). Elan shall have the right in its discretion to control such filing, prosecution, defense and maintenance provided that Newco and Isis at their request shall be provided with copies of all documents relating to such filing, prosecution, defense and maintenance in sufficient time to review such documents and comment thereon prior to filing.

10.2.2 Isis, at its expense, shall make a good faith effort (i) to secure the grant of any material patent applications within the Isis Delivery Patents that relate

to the Field and the Isis Development Candidate Patents; (ii) to file and prosecute patent applications on material patentable inventions and discoveries within the Isis Improvements that relate to the Field and the Development Candidate; (iii) to defend all such applications against third party oppositions; and (iv) to maintain in force any material issued letters patent within the Isis Delivery Patents that relate to the Field and the Isis Development Candidate Patents (including any letters patent that may issue covering any such Isis Improvements that relate to the Field). Isis shall have the right in its discretion to control such filing, prosecution, defense and maintenance provided that Elan and Newco at their request shall be provided with copies of all documents relating to such filing, prosecution, defense and maintenance in sufficient time to review such documents and comment thereon prior to filing.

10.2.3 In the event that a Participant informs the other Participant that it does not intend to file patent applications on patentable inventions and discoveries within the Isis Intellectual Property or Elan Intellectual Property as the case may be that relate to the Field in one or more countries in the Territory or fails to file such an application within a reasonable period of time, Newco shall have the option at its expense to file and prosecute such patent application(s) in the joint names of Newco and the Participant not intending or failing to so file (or, if required by law, on behalf of the inventors and assignable to Newco and the Participant). Upon written request from Newco, such Participant shall execute all documents, forms and declarations and to do all things as shall be reasonably necessary to enable Newco to exercise such option.

10.2.4 Elan and Isis, at their joint expense on behalf of Newco, shall (i) file and prosecute patent applications on patentable inventions and discoveries within the Newco Technology; (ii) defend all such applications against third party oppositions; and (iii) maintain in force any issued letters patent within the Newco Patents (including any patents that issue on patentable inventions and discoveries within the Newco Technology). Elan and Isis, directly or through the Management Committee, shall control such filing, prosecution, defense and maintenance. Elan and Isis agree to negotiate in good faith on the course of action to be taken with respect to Newco Technology.

10.2.5 Newco, Elan and Isis shall promptly inform each other in writing of any alleged infringement of any patents within the Elan Patents, the Isis Delivery Patents, the Isis Development Candidate Patents or the Newco Patents or any alleged misappropriation of trade secrets within the Elan Intellectual Property, the Isis Intellectual Property or the Newco Technology by a third party of which it becomes aware and provide the others with any available evidence of such infringement or

misappropriation insofar as such infringements or misappropriation relate solely to the Field.

10.2.6 Newco shall have the right to prosecute at its own expense and for its own benefit any infringements of the Elan Patents, the Isis Delivery Patents and the Isis Development Candidate Patents or misappropriation of the Elan Intellectual Property and the Isis Intellectual Property, insofar as such infringements or misappropriation relate solely to the Field. In the event that Newco takes such action, Newco shall do so at its own cost and expense. At Newco's request, the Participants shall cooperate with such action. Any recovery remaining after the deduction by Newco of the reasonable expenses (including attorney's fees and expenses) incurred in relation to such infringement proceeding shall belong to Newco. Should Newco decide not to pursue such infringers, within a reasonable period but in any event within twenty (20) days after receiving written notice of such alleged infringement or misappropriation each of the Participants may in its discretion initiate such proceedings in its own name, at its expense and for its own benefit, and at such Participant's request, Newco shall cooperate with such action. Alternatively, the Participants may agree to institute such proceedings in their joint names and shall reach agreement as to the proportion in which they shall share the proceeds of any such proceedings, and the expense of any costs not recovered, or the costs or damages payable to the third party. If the infringement of the Elan Patents, the Isis Delivery Patents or the Isis Development Candidate Patents affects both the Field as well as other products being developed or commercialized by Isis or Elan or its commercial partners outside the Field, Isis or Elan shall endeavor to agree as to the manner in which the proceedings should be instituted and as to the proportion in which they shall share the proceeds of any such proceedings, and the expense of any costs not recovered, or the costs or damages payable to the third party.

10.2.7 Newco shall have the first right but not the obligation to bring suit or otherwise take action against any alleged infringement of the Newco Patents or alleged misappropriation of the Newco Technology. If any such alleged infringement or misappropriation occurs that gives rise to a cause of action both inside and outside the Field, Newco, in consultation with the Participants, shall determine the cause of action to be taken. In the event that Newco takes such action, Newco shall do so at its own cost and expense and all damages and monetary award recovered in or with respect to such action shall be the property of Newco. Newco shall keep Elan and Isis informed of any action in a timely manner so as to enable Isis and Elan to provide input in any such action and Newco shall reasonably take into consideration any such input. At Newco's request, the Participants shall cooperate with any such action at Newco's cost and expense.

10.2.8 In the event that Newco does not bring suit or otherwise take action against all infringement of the Newco Patents or misappropriation of the Newco Technology, then (i) if only one Participant determines to pursue such suit or take such action at its own cost and expense, it shall be entitled to all damages and monetary award recovered in or with respect to such action and (ii) if the Participants pursue such suit or action outside of Newco, they shall negotiate in good faith an appropriate allocation of costs, expenses and recovery amounts.

10.2.9 In the event that a claim is, or proceedings are, brought against Newco by a third party alleging that the sale, distribution or use of a Product in the Territory or use of the Elan Intellectual Property or the Isis Intellectual Property, as the case may be, infringes the intellectual property rights of such party, Newco shall promptly advise the other Participants of such threat or suit.

10.2.10 Newco shall indemnify, defend and hold harmless Elan or Isis, as the case may be, against all actions, losses, claims, demands, damages, costs and liabilities (including reasonable attorneys fees) relating directly or indirectly to all such claims or proceedings referred to herein, provided that Elan or Isis, as the case may be, shall not acknowledge to the third party or to any other person the validity of any claims of such a third party, and shall not compromise or settle any claim or proceedings relating thereto without the prior written consent to Newco, not to be unreasonably withheld or delayed. At its option, Elan or Isis, as the case may be, may elect to take over the conduct of such proceedings from Newco provided that Newco's indemnification obligations shall continue; the costs of defending such claim shall be borne by Elan or Isis, as the case may be and such Participant shall not compromise or settle any such claim or proceeding without the prior written consent of Newco, such consent not to be unreasonably withheld or delayed.

10.3 Newco shall not encumber any of its rights under the Licenses or the Newco Technology without the prior written consent of Elan and Isis. Newco shall not be permitted to assign or sublicense any of its rights under the Licenses or the Program Technology without the prior written consent of Elan and Isis, respectively, which may be withheld in Elan's or Isis' sole discretion, as the case may be. Any permitted agreement between Newco and any permitted third party for the development or exploitation of the Elan Intellectual Property and/or Isis Intellectual Property in the Field shall require such third party to maintain the confidentiality of all information concerning the Elan Intellectual Property and the Isis Intellectual Property and shall provide that any improvements to the Elan Intellectual Property shall belong to Elan and any improvements to the Isis Intellectual Property shall belong to Isis.

CLAUSE 11

EXPLOITATION OF PRODUCTS OUTSIDE THE FIELD

11.1 LICENSES TO ELAN PROGRAM TECHNOLOGY AND ISIS PROGRAM TECHNOLOGY. Subject to the provisions of the License Agreements, Newco shall grant to Elan a perpetual, exclusive, royalty free and sublicensable license in the Territory to Elan Program Technology outside of the Field, and to Isis a perpetual, exclusive, royalty free and sublicensable license in the Territory to the Isis Program Technology outside of the Field.

11.2 LICENSES FOR NEWCO PROGRAM TECHNOLOGY. Newco shall grant (i) to Isis an exclusive license of Newco Program Technology outside the Field in the Territory solely for use in connection with Isis proprietary drug products (including drug products discovered or developed in collaborative partnerships) and (ii) to Elan an exclusive license in the Territory for the use of Newco Program Technology in all fields other than the Field or in connection with Isis proprietary drug products. All such licenses shall contain such customary provisions as are contained in similar licenses in the industry, as agreed to by the licensee and the unanimous decision of the Management Committee, acting in good faith. (including all material provisions thereof). The financial terms of the said license agreement shall have regard, inter alia, to:

11.1.1 the amount of monies expended by Newco in developing the licensed Newco Program Technology;

11.1.2 the materiality of the contribution of the Newco Intellectual Property by comparison to the further research and development work to be conducted, and of the Elan Intellectual Property and Isis Intellectual Property;

11.1.3 the financial return likely to be earned by Isis or Elan, as the case may be, from the proposed exploitation outside the Field; and

11.1.4 the impact of the proposed exploitation of the Newco Program Technology outside the Field on the exploitation of the Newco Program Technology within the Field.

CLAUSE 12

COMMERCIALIZATION

12.1 The Participants shall assist Newco in diligently pursuing the research, development, prosecution and commercialization of Products in accordance with the Business Plan. During the Research Term, Elan and Isis shall meet to discuss the commercial strategy for Newco, Commercialization of the Development

Product and the further exploitation of the Newco Technology. For example, Isis and Elan shall discuss strategy and terms relating to product and clinical development, corporate partnering, licensing and supply agreements. It is contemplated that Isis, either as agent for Newco or through its representatives on the Management Committee, shall locate and negotiate with Independent Third Party marketing partners for the Development Product. In the course of such representation, Isis shall keep Newco and Elan fully informed of its efforts and progress with respect to the foregoing.

12.2 In the event Isis shall propose to Newco the development of one or more Isis Products, the Management Committee, by unanimous decision, shall determine whether or not to develop any such Isis Product. It is contemplated that Isis shall locate and negotiate with Independent Third Party marketing partners for Isis Products. Isis shall keep Newco and Elan apprised of its efforts and progress with respect to the foregoing; provided, however, that any such information shall be kept confidential and shall not be disclosed to EPT (excluding senior executive personnel of Elan).

12.3 The Business Plan shall be reviewed and mutually agreed to by Isis and Elan on an annual basis.

12.4 If Isis wishes to research, develop, and/or Commercialize one or more Isis Oligonucleotide Drugs other than the Development Candidate, Newco shall have an option to negotiate in good faith the terms of the formulation research, development, and/or Commercialization of any such Isis Oligonucleotide Drugs. Provided Newco has the capability and technology to substantially perform the services sought by Isis with respect to such Isis Oligonucleotide Drugs, Isis will not offer such arrangement to Newco on terms less favorable than those it offers to Independent Third Parties and Newco shall not offer such arrangement to Isis on terms less favorable than those it offers to Independent Third Parties.

12.5 In the event an Independent Third Party shall propose to Newco the development of Third Party Products, the Management Committee, by unanimous decision, shall determine whether or not to develop any such Third Party Product. Newco shall be responsible for negotiating with any Independent Third Parties commercially reasonable terms (e.g., royalties, milestones, development fees, manufacturing rights) for developing and licensing Third Party Products. It is contemplated that Elan, either as agent for Newco or through its representatives on the Management Committee, shall locate and negotiate Independent Third Party marketing partners for Third Party Products. In the course of such representation, Elan shall keep Newco and Elan fully informed of its efforts and their progress with respect to the foregoing.

12.6 Notwithstanding anything set forth herein, at such time as Newco intends to Commercialize the Development Product, Elan shall have the right of first negotiation with respect to the world-wide commercialization of the Development Product in accordance with the terms of the Elan License Agreement.

12.7 Subject to the rights of Elan with respect to the Development Product, Newco shall not be permitted to contract the Commercialization of the Development Product or any other Product without the prior written consent of Elan and Isis, which consent will not be unreasonably withheld or delayed; provided that such reasonableness standard, in the case of Elan, shall not be applicable in the case of a proposed sublicense to any Technological Competitor of Elan and in the case of Isis, shall not be applicable in the case of a proposed sublicense to any Technological Competitor of Isis.

CLAUSE 13

MANUFACTURING

13.1 Elan shall have a first right of negotiation for the commercial production of the Development Product on behalf of Newco, in accordance with the provisions of section 2.13 of the Elan License Agreement. Subject to the foregoing rights of Elan with respect to the Development Product, Newco shall not be permitted to contract the manufacture of the Development Product or any other Product without the prior written consent of Elan and Isis, which consent will not be unreasonably withheld or delayed; provided that such reasonableness standard, in the case of Elan, shall not be applicable in the case of a proposed sublicense to any Technological Competitor of Elan and in the case of Isis, shall not be applicable in the case of a proposed sublicense to any Technological Competitor of Isis.

CLAUSE 14

TECHNICAL SERVICES AND ASSISTANCE

14.1 Whenever commercially and technically feasible, Newco shall contract with Isis or Elan, as the case may be, to perform such other services as Newco may require, other than those specifically dealt with hereunder or in the License Agreements. In determining which Party should provide such services, the Management Committee shall take into account the respective infrastructure, capabilities and experience of Elan and Isis.

14.2 Newco shall, if appropriate, conclude an administrative support agreement with Elan and/or Isis on such terms as the Parties thereto shall in good faith negotiate. The administrative services shall include one or more of the following administrative services as requested by Newco:

14.2.1 accounting, financial and other services;

14.2.2 tax services;

14.2.3 insurance services;

14.2.4 human resources services;

14.2.5 legal and company secretarial services;

14.2.6 patent and related intellectual property services; and

14.2.7 all such other services consistent with and of the same type as those services to be provided pursuant to this Agreement, as may be required.

The foregoing list of services shall not be deemed exhaustive and may be changed from time to time upon written request by Newco.

14.3. The Parties agree that each Party shall effect and maintain comprehensive general liability insurance in respect of all clinical trials and other activities performed by them on behalf of Newco. The Stockholders and Newco shall ensure that the industry standard insurance policies shall be in place for all activities to be carried out by Newco.

14.4 If Elan or Isis so requires, Isis or Elan, as the case may be, shall receive, at times and for periods mutually acceptable to the Parties, employees of the other Party (such employees to be acceptable to the receiving Party in the matter of qualification and competence) for instruction in respect of the Elan Intellectual Property or the Isis Intellectual Property, as the case may be, as necessary to further the Project.

14.5 The employees received by Elan or Isis, as the case may be, shall be subject to obligations of confidentiality no less stringent than those set out in Clause 22 and such employees shall observe the rules, regulations and systems adopted by the Party receiving the said employees for its own employees or visitors.

CLAUSE 15

AUDITORS, BANKERS, REGISTERED OFFICE, ACCOUNTING REFERENCE DATE; SECRETARY; COUNSEL

Unless otherwise agreed by the Stockholders and save as may be provided to the contrary herein:

15.1 the auditors of Newco shall be Ernst & Young;

15.2 the bankers of Newco shall be Bank of Bermuda or such other bank as may be mutually agreed from time to time;

15.3 the accounting reference date of Newco shall be December 31st in each Financial Year; and

15.4 the secretary of Newco shall be Diana Martin or such other Person as may be appointed by the Directors from time to time.

CLAUSE 16

REGULATORY

16.1 Newco shall keep the other Parties promptly and fully advised of Newco's regulatory activities, progress and procedures. Newco shall inform the other Parties of any dealings it shall have with an RHA, and shall furnish the other Parties with copies of all correspondence relating to the Products. The Parties shall collaborate to obtain any required regulatory approval of the RHA to market the Products.

16.2 Newco shall, at its own cost, file, prosecute and maintain any and all Regulatory Applications for the Products in the Territory in accordance with the Business Plan.

16.3 Any and all Regulatory Approvals obtained hereunder for any Product shall remain the property of Newco, provided that Newco shall allow Elan and Isis access thereto to enable Elan and Isis to fulfill their respective obligations and exercise their respective rights under this Agreement. Newco shall maintain such Regulatory Approvals at its own cost.

16.4 It is hereby acknowledged that there are inherent uncertainties involved in the registration of pharmaceutical products with the RHAs insofar as obtaining approval is concerned and such uncertainties form part of the business risk involved in undertaking the form of commercial collaboration as set forth in this Agreement. Therefore, except for liabilities resulting from failure to use reasonable efforts, none of Elan, EIS or Isis shall have any liability to Newco solely as a result of any failure of a Product to achieve the approval of any RHA.

CLAUSE 17

TRANSFERS OF SHARES; RIGHT OF FIRST OFFER; TAG ALONG RIGHTS

17.1 GENERAL:

No Stockholder shall, directly or indirectly, sell or otherwise transfer (each, a "TRANSFER") any Shares held by it except in accordance with this Agreement. Newco shall not, and shall not permit any transfer agent or registrar for any Shares to, transfer upon the books of Newco any Shares from any Stockholder to

any transferee, in any manner, except in accordance with this Agreement, and any purported transfer not in compliance with this Agreement shall be void.

17.2 RIGHTS OF FIRST OFFER:

If at any time after the end of the Term, a Stockholder shall desire to Transfer any Shares owned by it (a "SELLING STOCKHOLDER"), in any transaction or series of related transactions other than a Transfer to an Affiliate or subsidiary or in the case of EIS to an off-balance sheet special purpose entity established by EIS, then such Selling Stockholder shall deliver prior written notice of its desire to Transfer (a "NOTICE OF INTENTION") (i) to Newco and (ii) to the Stockholders who are not the Selling Stockholder (and any transferee thereof permitted hereunder, if any), as applicable, setting forth such Selling Stockholder's desire to make such Transfer, the number of Shares proposed to be transferred (the "OFFERED SHARES") and the proposed form of transaction (the "TRANSACTION PROPOSAL"), together with any available documentation relating thereto and the price at which such Selling Stockholder proposes to Transfer the Offered Shares (the "OFFER PRICE"). The "Right of First Offer" provided for in this Clause 17 shall be subject to any "Tag Along Right" benefiting a Stockholder which may be provided for by Clause 17, subject to the exceptions set forth therein.

Upon receipt of the Notice of Intention, the Stockholders who are not the Selling Stockholder shall have the right to purchase at the Offer Price the Offered Shares, exercisable by the delivery of notice to the Selling Stockholder (the "NOTICE OF EXERCISE"), with a copy to Newco, within 10 business days from the date of receipt of the Notice of Intention. If no such Notice of Exercise has been delivered by the Stockholders who are not the Selling Stockholder within such 10-business day period, or such Notice of Exercise does not relate to all of the Offered Shares covered by the Notice of Intention, then the Selling Stockholder shall be entitled to Transfer all of the Offered Shares to the intended transferee. In the event that all of the Offered Shares are not purchased by the non-selling Stockholders, the Selling Stockholder shall sell the available Offered Shares within 30 days after the delivery of such Notice of Intention on terms no more favorable to a third party than those presented to the non-selling Stockholders. If such sale does not occur, the Offered Shares shall again be subject to the Right of First Offer set forth in Clause 17.2.

In the event that any of the Stockholders who are not the Selling Stockholder exercises their right to purchase all of the Offered Shares (in accordance with this Clause 17), then the Selling Stockholder shall sell all of the Offered Shares to such Stockholder(s), in the amounts set forth in the Notice of Intention, after not less than 10 business days and not more than 25 business days from the date of the delivery of the Notice of Exercise. In the event that more than one of the Stockholders who are not the Selling Stockholders wish to purchase the Offered Shares, the Offered Shares shall be allocated to such Stockholders on the basis of their pro rata equity interests in Newco.

The rights and obligations of each of the Stockholders pursuant to the Right of First Offer provided herein shall terminate upon the date that the Common Stock is registered under Section 12(b) or 12(g) of the Exchange Act.

At the closing of the purchase of all of the Offered Shares by the Stockholders who are not the Selling Stockholder (scheduled in accordance with Clause 17), the Selling Stockholder shall deliver certificates evidencing the Offered Shares being sold, duly endorsed, or accompanied by written instruments of transfer in form reasonably satisfactory to the Stockholders who are not the Selling Stockholder, duly executed by the Selling Stockholder, free and clear of any adverse claims, against payment of the purchase price therefor in cash, and such other customary documents as shall be necessary in connection therewith.

Notwithstanding any other provision of this Clause 17.2, a Change in Control of any Stockholder shall not trigger a "Right of First Offer" in favor of any other Stockholder.

17.3 TAG ALONG RIGHTS:

Subject to Clause 17.2, a Stockholder (the "TRANSFERRING STOCKHOLDER") shall not Transfer (either directly or indirectly), in any one transaction or series of related transactions, to any Person or group of Persons, any Shares, unless the terms and conditions of such Transfer shall include an offer to the other Stockholders (the "REMAINING STOCKHOLDERS"), to sell Shares at the same price and on the same terms and conditions as the Transferring Stockholder has agreed to sell its Shares (the "TAG ALONG RIGHT").

In the event a Transferring Stockholder proposes to Transfer any Shares in a transaction subject to this Clause 17.3, it shall notify, or cause to be notified, the Remaining Stockholders in writing of each such proposed Transfer. Such notice shall set forth: (i) the name of the transferee and the amount of Shares proposed to be transferred, (ii) the proposed amount and form of consideration and terms and conditions of payment offered by the transferee (the "TRANSFEREE TERMS") and (iii) that the transferee has been informed of the Tag Along Right provided for in this Clause 17, if such right is applicable, and the total number of Shares the transferee has agreed to purchase from the Stockholders in accordance with the terms hereof.

The Tag Along Right may be exercised by each of the Remaining Stockholders by delivery of a written notice to the Transferring Stockholder (the "CO-SALE NOTICE") within 10 business days following receipt of the notice specified in the preceding subsection. The Co-sale Notice shall state the number of Shares owned by such Remaining Stockholder which the Remaining Stockholder wishes to include in such Transfer; provided, however, that without the written consent of the Transferring Stockholder, the amount of such securities belonging to the

Remaining Stockholder included in such Transfer may not be greater than such Remaining Stockholder's percentage beneficial ownership of Fully Diluted Common Stock multiplied by the total number of shares of Fully Diluted Common Stock to be sold by both the Transferring Stockholder and all Remaining Stockholders. Upon receipt of a Co-sale Notice, the Transferring Stockholder shall be obligated to transfer at least the entire number of Shares set forth in the Co-sale Notice to the transferee on the Transferee Terms; provided, however, that the Transferring Stockholder shall not consummate the purchase and sale of any Shares hereunder if the transferee does not purchase all such Shares specified in all Co-sale Notices. If no Co-sale Notice has been delivered to the Transferring Stockholder prior to the expiration of the 10 business day period referred to above and if the provisions of this Section have been complied with in all respects, the Transferring Stockholder shall have the right for a 45 day calendar day period to Transfer Shares to the transferee on the Transferee Terms without further notice to any other party, but after such 45-day period, no such Transfer may be made without again giving notice to the Remaining Stockholders of the proposed Transfer and complying with the requirements of this Clause 17.

At the closing of any Transfer of Shares subject to this Clause 17, the Transferring Stockholder, and the Remaining Stockholder, in the event such Tag Along Right is exercised, shall deliver certificates evidencing such securities as have been Transferred by each, duly endorsed, or accompanied by written instruments of transfer in form reasonably satisfactory to the transferee, free and clear of any adverse claim, against payment of the purchase price therefor.

Notwithstanding the foregoing, this Clause 17 shall not apply to any sale of Common Stock pursuant to an effective registration statement under the Securities Act in a bona fide public offering.

The rights and obligations of each of the Stockholders pursuant to the "Tag Along Right" provided herein shall terminate upon the date that the Common Stock is registered under Section 12(b) or 12(g) of the Exchange Act.

Notwithstanding any other provision of this Clause 17.3, a Change in Control of any Stockholder shall not trigger a "Tag Along Right" in favor of any other Stockholder.

CLAUSE 18

MATTERS REQUIRING PARTICIPANTS' APPROVAL

18.1 In consideration of Isis and Elan agreeing to enter into the License Agreements, the Parties hereby agree that Newco shall not without the prior approval of the EIS Director and at least two of the Isis Directors:

18.1.1. engage in any activity other than the Business;

18.1.2. acquire or dispose of assets of a value in excess of $25,000 or sell the principal assets, undertaking or Business of Newco;

18.1.3. create any fixed or floating charge, lien (other than a lien arising by operation of law) or other encumbrance over the whole or any part of the undertaking, property or assets of Newco or of any Subsidiary;

18.1.4. borrow any sum in excess of a maximum aggregate sum outstanding at any time of US $25,000;

18.1.5. make any loan or advance or give any credit (other than normal trade credit) in excess of US$25,000 to any Person;

18.1.6. give any guarantee or indemnity to secure the liabilities or obligations of any Party other than those which it is usual to give in the ordinary course of a business similar to the Business;

18.1.7. enter into any contract, arrangement or commitment involving expenditure on capital account or the realization of capital assets if the amount or the aggregate amount of such expenditure or realization by Newco would exceed US$50,000 in any one year or in relation to any one project, and for the purpose of this paragraph the aggregate amount payable under any agreement for hire, hire purchase or purchase on credit sale or conditional sale terms shall be deemed to be capital expenditure incurred in the year in which such agreement is entered into;

18.1.8. issue any unissued Shares or create or issue any new shares;

18.1.9. alter any rights attaching to any class of share in the capital of Newco or alter the Newco Memorandum of Association and Bye-Laws;

18.1.10. consolidate, sub-divide or convert any of Newco's share capital or in any way alter the rights attaching thereto;

18.1.11. dispose of Newco or of any shares in Newco;

18.1.12. enter into any partnership or profit sharing agreement with any Person other than arrangements with trade representatives and similar Persons in the ordinary course of business;

18.1.13. do or permit or suffer to be done any act or thing whereby Newco may be wound up (whether voluntarily or compulsorily), save as otherwise expressly provided for in this Agreement;

18.1.14. issue any debentures or other securities convertible into shares or debentures or any share warrants or any options in respect of shares in Newco;

18.1.15. enter into any contract or transaction except in the ordinary and proper course of the Business on arm's length terms;

18.1.16. acquire, purchase or subscribe for any shares, debentures, mortgages or securities (or any interest therein) in any company, trust or other Person;

18.1.17. adopt any employee benefit program or incentive schemes;

18.1.18. engage any new employee at remuneration of greater than US$60,000 per annum;

18.1.19. pay any remuneration to the Directors by virtue of holding such office other than Directors who hold executive office;

18.1.20. license or sub-license any of the Elan Intellectual Property, Isis Intellectual Property, or Newco Technology;

18.1.21. amend or vary the terms of the Isis License Agreement or the Elan License Agreement;

18.1.22. permit a person other than Newco to own a regulatory approval relating to the Product(s);

18.1.23. change the authorized signatories on Newco bank accounts;

18.1.24. amend or vary the Business Plan or agree the Budget;

18.1.25. alter the number of Directors;

18.1.26. pay dividends or distributions in respect of, or redeem or repurchase, the equity of Newco;

18.1.27. enter into joint venture agreements or any similar arrangements with any Person; or

18.1.28. create, acquire or dispose of any Subsidiary or of any shares in any Subsidiary.

CLAUSE 19

DISPUTES

19.1 Should any dispute or difference arise between Elan and Isis, or between Elan or Isis and Newco, during the period that this Agreement is in force, other than a dispute or difference relating to (i) the interpretation of any provision of this Agreement, (ii) the interpretation or application of law, or (iii) the ownership of any intellectual property, then any Party may forthwith give notice to the other Parties that it wishes such dispute or difference to be referred to the Chief Executive Officer of Isis and the President of EPT.

19.2 In any event of a notice being served in accordance with Clause 19.1, each of the Participants shall within 14 days of the service of such notice prepare and circulate to the Chief Executive Officer of Isis and the President of EPT a memorandum or other form of statement setting out its position on the matter in dispute and its reasons for adopting that position. Each memorandum or statement shall be considered by the Chief Executive Officer of Isis and the President of EPT who shall endeavor to resolve the dispute. If the chief executive officers of the Participants agree upon a resolution or disposition of the matter, they shall each sign a statement which sets out the terms of their agreement. The Participants agree that they shall exercise the voting rights and other powers available to them in relation to Newco to procure that the agreed terms are fully and promptly carried into effect.

CLAUSE 20

CERTAIN CHANGES OF CONTROL

20.1 [...***...].

20.2 In the event that [...***...] pursuant to Clause 20.1 above, the Participants shall jointly select a nationally recognized investment banking firm as arbitrator to make such determination. In the event the Participants do not agree upon the selection of such investment banking firm, Elan may contact the presiding justice of the Supreme Court of the State of New York sitting in the City, County, and State of

*CONFIDENTIAL TREATMENT REQUESTED

New York (the "PRESIDING JUSTICE") and request that an independent US-based nationally recognized investment banking firm which is knowledgeable of the pharmaceutical/biotechnology industry be appointed within 10 Business Days. The Presiding Justice shall endeavor to select an investment banking firm as arbitrator which is technically knowledgeable in the pharmaceutical/biotechnology industry (and which directly and through its Affiliates, has no business relationship with, or shareholding in, either of the Participants). Promptly upon being notified of the arbitrator's appointment, the Participants shall submit to the arbitrator details of their assessment of [...***...] together with such information as they think necessary to validate their assessment. The arbitrator shall notify Isis of [...***...] and shall notify Elan of [...***...]. The Participants shall then be entitled to make further submissions to the arbitrator within five Business Days explaining why [...***...], as the case may be, are unjustified. The arbitrator shall thereafter meet with Isis and Elan and shall thereafter choose either [...***...] on the basis of [...***...]. The arbitrator shall use its best efforts to determine [...***...] within 30 Business Days of his appointment. The Participants shall bear the costs of the arbitrator equally provided that the arbitrator may, in its discretion, allocate all or a portion of such costs to one Party. Any decision of the arbitrator shall be final and binding.

20.3 Elan shall purchase the Shares beneficially owned by Isis by delivery of the Purchase Price in cash no later than the 15th Business Day following determination of the Purchase Price by the arbitrator.

20.4 The Shares so transferred shall be sold by Isis with effect from the date of such transfer free from any lien, charge or encumbrance, but with all rights and restrictions attaching thereto.

20.5 If Elan exercises the Buyout Option, Newco shall continue to develop Isis Products on terms which are substantially the same as those which would be provided to an Independent Third Party negotiating on an arm's length basis.

20.6 If Elan exercises the Buyout Option, both parties will negotiate in good faith to agree to additional reasonable provisions and/or amendments to the License Agreements to protect the intellectual property rights of the Participants.

20.7 If Elan exercises the Buyout Option, the provisions of Clauses 1, 3, 11.1, 17, 20.7, 21.4, 22, 23 and 24 shall survive the termination of this Agreement under this Clause 20.7; all other terms and provisions of this Agreement shall cease to have effect and be null and void.

*CONFIDENTIAL TREATMENT REQUESTED

CLAUSE 21

TERMINATION

21.1 This Agreement shall govern the operation and existence of Newco until (i) terminated by written agreement of all Parties hereto or (ii) otherwise terminated in accordance with this Clause 21.

21.2 For the purpose of this Clause 21, a "RELEVANT EVENT" is committed or suffered by a Participant if:

21.2.1 it commits a material breach of its obligations under this Agreement or the applicable License, which breach remains uncured 60 days after written notice thereof; provided, however, that (x) if the breaching Participant has proposed a course of action to rectify the breach and is acting in good faith to rectify same but has not cured the breach by the 60th day, such period shall be extended by such period as is reasonably necessary to permit the breach to be rectified and (y) if a default involves a good faith dispute regarding the amount of any required payment, provided any undisputed amount is paid, such default shall be stayed and the remainder may be withheld for a reasonable period during which a good faith resolution of the amount owed is being pursued;

21.2.2 a distress, execution, sequestration or other process is levied or enforced upon or sued out against a material part of its property which is not discharged or challenged within 30 days;

21.2.3 it is unable to pay its debts in the normal course of business;

21.2.4 it ceases wholly or substantially to carry on its business, otherwise than for the purpose of a reconstruction or amalgamation, without the prior written consent of the other Participant (such consent not to be unreasonably withheld);

21.2.5 the appointment of a liquidator, receiver, administrator, examiner, trustee or similar officer of such Participant or over all or substantially all of its assets under the law of any applicable jurisdiction, including without limitation, the United States of America, Bermuda or Ireland;

21.2.6 an application or petition for bankruptcy, corporate re-organization, composition, administration, examination, arrangement or any other procedure similar to any of the foregoing under the law of any applicable jurisdiction, including without limitation, the United States of America, Bermuda or Ireland, is filed, and is not discharged within 60 days, or a Participant applies for or consents to the appointment of a receiver, administrator, examiner or similar officer of it or of all or a material part

of its assets, rights or revenues or the assets and/or the business of a Participant are for any reason seized, confiscated or condemned.

21.3 If either Participant commits a Relevant Event, the other Stockholder shall have in addition to all other legal and equitable rights and remedies hereunder, the right to terminate this Agreement upon 30 days' written notice.

21.4 In the event of a termination of the Elan License Agreement and/or the Isis License Agreement, both parties will negotiate in good faith to determine whether this Agreement should be terminated and if so, which provisions should survive termination.

21.5 The provisions of Clauses 1, 3, 7.1, 11.1, 17, 21.4, 21.5, 22, 23 and 24 shall survive the termination of this Agreement under Clause 21.3 or by mutual consent pursuant to Clause 21.1 in accordance with their terms; all other terms and provisions of this Agreement shall cease to have effect and be null and void upon the termination of this Agreement under Clause 21.3 or by mutual consent pursuant to Clause 21.1.

CLAUSE 22

CONFIDENTIALITY

22.1 The Parties and/or Newco acknowledge and agree that it may be necessary, from time to time, to disclose to each other confidential and/or proprietary information, including without limitation, inventions, works of authorship, trade secrets, specifications, designs, data, know-how and other information, relating to the Field, the Products, present or future products, the Newco Technology, the Elan Intellectual Property or the Isis Intellectual Property, as the case may be, methods, compounds, research projects, work in process, services, sales suppliers, customers, employees and/or business of the disclosing Party, whether in oral, written, graphic or electronic form (collectively "CONFIDENTIAL INFORMATION").

22.2 Any Confidential Information revealed by a Party to another Party shall be maintained as confidential and shall be used by the receiving Party exclusively for the purposes of fulfilling the receiving Party's rights and obligations under this Agreement, and for no other purpose. Confidential Information shall not include:

22.2.1 information that is generally available to the public;

22.2.2 information that is made public by the disclosing Party;

22.2.3 information that is independently developed by the receiving Party, as evidenced by such Party's written records, without the aid, application or use of the disclosing Party's Confidential Information;

22.2.4 information that is published or otherwise becomes part of the public domain without any disclosure by the receiving Party, or on the part of the receiving Party's directors, officers, agents, representatives or employees;

22.2.5 information that becomes available to the receiving Party on a non-confidential basis, whether directly or indirectly, from a source other than the disclosing Party, which source did not acquire this information on a confidential basis;

22.2.6 information which the receiving Party is required to disclose pursuant to:

(i) a valid order of a court or other governmental body or any political subdivision thereof or as otherwise required by law, rule or regulation; or

(ii) other requirement of law; provided, however, that if the receiving Party becomes legally required to disclose any Confidential Information, the receiving Party shall give the disclosing Party prompt notice of such fact so that the disclosing Party may obtain a protective order or seek confidential treatment or other appropriate remedy concerning any such disclosure. The receiving Party shall fully co-operate with the disclosing Party in connection with the disclosing Party's efforts to obtain any such order or other remedy. If any such order or other remedy does not fully preclude disclosure, the receiving Party shall make such disclosure only to the extent that such disclosure is legally required;

22.2.7 information which was already in the possession of the receiving Party at the time of receiving such information, as evidenced by its written records, provided such information was not previously provided to the receiving Party from a source which was under an obligation to keep such information confidential; or

22.2.8 information that is the subject of a written permission to disclose, without restriction or limitation, by the disclosing Party.

22.3 Each Party agrees to disclose Confidential Information of another Party only to those employees, representatives and agents requiring knowledge thereof in connection with their duties directly related to the fulfilling of the Party's obligations under this Agreement, so long as such persons are under an obligation of confidentiality no less stringent than as set forth herein. Each Party further agrees to inform all such employees, representatives and agents of the terms and provisions of the Transaction Documents and their duties hereunder and to obtain their consent hereto as a condition of receiving Confidential Information. Each Party agrees that it will exercise the same degree of care and protection to preserve the proprietary and confidential nature of the Confidential Information

disclosed by a Party, as the receiving Party would exercise to preserve its own Confidential Information. Each Party agrees that it will, upon request of another Party, return all documents and any copies thereof containing Confidential Information belonging to or disclosed by such other Party. Each Party shall promptly notify the other Parties upon discovery of any unauthorized use or disclosure of the other Parties' Confidential Information.

22.4 Notwithstanding the above, each Party may use or disclose Confidential Information disclosed to it by another Party to the extent such use or disclosure is reasonably necessary in filing or prosecuting patent applications, prosecuting or defending litigation, complying with patent applications, prosecuting or defending litigation, complying with applicable governmental regulations or otherwise submitting information to tax or other governmental authorities, conducting clinical trials, or granting a permitted sub-license or otherwise exercising its rights hereunder; provided, that if a Party is required to make any such disclosure of the other Party's Confidential Information, other than pursuant to a confidentiality agreement, such Party shall inform the third party recipient of the terms and provisions of this Agreement and their duties hereunder and shall obtain their consent hereto as a condition of releasing to the third party recipient the Confidential Information.

22.5 Nothing contained herein shall obligate or restrict any Party from utilizing public, non-proprietary information which is not subject to the protection of applicable patent laws.

22.6 Any breach of this Clause 22 by any employee, representative or agent of a Party shall be considered a breach by the Party itself.

22.7 The provisions relating to confidentiality in this Clause 22 shall remain in effect during the Term and for a period of seven years following the termination of this Agreement.

22.8 The Parties agree that the obligations of this Clause 22 are necessary and reasonable in order to protect the Parties' respective businesses, and each Party expressly agrees that monetary damages would be inadequate to compensate a Party for any breach by the other Party of its covenants and agreements set forth herein. Accordingly, the Parties agree and acknowledge that any such violation or threatened violation will cause irreparable injury to a Party and that, in addition to any other remedies that may be available, in law or in equity or otherwise, any Party shall be entitled to obtain injunctive relief against the threatened breach of the provisions of this Clause 22, or a continuation of any such breach by the other Party, specific performance and other equitable relief to redress such breach together with its damages and reasonable counsel fees and expenses to enforce its rights hereunder, without the necessity of proving actual or express damages.

CLAUSE 23

COSTS

23.1 Each Stockholder shall bear its own legal and other costs incurred in relation to preparing and concluding this Agreement and the other Transaction Documents.

23.2 All other costs, legal fees, registration fees and other expenses relating to the transactions contemplated hereby, including the costs and expenses incurred in relation to the incorporation of Newco, shall be borne by Newco.

CLAUSE 24

GENERAL

24.1 GOOD FAITH:

Each of the Parties hereto undertakes with the others to do all things reasonably within its power that are necessary or desirable to give effect to the spirit and intent of this Agreement.

24.2 FURTHER ASSURANCE:

At the request of any of the Parties, the other Party or Parties shall (and shall use reasonable efforts to procure that any other necessary parties shall) execute and perform all such documents, acts and things as may reasonably be required subsequent to the signing of this Agreement for assuring to or vesting in the requesting Party the full benefit of the terms hereof.

24.3 RELIANCE ON REPRESENTATION AND WARRANTIES:

Each of the Parties hereto hereby acknowledges that in entering into this Agreement it has not relied on any representation or warranty except as expressly set forth herein or in any document referred to herein.

24.4 FORCE MAJEURE:

Neither Party to this Agreement shall be liable for delay in the performance of any of its obligations hereunder if such delay is caused by or results from causes beyond its reasonable control, including without limitation, acts of God, fires, strikes, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts or other labor disturbances or intervention of any relevant government authority, but any such delay or failure shall be remedied by such Party as soon as practicable.

24.5 RELATIONSHIP OF THE PARTIES:

Nothing contained in this Agreement is intended or is to be construed to constitute Elan/EIS and Isis as partners, or Elan/EIS as an employee or agent of Isis, or Isis as an employee or agent of Elan/EIS.

No Party hereto shall have any express or implied right or authority to assume or create any obligations on behalf of or in the name of another Party or to bind another Party to any contract, agreement or undertaking with any third Party.

24.6 COUNTERPARTS:

This Agreement may be executed in any number of counterparts, each of which when so executed shall be deemed to be an original and all of which when taken together shall constitute this Agreement.

24.7 NOTICES:

Any notice to be given under this Agreement shall be sent in writing by registered or recorded delivery post or reputable overnight courier such as Federal Express or telecopied to:

Elan at:

Lincoln House, Lincoln Place, Dublin 2
Ireland
Attention: Vice President & General Counsel,
Elan Pharmaceutical Technologies,
a division of Elan Corporation, plc
Telephone: 353-1-709-4000
Fax: 353-1-709-4124

with a copy to:

Brock Silverstein LLC
One Citicorp Center, 56th Floor
New York, NY 10022
Attention: David Robbins, Esq.
Telephone: 212-371-2000
Fax: 212-371-5500

EIS at:

Elan International Services, Ltd.
102 St. James Court
Flatts, Smiths Parish FL04

Bermuda
Attention: President
Telephone: 441-292-9169
Fax: 441-292-2224

with a copy to:

Brock Silverstein LLC
One Citicorp Center, 56th Floor
New York, NY 10022
Attention: David Robbins, Esq.
Telephone: 212-371-2000
Fax: 212-371-5500

Isis at:

2292 Faraday Avenue
Carlsbad, CA 92008
Attention: B. Lynne Parshall
Telephone: 760-603-2460
Fax: 760-931-9639

with a copy to:

Cooley Godward LLP
4365 Executive Drive
San Diego, CA 92121
Attention: L. Kay Chandler, Esq.
Telephone: 619-550-6000
Fax: 619-453-3555

Newco at:

Orasense Ltd.
c/o Appleby, Spurling & Kempe
Cedar House, 41 Cedar Avenue
P.O. Box HM 1179
Hamilton, Bermuda HM EX
Attention: Timothy Faries
Telephone: 441-295-2244
Fax: 441-295-7768

with a copy to each of Isis, EIS and their respective counsel at the addresses indicated above;

or to such other address(es) as may from time to time be notified by any Party to the others hereunder.

Any notice sent by mail shall be deemed to have been delivered within three Business Days after dispatch or delivery to the relevant courier and any notice sent by telecopy shall be deemed to have been delivered upon confirmation of receipt by telephone. Notices of change of address shall be effective upon receipt.

24.8 GOVERNING LAW

This Agreement shall be governed by and construed in accordance with the laws of the State of New York without giving effect to any choice or conflict or law provision or rule.

24.9 ARBITRATION

(a) Any dispute under this Agreement or the other Transaction Documents which is not settled by mutual consent (whether pursuant to the provisions in Clause 19 hereof or otherwise) shall be finally settled by binding arbitration, conducted in accordance with the Commercial Arbitration Rules of the American Arbitration Association by one (1) arbitrator appointed in accordance with said rules. Such arbitrator shall be reasonably satisfactory to each of the Parties; provided, that if the Parties are unable to agree upon the identity of such arbitrator within 15 days of demand by either Party, then either Party shall have the right to petition the Presiding Justice to appoint an arbitrator.

The arbitration shall be held in New York, New York and the arbitrator shall be an independent expert in pharmaceutical product development and marketing (including clinical development and regulatory affairs).

(b) The arbitrator shall determine what discovery will be permitted, consistent with the goal of limiting the cost and time which the Parties must expend for discovery; provided the arbitrator shall permit such discovery as they deem necessary to permit an equitable resolution of the dispute.

Any written evidence originally in a language other than English shall be submitted in English translation accompanied by the original or a true copy thereof.

The costs of the arbitration, including administrative and arbitrators' fees, shall be shared equally by the Parties and each Party shall bear its own costs and attorneys' and witness' fees incurred in connection with the arbitration.

(c) In rendering judgment, the arbitrator shall be instructed by the Parties that he shall be permitted to select solely from between the proposals for resolution of the relevant issue presented by each Party, and not any other proposal.

A disputed performance or suspended performances pending the resolution of the arbitration must be completed within thirty (30) days following the final decision of the arbitrators or such other reasonable period as the arbitrators determine in a written opinion.

(d) Any arbitration under the Transaction Documents shall be completed within one year from the filing of notice of a request for such arbitration.

The arbitration proceedings and the decision shall not be made public without the joint consent of the Parties and each Party shall maintain the confidentiality of such proceedings and decision unless otherwise permitted by the other Party.

(e) The Parties agree that the decision shall be the sole, exclusive and binding remedy between them regarding any and all disputes, controversies, claims and counterclaims presented to the arbitrators. Application may be made to any court having jurisdiction over the Party (or its assets) against whom the decision is rendered for a judicial recognition of the decision and an order of enforcement.

24.10 SEVERABILITY:

If any provision in this Agreement is agreed by the Parties to be, deemed to be or becomes invalid, illegal, void or unenforceable under any law that is applicable hereto, such provision will be deemed amended to conform to applicable laws so as to be valid and enforceable or, if it cannot be so amended without materially altering the intention of the Parties, it will be deleted, with effect from the date of such agreement or such earlier date as the Parties may agree, and the validity, legality and enforceability of the remaining provisions of this Agreement shall not be impaired or affected in any way.

24.11 AMENDMENTS:

No amendment, modification or addition hereto shall be effective or binding on any Party unless set forth in writing and executed by a duly authorized representative of all Parties.

24.12 WAIVER:

No waiver of any right under this Agreement shall be deemed effective unless contained in a written document signed by the Party charged with such waiver,

and no waiver of any breach or failure to perform shall be deemed to be a waiver of any future breach or failure to perform or of any other right arising under this Agreement.

24.13 ASSIGNMENT:

None of the Parties shall be permitted to assign its rights or obligations hereunder without the prior written consent of the other Parties except as follows:

24.13.1 Elan, EIS and/or Isis shall have the right to assign their rights and obligations hereunder to their Affiliates provided, however, that such assignment does not result in adverse tax consequences for any other Parties.

24.13.2 Elan and EIS shall have the right to assign their rights and obligations hereunder to an off-balance sheet special purpose entity established by Elan or EIS.

24.13.3 Elan, EIS and/or Isis shall have the right to assign or otherwise transfer their rights and obligations hereunder in connection with a sale of all or substantially all of the business of such Party to which the transaction Documents relate, whether by merger, sale of stock, sale of assets or otherwise, subject, however, to the Elan's right to exercise the Buyout Option pursuant to the provisions of Clause 20 hereof in the event of a Change of Control of Isis and/or Newco.

24.14 WHOLE AGREEMENT/NO EFFECT ON OTHER AGREEMENTS:

This Agreement (including the Schedules attached hereto) and the other Transaction Documents set forth all of the agreements and understandings between the Parties with respect to the subject matter hereof, and supersedes and terminates all prior agreements and understandings between the Parties with respect to the subject matter hereof. There are no agreements or understandings with respect to the subject matter hereof, either oral or written, between the Parties other than as set forth in this Agreement and the other Transaction Documents.

In the event of any ambiguity or conflict arising between the terms of this Agreement and those of the Newco Memorandum of Association and Bye-Laws, the terms of this Agreement shall prevail.

No provision of this Agreement shall be construed so as to negate, modify or affect in any way the provisions of any other agreement between any of the Parties unless specifically referred to, and solely to the extent provided herein. In the event of a conflict between the provisions of this Agreement and the

provisions of the License Agreements, the terms of this Agreement shall prevail unless this Agreement specifically provide otherwise.

24.15 SUCCESSORS:

This Agreement shall be binding upon and inure to the benefit of the Parties hereto, their successors and permitted assigns.

[Signature Page Follows]

IN WITNESS WHEREOF, the Parties hereto have executed this Agreement on the day first set forth above.

SIGNED

BY:_____

for and on behalf of
ELAN CORPORATION, PLC

in the presence of:_____

SIGNED

BY:_____

for and on behalf of
ELAN INTERNATIONAL SERVICES, LTD.

in the presence of:_____

SIGNED

BY:_____

for and on behalf of
ISIS PHARMACEUTICALS, INC.

in the presence of:_____

SIGNED

BY:_____

for and on behalf of
ORASENSE LTD.

in the presence of:_____

EXHIBIT 10.2

SECURITIES PURCHASE AGREEMENT

SECURITIES PURCHASE AGREEMENT (this "Agreement"), dated as of April 20, 1999, between ISIS PHARMACEUTICALS, INC., a Delaware corporation (the "Company"), and ELAN INTERNATIONAL SERVICES, LTD., a Bermuda private limited company ("EIS").

R E C I T A L S:

A. The Company desires to issue and sell to EIS, and EIS desires to purchase from the Company, (i) 120,150 shares of a newly-created series of the Company's Preferred Stock, par value $.001 per share, captioned "Series A Convertible Preferred Stock" (the "Series A Preferred Stock"), (ii) 910,844 shares of the Company's Common Stock, par value $.001 per share (the "Common Stock") ((i) and (ii) together, the "Shares"), and (iii) a warrant (the "Warrant") to purchase up to 215,000 shares of Common Stock as provided for therein. In addition, EIS has agreed to lend certain funds to the Company pursuant to a convertible promissory note in the form attached hereto as Exhibit A (as amended at any time, the "Note" and, together with the Series A Preferred Stock, the Common Stock, and the Warrant, the "Securities"), with a maximum aggregate principal amount of U.S.$18,400,000, amounts in respect of which shall be disbursed in accordance with its terms and subject to the conditions contained herein and therein. The rights, preferences and privileges of the Series A Preferred Stock are as set forth in the Certificate of Designations, Preferences and Rights (the "Certificate of Designations"), the form of which is attached hereto as Exhibit B.

B. The Company and EIS have previously caused to be formed Orasense Ltd., a Bermuda private limited company ("Newco"), and pursuant to the terms of a Subscription, Joint Development and Operating Agreement, dated as of the date hereof (as amended at any time, the "JDOA"), simultaneously with the transactions contemplated by this Agreement, (i) the Company shall acquire 9,612 common shares of Newco, par value U.S.$1.00 per share (the "Newco Common Stock"), and (ii) EIS shall acquire 2,388 shares of Newco Common Stock. Additionally, as of the date hereof, Newco has entered into license agreements with (i) ELAN CORPORATION, PLC, an Irish public limited company and parent corporation of EIS ("Elan;" such agreement, as amended at any time, the "Elan License Agreement"), and (ii) the Company (such agreement, as amended at any time, the "Newco License Agreement" and, together with the Elan License Agreement, the "License Agreements").

C. The Company and EIS are executing and delivering on the date hereof a Registration Rights Agreement, in the form attached hereto as Exhibit C (as amended at any time, the "Registration Rights Agreement"), in respect of the Common Stock issued or issuable upon conversion of the Series A Preferred Stock and the Note and exercise of the Warrant, the Common Stock being purchased hereunder, and any other Common Stock issued to EIS or any of its affiliates or permitted transferees upon any stock split, stock dividend, recapitalization or similar event affecting the Securities. The Company, EIS and Newco are also executing and delivering on the date hereof a Registration Rights Agreement in the form attached hereto as

Exhibit D (as amended at any time, the "Newco Registration Rights Agreement"). Additionally, the Company and EIS are executing and delivering on the date hereof a Funding Agreement in the form attached hereto as Exhibit E (the "Funding Agreement;" and, together with this Agreement, the Certificate of Designations, the JDOA, the Registration Rights Agreement, the Newco Registration Rights Agreement, the License Agreements and each other document or instrument executed and delivered in connection with the transactions contemplated hereby and by the JDOA, the "Transaction Documents").

A G R E E M E N T:

The parties hereto agree as follows:

SECTION 1. Closing.

(a) Time and Place. The closing of the transactions contemplated hereby (the "Closing") shall occur on the date hereof (the "Closing Date"), at the offices of Brock Silverstein LLC, One Citicorp Center, 56th Floor, New York, NY 10022.

(b) Issuance of Securities. At the Closing, the Company shall issue and sell to EIS, and EIS shall purchase from the Company: (i) 120,150 shares of Series A Preferred Stock, (ii) 910,844 shares of Common Stock, (iii) the Warrant, and (iv) the Note, the principal amount of which shall be disbursed by EIS subsequent to the Closing in accordance with its terms.

(c) Purchase Price. The purchase price (the "Purchase Price") shall be the sum of (i) U.S.$12,015,000, the purchase price for the Series A Preferred Stock, and (ii) U.S.$15,000,000, the purchase price for the Common Stock.

(d) Delivery. At the Closing:

(i) EIS shall pay the Purchase Price by wire transfer to an account designated by the Company and the parties hereto shall execute and deliver to each other, as applicable: (A) a certificate or certificates for the Series A Preferred Stock and the Common Stock; (B) the Note; (C) the Warrant; (D) the Registration Rights Agreement; (E) the Newco Registration Rights Agreement; (F) the JDOA; (G) the Certificate of Designations, as filed with the Secretary of State of the State of Delaware; (H) the License Agreements; (I) the Funding Agreement; (J) certificates as to the incumbency of the officers of the Company executing any of the Transaction Documents; and (K) any other documents or instruments reasonably requested by a party hereto; and

(ii) The Company shall cause to be delivered to EIS an opinion of counsel in the form attached hereto as Exhibit C to the Letter Agreement, dated March 31, 1998, by and among Elan, EIS and the Company (the "Letter Agreement").

(e) Exemption from Registration. The Securities and any underlying shares of Common Stock will be issued under an exemption or exemptions from registration under the Securities Act of 1933, as amended (the "Securities Act"). Accordingly, the certificates evidencing the Series A Preferred Stock and the Common Stock, the Warrant, the Note and any shares of Common Stock or other securities issuable upon the exercise, conversion or exchange of any of the Securities shall, upon issuance, contain a legend, substantially in the form as follows:

> THE SECURITIES REPRESENTED HEREBY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND MAY NOT UNDER ANY CIRCUMSTANCES BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF WITHOUT AN EFFECTIVE REGISTRATION STATEMENT FOR SUCH SECURITIES UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND ANY APPLICABLE STATE SECURITIES LAWS OR AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY THAT REGISTRATION IS NOT REQUIRED UNDER SUCH ACT OR APPLICABLE STATE SECURITIES LAWS.
>
> THE TRANSFER OF THE SECURITIES REPRESENTED BY THIS CERTIFICATE IS ALSO SUBJECT TO THE RESTRICTIONS CONTAINED IN THAT CERTAIN SECURITIES PURCHASE AGREEMENT, DATED APRIL 20, 1999, BY AND BETWEEN ISIS PHARMACEUTICALS, INC. AND ELAN INTERNATIONAL SERVICES, LTD.

SECTION 2. Representations and Warranties of the Company. The Company hereby represents and warrants to EIS, as of the date hereof, as follows:

(a) Organization. The Company is duly organized, validly existing and in good standing under the laws of the State of Delaware and has all requisite corporate power and authority to own and lease its properties, to carry on its business as presently conducted and as proposed to be conducted and to consummate the transactions contemplated hereby. The Company is duly qualified as a foreign corporation and in good standing to do business in each jurisdiction in which the nature of the business conducted or the property owned by it requires such qualification, except where the failure to be so qualified would not, individually or in the aggregate, have a material adverse effect on the business, assets, liabilities (contingent or otherwise), operations, condition (financial or otherwise), or prospects of the Company (a "Company Material Adverse Effect").

(b) Capitalization. As of the Closing Date, the Company has reserved a sufficient number of shares of Common Stock (i) for issuance upon conversion of the Series A

Preferred Stock being purchased hereunder by EIS (including dividends in-kind thereon), (ii) for issuance upon exercise of the Warrant, and (iii) for issuance upon conversion of the Note (including interest payable thereon). The Shares, when issued against payment therefor in accordance with this Agreement, will be duly and validly issued, fully paid and nonassessable, will not be issued in violation of any preemptive or similar rights. The shares of Common Stock underlying the Series A Preferred Stock, the Note and the Warrant (the "Underlying Shares"), when issued upon conversion or exercise in accordance with the terms thereof, will be duly and validly issued, fully paid and nonassessable, will not be issued in violation of any preemptive or similar rights.

(c) Authorization of Transaction Documents. The Company has full corporate power and authority to execute and deliver this Agreement and each of the other Transaction Documents to which it is a party, and to perform its obligations hereunder and thereunder. The execution, delivery and performance by the Company of this Agreement and each of the other Transaction Documents to which it is a party, including the issuance and sale of the Securities, have been duly authorized by all requisite corporate action by the Company and, when executed and delivered by the Company, this Agreement and each of the other Transaction Documents to which it is a party will be the valid and binding obligations of the Company, enforceable against the Company in accordance with their respective terms, except (A) that enforcement may be limited by (i) applicable bankruptcy, insolvency, reorganization, arrangement, moratorium or other similar laws affecting creditors' rights, and (ii) general equity principles and limitations on the availability of equitable relief, including specific performance, and (B) that any rights to indemnity or contribution hereunder or thereunder may be limited by state and federal securities laws and by public policy considerations.

(d) No Violation. The execution, delivery and performance by the Company of this Agreement and each other Transaction Document to which it is a party, including the issuance and sale of the Securities, and compliance with the provisions hereof and thereof by the Company, does not conflict with or constitute or result in a breach of or default under (or an event which with notice or passage of time or both would constitute a default) or give rise to any right of termination, cancellation or acceleration under (i) the Certificate of Incorporation, as amended, or by-laws, of the Company, (ii) applicable law, statute, rule or regulation, or any ruling, writ, injunction, order, judgment or decree of any court, arbitrator, administrative agency or other governmental body applicable to the Company or any of its properties or assets, or (iii) any contract filed as an exhibit to the Company's Annual Report on Form 10-K for the year ended December 31, 1998 (the "1998 Form 10-K"), except where such breach, default, termination, cancellation or acceleration would not, individually or in the aggregate, have a Company Material Adverse Effect.

(e) Approvals. No material permit, authorization, consent, approval, or order of or by, or any notification of or filing with, any person or entity (governmental or otherwise) is required in connection with the execution, delivery or performance of this Agreement or the Transaction Documents, including the issuance and sale of the Securities, by the Company, other

than the filing of a Form D by the Company pursuant to Regulation D under the Securities Act ("Regulation D").

(f) SEC Filings. The Company has filed with the Securities and Exchange Commission (the "SEC") all forms, reports, schedules, statements, exhibits and other documents (collectively, the "SEC Filings") required to be filed by the Company on or before the date hereof. At the time filed, the SEC Filings, including without limitation, any financial statements, exhibits and schedules included therein or documents incorporated therein by reference (i) did not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary in order to make the statements therein, in light of the circumstances under which they were made, not misleading and (ii) complied in all material respects with the applicable requirements of the Securities Act or the Securities Exchange Act of 1934, as amended (the "Exchange Act"), as the case may be.

(g) Financial Statements. The audited balance sheets of the Company at December 31, 1997 and 1998, together with the related statements of operations, stockholders' equity (deficit) and cash flows for each of the three years ended December 31, 1998, together with the reports and opinions thereon of Ernst & Young LLP, contained in the 1998 Form 10-K, comply as to form in all material respects with applicable accounting requirements and the published rules and regulation of the SEC with respect thereto, and fairly present, in all material respects, the financial position of the Company and the results of its operations and its cash flows at such dates and for the years then ended and were prepared in conformity in all material respects with generally accepted accounting principles applied on a consistent basis.

(h) Litigation. Except as disclosed in the 1998 Form 10-K, there is no legal, administrative, arbitration or other action or proceeding or governmental investigation pending, or to the Company's knowledge, threatened against the Company, or any director, officer or employee of the Company that challenges the validity or performance of this Agreement or the other Transaction Documents to which the Company is a party.

(i) Absence of Certain Events. Since March 31, 1998, except as contemplated by the Transaction Documents, (A) the Company has not (i) made, paid or declared any dividend or distribution to any equity holder (in such capacity) or redeemed any of its capital stock, (ii) varied its business plan or practices, in any material respect, from past practices, (iii) entered into any financing, joint venture, license or similar arrangement that would limit or restrict its ability to perform its obligations hereunder and under each of the other Transaction Documents to which it is a party, or (iv) suffered or permitted to be incurred any liability or obligation or any lien or encumbrance against any of its properties or assets that would limit or restrict its ability to perform its obligations hereunder and under each of the other Transaction Documents to which it is a party, and (B) there has not been any change or development which has had, or in the Company's reasonable judgment is likely to have, a Company Material Adverse Effect.

(j) Brokers or Finders. The Company has not retained any investment banker, broker, finder or person or entity acting in a similar capacity, and is not liable for any fee or payment to any such person, in connection with the transactions contemplated by the Transaction Documents.

SECTION 3. Representation and Warranties of EIS. EIS hereby represents and warrants to the Company, as of the date hereof, as follows:

(a) Organization. EIS is duly organized, validly existing and in good standing under the laws of Bermuda and has all requisite corporate power and authority to own and lease its properties, to carry on its business as presently conducted and as proposed to be conducted and to consummate the transactions contemplated hereby. EIS is duly qualified as a foreign corporation and in good standing to do business in each jurisdiction in which the nature of the business conducted or the property owned by it requires such qualification, except where the failure to be so qualified would not, individually or in the aggregate, have a material adverse effect on the business, assets, liabilities (contingent or otherwise), operations, condition (financial or otherwise), or prospects of EIS (an "EIS Material Adverse Effect").

(b) Authorization of Transaction Documents. EIS has full corporate power and authority to execute and deliver this Agreement and each of the other Transaction Documents to which it is a party, and to perform its obligations hereunder and thereunder. The execution, delivery, and performance by EIS of this Agreement and each other Transaction Document to which it is a party, including the purchase and acceptance of the Securities, have been duly authorized by all requisite corporate action by EIS and, when executed and delivered by EIS, this Agreement and each of the other Transaction Document to which it is a party, will be the valid and binding obligations of EIS, enforceable against it in accordance with their respective terms, except (A) that enforcement may be limited by (i) applicable bankruptcy, insolvency, reorganization, arrangement, moratorium or other similar laws affecting creditors' rights, and (ii) general equity principles and limitations on the availability of equitable relief, including specific performance, and (B) that any rights to indemnity or contribution hereunder or thereunder may be limited by state and federal securities laws and by public policy considerations.

(c) No Violation. The execution, delivery and performance by EIS of this Agreement and each other Transaction Document to which it is a party, including the purchase and acceptance of the Securities, and compliance with provisions hereof and thereof by EIS, will not conflict with or constitute or result in a breach of or default under (or an event which with notice or passage of time or both would constitute a default) or give rise to any right of termination, cancellation or acceleration under (i) the Memorandum and Articles of Association of EIS, (ii) applicable law, statute, rule or regulation, or any ruling, writ, injunction, order, judgment or decree of any court, arbitrator, administrative agency or other governmental body applicable to EIS or any of its properties or assets, or (iii) any material contract to which EIS is party, except where such breach, default, termination, cancellation or acceleration would not, individually or in the aggregate, have an EIS Material Adverse Effect.

(d) Approvals. No material permit, authorization, consent, approval or order of or by, or any notification of or filing with, any person or entity (governmental or otherwise) is required in connection with the execution, delivery or performance of this Agreement or the Transaction Documents by EIS.

(e) Investment Representations.

(i) EIS is sophisticated in transactions of this type and capable of evaluating the merits and risks of the transactions described herein and in the other Transaction Documents to which it is a party, and has the capacity to protect its own interests. EIS has not been formed solely for the purpose of entering into the transactions described herein and therein and is acquiring the Securities (and the Underlying Shares) for investment for its own account, not as a nominee or agent, and not with the view to, or for resale, distribution or fractionalization thereof, in whole or in part, and no other person (other than Elan) has a direct or indirect interest, beneficial or otherwise in the Securities (or the Underlying Shares); provided, however, that EIS shall be permitted to convert or exchange such Securities in accordance with their terms.

(ii) EIS has not and does not intend to enter into any contract, undertaking, agreement or arrangement with any person or entity to sell, transfer or pledge the Securities (or the Underlying Shares).

(iii) EIS acknowledges its understanding that the private placement and sale of the Securities (and the Underlying Shares) is exempt from registration under the Securities Act by virtue of the provisions of Regulation D. In furtherance thereof, EIS represents and warrants that it is an "accredited investor" as that term is defined in Regulation D, has the financial ability to bear the economic risk of its investment, has adequate means for providing for its current needs and personal contingencies and has no need for liquidity with respect to its investment in the Company.

(iv) EIS agrees that it shall not sell or otherwise transfer any of the Securities (or the Underlying Shares) without registration under the Securities Act or pursuant to an opinion of counsel reasonably satisfactory to the Company that an exemption from registration is available, and fully understands and agrees that it must bear the total economic risk of its purchase for an indefinite period of time because, among other reasons, none of the Securities (or the Underlying Shares) have been registered under the Securities Act or under the securities laws of any applicable state or other jurisdiction and, therefore, cannot be resold, pledged, assigned or otherwise disposed of unless subsequently registered under the Securities Act and under the applicable securities laws of such states or jurisdictions or an exemption from such registration is available. EIS understands that the Company is under no obligation to register the Securities (or the Underlying Shares) on its behalf with the exception of certain registration rights with respect to certain of the Securities (and the Underlying

Shares), as provided in the Registration Rights Agreement. EIS understands the lack of liquidity and restrictions on transfer of the Securities (and the Underlying Shares) and that this investment is suitable only for a person or entity of adequate financial means that has no need for liquidity of this investment and that can afford a total loss of its investment.

(f) Litigation. There is no legal, administrative, arbitration or other action or proceeding or governmental investigation pending, or to EIS's knowledge threatened, against EIS that challenges the validity or performance of this Agreement or the other Transaction Documents to which EIS is a party.

(g) Brokers or Finders. EIS has not retained any investment banker, broker, finder or person or entity acting in a similar capacity, and is not liable for any fee or payment to any such person, in connection with the transactions contemplated by the Transaction Documents.

SECTION 4. Covenants of the Parties.

(a) Operating Covenants. From and after the Closing Date and until the earlier to occur of the exercise or expiration of the EIS Exchange Right (as such term is defined in Section 6 hereof), the Company shall not without the prior written consent of EIS: (i) encumber, pledge or otherwise affect, in any respect, (A) any shares of Newco Common Stock owned by the Company, including, without limitation, those shares of Newco Common Stock transferable to EIS upon exercise by EIS of the EIS Exchange Right, or (B) its ability to permit EIS to exercise the EIS Exchange Right in full, as provided herein, or (ii) enter into any Significant Transaction (as such term is defined in the Letter Agreement) with a director, officer or more than 20% beneficial owner of Common Stock on other than an arm's length basis. From and after the Closing Date and until the earlier to occur of the exercise or expiration of the EIS Exchange Right, EIS shall not without the prior written consent of the Company encumber, pledge or otherwise affect, in any respect, any shares of Newco Common Stock owned by EIS.

(b) Fully-diluted Stock Ownership. Notwithstanding any other provision of this Agreement, in the event that EIS shall have determined that at any time it (together with its affiliates, if applicable) holds or has the right to receive Common Stock (or securities or rights, options or warrants exercisable, exchangeable or convertible for or into Common Stock) representing in the aggregate in excess of 19.9% of the Company's outstanding Common Stock on a fully diluted basis (assuming the exercise, exchange or conversion of such securities beneficially owned by EIS or its affiliates, but not the exercise, exchange or conversion of any other similar securities), EIS shall have the right, in its sole discretion, rather than acquiring such securities from the Company, to exchange such number of securities, as are necessary to bring its holdings to below 19.9% of the voting securities of the Company, for non-voting, convertible liquidation preferred stock of the Company (which shall be reasonably satisfactory to each of the Company and EIS), which equity securities shall be entitled to all of the other rights and benefits of the Common Stock. In the event that EIS shall undertake to exercise such right, EIS shall

retain the additional right to exchange such new class of equity security for Common Stock, in its discretion at any time. Each of the Company and EIS shall use commercially reasonable effort to effect such transactions and any required subsequent conversions or adjustments to such securities, on a quarterly basis, within 10 business days of the end of each of EIS' fiscal quarter.

(c) Use of Proceeds. The Company shall use the proceeds of (i) the issuance and sale of the Series A Preferred Stock solely to meet its initial capitalization obligations to Newco as described in the JDOA, and (ii) the issuance and funding of the Note solely to meet its developmental funding obligations to Newco, as described in the Funding Agreement.

(d) Confidentiality; Non-Disclosure.

(i) Subject to clauses (ii) and (iii) below, from and after the date hereof, neither the Company nor EIS (nor their respective affiliates) shall disclose to any person or entity this Agreement or the other Transaction Documents or the contents thereof or the parties thereto, except that such parties may make such disclosure (x) to their directors, officers, employees and advisors, so long as they shall have advised such persons of the obligation of confidentiality herein and for whose breach or default the disclosing party shall be responsible, or (y) as required by applicable law, rule, regulation or judicial or administrative process, provided that the disclosing party uses reasonable efforts to obtain an order or ruling protecting the confidentiality of confidential information of the other party contained herein or therein. The parties shall be entitled to seek injunctive or other equitable relief in respect of any breach or threatened breach of the foregoing covenant without the requirement of posting a bond or other collateral.

(ii) Prior to issuing any press release or public disclosure in respect of this Agreement or the transactions contemplated hereby, the party proposing such issuance shall obtain the consent of the other party to the contents thereof, which consent shall not be unreasonably withheld or delayed; it being understood that if such second party shall not have responded to such consent request within five business days, such consent shall be deemed given.

(iii) This Section 4(d) shall not be construed to prohibit disclosure by the receiving party of any information which has not been previously determined to be confidential by the disclosing party, or which shall have become publicly disclosed (other than by breach of the receiving party's obligations hereunder).

(e) Further Assurances. From and after the date hereof, each of the parties hereto agree to do or cause to be done such further acts and things and deliver or cause to be delivered to each other such additional assignments, agreements, powers and instruments, as each may reasonably require or deem advisable to carry into effect the purposes of this Agreement and the other Transaction Documents.

SECTION 5. Standstill.

(a) Provided that nothing contained herein will prevent or prohibit EIS from purchasing Voting Stock (as defined below) of the Company pursuant to subsection 5(b) or from acquiring Voting Stock pursuant to the conversion of the Series A Preferred Stock or the Note or the exercise of the Warrant in accordance with their respective terms, EIS will not, directly or indirectly, without the prior consent of a majority of the Board of Directors of the Company (the "Board"), (i) acquire (or offer or agree to acquire) any Voting Stock if, as a result, EIS would beneficially own more than 20% of the then outstanding Voting Stock; (ii) directly or indirectly solicit proxies or consents or become a participant in a solicitation (as such terms are defined in Regulation 14A under the Exchange Act) in opposition to the recommendation of the majority of the Board for a Takeover Event (as defined below); or (iii) transfer to any third party, other than its "affiliates," "associates" (as such terms are defined in Rule 12b-2 under the Exchange Act), officers, directors or employees, the right to vote any Voting Stock except in connection with the transfer of ownership of such Voting Stock for fair value. EIS also agrees that it will not advise, assist or encourage any third party to do any of the foregoing. Notwithstanding the foregoing, EIS will not be obligated to dispose of any Voting Stock it owns if its percentage ownership is increased as a result of a decrease in the number of shares of Voting Stock outstanding.

(b) The provisions of this Section 5 will terminate: (i) if EIS owns less than 2% of Voting Stock; (ii) if EIS makes a tender offer to purchase 100% of the then outstanding Voting Stock and such offer is accepted by the holders of more than 50% of the Voting Stock not owned directly or indirectly by EIS (which tender offer, if it contains such acceptance as a condition to consummation, will not be a violation of subsection 5(a)); (iii) if any person or group, excluding EIS, makes a bona fide offer to acquire Voting Stock which would, if successful, result in the bidder's beneficial ownership of at least 15% of the then outstanding Voting Stock; or (iv) upon the third anniversary of the date of this Agreement. For purposes of clause (iii), the provisions of this Section 5 will not terminate until such time as such offer is rejected or revoked, however, EIS will not have to dispose of any Voting Stock acquired by it before such offer is rejected or revoked, and EIS will be permitted to consummate pending transactions which are not cancelable without a penalty.

(c) The Company will give EIS prompt notice of the receipt by the Company of any written notice couched in such terms as to put the Company reasonably on notice of the likelihood that a person or group has acquired or is proposing to acquire an aggregate position of at least 5% of the Voting Stock, the Company's receiving any bona fide offer to purchase or acquire 15% or more of the Voting Stock or all or substantially all of the assets of the Company, and any Board determination to seek an acquiror for in excess of 50% of the Voting Stock.

(d) EIS will cause its affiliates and associates to comply with the provisions of this Section 5, whether directly or indirectly, individually or as part of a "group" (as such term is defined in Rule 13d-5 under the Exchange Act). When used in this Section 5, the term EIS includes EIS together with its affiliates and associates.

(e) For purposes of this Section 5, the term "Takeover Event" means any proposal for any merger or business combination involving the Company or any of its subsidiaries, the purchase or sale of any assets of the Company or any of its subsidiaries, or the purchase of any of the Voting Stock, by tender offer or otherwise (except pursuant to the exercise of rights, warrants, options or similar securities distributed by the Company to holders of Voting Stock generally), and the term "Voting Stock" means the Common Stock and any preferred stock of the Company possessing voting rights and eligible to participate in votes of all of the Company's stockholders pursuant to the Company's Certificate of Incorporation and Delaware law, and includes any options, convertible securities or other rights to acquire such stock.

SECTION 6. Conversion and Exchange Rights. The Certificate of Designations sets forth certain rights of the holders of shares of Series A Preferred Stock to convert such shares of preferred stock into newly issued shares of Common Stock, or to exchange such shares of Series A Preferred Stock into certain shares of Newco Common Stock owned by the Company (the "EIS Exchange Right"), both on the terms and conditions set forth therein.

SECTION 7. Survival Period. The representations and warranties of the Company and EIS contained herein shall survive for a period of two years from and after the date hereof.

SECTION 8. Notices. All notices, demands and requests of any kind to be delivered to any party in connection with this Agreement shall be in writing and shall be deemed to have been duly given if personally or hand delivered or if sent by an internationally-recognized overnight delivery or by registered or certified mail, return receipt requested and postage prepaid, or by facsimile transmission (with receipt confirmed by telephone) addressed as follows:

(i) if to the Company, to:

Isis Pharmaceuticals, Inc.
2292 Faraday Avenue
Carlsbad, CA 92008
Attn: B. Lynne Parshall
Tel.: 760-603-2460
Fax: 760-931-9639

with a copy to:
Cooley Godward LLP
4365 Executive Drive
San Diego, CA 92121
Attn: L. Kay Chandler, Esq.
Tel.: 619-550-6000
Fax: 619-453-3555

(ii) if to EIS, to:

Elan International Services, Ltd.
Flatts, Smiths Parish
Bermuda, FL 04
Attention: Director
Tel.: 441-292-9169
Fax: 441-292-2224

with a copy to:

Brock Silverstein LLC
153 East 53rd Street , 56th Floor
New York, New York 10022
Attention: David Robbins, Esq.
Tel.: 212-371-2000
Fax: 212-371-5500

or to such other address as the party to whom notice is to be given may have furnished to the other party hereto in writing in accordance with provisions of this Section 8. Any such notice or communication shall be deemed to have been effectively given (i) in the case of personal or hand delivery, on the date of such delivery, (ii) in the case of an internationally-recognized overnight delivery service, on the second business day after the date when sent, (iii) in the case of mailing, on the fifth business day following that day on which the piece of mail containing such communication is posted, and (iv) in the case of facsimile transmission, on the date of telephone confirmation of receipt.

SECTION 9. Entire Agreement. This Agreement and the other Transaction Documents contain the entire understanding of the parties with respect to the subject matter hereof and thereof and supersede all prior agreements and understandings among the parties with respect thereto.

SECTION 10. Amendments. This Agreement may not be modified or amended, or any of the provisions hereof waived, except by written agreement of the Company and EIS.

SECTION 11. Counterparts and Facsimile. The Transaction Documents may be executed in any number of counterparts, and each such counterpart hereof shall be deemed to be an original instrument, but all such counterparts together shall constitute one agreement. Each of the Transaction Documents may be signed and delivered to the other party by facsimile transmission; such transmission shall be deemed a valid signature.

SECTION 12. Headings. The section and paragraph headings contained in this Agreement are for reference purposes only and shall not affect in any way the meaning or interpretation of the Agreement.

SECTION 13. Governing Law. This Agreement shall be governed by and construed in accordance with the laws of the State of New York, without giving effect to principles thereof relating to conflicts of laws, except that all issues concerning the relative rights of the Company and its stockholders shall be governed by the Delaware General Corporation Law, without giving effect to the principles thereof relating to conflicts of laws.

SECTION 14. Arbitration.

(a) Any dispute under the Transaction Documents which is not settled by mutual consent shall be finally settled by binding arbitration, conducted in accordance with the Commercial Arbitration Rules of the American Arbitration Association by one arbitrator appointed in accordance with said rules. Such arbitrator shall be reasonably satisfactory to each of the parties; provided, that if the parties are unable to agree upon the identity of such arbitrator within 15 days of demand by either party, then either party shall have the right to petition a presiding justice of the Supreme Court of New York, New York County, to appoint an arbitrator. The arbitration shall be held in New York, New York and the arbitrator shall be an independent expert in pharmaceutical product development and marketing (including clinical development and regulatory affairs).

(b) The arbitrator shall determine what discovery will be permitted, consistent with the goal of limiting the cost and time which the parties must expend for discovery; provided the arbitrator shall permit such discovery as they deem necessary to permit an equitable resolution of the dispute. Any written evidence originally in a language other than English shall be submitted in English translation accompanied by the original or a true copy thereof. The costs of the arbitration, including administrative and arbitrators' fees, shall be shared equally by the parties and each party shall bear its own costs and attorneys' and witness' fees incurred in connection with the arbitration.

(c) In rendering judgment, the arbitrator shall be instructed by the parties that he shall be permitted to select solely from between the proposals for resolution of the relevant issue presented by each party, and not any other proposal. A disputed performance or suspended performances pending the resolution of the arbitration must be completed within 30 days following the final decision of the arbitrators or such other reasonable period as the arbitrators determine in a written opinion.

(d) Any arbitration under the Transaction Documents shall be completed within one year from the filing of notice of a request for such arbitration. The arbitration proceedings and the decision shall not be made public without the joint consent of the parties and each party shall maintain the confidentiality of such proceedings and decision unless otherwise permitted by the other party.

(e) The parties agree that the decision shall be the sole, exclusive and binding remedy between them regarding any and all disputes, controversies, claims and counterclaims

presented to the arbitrators. Application may be made to any court having jurisdiction over the party (or its assets) against whom the decision is rendered for a judicial recognition of the decision and an order of enforcement.

SECTION 15. Expenses. Each of the parties shall be responsible for its own costs and expenses incurred in connection with the transactions contemplated hereby and by the other Transaction Documents.

SECTION 16. Schedules, etc. All statements contained in any exhibit or schedule delivered by the parties hereto, or in connection with the transactions contemplated hereby, are an integral part of this Agreement and shall be deemed representations and warranties hereunder.

SECTION 17. Assignments and Transfers. This Agreement and all of the provisions hereof shall be binding upon and inure to the benefit of the parties hereto and their respective successors and permitted assigns. This Agreement, the shares of Series A Preferred Stock and Common Stock being purchased hereunder by EIS, the Note, the Warrant, and the shares of Common Stock underlying the Series A Preferred Stock, the Note and the Warrant may be transferred by EIS to its affiliates and subsidiaries, as well as any off-balance sheet special purpose entity established by EIS, provided, however, that EIS shall remain liable for its obligations hereunder after any such assignment. Other than as set forth above, no party shall transfer or assign this Agreement, the shares of Series A Preferred Stock and Common Stock being purchased hereunder by EIS, the Note, the Warrant, and the shares of Common Stock underlying the Series A Preferred Stock, the Note and the Warrant, or any interest therein, without the prior written consent of the other party; provided, however, that no consent shall be required in connection with any such transfer or assignment by a party pursuant to a sale of all or substantially all of the business of such party to which the Transaction Documents relate, whether by merger, sale of stock, sale of assets or otherwise.

SECTION 18. Severability. In case any provision of this Agreement shall be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not be in any way affected or impaired thereby.

[Signature Page Follows.]

IN WITNESS WHEREOF, each of the undersigned has duly executed this Agreement as of the date first written above.

ISIS PHARMACEUTICALS, INC.

By: /s/ B. Lynne Parshall

B. Lynne Parshall
Executive Vice President

ELAN INTERNATIONAL SERVICES, LTD.

By: /s/ Kevin Insley

Kevin Insley
President

EXHIBIT 10.3

THIS CONVERTIBLE PROMISSORY NOTE AND THE SHARES OF COMMON STOCK ISSUABLE UPON CONVERSION HEREOF HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND MAY NOT UNDER ANY CIRCUMSTANCES BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF WITHOUT AN EFFECTIVE REGISTRATION STATEMENT FOR SUCH SECURITIES UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND ANY APPLICABLE STATE SECURITIES LAWS OR AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY THAT REGISTRATION IS NOT REQUIRED UNDER SUCH ACT OR APPLICABLE STATE SECURITIES LAWS.

THE TRANSFER OF THE SECURITIES REPRESENTED BY THIS CERTIFICATE IS ALSO SUBJECT TO THE RESTRICTIONS CONTAINED IN THAT CERTAIN SECURITIES PURCHASE AGREEMENT, DATED APRIL 20, 1999, BY AND BETWEEN ISIS PHARMACEUTICALS, INC. AND ELAN INTERNATIONAL SERVICES, LTD.

ISIS PHARMACEUTICALS, INC.
CONVERTIBLE PROMISSORY NOTE

U.S. $18,400,000

APRIL 20, 1999
NEW YORK, NEW YORK

The undersigned, ISIS PHARMACEUTICALS, INC., a Delaware corporation with offices at 2292 Faraday Avenue, Carlsbad, California 92008 (the "Company"), unconditionally promises to pay to ELAN INTERNATIONAL SERVICES, LTD., a Bermuda private limited company ("EIS"), or its permitted assigns, transferees and successors as provided herein (collectively, the "Holder"), on April 19, 2005 (the "Maturity Date"), at such place as may be designated by the Holder to the Company, the principal amount outstanding hereunder (not to exceed U.S.$18,400,000), together with interest thereon accrued at a rate per annum equal to 12.0%, from and after the date of the initial disbursement of funds hereunder (the "Original Issue Date"), compounded on a semi-annual basis, the initial such compounding to commence on the date that is six months from and after the Original Issue Date (each such date, a "Compounding Date").

SECTION 1. SECURITIES PURCHASE AGREEMENT AND FUNDING AGREEMENT.

This Note is issued pursuant to a Securities Purchase Agreement dated as of the date hereof, by and between the Company and EIS (as amended at any time, the "Securities Purchase Agreement"), and is intended to be afforded the benefits thereof, including the representations and warranties set forth therein. The Company shall use the proceeds of the

issuance and sale of this Note solely in accordance with the provisions set forth therein and in a certain Funding Agreement, dated as of the date hereof (as amended at any time, the "Funding Agreement"), by and among Elan Corporation, plc, an Irish public limited company and the parent corporation of EIS, EIS and the Company, and as described in Section 6 below. Capitalized terms used but not otherwise defined herein shall have the meanings given such terms in the Securities Purchase Agreement.

SECTION 2. DISBURSEMENTS.

(a) From and after the date that is 10 days after the approval of Newco's budget and until March 31, 2002, disbursements shall be made by the Holder to the Company hereunder in minimum increments of U.S.$250,000 (except in the event that an amount less than U.S.$250,000 shall be remaining and available for funding hereunder, in which case such lesser amount may be funded hereunder); provided, that the Company shall deliver notice of a request therefor to the Holder in the form attached hereto as Exhibit A (the "Disbursement Notice"), together with an Officer's Certificate confirming that as of such date no Event of Default exists hereunder; the Holder shall, subject to the terms and conditions hereof, fund such amount within 10 business days of the receipt of the Disbursement Notice, subject to the receipt by the Holder of any required approvals under the Mergers and Takeovers (Control) Acts 1978-1996. A "business day" is any day that commercial banks are open for the transaction of business in the City of New York.

(b) The Holder shall not be required to disburse more than a maximum principal amount of U.S.$18,400,000.

SECTION 3. PAYMENTS AND COVENANTS.

(a) Unless earlier converted in accordance with the terms of Section 4 below, or prepaid in accordance with the terms hereof, the entire outstanding principal amount of this Note, together with any accrued and unpaid interest thereon, shall be due and payable on the Maturity Date.

(b) Accrued interest hereon shall not be paid in cash, but shall be capitalized and added to principal amount outstanding hereunder on each Compounding Date.

(c) This Note may be prepaid by the Company, in whole or in part,

(i) in cash, upon not less than 30 days' prior written notice to EIS; or

(ii) in shares of the Company's Common Stock, par value $.001 per share (the "Common Stock"), at any time, at a price equal to the average of the closing price of the Common Stock for the 60 trading days ending two business days prior to the date of repayment.

SECTION 4. CONVERSION.

(a) Conversion Right.

(i) From and after the Original Issue Date and until this Note is repaid in full, the Holder shall have the right from time to time, in its sole discretion, to convert the outstanding principal amount and accrued and unpaid interest then-outstanding hereunder, on a per tranche basis (each, a "Conversion Right"), into such number of shares of Common Stock that shall be obtained by dividing the sum of the outstanding principal amount of such tranche and all accrued and unpaid interest thereon by a per share price calculated as 150% of the average of the closing price of the Common Stock for the 60 trading days ending two business days prior to the date of disbursement of such tranche (each, a "Conversion Price").

(ii) The Holder shall be entitled to exercise a Conversion Right upon at least five days' prior written notice to the Company, such notice to be in the form attached hereto as Exhibit B. Within 10 days of the conversion date specified in such notice, the Company shall issue stock certificates to EIS representing the aggregate number of shares of Common Stock due to EIS as a result of such conversion.

(b) Reclassification, Etc. In case of (i) any reclassification, reorganization, change or conversion of securities of the class issuable upon conversion of the outstanding principal amount and accrued and unpaid interest then-outstanding hereunder (other than a change in par value, or from par value to no par value), or (ii) any consolidation of the Company with or into another entity (other than a merger or consolidation with another entity in which the Company is the surviving entity and that does not result in any reclassification or change of the class of securities issuable upon the conversion of the outstanding principal amount and accrued and unpaid interest then-outstanding hereunder), or (iii) any sale of all or substantially all the assets of the Company (excluding the transactions contemplated by the Transaction Documents), then the Company, or such successor or purchasing entity, as the case may be, shall duly execute and deliver to the Holder a new Note or a supplement hereto (in form and substance reasonably satisfactory to the Holder of this Note), so that the Holder shall have the right to receive, at a total purchase price not to exceed the outstanding principal amount and accrued and unpaid interest then-outstanding hereunder, and in lieu of the shares of Common Stock theretofore issuable upon the conversion of such outstanding principal amount and accrued and unpaid interest then-outstanding hereunder, the kind and amount of shares of stock and other securities, money and property receivable upon such reclassification, reorganization, change, merger, consolidation or conversion by a holder of the number of shares of Common Stock then issuable under this Note. Such new Note shall provide for adjustments that shall be as nearly equivalent as may be practicable to the adjustments provided for in this Section 4. The provisions of this Section 4(b) shall similarly attach to successive reclassifications, reorganizations, changes, mergers, consolidations, transfers or conversions.

(c) No Impairment. The Company will not, by amendment of its Certificate of Incorporation or by-laws or through any reorganization, recapitalization, transfer of assets,

consolidation, merger, dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms to be observed or performed hereunder by the Company, but will at all times in good faith assist in the carrying out of all the provisions of this Section 4 and in the taking of all such action as may be necessary or appropriate in order to protect the rights of EIS against impairment. This provision shall not restrict the Company from otherwise amending and/or restating its Certificate of Incorporation in accordance with Delaware General Corporation Law.

(d) Notice of Adjustments. Whenever the consideration issuable upon a conversion hereunder shall be changed pursuant to this Section 4, the Company shall prepare a certificate setting forth, in reasonable detail, the event requiring the change and the kind and amount of shares of stock and other securities, money and property subsequently issuable upon a conversion hereof. Such certificate shall be signed by its chief financial officer and shall be delivered to EIS.

(e) Fractional Shares; Rounding. No fractional shares of Common Stock will be issued in connection with any exercise hereunder, but in lieu of such fractional shares the Company shall make a cash payment therefor based on the applicable Conversion Price. All calculations under this Section 4 shall be made to the nearest cent or to the nearest one-hundredth of a share, as the case may be.

SECTION 5. EXCHANGE RIGHT.

(a) In the event that EIS shall exercise the EIS Exchange Right, a principal amount outstanding hereunder equal to 30.1% of the total amount of development funding expenditures to date provided by each of the parties to Newco, in accordance with the terms of the Funding Agreement, together with all accrued interest thereon, shall be canceled upon the closing of such exchange.

(b) In no event shall the amount determined in accordance with subsection (a) above exceed the aggregate principal amount issued hereunder and accrued interest thereon.

SECTION 6. USE OF PROCEEDS.

The Company shall use the proceeds of this Note solely for developmental funding of Newco, provided that the Board of Directors of Newco has determined that such developmental funding is necessary (which shall include the consent of at least one of the Company's directors and the EIS director).

SECTION 7. EVENTS OF DEFAULT.

The occurrence of any of the following events shall constitute an event of default (an "Event of Default"):

(a) a default in the payment of the principal amount of this Note, when and as the same shall become due and payable;

(b) a default in the payment of any accrued and unpaid interest on this Note, when and as the same shall become due and payable;

(b) a material breach by the Company of its obligations under the JDOA or the Isis License Agreement, which breach remains uncured 60 days after written notice thereof by EIS; provided, however, that (x) if the Company has proposed a course of action to rectify the breach and is acting in good faith to rectify same but has not cured the breach by the 60th day, such period shall be extended by such period as is reasonably necessary to permit the breach to be rectified and (y) if such default involves a good faith dispute regarding the amount of any required payment, provided any undisputed amount is paid, such default shall be stayed and the remainder may be withheld for a reasonable period during which a good faith resolution of the amount owed is being pursued;

(c) a distress, execution, sequestration or other process is levied or enforced upon the Company or sued out against a material part of its property which is not discharged or challenged within 30 days;

(d) the Company is unable to pay its debts in the normal course of business;

(e) the Company ceases wholly or substantially to carry on its business, otherwise than for the purpose of a reconstruction or amalgamation, without the prior written consent of the EIS (such consent not to be unreasonably withheld);

(f) the appointment of a liquidator, receiver, administrator, examiner, trustee or similar officer of the Company or over all or substantially all of its assets under the law; or

(g) any other termination of the JDOA.

SECTION 8. REMEDIES IN THE EVENT OF DEFAULT.

(a) In the case of any Event of Default by the Company, the Holder, may in its sole discretion, demand that the aggregate amount of funds advanced to the Company under this Note and outstanding hereunder and accrued and unpaid interest thereon shall, in addition to all other rights and remedies of the Holder hereunder and under applicable law, be and become immediately due and payable upon written notice delivered by the Holder to the Company. Notwithstanding the preceding sentence, the rights of the Holder as set forth in Section 4 hereunder shall survive any such acceleration and payment. If the Holder shall accelerate and be paid and then elect to exercise the Conversion Right, the Holder shall pay the Company for shares of Common Stock issued under such Conversion Right.

(b) The Company hereby waives demand and presentment for payment, notice of nonpayment, protest and notice of protest, diligence, filing suit, and all other notice and promises

to pay the Holder its costs of collection of all amounts due hereunder, including reasonable attorneys' fees.

(c) In the case of any Event of Default under this Note by the Company this Note shall continue to bear interest after such default at the interest rate otherwise in effect hereunder plus 3% per annum (but in any event not in excess of the maximum rate of interest permitted by applicable law).

SECTION 9. VOTING RIGHTS.

This Note shall not entitle the holder hereof to any voting rights or other rights as a stockholder of the Company prior to its conversion.

SECTION 10. SENIORITY.

(a) The Holder acknowledges and agrees that the obligations evidenced hereby are subordinate in right to payment in full of interest and principal relating to the Company's 14% Senior Subordinated Discount Notes due November 2007 (the "Discount Notes") and therefore the obligations evidenced hereby are "Subordinated Indebtedness" as defined in that certain Purchase Agreement, dated October 24, 1997, between the Company and the purchasers listed on Schedule I thereto (the "Purchase Agreement"); it being understood that in the event there is any event of default in respect of the Purchase Agreement, the Company shall not pay to the Holder hereof in cash any amounts due hereunder until such event of default is cured or waived pursuant to the terms of such indenture.

(b) The Company shall not incur any indebtedness for money borrowed which shall rank senior to this Note without the prior written consent of the Holder; provided, however, that the Company may incur additional indebtedness which ranks pari passu with the obligations evidenced hereby.

SECTION 11. MISCELLANEOUS.

(a) EIS may assign this Note to its affiliates and subsidiaries, as well as any off-balance sheet special purpose entity established by EIS. This Note and all of the provisions hereof shall be binding upon and inure to the benefit of the parties hereto and their respective successors and permitted assigns; provided, however, that EIS and the Company shall remain liable for their respective obligations hereunder after any such assignment.

(b) All notices, demands and requests of any kind to be delivered to any party in connection with this Agreement shall be in writing and shall be deemed to have been duly given if personally delivered or if sent by nationally-recognized overnight courier or by registered or certified mail, return receipt requested and postage prepaid, or by facsimile transmission, addressed as follows:

(i) if to the Company:

Isis Pharmaceuticals, Inc.
2292 Faraday Avenue
Carlsbad, CA 92008
Attn: B. Lynne Parshall
Tel.: 760-603-2460
Fax: 760-931-9639

with a copy to:

Cooley Godward LLP
4365 Executive Drive
San Diego, CA 92121
Attention: L. Kay Chandler, Esq.
Tel: 619-550-6000
Fax: 619-453-3555

(ii) if to EIS, to:

Elan International Services, Ltd.
102 St. James Court
Flatts, Smiths Parish
Bermuda SL04
Attention: President
Tel: 441-292-9169
Fax: 441-292-2224

with a copy to:

Brock Silverstein LLC
153 East 53rd Street
New York, New York 10022
Attention: David Robbins, Esq.
Tel: 212-371-2000
Fax: 212-371-5500

Each party, by written notice given to the other in accordance with this Section 11(b) may change the address to which notices, other communication or documents are to be sent to such party. All notices, other communications or documents shall be deemed to have been duly given when received. Any such notice or communication shall be deemed to have been effectively given, (a) in the case of personal delivery, on the date of such delivery, (b) in the case of nationally-recognized overnight courier, on the second business day after the date when sent, (c) in the case of mailing, on the fifth business day following that day on which the piece of mail

containing such communication is posted, and (d) in the case of facsimile transmission, on the date of telephone conformation of receipt.

(c) This Note may not be modified or amended, or any of the provisions hereof waived, except by written agreement of the Company and EIS.

(d) This Note shall be governed by and construed in accordance with the laws of the State of New York, without giving effect to principles thereof relating to conflicts of laws, except that all issues concerning the relative rights of the Company and its stockholders shall be governed by the Delaware General Corporation Law, without giving effect to the principles thereof relating to conflicts of laws.

(e) This Note may be executed in any number of counterparts, and each such counterpart hereof shall be deemed to be an original instrument, but all such counterparts together shall constitute one note. The Note may be signed and delivered to the other party by a facsimile transmission; such transmission shall be deemed a valid signature.

(f) Each of the parties shall be responsible for its own costs and expenses incurred in connection with the transactions contemplated hereby.

[Signature page follows]

IN WITNESS WHEREOF, the Company and EIS have executed this Note on the date first above written.

ISIS PHARMACEUTICALS, INC.

By: /s/ B. Lynne Parshall

B. Lynne Parshall
Executive Vice President

ELAN INTERNATIONAL SERVICES, LTD.

By: /s/ Kevin Insley

Kevin Insley
President

EXHIBIT A

NOTICE OF REQUEST FOR DISBURSEMENT

Date:

To: Elan International Services, Ltd.

From: Isis Pharmaceuticals, Inc.

Re: Disbursement Request

- ---

Pursuant to the terms of the Convertible Promissory Note (the "Note") issued by Isis Pharmaceuticals, Inc. (the "Company") to Elan International Services, Ltd. ("EIS"), dated April 20, 1999, the Company hereby notifies EIS of its request for a disbursement thereunder in the amount of $_____. Please provide funding in the requested amount to the Company in accordance with the following wire instructions

[

]

Sincerely,

ISIS PHARMACEUTICALS, INC.

By: _____
Name:
Title:

EXHIBIT B

NOTICE OF ELECTION TO EXERCISE A CONVERSION RIGHT

Date:

To: Isis Pharmaceuticals, Inc.

From: Elan International Services, Ltd.

Re: Exercise of a Conversion Right

- ---

Pursuant to the terms of the Convertible Promissory Note (the "Note") issued by Isis Pharmaceuticals, Inc. (the "Company") to Elan International Services, Ltd. ("EIS"), dated April 20, 1999, specifically Section 4 thereof, EIS hereby notifies the Company of its intention to exercise a right of conversion.

Pursuant to Section 4 of the Note, EIS hereby elects to convert [$_____]* in aggregate principal amount and all accrued and unpaid interest thereon for shares of the Company's Common Stock, par value $.001 per share, effective [_____, ____]

We have instructed our attorneys to contact the Company to discuss the timing and documentation of the conversion.

Sincerely,

ELAN INTERNATIONAL SERVICES, LTD.

By: _____
Name:
Title:

- --------
* Amount must represent one or more tranches drawn down by the Company under the Note.

EXHIBIT 10.4

THIS WARRANT AND THE SHARES OF COMMON STOCK ISSUABLE UPON EXERCISE HEREOF HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND MAY NOT UNDER ANY CIRCUMSTANCES BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF WITHOUT AN EFFECTIVE REGISTRATION STATEMENT FOR SUCH SECURITIES UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND ANY APPLICABLE STATE SECURITIES LAWS OR AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY THAT REGISTRATION IS NOT REQUIRED UNDER SUCH ACT OR APPLICABLE STATE SECURITIES LAWS.

THE TRANSFER OF THE SECURITIES REPRESENTED BY THIS CERTIFICATE IS ALSO SUBJECT TO THE RESTRICTIONS CONTAINED IN THAT CERTAIN SECURITIES PURCHASE AGREEMENT, DATED APRIL 20, 1999, BY AND BETWEEN ISIS PHARMACEUTICALS, INC. AND ELAN INTERNATIONAL SERVICES, LTD.

APRIL 20, 1999

ISIS PHARMACEUTICALS, INC.

WARRANT TO PURCHASE SHARES
OF COMMON STOCK

THIS CERTIFIES THAT for value received, Elan International Services, Ltd., a Bermuda corporation ("EIS"), or its permitted transferees and successors as provided herein (each, a "Holder"), is entitled to subscribe for and purchase up to 215,000 shares, as adjusted pursuant to Section 4 (the "Shares"), of the fully paid and nonassessable common stock, par value $.001 per share (the "Common Stock"), of Isis Pharmaceuticals, Inc., a Delaware corporation (the "Company"), with offices located at 2292 Faraday Avenue, Carlsbad, CA 92008, at the price of U.S.$24.00 per share (such price, and such other prices that shall result from time to time, from the adjustments specified in Section 4, the "Warrant Price"), subject to the provisions and upon the terms and conditions hereinafter set forth.

1. Term. The purchase right represented by this Warrant is exercisable, in whole or in part, at any time, and from time to time, from and after the date hereof and until 5:00 p.m. Eastern Standard Time on April 19, 2004. To the extent not exercised at 5:00 p.m. Eastern Standard Time on April 19, 2004, this Warrant shall completely and automatically terminate and expire, and thereafter it shall be of no force or effect.

2. Method of Exercise; Payment; Issuance of New Warrant.

(a) The purchase right represented by this Warrant may be exercised by the Holder, in whole or in part and from time to time, by the surrender of this Warrant (with the notice of exercise form attached hereto as Annex A duly executed) at the principal office of the

Company and by the payment to the Company of an amount, in cash or other immediately available funds, equal to the then-applicable Warrant Price per Share multiplied by the number of Shares then being purchased or pursuant to the cashless exercise procedure described below.

(b) In lieu of delivering cash or other immediately available funds, the Holder may instruct the Company in writing to deduct from the number of Shares that would otherwise be issued upon such exercise, a number of shares of Common Stock equal to the quotient obtained from dividing (x) the product obtained by multiplying (A) the number of Shares for which the Warrant is being exercised and (B) the Warrant Price then in effect by (y) a price equal to the average of the closing price of the Common Stock for the 60 trading days ending two business days prior to the date of exercise.

(c) The persons or entities in whose name(s) any certificate(s) representing Shares shall be issuable upon exercise of this Warrant shall be deemed to have become the holder(s) of record of, and shall be treated for all purposes as the record holder(s) of, the Shares represented thereby (and such Shares shall be deemed to have been issued) immediately prior to the close of business on the date or dates upon which this Warrant is properly exercised and full payment for the Shares acquired pursuant to such exercise is made. Upon any exercise of the rights represented by this Warrant, certificates for the Shares purchased shall be delivered to the Holder hereof as soon as possible and in any event within 15 days of receipt of such notice and payment, and unless this Warrant has been fully exercised or expired, a new Warrant representing the portion of Shares, if any, with respect to which this Warrant shall not then have been exercised shall also be issued to the Holder hereof as soon as possible and in any event within such 15-day period.

3. Stock Fully Paid, Reservation of Shares. All Shares that may be issued upon the exercise of this Warrant, when issued upon exercise in accordance with the terms hereof, will be duly and validly issued, fully paid and nonassessable, will not be issued in violation of any preemptive or similar rights. During the period within which this Warrant may be exercised, the Company will at all times have authorized and reserved for the purpose of the issue upon the exercise of the purchase rights evidenced by this Warrant a sufficient number of shares of its Common Stock to provide for the exercise of the rights represented by this Warrant.

4. Adjustment of Warrant Price and Number of Shares. The number and kind of securities purchasable upon the exercise of this Warrant and the Warrant Price shall be subject to the adjustment from time to time upon the occurrence of certain events, as follows:

(a) Reclassification, Etc. In case of (i) any reclassification, reorganization, change or conversion of securities of the class issuable upon exercise of this Warrant (other than a change in par value, or from par value to no par value), or (ii) any consolidation of the Company with or into another entity (other than a merger or consolidation with another entity in which the Company is the surviving entity and that does not result in any reclassification or change of outstanding securities issuable upon exercise of this Warrant), or (iii) any sale of all or substantially all the assets of the Company, then the Company, or such successor or purchasing entity, as the case may be, shall duly execute and deliver to the Holder of this Warrant a new Warrant or a supplement hereto (in form and substance reasonably satisfactory to the Holder of

this Warrant), so that the Holder shall have the right to receive, at a total purchase price not to exceed that payable upon the exercise of the unexercised portion of this Warrant, and in lieu of the shares of Common Stock theretofore issuable upon the exercise of this Warrant, the kind and amount of shares of stock and other securities, receivable upon such reclassification, reorganization, change or conversion by a holder of the number of shares of Common Stock then purchasable under this Warrant. Such new Warrant shall provide for adjustments that shall be as nearly equivalent as may be practicable to the adjustments provided for in this Section 4. The provisions of this Section 4(a) shall similarly attach to successive reclassifications, reorganizations, changes, and conversions.

(b) Subdivision or Combination of Shares. If the Company at any time during which this Warrant remains outstanding and unexpired shall subdivide or combine its Common Stock, (i) in the case of a subdivision, the Warrant Price shall be proportionately decreased and the number of Shares purchasable hereunder shall be proportionately increased, and (ii) in the case of a combination, the Warrant Price shall be proportionately increased and the number of Shares purchasable hereunder shall be proportionately decreased.

(c) No Impairment. The Company will not, by amendment of its Certificate of Incorporation or by-laws or through any reorganization, recapitalization, transfer of assets, consolidation, merger, dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms to be observed or performed hereunder by the Company, but will at all times in good faith assist in the carrying out of all the provisions of this Section 4 and in the taking of all such action as may be necessary or appropriate in order to protect the rights of the Holder against impairment.

(d) Notice of Adjustments. Whenever the Warrant Price or the number of Shares purchasable hereunder shall be adjusted pursuant to this Section 4, the Company shall prepare a certificate setting forth, in reasonable detail, the event requiring the adjustment, the amount of the adjustment, the method by which such adjustment was calculated. Such certificate shall be signed by its chief financial officer and shall be delivered to the Holder.

(e) Fractional Shares. No fractional shares of Common Stock will be issued in connection with any exercise hereunder, but in lieu of such fractional shares the Company shall make a cash payment therefor based on the average of the closing price of the Common Stock for the 60 trading days ending two business days prior to date of exercise.

(f) Cumulative Adjustments. No adjustment in the Warrant Price or the number of Shares purchasable hereunder shall be required under this Section 4 until cumulative adjustments result in a concomitant change of 1% or more of the Warrant Price or in the number of Shares purchasable upon exercise of this Warrant as in effect prior to the last such adjustment; provided, however, that any adjustment that by reason of this Section 4 are not required to be made shall be carried forward and taken into account in any subsequent adjustment. All calculations under this Section 4 shall be made to the nearest cent or to the nearest one-hundredth of a share, as the case may be.

5. Compliance with Securities Act; Disposition of Warrant or Shares of Common Stock.

(a) The Holder, by acceptance hereof, confirms the investment representations made in the Securities Purchase Agreement, dated April 20, 1999, by and between the Company and EIS, with regard to this Warrant and the Shares to be issued upon exercise hereof and, without limiting the foregoing, agrees that this Warrant and the Shares to be issued upon exercise hereof are being acquired for investment and that such Holder will not offer, sell or otherwise dispose of this Warrant or any Shares to be issued upon exercise hereof except under circumstances which will not result in a violation of applicable securities laws. Upon exercise of this Warrant, unless the Shares being acquired are registered under the Securities Act, or an exemption from the registration requirements of the Securities Act is available, the Holder shall confirm in writing, by executing an instrument in form reasonably satisfactory to the Company, that the Shares so purchased are being acquired for investment and not with a view toward distribution or resale. This Warrant and all Shares issued upon exercise of this Warrant (unless registered under the Securities Act) shall be stamped or imprinted with a legend in substantially the following form:

> THE SECURITIES REPRESENTED HEREBY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND MAY NOT UNDER ANY CIRCUMSTANCES BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF WITHOUT AN EFFECTIVE REGISTRATION STATEMENT FOR SUCH SECURITIES UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND ANY APPLICABLE STATE SECURITIES LAWS OR AN OPINION OF COUNSEL SATISFACTORY TO THE COMPANY THAT REGISTRATION IS NOT REQUIRED UNDER SUCH ACT OR APPLICABLE STATE SECURITIES LAWS.
>
> THE TRANSFER OF THE SECURITIES REPRESENTED BY THIS CERTIFICATE IS ALSO SUBJECT TO THE RESTRICTIONS CONTAINED IN THAT CERTAIN SECURITIES PURCHASE AGREEMENT, DATED APRIL 20, 1999, BY AND BETWEEN ISIS PHARMACEUTICALS, INC. AND ELAN INTERNATIONAL SERVICES, LTD.

(b) (i) This Warrant may be transferred or assigned, in whole or in part, by EIS to its affiliates and/or subsidiaries, as well as any off-balance sheet special purpose entity established by EIS; provided, that the transferor shall continue to be liable and obligated for its obligations hereunder. Subject to the foregoing, this Warrant and all of the provisions hereof shall be binding upon and inure to the benefit of the parties hereto and their respective successors and permitted assigns. Other than as set forth above, this Warrant may not be transferred or assigned by either party without the prior written consent of the other; provided, however, that no consent shall be required in connection with any transfer or assignment by a party pursuant to a sale of all or substantially all of

the business of such party to which the Transaction Documents relate, whether by merger, sale of stock, sale of assets or otherwise.

(ii) With respect to any offer, sale or other disposition of this Warrant or any Shares acquired pursuant to the exercise of this Warrant prior to registration of such Shares, the Holder shall give written notice to the Company prior thereto, describing briefly the manner thereof, together with a written opinion of such Holder's counsel, if requested by the Company, to the effect that such offer, sale or other disposition may be effected without registration or qualification (under the Securities Act as then in effect or any other applicable federal or state securities law then in effect) of this Warrant or such Shares and indicating whether or not under the Securities Act certificates for this Warrant or such Shares to be sold or otherwise disposed of require any restrictive legend as to applicable restrictions on transferability in order to ensure compliance with the Securities Act. Promptly upon receiving such written notice and reasonably satisfactory opinion, if so requested, the Company, as promptly as practicable, shall notify such Holder that such Holder may sell or otherwise dispose of this Warrant or such Shares, all in accordance with the terms of the notice delivered to the Company. Each certificate representing this Warrant or the Shares thus transferred shall bear a legend as to the applicable restrictions on transferability in order to insure compliance with the Securities Act, unless in the aforesaid opinion of counsel for the Holder such legend is not required in order to insure compliance with the Securities Act. The Company may issue stop transfer instructions to its transfer agent in connection with such restrictions.

(iii) The shares of Common Stock underlying this Warrant are entitled to the benefit of certain registration rights as set forth in a Registration Rights Agreement dated as of the date hereof between the Company and the initial Holder named herein.

6. Rights as Shareholders. No Holder, as such, shall be entitled to vote or receive dividends or be deemed the holder of Shares or any other securities of the Company which may at any time be issuable upon the exercise hereof for any purpose, nor shall anything contained herein be construed to confer upon the Holder, as such, any right to vote for the election of directors or upon any matter submitted to shareholders at any meeting thereof, or to receive notice of meetings, or to receive dividends or subscription rights or otherwise until this Warrant is exercised and the Shares purchasable upon the exercise hereof shall have become deliverable, as provided herein.

7. Miscellaneous.

(a) This Warrant may not be modified or amended, or any provisions hereof waived, except by written agreement of the Company and the Holder.

(b) Any notice, request or other document required or permitted to be given or delivered to the Holder or the Company shall (i) be in writing, (ii) be delivered personally or sent by mail or overnight courier to the intended recipient to Holder at 102 St. James Court, Flatts, Smiths Parish, Bermuda FL 04, Attn: President, or to the Company at the address indicated on the first page of this Warrant, unless the recipient has given notice of another address in

accordance with this paragraph, and (iii) be effective on receipt if delivered personally, two business days after dispatch if mailed, and one business day after dispatch if sent by overnight courier service.

(c) The Company covenants to the Holder that upon receipt of evidence reasonably satisfactory to the Company of the loss, theft, destruction or mutilation of this Warrant and, in the case of any such loss, theft or destruction, upon receipt of a bond or indemnity reasonably satisfactory to the Company, or in the case of any such mutilation upon surrender and cancellation of such Warrant, the Company will prepare and deliver a new Warrant, of like tenor, in lieu of the lost, stolen, destroyed or mutilated Warrant.

(d) The descriptive headings of the several sections and paragraphs of this Warrant are inserted for convenience only and do not constitute a part of this Warrant.

(e) This Warrant shall be governed by and construed in accordance with the laws of the State of New York without giving effect to the principles thereof relating to conflicts of laws, except that all issues concerning the relative rights of the Company and its stockholders shall be governed by the Delaware General Corporation Law, without giving effect to the principles thereof relating to conflicts of laws.

(f) This Warrant may be executed in any number of counterparts, and each such counterpart hereof shall be deemed to be an original instrument, but all such counterparts together shall constitute one Warrant.

(g) Each of the parties shall be responsible for its own costs and expenses incurred in connection with the transactions contemplated hereby.

[Signature page follows]

IN WITNESS WHEREOF, Isis Pharmaceuticals, Inc. has caused this Warrant to be executed and delivered by its duly authorized corporate officers on the date first above written.

ISIS PHARMACEUTICALS, INC.

By: /s/ B. Lynne Parshall

B. Lynne Parshall
Executive Vice President

Attest:

By: /s/ Debbie Jo Blank

Debbie Jo Blank

Agreed and accepted by:

ELAN INTERNATIONAL SERVICES, LTD.

By: /s/ Kevin Insley

Kevin Insley
President

ANNEX A

NOTICE OF EXERCISE

To: Isis Pharmaceuticals, Inc.

1. The undersigned hereby elects to purchase _____ shares of Common Stock of Isis Pharmaceuticals, Inc. pursuant to the terms of the attached Warrant, and

[ ] (a) tenders herewith full payment of the purchase price of such shares, in cash or other immediately available funds.

[ ] (b) instructs and agrees that pursuant to paragraph 2(b) of the attached Warrant, _____ shares of Common Stock be withheld in payment therefor.

2. Please issue a certificate or certificates representing said shares in the name of the undersigned or in such other name or names as are specified below:

_____(Name)

_____(Address)

3. The undersigned represents that the aforesaid shares are being acquired for the account of the undersigned for investment and not with a view to, or for resale in connection with, the distribution thereof and that the undersigned has no present intention of distributing or reselling such shares and otherwise confirms the investment representations made in Section 5 of the Warrant with regard to the shares of Common Stock being acquired.

Signature:_____

Name:_____

Address:_____

Social Security or taxpayer identification number:

_____

EXHIBIT 10.5

ISIS PHARMACEUTICALS, INC.
REGISTRATION RIGHTS AGREEMENT

THIS REGISTRATION RIGHTS AGREEMENT (the "Agreement") is made as of April 20, 1999 by and among ISIS PHARMACEUTICALS, INC., a Delaware corporation (the "Company"), and ELAN INTERNATIONAL SERVICES, LTD., a Bermuda corporation ("EIS").

R E C I T A L S:

A. Pursuant to a securities purchase agreement dated as of the date hereof by and between the Company and EIS (the "Purchase Agreement"), EIS has acquired certain shares of common stock of the Company (the "Common Stock"), Series A Convertible Preferred Stock of the Company (the "Series A Convertible Preferred Stock"), a convertible promissory note (the "Note"), which Series A Convertible Preferred Stock and Note are convertible into shares of Common Stock, and a warrant (the "Warrant") to purchase shares of Common Stock.

B. The execution of the Purchase Agreement has occurred on the date hereof and it is a condition to the closing of the transactions contemplated thereby that the parties execute and deliver this Agreement.

C. The parties desire to set forth herein their agreement on the terms and subject to the conditions set forth herein related to the granting of certain registration rights to the Holders (as defined below) relating to the Common Stock held by such Holders and the Common Stock underlying the Series A Convertible Preferred Stock, the Note and the Warrant.

A G R E E M E N T:

The parties hereto agree as follows:

1. Certain Definitions. As used in this Agreement, the following terms shall have the following respective meanings:

"Commission" shall mean the U.S. Securities and Exchange Commission.

"Exchange Act" shall mean the Securities Exchange Act of 1934, as amended, and the rules and regulations of the Commission thereunder, all as the same shall be in effect from time to time.

"Holders" or "Holders of Registrable Securities" shall mean EIS and any Person who shall have acquired Registrable Securities from EIS as permitted herein, either individually or jointly, as the case may be, in a transaction pursuant to which registration rights are transferred pursuant to Section 10 hereof.

"Person" shall mean an individual, a partnership, a company, an association, a joint stock company, a trust, a joint venture, an unincorporated organization and a governmental or quasi-governmental entity, or any department, agency or political subdivision thereof.

"Registrable Securities" means (i) any shares of Common Stock purchased pursuant to the Purchase Agreement, any shares of Common Stock issued or issuable upon conversion of shares of Series A Convertible Preferred Stock (or issued as dividends thereon) or the Note, and any shares of Common Stock issued or issuable upon exercise of the Warrant, and (ii) any Common Stock issued or issuable in respect of the securities referred to in clause (i) above upon any stock split, stock dividend, recapitalization or similar event; excluding in all cases, however, any Registrable Securities sold by a Person in a transaction (including a transaction pursuant to a registration statement under this Agreement and a transaction pursuant to Rule 144 promulgated under the Securities Act) in which registration rights are not transferred pursuant to Section 10 hereof.

The terms "register," "registered" and "registration" refer to a registration effected by preparing and filing a registration statement in compliance with the Securities Act, and the declaration or order of the effectiveness of such registration statement.

"Registration Expenses" shall mean all expenses, other than Selling Expenses, incurred by the Company in complying with Sections 2 or 3 hereof, including without limitation, all registration, qualification and filing fees, exchange listing fees, printing expenses, escrow fees, fees and disbursements of counsel for the Company, blue sky fees and expenses, the expense of any special audits incident to or required by any such registration and the reasonable fees and disbursements, not to exceed $10,000, of one counsel for the Holders, such counsel to be selected by Holders holding a majority of the Registrable Securities included in such registration.

"Securities Act" shall mean the Securities Act of 1933, as amended, and the rules and regulations of the Commission thereunder, all as the same shall be in effect from time to time.

"Selling Expenses" shall mean all underwriting discounts, selling commissions and stock transfer taxes applicable to the securities registered by the Holders and the costs of any accountants or other experts retained by the Holders.

2. Demand Registration.

(a) Requests for Registration. From and after the date hereof until the date of filing of the Shelf Registration Statement (as defined herein), any Holder or Holders who collectively hold Registrable Securities representing at least 50% of the Registrable Securities then outstanding shall have the right at any time from time to time, to request one registration under the Securities Act of a minimum of 400,000 shares of Common Stock (as adjusted for any combinations, consolidations, stock distributions, stock dividends or other recapitalizations with respect to such shares) on Form S-1, S-2 or S-3 (if available) or any similar registration statement (a "Demand Registration"), such form to be selected by the Company as appropriate. The request for the Demand Registration shall specify the approximate number of Registrable

Securities requested to be registered. Within 20 days after receipt of any such request, the Company will give written notice of such requested registration to all other Holders of Registrable Securities. The Company shall include such other Holders' Registrable Securities in such offering if they have responded affirmatively within 20 days after the receipt of the Company's notice. The Holders in aggregate will be entitled to request only one Demand Registration hereunder. A registration will not count as the permitted Demand Registration until it has become effective (unless such Demand Registration has not become effective due solely to the fault of the Holders requesting such registration, including a request by such Holders that such registration be withdrawn). The Company shall pay all Registration Expenses in connection with any Demand Registration whether or not such Demand Registration has become effective.

(b) Priority on Demand Registration. If a Demand Registration is an underwritten offering and the managing underwriters advise the Company in writing that in their opinion the number of Registrable Securities requested to be included in such offering exceeds the number of Registrable Securities which can be sold in such offering without adversely affecting the marketability of the offering, the Company will include in such registration such number of Registrable Securities allocated pro rata among the Holders thereof based upon the number of Registrable Securities owned by each such Holder. No securities other than Registrable Securities hereunder shall be included in such Demand Registration without the prior written consent of Holders who collectively hold Registrable Securities representing at least 50% of the Registrable Securities then outstanding.

(c) Restrictions on Demand Registration. The Company may postpone the filing or the effectiveness of a registration statement for a Demand Registration if the Company determines in good faith that such Demand Registration would reasonably be expected to have a material adverse effect on any proposal or plan by the Company to engage in any financing, acquisition or disposition of assets (other than in the ordinary course of business) or any merger, consolidation, tender offer or similar transaction or would require disclosure of any information that the board of directors of the Company determines in good faith the disclosure of which would be detrimental to the Company; provided, however, that in such event, the Holders initially requesting such Demand Registration will be entitled to withdraw such request and, if such request is withdrawn, such Demand Registration will not count as the permitted Demand Registration hereunder and the Company will pay any Registration Expenses in connection with such registration.

(d) Selection of Underwriters. The Holders will have the right to select the investment banker(s) and manager(s) to administer an offering pursuant to the Demand Registration, subject to the Company's prior written approval, which will not be unreasonably withheld or delayed.

(e) Other Registration Rights. Except as provided in this Agreement, so long as any Holder owns any Registrable Securities, the Company will not grant to any Persons the right to request the Company to register any equity securities of the Company, or any securities convertible or exchangeable into or exercisable for such securities, which conflicts with the

rights granted to the Holders hereunder, without the prior written consent of the Holders of at least 50% of the Registrable Securities.

3. Shelf Registration Statement.

(a) The Company will cause, by May 30, 2002, to be prepared and filed, and will use commercially reasonable to have declared effective with the Commission within 60 days after filing, a Registration Statement on Form S-3 (or such other form of registration statement that the Company shall determine and that is reasonably satisfactory to the Holders) for an offering to be made on a continuous basis pursuant to Rule 415 (or any similar rule that may be adopted by the Commission) under the Securities Act covering the Registrable Securities (the "Shelf Registration Statement"); provided, however, that if the Company shall furnish to the Holders a certificate signed by any executive officer of the Company stating that in the good faith judgment of the Board of Directors of the Company it would be seriously detrimental to the Company to file the Shelf Registration Statement at such time and it is therefore essential to defer the filing of the Shelf Registration Statement, the Company shall have the right to defer such filing for a reasonable period, not to exceed 60 days. The Shelf Registration Statement may be terminated (and the Company shall have no obligation to update the Shelf Registration Statement and may suspend sales thereunder) at such time as all Registrable Securities can be sold by their Holders within a three-month period without compliance with the registration requirements of the Securities Act pursuant to Rule 144 (including Rule 144(k)) promulgated thereunder (the "Termination Date"). The Holder shall furnish to the Company such information regarding themselves, the Registrable Securities held by them, and the intended method of distribution of such securities as shall be required to effect the Shelf Registration Statement. In that connection, each Holder shall be required to represent that all such information which is given is both complete and accurate in all material respects.

(b) So long as the Shelf Registration Statement is effective, the Company will furnish to the Purchaser as soon as practicable after available (but in the case of the Company's Annual Report to Stockholders, within 120 days after the end of each fiscal year of the Company), (i) one copy of (A) its Annual Report to Stockholders (which Annual Report shall contain financial statements audited in accordance with generally accepted auditing standards certified by a national firm of certified public accountants), (B) if not included in substance in the Annual Report to Stockholders, its Annual Report on Form 10-K, (C) if not included in substance in its Quarterly Reports to Stockholders, its quarterly reports on Form 10-Q, and (D) a full copy of the particular Registration Statement covering the Registrable Securities (the foregoing, in each case, excluding exhibits), (ii) upon the reasonable request of any Holder, all exhibits excluded by the parenthetical in clause (i) of this paragraph, in the form generally available to the public, and (c) upon the reasonable request of any Holder, an adequate number of copies of the prospectuses and supplements to supply to any other party requiring such prospectuses.

4. Expenses of Registration. Except as otherwise provided herein, all Registration Expenses incurred in connection with all registrations pursuant to Sections 2 and 3 shall be borne by the Company. All Selling Expenses relating to securities registered on behalf of the Holders of Registrable Securities shall be borne by such Holders.

5. Holdback Agreements.

(a) The Company agrees (i) not to effect any public sale or distribution of its equity securities, or any securities convertible into or exchangeable or exercisable for such securities, for its own account during the seven days prior to and during the 90-day period beginning on the effective date of any underwritten Demand Registration (except (A) as part of such underwritten registration, (B) pursuant to registration statements on Form S-4 or Form S-8 or any successor form, (C) pursuant to a registration statement then in effect or (D) as required under any existing contractual obligation of the Company), unless the underwriters managing the registered public offering otherwise agree, and (ii) to use reasonable efforts to cause each holder of at least 5% (on a fully-diluted basis) of its outstanding Common Stock, or any securities convertible into or exchangeable or exercisable for Common Stock, purchased from the Company at any time after the date of this Agreement (other than in a registered public offering) to agree not to effect any public sale or distribution (including sales pursuant to Rule 144) of any such securities during such periods (except as part of such underwritten registration, if otherwise permitted), unless the underwriters managing the registered public offering otherwise agree.

(b) Each Holder agrees, if requested by the managing underwriter or underwriters in an underwritten offering of securities of the Company, not to effect any offer, sale, distribution or transfer, including a sale pursuant to Rule 144 (or any similar provision then effect) under the Securities Act (except as part of such underwritten registration), during the seven-day period prior to, and during the 180-day period (or such shorter period as may be agreed to in writing by the Company and the Holders of at least 50% of the Registrable Securities) following the effective date of such Registration Statement to the extent timely notified in writing by the managing underwriter or underwriters.

6. Registration Procedures. Whenever the Company is under the obligation to register Registrable Securities hereunder, the Company will use all reasonable efforts to effect the registration and the sale of such Registrable Securities, and pursuant thereto the Company will as expeditiously as possible:

(a) subject to Section 2(c) and 3(a) hereof, prepare and file with the Commission a registration statement on any form for which the Company qualifies with respect to such Registrable Securities and use all reasonable efforts to cause such registration statement to become effective (provided that before filing a registration statement or prospectus or any amendments or supplements thereto, the Company will (i) furnish to the counsel selected by the Holders copies of all such documents proposed to be filed, which documents will be subject to the review of such counsel, and (ii) notify each Holder of Registrable Securities covered by such registration of any stop order issued or threatened by the Commission);

(b) subject to Section 2(c), 3(b) and 6(e) hereof, prepare and file with the Commission such amendments and supplements to such registration statement and the prospectus used in connection therewith as may be necessary to keep such registration statement effective for, in the case of a Demand Registration, a period equal to the shorter of (i) six months and (ii) the time by which all securities covered by such registration statement have been sold,

and in the case of the Shelf Registration Statement, until the Termination Date, and comply with the provisions of the Securities Act with respect to the disposition of all securities covered by such registration statement during such period in accordance with the intended methods of disposition by the sellers thereof set forth in such registration statement;

(c) furnish to each seller of Registrable Securities such number of copies of such registration statement, each amendment and supplement thereto, the prospectus included in such registration statement (including each preliminary prospectus) and such other documents as such seller may reasonably request in order to facilitate the disposition of the Registrable Securities owned by such seller;

(d) use all reasonable efforts to register or qualify such Registrable Securities under the securities or blue sky laws of such jurisdictions as any seller reasonably requests and do any and all other acts and things which may be reasonably necessary or advisable to enable such seller to consummate the disposition in such jurisdictions of the Registrable Securities owned by such seller (provided that the Company will not be required to (i) qualify generally to do business in any jurisdiction where it would not otherwise be required to qualify but for this Section 6(d), (ii) subject itself to taxation in any jurisdiction, or (iii) consent to general service of process in any such jurisdiction);

(e) notify each seller of such Registrable Securities, at any time when a prospectus relating thereto is required to be delivered under the Securities Act, of the happening of any event as a result of which the prospectus included in such registration statement contains an untrue statement of a material fact or omits any fact necessary to make the statements therein not misleading, and, at the request of any such seller, the Company will prepare a supplement or amendment to such prospectus so that, as thereafter delivered to the purchasers of such Registrable Securities, such prospectus will not contain an untrue statement of a material fact or omit to state any fact necessary to make the statements therein not misleading; provided, however, that the Company shall not be required to amend the registration statement or supplement the Prospectus for a period of up to six months if the board of directors determines in good faith that to do so would reasonably be expected to have a material adverse effect on any proposal or plan by the Company to engage in any financing, acquisition or disposition of assets (other than in the ordinary course of business) or any merger, consolidation, tender offer or similar transaction or would require the disclosure of any information that the board of directors determines in good faith the disclosure of which would be detrimental to the Company, it being understood that the period for which the Company is obligated to keep the Registration Statement effective shall be extended for a number of days equal to the number of days the Company delays amendments or supplements pursuant to this provision. Upon receipt of any notice pursuant to this Section 6(e), the Holders shall suspend all offers and sales of securities of the Company and all use of any prospectus until advised by the Company that offers and sales may resume, and shall keep confidential the fact and content of any notice given by the Company pursuant to this Section 6(e);

(f) cause all such Registrable Securities to be listed on each securities exchange on which similar securities issued by the Company are then listed;

(g) provide a transfer agent and registrar for all such Registrable Securities not later than the effective date of such registration statement;

(h) enter into such customary agreements (including underwriting agreements in customary form) and take all such other actions as the Holders of a majority of the Registrable Securities being sold or the underwriters, if any, reasonably request in order to expedite or facilitate the disposition of such Registrable Securities;

(i) make available for inspection by a representative of the Holders of Registrable Securities included in the registration statement, any underwriter participating in any disposition pursuant to such registration statement and any attorney, accountant or other agent retained by any such seller or underwriter, all pertinent financial and other records, pertinent corporate documents and properties of the Company, and cause the Company's officers, directors, employees and independent accountants to supply all information reasonably requested by any such seller, underwriter, attorney, accountant or agent in connection with such registration statement;

(j) otherwise use its reasonable efforts to comply with all applicable rules and regulations of the Commission, and make available to its security holders, as soon as reasonably practicable, an earnings statement covering the period of at least 12 months beginning with the first day of the Company's first full calendar quarter after the effective date of the registration statement, which earnings statement shall satisfy the provisions of Section 11(a) of the Securities Act and Rule 158 thereunder;

(k) in the event of the issuance of any stop order suspending the effectiveness of a registration statement, or of any order suspending or preventing the use of any related prospectus or suspending the qualification of any Common Stock included in such registration statement for sale in any jurisdiction, use all reasonable efforts promptly to obtain the withdrawal of such order; and

(l) if the registration is an underwritten offering, use all reasonable efforts to obtain a so-called "cold comfort" letter from the Company's independent public accountants in customary form and covering such matters of the type customarily covered by cold comfort letters.

7. Obligations of Holders. Whenever the Holders of Registrable Securities sell any Registrable Securities pursuant to a Demand Registration or the Shelf Registration Statement, such Holders shall be obligated to comply with the applicable provisions of the Securities Act, including the prospectus delivery requirements thereunder, and any applicable state securities or blue sky laws.

8. Indemnification. (a) In connection with any registration statement for a Demand Registration or any Shelf Registration Statement in which a Holder of Registrable Securities is participating, the Company agrees to indemnify, to the fullest extent permitted by applicable law, each such Holder of Registrable Securities, its officers and directors and each Person who controls such Holder (within the meaning of the Securities Act) against all losses,

claims, damages, liabilities, expenses or any amounts paid in settlement of any litigation, investigation or proceeding commenced or threatened to which each such indemnified party may become subject under the Securities Act (collectively, "Claims") insofar as such Claim arose out of (i) any untrue or alleged untrue statement of material fact contained, on the effective date thereof, in any such registration statement, prospectus or preliminary prospectus or any amendment thereof or supplement thereto or (ii) any omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, except insofar as the same are caused by or contained in any information furnished in writing to the Company by such Holder expressly for use therein or by such Holder's failure to deliver a copy of the registration statement or prospectus or any amendments or supplements thereto after the Company has furnished such Holder with a sufficient number of copies of the same. In connection with an underwritten offering, the Company will indemnify the underwriters, their officers and directors and each Person who controls the underwriters (within the meaning of the Securities Act) to the same extent as provided above with respect to the indemnification of the Holders of Registrable Securities.

(b) In connection with any registration statements for a Demand Registration or any Shelf Registration Statement in which a Holder of Registrable Securities is participating, each such Holder will furnish to the Company in writing such customary information as the Company reasonably requests for use in connection with any such registration statement or prospectus (the "Seller's Information") and, to the fullest extent permitted by applicable law, will indemnify the Company, its directors and officers and each Person who controls the Company (within the meaning of the Securities Act) against any and all Claims to which each such indemnified party may become subject under the Securities Act insofar as such Claim arose out of (i) any untrue or alleged untrue statement of material fact contained, on the effective date thereof, in any such registration statement, prospectus or preliminary prospectus or any amendment thereof or supplement thereto or (ii) any omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading; provided that with respect to a Claim arising pursuant to clause (i) or (ii) above, the material misstatement or omission is contained in such Seller's Information; provided, further, that the obligation to indemnify will be individual to each Holder and will be limited to the amount of proceeds received by such Holder from the sale of Registrable Securities pursuant to such registration statement.

(c) Any Person entitled to indemnification hereunder will (i) give prompt written notice to the indemnifying party of any claim with respect to which it seeks indemnification (but the failure to provide such notice shall not release the indemnifying party of its obligation under paragraphs (a) and (b), unless and then only to the extent that, the indemnifying party has been prejudiced by such failure to provide such notice) and (ii) unless in such indemnified party's reasonable judgment a conflict of interest between such indemnified and indemnifying parties may exist with respect to such claim, permit such indemnifying party to assume the defense of such claim with counsel reasonably satisfactory to the indemnified party. An indemnifying party who is not entitled to, or elects not to, assume the defense of a claim will not be obligated to pay the fees and expenses of more than one counsel for all parties indemnified by such indemnifying party with respect to such claim, unless in the reasonable judgment of any indemnified party a

conflict of interest may exist between such indemnified party and any other of such indemnified parties with respect to such claim.

(d) The indemnifying party shall not be liable to indemnify an indemnified party for any settlement, or consent to judgment of any such action effected without the indemnifying party's consent (but such consent will not be unreasonably withheld). Furthermore, the indemnifying party shall not, except with the prior written approval of each indemnified party, consent to entry of any judgment or enter into any settlement which does not include as an unconditional term thereof the giving by the claimant or plaintiff to each indemnified party of a release from all liability in respect of such claim or litigation without any payment or consideration provided by each such indemnified party.

(e) If the indemnification provided for in this Section 8 is unavailable to an indemnified party under clauses (a) and (b) above in respect of any losses, claims, damages or liabilities referred to therein, then each indemnifying party, in lieu of indemnifying such indemnified party, shall contribute to the amount paid or payable by such indemnified party as a result of such losses, claims, damages or liabilities in such proportion as is appropriate to reflect not only the relative benefits received by the Company (if any), the underwriters, the sellers of Registrable Securities and any other sellers participating in the registration statement from the sale of shares pursuant to the registered offering of securities for which indemnity is sought but also the relative fault of the Company, the underwriters, the sellers of Registrable Securities and any other sellers participating in the registration statement in connection with the statement or omission which resulted in such losses, claims, damages or liabilities, as well as any other relevant equitable considerations. The relative benefits received by the Company (if any), the underwriters, the sellers of Registrable Securities and any other sellers participating in the registration statement shall be deemed to be based on the relative relationship of the total net proceeds from the offering (before deducting expenses) to the Company (if any), the total underwriting commissions and fees from the offering (before deducting expenses) to the underwriters and the total net proceeds from the offering (before deducting expenses) to the sellers of Registrable Securities and any other sellers participating in the registration statement. The relative fault of the Company, the underwriters, the sellers of Registrable Securities and any other sellers participating in the registration statement shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the Company or by the sellers of Registrable Securities and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

(f) The indemnification provided for under this Agreement will remain in full force and effect regardless of any investigation made by or on behalf of the indemnified party or any officer, director or controlling person of such indemnified party and will survive the transfer of the Registrable Securities.

9. Participation in Underwritten Registrations. No Holder may participate in any registration hereunder which is underwritten unless such Holder (a) agrees to sell such Holder's securities on the basis provided in any underwriting arrangements approved by the Holder or Holders entitled hereunder to approve such arrangements, (b) as expeditiously as possible

notifies the Company of the occurrence of any event as a result of which any prospectus contains an untrue statement of material fact or omits to state a material fact required to be stated therein or necessary to make the statements therein not misleading and (c) completes and executes all questionnaires, powers of attorney, indemnities, underwriting agreements and other documents reasonably required under the terms of such underwriting arrangements.

10. Transfer of Registration Rights. The rights granted to any Holder under this Agreement may be assigned to any permitted transferee of Registrable Securities, in connection with any transfer or assignment of Registrable Securities by a Holder; provided, however, that: (a) such transfer is otherwise effected in accordance with applicable securities laws, (b) if not already a party hereto, the assignee or transferee agrees in writing prior to such transfer to be bound by the provisions of this Agreement applicable to the transferor, (c) such transferee shall own Registrable Securities representing at least 200,000 shares of Common Stock (as adjusted for any combinations, consolidations, stock distributions, stock dividends or other recapitalizations with respect to such shares), and (d) EIS shall act as agent and representative for such Holder for the giving and receiving of notices hereunder.

11. Information by Holder. Each Holder shall furnish to the Company such written information regarding such Holder and any distribution proposed by such Holder as the Company may reasonably request in writing and as shall be reasonably required in connection with any registration, qualification or compliance referred to in this Agreement and shall promptly notify the Company of any changes in such information.

12. Exchange Act Compliance. The Company shall comply with all of the reporting requirements of the Exchange Act then applicable to it and shall comply with all other public information reporting requirements of the Commission which are conditions to the availability of Rule 144 for the sale of the Registrable Securities. The Company shall cooperate with each Holder in supplying such information as may be necessary for such Holder to complete and file any information reporting forms presently or hereafter required by the Commission as a condition to the availability of Rule 144.

13. Termination of Registration Rights. All registration rights granted under this Agreement shall terminate and be of no further force and effect, as to any particular Holder, at such time as all Registrable Securities held by such Holder can be sold within a three-month period without compliance with the registration requirements of the Securities Act pursuant to Rule 144 (including Rule 144(k)) promulgated thereunder or have been resold pursuant to a Demand Registration or the Shelf Registration Statement.

14. Miscellaneous.

(a) No Inconsistent Agreements. The Company will not hereafter enter into any agreement with respect to its securities which is inconsistent with or violates the rights granted to the Holders of Registrable Securities in this Agreement without the prior written consent of a majority in interest of such Registrable Securities.

(b) Remedies. Any Person having rights under any provision of this Agreement will be entitled to enforce such rights specifically to recover damages caused by reason of any breach of any provision of this Agreement and to exercise all other rights granted by law. The parties hereto agree and acknowledge that money damages may not be an adequate remedy for any breach of the provisions of this Agreement and that any party may in its sole discretion apply to any court of law or equity of competent jurisdiction (without posting any bond or other security) for specific performance and for other injunctive relief in order to enforce or prevent violation of the provisions of this Agreement; provided, however, that in no event shall any Holder have the right to enjoin, delay or interfere with any offering of securities by the Company.

(c) Amendments and Waivers. Except as otherwise provided herein, the provisions of this Agreement may be amended or waived only with the prior written consent of the Company and Holders of at least 50% of the Registrable Securities; provided, however, that without the prior written consent of all the Holders, no such amendment or waiver shall reduce the foregoing percentage required to amend or waive any provision of this Agreement.

(d) Successors and Assigns. All covenants and agreements in this Agreement by or on behalf of any of the parties hereto will bind and inure to the benefit of the respective successors and assigns of the parties hereto, and shall inure to the benefit and be enforceable by each Holder of Registrable Securities from time to time. In addition, whether or not any express assignment has been made, the provisions of this Agreement which are for the benefit of Holders of Registrable Securities are also for the benefit of, and enforceable by, any permitted transferee of Registrable Securities in accordance with Section 10 hereof.

(e) Severability. Whenever possible, each provision of this Agreement will be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be prohibited by or invalid under applicable law, such provision will be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of this Agreement.

(f) Counterparts. This Agreement may be executed simultaneously in two or more counterparts, any one of which need not contain the signatures of more than one party, but all such counterparts taken together will constitute one and the same Agreement.

(g) Descriptive Headings. The descriptive headings of this Agreement are inserted for convenience only and do not constitute a part of this Agreement.

(h) Governing Law. All questions concerning the construction, validity and interpretation of this Agreement will be governed by the laws of the State of New York without regard to principles of conflicts of laws, except that all issues concerning the relative rights of the Company and its stockholders shall be governed by the Delaware General Corporation Law, without giving effect to the principles thereof relating to conflicts of laws.

(i) Notices. All notices, demands and requests of any kind to be delivered to any party in connection with this Agreement shall be in writing and shall be deemed to have been

duly given if personally delivered or if sent by nationally-recognized overnight courier or by registered or certified airmail, return receipt requested and postage prepaid or by facsimile transmission (with receipt confirmed by telephone), addressed as follows:

(i) if to the Company, to:

Isis Pharmaceuticals, Inc.
2292 Faraday Avenue
Carlsbad, CA 92008
Facsimile: (760) 931-9639
telephone confirmation required at (760) 603-2460
Attention: B. Lynne Parshall

with a copy to:

Cooley Godward LLP
4365 Executive Drive
San Diego, CA 92121
Facsimile: (619) 453-3555
telephone confirmation required at (619) 550-6000
Attention: L. Kay Chandler, Esq.

(ii) if to EIS, to:

Elan International Services, Ltd.
Flatts, Smiths Parish
Bermuda, FL 04
Facsimile: (441) 292-2224
telephone confirmation required at (441) 292-9169
Attention: President

with a copy to:

Brock Silverstein LLC
153 East 53rd Street, 56th Floor
New York, New York 10022
Facsimile: (212) 371-5500
telephone confirmation required at (212) 371-2000
Attention: David Robbins, Esq.

(j) Entire Agreement. This Agreement constitutes the full and entire understanding and agreement between the parties with regard to the subject matter hereof.

[Signature page follows]

IN WITNESS WHEREOF, the parties have executed this Registration Rights Agreement as of the date first written above.

ISIS PHARMACEUTICALS, INC.

By: /s/ B. LYNNE PARSHALL

B. Lynne Parshall
Executive Vice President

ELAN INTERNATIONAL SERVICES, LTD.

By: /s/ KEVIN INSLEY

Kevin Insley
President

EXHIBIT 10.6

ORASENSE LTD.
REGISTRATION RIGHTS AGREEMENT

THIS REGISTRATION RIGHTS AGREEMENT (the "Agreement") is made as of April 20, 1999 by and among ORASENSE LTD., a Bermuda corporation (the "Company"), ISIS PHARMACEUTICALS, INC., a Delaware corporation ("Isis"), and ELAN INTERNATIONAL SERVICES, Ltd., a Bermuda corporation ("EIS").

R E C I T A L S:

A. Pursuant to a joint development and operating agreement dated as of the date hereof by and among the Company, Isis, ELAN CORPORATION, PLC, an Irish public limited company and EIS (the "JDOA"), Isis and EIS have acquired certain common shares, par value $1.00 per share (the "Common Shares"), of the Company.

B. The execution of the JDOA has occurred on the date hereof and it is a condition to the closing of the transactions contemplated thereby that the parties execute and deliver this Agreement.

C. The parties desire to set forth herein their agreement on the terms and subject to the conditions set forth herein related to the granting of certain registration rights to the Holders (as defined below) relating to the Common Shares held by such Holders.

A G R E E M E N T:

The parties hereto agree as follows:

1. Certain Definitions. As used in this Agreement, the following terms shall have the following respective meanings:

"Commission" shall mean the U.S. Securities and Exchange Commission.

"Exchange Act" shall mean the Securities Exchange Act of 1934, as amended, and the rules and regulations of the Commission thereunder, all as the same shall be in effect from time to time.

"Holders" or "Holders of Registrable Securities" shall mean Isis, EIS and any Person who shall have acquired Registrable Securities from either Isis or EIS as permitted herein, either individually or jointly, as the case may be, in a transaction pursuant to which registration rights are transferred pursuant to Section 10 hereof.

"Person" shall mean an individual, a partnership, a company, an association, a joint stock company, a trust, a joint venture, an unincorporated organization and a governmental or quasi-governmental entity, or any department, agency or political subdivision thereof.

"Registrable Securities" means (i) any Common Shares subscribed for pursuant to the JDOA and (ii) any Common Shares issued or issuable in respect of the securities referred to in clause (i) above upon any stock split, stock dividend, recapitalization or similar event; excluding in all cases, however, any Registrable Securities sold by a Person in a transaction (including a transaction pursuant to a registration statement under this Agreement and a transaction pursuant to Rule 144 promulgated under the Securities Act) in which registration rights are not transferred pursuant to Section 10 hereof.

The terms "register," "registered" and "registration" refer to a registration effected by preparing and filing a registration statement in compliance with the Securities Act, and the declaration or order of the effectiveness of such registration statement.

"Registration Expenses" shall mean all expenses, other than Selling Expenses, incurred by the Company in complying with Sections 2 or 3 hereof, including without limitation, all registration, qualification and filing fees, exchange listing fees, printing expenses, escrow fees, fees and disbursements of counsel for the Company, blue sky fees and expenses, the expense of any special audits incident to or required by any such registration and the reasonable fees and disbursements, not to exceed $10,000, of one counsel for the Holders, such counsel to be selected by Holders holding a majority of the Registrable Securities included in such registration.

"Securities Act" shall mean the Securities Act of 1933, as amended, and the rules and regulations of the Commission thereunder, all as the same shall be in effect from time to time.

"Selling Expenses" shall mean all underwriting discounts, selling commissions and stock transfer taxes applicable to the securities registered by the Holders and the costs of any accountants or other experts retained by the Holders.

2. Demand Registrations.

(a) Requests for Registration. From and after the occurrence of the initial public offering of the Company's Common Shares under the Securities Act, any Holder or Holders who collectively hold Registrable Securities representing at least 33% of the Registrable Securities then outstanding shall have the right at any time from time to time, to request two registrations under the Securities Act of all or part of their Registrable Securities on Form S-1, S-2 or S-3 (if available) or any similar registration statement (each, a "Demand Registration"), such form to be selected by the Company as appropriate. The request for the Demand Registration shall specify the approximate number of Registrable Securities requested to be registered, which must have a minimum expected aggregate offering price to the public of at least $1,000,000. Within 20 days after receipt of any such request, the Company will give written notice of such requested registration to all other Holders of Registrable Securities. The Company shall include such other

Holders' Registrable Securities in such offering if they have responded affirmatively within 20 days after the receipt of the Company's notice. The Holders in aggregate will be entitled to request only one Demand Registration hereunder within any 12-month period. A registration will not count as a permitted Demand Registration until it has become effective (unless such Demand Registration has not become effective due solely to the fault of the Holders requesting such registration, including a request by such Holders that such registration be withdrawn). The Company shall pay all Registration Expenses in connection with any Demand Registration whether or not such Demand Registration has become effective.

(b) Priority on Demand Registrations. If a Demand Registration is an underwritten offering and the managing underwriters advise the Company in writing that in their opinion the number of Registrable Securities and, if permitted hereunder, other securities requested to be included in such offering, exceeds the number of Registrable Securities and other securities, if any, which can be sold in such offering without adversely affecting the marketability of the offering, the Company will include in such registration:

(i) first, the Registrable Securities requested to be included in such registration by the Holders (or, if necessary, such Registrable Securities pro rata among the Holders thereof based upon the number of Registrable Securities owned by each such Holder) together with any securities held by third parties holding a similar, previously granted right to be included in such registration; and

(ii) thereafter, other securities requested to be included in such registration.

(c) Restrictions on Demand Registration. The Company may postpone for up to six months in any 12-month period, the filing or the effectiveness of a registration statement for a Demand Registration if the Company determines in good faith that such Demand Registration would reasonably be expected to have a material adverse effect on any proposal or plan by the Company to engage in any financing, acquisition or disposition of assets (other than in the ordinary course of business) or any merger, consolidation, tender offer or similar transaction or would require disclosure of any information that the board of directors of the Company determines in good faith the disclosure of which would be detrimental to the Company; provided, however, that in such event, the Holders initially requesting such Demand Registration will be entitled to withdraw such request and, if such request is withdrawn, such Demand Registration will not count as a permitted Demand Registration hereunder and the Company will pay any Registration Expenses in connection with such registration.

(d) Selection of Underwriters. The Holders will have the right to select the investment banker(s) and manager(s) to administer an offering pursuant to the Demand Registration, subject to the Company's prior written approval, which will not be unreasonably withheld or delayed.

(e) Other Registration Rights. Except as provided in this Agreement, so long as any Holder owns any Registrable Securities, the Company will not grant to any Persons the right to request the Company to register any equity securities of the Company, or any securities

convertible or exchangeable into or exercisable for such securities, which conflicts with the rights granted to the Holders hereunder, without the prior written consent of the Holders of at least 50% of the Registrable Securities; provided, however, that the Company may grant rights to other Persons to demand and piggyback registrations so long as the Holders of Registrable Securities are entitled to participate in any such registrations with such Persons pro rata on the basis of the number of shares owned by each such Holder.

3. Piggyback Registrations.

(a) Right to Piggyback. At any time the Company shall propose to register Common Shares under the Securities Act (other than in a registration statement on Form S-3 relating to sales of securities to participants in a Company dividend reinvestment plan, or Form S-4 or S-8 or any successor form or in connection with an acquisition or exchange offer or an offering of securities solely to the existing shareholders or employees of the Company) (each, a "Piggyback Registration"), the Company will give prompt written notice to all Holders of Registrable Securities of its intention to effect such a registration and, subject to Section 3(b) and the other terms of this Agreement, will include in such registration all Registrable Securities which are permitted under applicable securities laws to be included in the form of registration statement selected by the Company and with respect to which the Company has received written requests for inclusion therein within 20 days after the receipt of the Company's notice.

(b) Priority on Piggyback Registrations. If a Piggyback Registration is to be an underwritten offering, and the managing underwriters advise the Company in writing that in their opinion the number of securities requested to be included in such registration exceeds the number which can be sold in such offering without adversely affecting the marketability of the offering, the Company will include in such registration:

(i) first, the securities the Company proposes to sell;

(ii) any securities having the right to be included in such registration prior to the securities of the Holders;

(iii) the Registrable Securities requested to be included in such registration by the Holders and any securities requested to be included in such registration by any other Person having equal priority to registration with the Holders, pro rata among the Holders of such Registrable Securities and such other Persons, on the basis of the number of shares owned by each of such Holders; and

(iv) thereafter, other securities requested to be included in such registration.

The Holders of any Registrable Securities included in such an underwritten offering must execute an underwriting agreement, in customary form and in form and substance satisfactory to the managing underwriters.

(c) Right to Terminate Registration. If, at any time after giving written notice of its intention to register any of its securities as set forth in Section 3(a) and prior to the effective date of the registration statement filed in connection with such registration, the Company shall determine for any reason not to register such securities, the Company may, at its election, give written notice of such determination to each Holder of Registrable Securities and thereupon be relieved of its obligation to register any Registrable Securities in connection with such registration (but not from its obligation to pay the Registration Expenses in connection therewith as provided herein).

(d) Selection of Underwriters. The Company will have the right to select the investment banker(s) and manager(s) to administer an offering pursuant to a Piggyback Registration.

4. Expenses of Registration. Except as otherwise provided herein or as may otherwise be prohibited by applicable law, all Registration Expenses incurred in connection with all registrations pursuant to Sections 2 and 3 shall be borne by the Company. All Selling Expenses relating to securities registered on behalf of the Holders of Registrable Securities shall be borne by such Holders.

5. Holdback Agreements.

(a) The Company agrees (i) not to effect any public sale or distribution of its equity securities, or any securities convertible into or exchangeable or exercisable for such securities, during the seven days prior to and during the 180-day period beginning on the effective date of any underwritten Demand Registration or any underwritten Piggyback Registration (except as part of such underwritten registration or pursuant to registration statements on Form S-4 or Form S-8 or any successor form), unless the underwriters managing the registered public offering otherwise agree, and (ii) to use reasonable efforts to cause each holder of at least 5% (on a fully-diluted basis) of its outstanding Common Shares, or any securities convertible into or exchangeable or exercisable for Common Shares, purchased from the Company at any time after the date of this Agreement (other than in a registered public offering) to agree not to effect any public sale or distribution (including sales pursuant to Rule 144) of any such securities during such periods (except as part of such underwritten registration, if otherwise permitted), unless the underwriters managing the registered public offering otherwise agree.

(b) Each Holder agrees, if requested by the managing underwriter or underwriters in an underwritten offering of securities of the Company, not to effect any offer, sale, distribution or transfer, including a sale pursuant to Rule 144 (or any similar provision then effect) under the Securities Act (except as part of such underwritten registration), during the seven-day period prior to, and during the 180-day period (or such shorter period as may be agreed to in writing by the Company and the Holders of at least 50% of the Registrable Securities) following the effective date of such Registration Statement to the extent timely notified in writing by the managing underwriter or underwriters.

6. Registration Procedures. Whenever the Holders of Registrable Securities have requested that any Registrable Securities be registered pursuant to this Agreement, the Company will use all reasonable efforts to effect the registration and the sale of such Registrable Securities in accordance with the intended method of distribution thereof, and pursuant thereto the Company will as expeditiously as possible:

(a) subject to Section 2(c) hereof, prepare and file with the Commission a registration statement on any form for which the Company qualifies with respect to such Registrable Securities and use all reasonable efforts to cause such registration statement to become effective (provided that before filing a registration statement or prospectus or any amendments or supplements thereto, the Company will (i) furnish to the counsel selected by the Holders copies of all such documents proposed to be filed, which documents will be subject to the review of such counsel, and (ii) notify each Holder of Registrable Securities covered by such registration of any stop order issued or threatened by the Commission);

(b) subject to Section 2(c) hereof, prepare and file with the Commission such amendments and supplements to such registration statement and the prospectus used in connection therewith as may be necessary to keep such registration statement effective for a period equal to the shorter of (i) six months and (ii) the time by which all securities covered by such registration statement have been sold, and comply with the provisions of the Securities Act with respect to the disposition of all securities covered by such registration statement during such period in accordance with the intended methods of disposition by the sellers thereof set forth in such registration statement;

(c) furnish to each seller of Registrable Securities such number of copies of such registration statement, each amendment and supplement thereto, the prospectus included in such registration statement (including each preliminary prospectus) and such other documents as such seller may reasonably request in order to facilitate the disposition of the Registrable Securities owned by such seller;

(d) use all reasonable efforts to register or qualify such Registrable Securities under the securities or blue sky laws of such jurisdictions as any seller reasonably requests and do any and all other acts and things which may be reasonably necessary or advisable to enable such seller to consummate the disposition in such jurisdictions of the Registrable Securities owned by such seller (provided that the Company will not be required to (i) qualify generally to do business in any jurisdiction where it would not otherwise be required to qualify but for this Section 6(d), (ii) subject itself to taxation in any jurisdiction, or (iii) consent to general service of process in any such jurisdiction);

(e) notify each seller of such Registrable Securities, at any time when a prospectus relating thereto is required to be delivered under the Securities Act, of the happening of any event as a result of which the prospectus included in such registration statement contains an untrue statement of a material fact or omits any fact necessary to make the statements therein not misleading, and, at the request of any such seller, the Company will prepare a supplement or amendment to such prospectus so that, as thereafter delivered to the purchasers of such Registrable Securities, such prospectus will not contain an untrue statement of a material fact or

omit to state any fact necessary to make the statements therein not misleading; provided, however, that the Company shall not be required to amend the registration statement or supplement the Prospectus for a period of up to six months if the board of directors determines in good faith that to do so would reasonably be expected to have a material adverse effect on any proposal or plan by the Company to engage in any financing, acquisition or disposition of assets (other than in the ordinary course of business) or any merger, consolidation, tender offer or similar transaction or would require the disclosure of any information that the board of directors determines in good faith the disclosure of which would be detrimental to the Company, it being understood that the period for which the Company is obligated to keep the Registration Statement effective shall be extended for a number of days equal to the number of days the Company delays amendments or supplements pursuant to this provision. Upon receipt of any notice pursuant to this Section 6(e), the Holders shall suspend all offers and sales of securities of the Company and all use of any prospectus until advised by the Company that offers and sales may resume, and shall keep confidential the fact and content of any notice given by the Company pursuant to this Section 6(e);

(f) cause all such Registrable Securities to be listed on each securities exchange on which similar securities issued by the Company are then listed;

(g) provide a transfer agent and registrar for all such Registrable Securities not later than the effective date of such registration statement;

(h) enter into such customary agreements (including underwriting agreements in customary form) and take all such other actions as the Holders of a majority of the Registrable Securities being sold or the underwriters, if any, reasonably request in order to expedite or facilitate the disposition of such Registrable Securities;

(i) make available for inspection by a representative of the Holders of Registrable Securities included in the registration statement, any underwriter participating in any disposition pursuant to such registration statement and any attorney, accountant or other agent retained by any such seller or underwriter, all pertinent financial and other records, pertinent corporate documents and properties of the Company, and cause the Company's officers, directors, employees and independent accountants to supply all information reasonably requested by any such seller, underwriter, attorney, accountant or agent in connection with such registration statement;

(j) otherwise use its reasonable efforts to comply with all applicable rules and regulations of the Commission, and make available to its security holders, as soon as reasonably practicable, an earnings statement covering the period of at least 12 months beginning with the first day of the Company's first full calendar quarter after the effective date of the registration statement, which earnings statement shall satisfy the provisions of Section 11(a) of the Securities Act and Rule 158 thereunder;

(k) in the event of the issuance of any stop order suspending the effectiveness of a registration statement, or of any order suspending or preventing the use of any related prospectus or suspending the qualification of any Common Shares included in such registration statement

for sale in any jurisdiction, use all reasonable efforts promptly to obtain the withdrawal of such order; and

(l) if the registration is an underwritten offering, use all reasonable efforts to obtain a so-called "cold comfort" letter from the Company's independent public accountants in customary form and covering such matters of the type customarily covered by cold comfort letters.

7. Obligations of Holders. Whenever the Holders of Registrable Securities sell any Registrable Securities pursuant to a Demand Registration or a Piggyback Registration, such Holders shall be obligated to comply with the applicable provisions of the Securities Act, including the prospectus delivery requirements thereunder, and any applicable state securities or blue sky laws.

8. Indemnification. (a) The Company agrees to indemnify, to the fullest extent permitted by applicable law, each Holder of Registrable Securities, its officers and directors and each Person who controls such Holder (within the meaning of the Securities Act) against all losses, claims, damages, liabilities, expenses or any amounts paid in settlement of any litigation, investigation or proceeding commenced or threatened (collectively, "Claims") to which each such indemnified party may become subject under the Securities Act insofar as such Claim arose out of (i) any untrue or alleged untrue statement of material fact contained, on the effective date thereof, in any registration statement, prospectus or preliminary prospectus or any amendment thereof or supplement thereto or (ii) any omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, except insofar as the same are caused by or contained in any information furnished in writing to the Company by such Holder expressly for use therein or by such Holder's failure to deliver a copy of the registration statement or prospectus or any amendments or supplements thereto after the Company has furnished such Holder with a sufficient number of copies of the same. In connection with an underwritten offering, the Company will indemnify the underwriters, their officers and directors and each Person who controls the underwriters (within the meaning of the Securities Act) to the same extent as provided above with respect to the indemnification of the Holders of Registrable Securities.

(b) In connection with any registration statements in which a Holder of Registrable Securities is participating, each such Holder will furnish to the Company in writing such customary information as the Company reasonably requests for use in connection with any such registration statement or prospectus (the "Seller's Information") and, to the fullest extent permitted by applicable law, will indemnify the Company, its directors and officers and each Person who controls the Company (within the meaning of the Securities Act) against any and all Claims to which each such indemnified party may become subject under the Securities Act insofar as such Claim arose out of (i) any untrue or alleged untrue statement of material fact contained, on the effective date thereof, in any registration statement, prospectus or preliminary prospectus or any amendment thereof or supplement thereto or (ii) any omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading; provided that with respect to a Claim arising pursuant to clause (i) or (ii) above, the material misstatement or omission is contained in such Seller's

Information; provided, further, that the obligation to indemnify will be individual to each Holder and will be limited to the amount of proceeds received by such Holder from the sale of Registrable Securities pursuant to such registration statement.

(c) Any Person entitled to indemnification hereunder will (i) give prompt written notice to the indemnifying party of any claim with respect to which it seeks indemnification (but the failure to provide such notice shall not release the indemnifying party of its obligation under paragraphs (a) and (b), unless and then only to the extent that, the indemnifying party has been prejudiced by such failure to provide such notice) and (ii) unless in such indemnified party's reasonable judgment a conflict of interest between such indemnified and indemnifying parties may exist with respect to such claim, permit such indemnifying party to assume the defense of such claim with counsel reasonably satisfactory to the indemnified party. An indemnifying party who is not entitled to, or elects not to, assume the defense of a claim will not be obligated to pay the fees and expenses of more than one counsel for all parties indemnified by such indemnifying party with respect to such claim, unless in the reasonable judgment of any indemnified party a conflict of interest may exist between such indemnified party and any other of such indemnified parties with respect to such claim.

(d) The indemnifying party shall not be liable to indemnify an indemnified party for any settlement, or consent to judgment of any such action effected without the indemnifying party's consent (but such consent will not be unreasonably withheld). Furthermore, the indemnifying party shall not, except with the prior written approval of each indemnified party, consent to entry of any judgment or enter into any settlement which does not include as an unconditional term thereof the giving by the claimant or plaintiff to each indemnified party of a release from all liability in respect of such claim or litigation without any payment or consideration provided by each such indemnified party.

(e) If the indemnification provided for in this Section 8 is unavailable to an indemnified party under clauses (a) and (b) above in respect of any losses, claims, damages or liabilities referred to therein, then each indemnifying party, in lieu of indemnifying such indemnified party, shall contribute to the amount paid or payable by such indemnified party as a result of such losses, claims, damages or liabilities in such proportion as is appropriate to reflect not only the relative benefits received by the Company, the underwriters, the sellers of Registrable Securities and any other sellers participating in the registration statement from the sale of shares pursuant to the registered offering of securities for which indemnity is sought but also the relative fault of the Company, the underwriters, the sellers of Registrable Securities and any other sellers participating in the registration statement in connection with the statement or omission which resulted in such losses, claims, damages or liabilities, as well as any other relevant equitable considerations. The relative benefits received by the Company, the underwriters, the sellers of Registrable Securities and any other sellers participating in the registration statement shall be deemed to be based on the relative relationship of the total net proceeds from the offering (before deducting expenses) to the Company, the total underwriting commissions and fees from the offering (before deducting expenses) to the underwriters and the total net proceeds from the offering (before deducting expenses) to the sellers of Registrable Securities and any other sellers participating in the registration statement. The relative fault of the Company, the underwriters, the sellers of Registrable Securities and any other sellers

participating in the registration statement shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the Company or by the sellers of Registrable Securities and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

(f) The indemnification provided for under this Agreement will remain in full force and effect regardless of any investigation made by or on behalf of the indemnified party or any officer, director or controlling person of such indemnified party and will survive the transfer of the Registrable Securities.

9. Participation in Underwritten Registrations. No Holder may participate in any registration hereunder which is underwritten unless such Holder (a) agrees to sell such Holder's securities on the basis provided in any underwriting arrangements approved by the Holder or Holders entitled hereunder to approve such arrangements, (b) as expeditiously as possible notifies the Company of the occurrence of any event as a result of which any prospectus contains an untrue statement of material fact or omits to state a material fact required to be stated therein or necessary to make the statements therein not misleading and (c) completes and executes all questionnaires, powers of attorney, indemnities, underwriting agreements and other documents reasonably required under the terms of such underwriting arrangements.

10. Transfer of Registration Rights. The rights granted to any Holder under this Agreement may be assigned to any permitted transferee of Registrable Securities, in connection with any transfer or assignment of Registrable Securities by a Holder; provided, however, that: (a) such transfer is otherwise effected in accordance with applicable securities laws, (b) if not already a party hereto, the assignee or transferee agrees in writing prior to such transfer to be bound by the provisions of this Agreement applicable to the transferor, (c) such transferee shall own Registrable Securities representing at least 3,000 Common Shares (as adjusted for any combinations, consolidations, stock distributions, stock dividends or other recapitalizations with respect to such shares), and (d) Isis or EIS, as applicable, shall act as agent and representative for such Holder for the giving and receiving of notices hereunder.

11. Information by Holder. Each Holder shall furnish to the Company such written information regarding such Holder and any distribution proposed by such Holder as the Company may reasonably request in writing and as shall be reasonably required in connection with any registration, qualification or compliance referred to in this Agreement and shall promptly notify the Company of any changes in such information.

12. Exchange Act Compliance. The Company shall comply with all of the reporting requirements of the Exchange Act then applicable to it and shall comply with all other public information reporting requirements of the Commission which are conditions to the availability of Rule 144 for the sale of the Registrable Securities. The Company shall cooperate with each Holder in supplying such information as may be necessary for such Holder to complete and file any information reporting forms presently or hereafter required by the Commission as a condition to the availability of Rule 144.

13. Termination of Registration Rights. All registration rights granted under this Agreement shall terminate and be of no further force and effect, as to any particular Holder, at such time as all Registrable Securities held by such Holder can be sold within a three-month period without compliance with the registration requirements of the Securities Act pursuant to Rule 144 (including Rule 144(k)) promulgated thereunder or have been resold pursuant to a registration statement hereunder.

14. Miscellaneous.

(a) No Inconsistent Agreements. The Company will not hereafter enter into any agreement with respect to its securities which is inconsistent with or violates the rights granted to the Holders of Registrable Securities in this Agreement without the prior written consent of a majority in interest of such Registrable Securities.

(b) Remedies. Any Person having rights under any provision of this Agreement will be entitled to enforce such rights specifically to recover damages caused by reason of any breach of any provision of this Agreement and to exercise all other rights granted by law. The parties hereto agree and acknowledge that money damages may not be an adequate remedy for any breach of the provisions of this Agreement and that any party may in its sole discretion apply to any court of law or equity of competent jurisdiction (without posting any bond or other security) for specific performance and for other injunctive relief in order to enforce or prevent violation of the provisions of this Agreement; provided, however, that in no event shall any Holder have the right to enjoin, delay or interfere with any offering of securities by the Company.

(c) Amendments and Waivers. Except as otherwise provided herein, the provisions of this Agreement may be amended or waived only with the prior written consent of the Company and Holders of at least 50% of the Registrable Securities; provided, however, that without the prior written consent of all the Holders, no such amendment or waiver shall reduce the foregoing percentage required to amend or waive any provision of this Agreement.

(d) Successors and Assigns. All covenants and agreements in this Agreement by or on behalf of any of the parties hereto will bind and inure to the benefit of the respective successors and assigns of the parties hereto, and shall inure to the benefit and be enforceable by each Holder of Registrable Securities from time to time. In addition, whether or not any express assignment has been made, the provisions of this Agreement which are for the benefit of Holders of Registrable Securities are also for the benefit of, and enforceable by, any permitted transferee of Registrable Securities, in accordance with Section 10 hereof.

(e) Severability. Whenever possible, each provision of this Agreement will be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be prohibited by or invalid under applicable law, such provision will be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of this Agreement.

(f) Counterparts. This Agreement may be executed simultaneously in two or more counterparts, any one of which need not contain the signatures of more than one party, but all such counterparts taken together will constitute one and the same Agreement.

(g) Descriptive Headings. The descriptive headings of this Agreement are inserted for convenience only and do not constitute a part of this Agreement.

(h) Governing Law. All questions concerning the construction, validity and interpretation of this Agreement will be governed by the laws of the State of New York without regard to principles of conflicts of laws.

(i) Notices. All notices, demands and requests of any kind to be delivered to any party in connection with this Agreement shall be in writing and shall be deemed to have been duly given if personally delivered or if sent by nationally-recognized overnight courier or by registered or certified airmail, return receipt requested and postage prepaid or by facsimile transmission (with receipt confirmed by telephone), addressed as follows:

(i) if to the Company, to:

Orasense Ltd.
c/o Appleby, Spurling & Kempe
Cedar House, 41 Cedar Avenue
P.O. Box HM 1179
Hamilton, Bermuda HM EX
Facsimile: (441) 295-7768
telephone confirmation required at (441) 295-2244
Attention: Timothy Faries

with a copy to each of Isis, EIS and their respective counsel at the addresses indicated below

(ii) if to Isis, to:

Isis Pharmaceuticals, Inc.
2292 Faraday Avenue
Carlsbad, CA 92008
Facsimile: (760) 931-9639
telephone confirmation required at (760) 603-2460
Attention: B. Lynne Parshall

with a copy to:

Cooley Godward LLP
4365 Executive Drive
San Diego, CA 92121
Facsimile: (619) 453-3555
telephone confirmation required at (619) 550-6000
Attention: L. Kay Chandler, Esq.

(iii) if to EIS, to:

Elan International Services, Ltd.
Flatts, Smiths Parish
Bermuda, FL 04
Facsimile: (441) 292-2224
telephone confirmation required at (441) 292-9169
Attention: President

with a copy to:

Brock Silverstein LLC
153 East 53rd Street, 56th Floor
New York, New York 10022
Facsimile: (212) 371-5500
telephone confirmation required at (212) 371-2000
Attention: David Robbins, Esq.

(j) Entire Agreement. This Agreement constitutes the full and entire understanding and agreement between the parties with regard to the subject matter hereof.

[Signature page follows]

IN WITNESS WHEREOF, the parties have executed this Registration Rights Agreement as of the date first written above.

ORASENSE LTD.

By: _____
Name: B. Lynne Parshall
Title: President

ISIS PHARMACEUTICALS, INC.

By: _____
Name: B. Lynne Parshall
Title: Executive Vice President

ELAN INTERNATIONAL SERVICES, LTD.

By: _____
Name: Kevin Insley
Title: President

EXHIBIT 10.7

***TEXT OMITTED AND FILED SEPARATELY
CONFIDENTIAL TREATMENT REQUESTED
UNDER 17 C.F.R. SECTIONS 200.80(b)(4),
200.83 AND 240.24b-2

LICENSE AGREEMENT

BY AND BETWEEN

ORASENSE LTD

A BERMUDA LIMITED COMPANY

AND

ELAN PHARMACEUTICAL TECHNOLOGIES,
A DIVISION OF ELAN CORPORATION, PLC

AN IRISH COMPANY

APRIL 20, 1999

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LICENSE AGREEMENT dated as of March 31, 1999 between Orasense Ltd., a Bermuda limited company, and Elan Pharmaceutical Technologies, a division of Elan Corporation, plc, an Irish limited company.

RECITALS:

A. Contemporaneously herewith, Elan and Isis (capitalized terms used herein are defined below) propose to enter into the Development Agreement for the purpose of recording the terms and conditions of a joint venture and of regulating their relationship with each other and certain aspects of the affairs of and their dealings with Orasense.

B. Elan is beneficially entitled to the use of certain know-how and certain patents that have been granted or are pending in relation to the development and production of various drug delivery technologies.

C. Orasense desires to enter into this Agreement with Elan so as to permit Orasense to utilize the Elan Intellectual Property in the research, development, manufacture, distribution and sale of the Products in the Field and in the Territory.

D. Elan, EIS and Isis entered into a letter agreement dated March 31, 1999 (the "Letter Agreement") pursuant to which they agreed to enter into definitive documents, including this Agreement, and the Isis License Agreement relating to Orasense's use of the Isis Intellectual Property.

NOW THEREFORE IT IS HEREBY AGREED AS FOLLOWS:

1. DEFINITIONS.

A. In this Agreement, the following definitions shall apply:

1.1. "Affiliate" shall mean, with respect to Elan or Isis, any corporation or entity other than Orasense (and entities controlled by it) controlling, controlled or under the common control of Elan or Isis, as the case may be, and, with respect to Orasense, any corporation or entity under control of Orasense. A corporation or non-corporate entity shall be regarded as in control of another corporation if it owns or directly or indirectly controls at least fifty percent (50%) of the voting stock of the other corporation or (a) in the absence of the ownership of at least fifty percent (50%) of the voting stock of a corporation or (b) in the case of a non-corporate entity, the power to direct or cause the direction of the management and policies of such corporation or non-corporate entity, as applicable.

1.2. "Agreement" shall mean this agreement (which expression shall be deemed to include the Recitals and the Schedules hereto);

1.3. "cGCP", "cGLP" and "cGMP" shall mean current Good Clinical Practices, current Good Laboratory Practices and current Good Manufacturing Practices respectively;

1.4. "Commercialization" shall mean the manufacture, promotion, distribution, marketing and sale of the Products;

1.5. "Competitive Change of Control Event" shall mean that a Primary Technological Competitor of Elan acquires directly or indirectly voting stock or equivalent securities in Isis or Orasense representing [...***...] percent or more of the stock which carries entitlement to vote, or a Primary Technological Competitor of Elan acquires by all or substantially all of the business of Isis or Orasense to which the Transaction Documents relate, whether by merger, sale of stock, sale of assets or otherwise;

1.6. "Control" shall mean the ability to grant a license or sublicense as contemplated herein without violating the terms of any agreement with any third party;

1.7. "Cost of Living Increase" shall mean, with respect to any year of the Term, any increase in the Consumer Price Index published by the Bureau of Labor Statistics of the United States Department of Labor, All Urban Consumers, United States City Average, All Items (1982/84=100);

1.8. "Definitive Documents" shall have the same meaning as given to the term "Transaction Documents" in the Development Agreement;

1.9. "Development Agreement" shall mean the Joint Development and Operating Agreement of even date entered into among Isis, Elan, EIS and Orasense;

1.10. "Development Candidate" shall mean a [...***...] antisense inhibitor of TNF-(alpha), as more specifically detailed in Exhibit A hereto;

1.11. "Development Product" shall mean any product containing as an active ingredient the Development Candidate (or a Substituted Development Candidate) in an Oral formulation for humans;

1.12. "Effective Date" shall mean the date of execution and delivery of the Definitive Documents;

1.13. "EIS" shall mean Elan International Services, Ltd., a Bermuda limited company;

1.14. "Elan" shall mean Elan Pharmaceutical Technologies, a division of Elan Corporation, plc, a public limited company incorporated under the laws of Ireland, its, successors and permitted assigns;

1.15. "Elan Improvements" shall mean any improvements to the Elan Patents and Elan Know How developed by Elan (other than pursuant to the Research and Development Program). Subject to contractual restrictions, Elan Improvements shall be deemed part of and shall be included in the term "Elan Intellectual Property" and shall be deemed, immediately upon development by Elan, to be included in the license of the Elan Intellectual Property hereunder. If the inclusion of an Elan Improvement in the license of Elan Intellectual

Property is restricted or limited by a third party agreement, Elan shall use reasonable commercial efforts to exclude or where applicable minimize any such restriction or limitation;

1.16. "Elan Intellectual Property" shall mean the Elan Know-How, the Elan Patent Rights and/or the Elan Improvements. Examples of the Elan Intellectual Property existing as of the Effective Date include, but are not limited to, technology related to the modification of the solubility, intrinsic dissolution, stability and/or permeability of a drug or modification of the surface(s) of particles, pharmaceutical formulation excipient technology, formulation, scale-up and manufacturing know-how. Schedule 1 hereto shall contain, by way of illustration but not limitation, examples of Elan Intellectual Property. For the avoidance of doubt, Elan Intellectual Property shall consist of Oral drug delivery technology Controlled by Elan doing business as Elan Pharmaceutical Technologies and shall exclude (a) the Excluded Elan Technology, (b) inventions, patents and know-how Controlled by all other affiliates or subsidiaries of Elan, including, but not limited to the Elan Pharmaceuticals division which incorporates Athena Neurosciences, Inc., Carnrick Laboratories, Targon Corporation and Neurex Corporation and (c) inventions, patents and know-how that are subject to contractual obligations of Elan to third parties as of the Effective Date to the extent the licensing of such inventions, patents and know-how is restricted or limited;

1.17. "Elan Know-How" shall mean any and all rights Controlled by Elan as of the Effective Date to any discovery, invention (whether or not patentable), know-how, substances, data, techniques, processes, systems, formulations and designs relating to Oral drug delivery;

1.18. "Elan License" shall have the meaning set forth in Section 2.1 hereof;

1.19. "Elan Patents" shall mean any and all patents and patent applications Controlled by Elan, existing and/or pending as of the Effective Date or hereafter filed or obtained relating to Oral drug delivery technology Controlled by Elan on the Effective Date. Elan Patent Rights shall also include all extensions, continuations, continuations-in-part, divisionals, patents-of-additions, re-examinations, re-issues, supplementary protection certificates and foreign counterparts of such patents and patent applications and any patents issuing thereon and extensions of any patents licensed hereunder;

1.20. "Elan Program Technology" shall mean all Program Technology solely conceived or made by Elan and/or its agents;

1.21. "Elan Right of First Negotiation" shall have the meaning provided in Section 2.11 hereof;

1.22. "Elan Targeting Technology" shall mean drug targeting technology to target a drug to a [...***...] or into a [...***...] or into a [...***...];

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1.23. "Excluded Elan Technology" shall mean (i) Oral Delivery Devices and (ii) Elan Targeting Technology;

1.24. "FDA" shall mean the United States Food and Drug Administration or any successors or agency the approval of which is necessary to market a product in the United States of America;

1.25. "Field" shall mean the research, development and Commercialization of in an Oral Platform for delivery of Oligonucleotide Drugs;

1.26. "Full Time Equivalent Rate" shall mean, for the services proposed to be rendered by Elan, [...***...] United States dollars (US $[...***...]);

1.27. "Independent Third Party" shall mean any person other than Orasense, Isis, Elan or any of their respective Affiliates;

1.28. "In market" shall mean sales of Products whether by Orasense or its Affiliates, or where applicable by a sublicensee, to an Independent Third Party being a wholesaler, distributor, managed care organization, hospital, pharmacy and/or the like;

1.29. "Isis" shall mean Isis Pharmaceuticals, Inc., a Delaware corporation;

1.30. "Isis Intellectual Property" shall have the meaning set forth in the Isis License Agreement;

1.31. "Isis License" shall have the meaning set forth in the Isis License Agreement;

1.34. "Isis License Agreement" shall mean that certain license agreement, of even date herewith, entered into between Isis and Orasense;

1.35. "Isis Oligonucleotide" shall mean any Oligonucleotide Drug Controlled by Isis other than the Development Candidate;

1.36. "Isis Products" shall mean Products based upon Isis Oligonucleotides that are made, designed, or otherwise created by or on behalf of Isis or any of its Affiliates after the date hereof pursuant to the Project using the Orasense Technology and/or the Licensed Technologies;

1.37. "Isis Program Technology" shall mean all Program Technology solely conceived by Isis and/or its agents.

1.38. "Licensed Technologies" shall mean the Elan Intellectual Property and the Isis Intellectual Property;

1.39. "Licenses" shall mean the Elan License and the Isis License;

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1.40. "Lien" shall mean any and all liens, security interests, restrictions, claims, encumbrances or rights of third parties of every kind and nature;

1.41. "Management Committee" shall have the meaning given to such term in the Development Agreement;

1.42. "Marketing Authorization" shall mean the procurement of registrations and permits required by applicable government authorities in a country in the Territory for the marketing, sale, and distribution of a Product in such country;

1.43. "Net Sales" shall mean the amount billed, invoiced and/or received on sales of a Product sold by Orasense or its Affiliates or sublicensees to an Independent Third Party, less, to the extent included in such invoice price the total of: (1) ordinary and customary trade quantity or cash discounts and nonaffiliated brokers' or agents' commissions actually allowed, including government managed care and other contract rebates, pharmacy incentive programs, including chargebacks of pharmacy or hospital performance incentive programs or similar programs; (2) credits, rebates and returns (including, but not limited to, wholesaler and retailer returns); (3) freight, postage and duties paid for and separately identified on the invoice or other documentation maintained in the ordinary course of business, and (4) import, export and sales taxes, excise taxes, other consumption taxes, customs duties, tariffs and compulsory payments to governmental authorities actually paid and separately identified on the invoice or other documentation maintained in the ordinary course of business and based on sales or turnover or delivery of the Products. Net Sales shall also include the amount or fair market value of all other consideration received by Orasense or its Affiliates or sublicensees in respect of Products, whether such consideration is payment in kind, exchange or another form. If a Product is provided to an Independent Third Party by Orasense or its Affiliates or sublicensees without charge or provision of invoice and used by such Independent Third Party, then Orasense or its Affiliates or sublicensees shall be treated as having sold such Product to such Independent Third Party for an amount equal to the fair market value of such Product. Sales between or among Orasense and its respective Affiliates or authorized licensees shall be excluded from the computation of Net Sales. A "sale" of a Product is deemed to occur upon the earlier of invoicing, shipment or transfer of title in the Product to an Independent Third Party. For avoidance of doubt, Net Sales shall include royalties received by Orasense or its Affiliates from any Independent Third Party in respect of Products;

1.44. "Oligonucleotide Drug" shall mean any single stranded, [...***...] oligonucleotide including those [...***...] used as a human therapeutic and/or prophylactic compound containing between [...***...] nucleotides and/or nucleosides including oligonucleotide analogs which may include [...***...]. For purposes of this agreement, Oligonucleotide Drug shall specifically exclude oligonucleotides used in [...***...], oligonucleotides used as [...***...] an oligonucleotide,

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oligonucleotides used as [...***...] or oligonucleotides used as [...***...]. Oligonucleotide Drug shall also specifically exclude polymers in which the [...***...]but shall not exclude [...***...]. Should Isis develop [...***...] oligonucleotides or should Elan independently discover drug delivery technology it believes to be potentially applicable to [...***...] oligonucleotides, then the Participants shall discuss in good faith whether such oligonucleotides can be formulated for Oral delivery using the Oral Platform, and whether such formulation appears feasible without requiring a significant further investment in developing or enhancing the Oral Platform; if such formulation appears feasible, the Participants shall discuss in good faith the inclusion of such oligonucleotides as Oligonucleotide Drugs;

1.45. "Oral" shall mean administration by way of the mouth for the purpose of topical or systemic delivery by way of the alimentary canal;

1.46. "Oral Delivery Devices" shall mean devices for delivering an active agent orally such as those employing [...***...] technologies;

1.47. "Oral Platform" shall mean formulation and excipient systems and technologies including [...***...] and including the use of [...***...], which can be employed to develop dosage forms of Oligonucleotide Drugs, deliver said dosage forms to the alimentary canal and facilitate and promote the systemic and topical delivery of Oligonucleotide Drugs;

1.48. "Orasense" shall mean Orasense, Ltd., a Bermuda limited company;

1.49. "Orasense Program Technology" shall mean all Program Technology other than Elan Program Technology and Isis Program Technology;

1.50. "Orasense Technology" shall mean all Program Technology and all technology licensed or acquired by Orasense or developed by Orasense whether or not pursuant to the Research and Development Program, excluding, however, Isis Intellectual Property and Elan Intellectual Property;

1.51. "Participant" shall mean Elan or Isis, as the case may be. "Participants" shall mean both Elan and Isis;

1.52. "Parties" shall mean Elan and Orasense;

1.53. "Person" shall mean an individual, partnership, corporation, limited liability company, business trust, joint stock company, trust, unincorporated association, joint venture, or other entity of whatever nature;

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1.54. "Plan" shall mean the business plan and program of development agreed to by Elan and Isis within sixty (60) days of the date hereof, with respect to the research, development, prosecution and commercialization of the Products, which Plan shall be reviewed and mutually agreed to in writing by Elan and Isis on an annual basis;

1.54. "Primary Technological Competitor of Elan" shall mean those entities listed on Schedule 2A hereto.

1.55. "Project" shall mean all activity as undertaken by Elan, Isis and Orasense to develop the Products in accordance with the Plan;

1.56. "Product" shall mean any Oligonucleotide Drug under development or developed by or on behalf of Orasense in an Oral formulation for administration to humans;

1.59. "Program Technology" shall mean all technology developed by or on behalf of Orasense, whether by Elan, Isis, a third party or jointly by any combination thereof, pursuant to the Research and Development Program;

1.60. "Regulatory Authority" shall mean any regulatory authority outside the United States of America, the approval of which is necessary to market a Product;

1.61. "Research and Development Program" shall have the same meaning given to such term in the Development Agreement;

1.62. "Research Term" shall mean the period commencing on the Effective Date and continuing for a period of [...***...] thereafter, unless extended by the mutual written agreement of Elan and Isis; provided, however, that if a Participant shall be prevented by (i) events beyond the Participants' control, or (ii) by such Participant's delay or negligent act or omission, from performing its obligations under the Definitive Documents within said [...***...] period, then the other Participant at its option, may extend the duration of the Research Term by a term equal in length to the period during which the first Participant was unable to perform its obligations hereunder;

1.63. "Technological Competitor of Elan" shall mean any entity listed on Schedule 2B hereto, subject to amendment from time to time upon mutual written agreement of Orasense, Isis and Elan;

1.64. "Technological Competitor of Isis" shall have the meaning given to such term in the Isis License Agreement, as the same shall be amended from time to time in accordance with such agreement;

1.65. "Term" shall have the meaning given to it in Clause 12 below;

1.66. "Territory" shall mean all the countries of the world;

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1.67. "Third Party Oligonucleotide Drug" shall mean any Oligonucleotide Drug Controlled by an Independent Third Party, other than an Isis Oligonucleotide Drug;

1.68. "Third Party Product" shall mean Products based upon Third Party Oligonucleotide Drug that are made, designed, or otherwise created by or on behalf of an Independent Third Party after the date hereof pursuant to the Project using the Orasense Technology and/or the Licensed Technologies. For avoidance of doubt, any Product based upon an Oligonucleotide Drug jointly developed by an Independent Third Party and Isis other than pursuant of the Program shall be deemed to be an Isis Product;

1.69. "Trademark" shall mean the trademark(s) belonging to Elan as may be selected by Orasense or its permitted sub-licensees, with Elan's consent, for use in connection with the Products. By way of example, the Trademarks include, but are not limited to, [...***...].

1.70. "United States Dollar" and "US$" shall mean the lawful currency for the time being of the United States of America;

B. Interpretation. In this Agreement the following shall apply:

1.1 The singular includes the plural and vice versa, the masculine includes the feminine and vice versa.

1.2. Any reference to a Clause or Schedule shall, unless otherwise specifically provided, be to a Clause or Schedule of this Agreement.

1.3. The headings of this Agreement are for ease of reference only and shall not affect its construction or interpretation.

2. GRANT OF RIGHTS

2.1. Subject to the terms and conditions contained herein and, in consideration of the payments specified in Clause 6.1(i), Elan hereby grants to Orasense for the Term a non-exclusive license, including the limited right to grant sublicenses pursuant to Clause 2.6 hereof, of the Elan Intellectual Property within the Field for the Territory, solely to research, develop, manufacture, have manufactured, and Commercialize the Products in the Territory, subject to any contractual obligations of Elan to Independent Third Parties as of the Effective Date and, unless prohibited by the paragraph below titled Non Competition, contractual obligations to Independent Third Parties that Elan may enter into after the Effective Date (the "Elan License").

2.2. Elan hereby grants an option, to be exercised upon written notice to Elan by Orasense and payment of an option price of [...***...], to Elan patents and know-how related to Oral delivery systems held by Elan Transdermal Technologies, Inc. (formerly

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Sano Corporation) and Elan Pharmaceutical International Ltd. (but only to the extent such technology consists of NanoCrystal(TM) technology formerly held by NanoSystems, a division of the Eastman Kodak Company). Upon exercise of such option by Orasense, such technology, shall, subject to any contractual obligations to Independent Third Parties that Elan may have as of the date of exercise of the such option, and, unless prohibited by the paragraph below titled Non Competition, contractual obligations to Independent Third Parties that Elan may enter into after the exercise of such option, be deemed included within the Elan License, the Elan Intellectual Property, the Elan Patents, and the Elan Know-How, as appropriate, and subject to the provisions hereof with respect thereto.

2.3. In the event, as of the Effective Date, the Elan License granted to Orasense hereunder is restricted or limited by any contractual obligations of Elan to Independent Third Parties, then Elan shall use reasonable commercial efforts to exclude or, where applicable, to minimize any such restriction or limitation. Except as expressly provided herein, all proprietary rights and rights of ownership with respect to the Elan Intellectual Property shall at all times remain solely with Elan. Elan shall disclose to Orasense inventions made by or on behalf of Elan in connection with the performance of the Project, any patentable inventions and discoveries within the Elan Intellectual Property that relate to the Field and any patentable Elan Improvements developed by or on behalf of Elan.

2.4. To the extent royalty or other compensation obligations to Independent Third Parties that are payable with respect to Elan Intellectual Property would be triggered by a proposed use of Elan Intellectual Property in connection with the Project, Elan will inform Orasense and Isis of such royalty or compensation obligation. If Orasense decides to utilize such Elan Intellectual Property in connection with the Project, Orasense will be responsible for the payment of such royalty or other compensation obligations relating thereto.

2.5. Notwithstanding anything contained in this Agreement to the contrary, Elan shall have the right, and subject to the paragraph below titled Non-Competition, to fully exploit and grant licenses and sublicenses with respect to the Elan Intellectual Property. Elan's rights to exploit and grant licenses referred to in the immediately preceding sentence shall include the right to research, develop, manufacture, license or Commercialize products.

2.6. Orasense shall not be permitted to (a) encumber any of its rights under the Licenses or the Orasense Technology without the prior written consent of Elan; (b) assign or sublicense any of its rights under the licenses for the Licensed Technologies and the Orasense Technology without the prior written consent of Elan, which consent may be withheld in Elan's sole discretion. Any agreement between Orasense and any permitted third party for the development or exploitation of the Elan Intellectual Property shall require such third party to maintain the confidentiality of all information concerning the Elan Intellectual Property and shall provide that any Elan Improvements shall belong to Elan and shall permit an assignment of rights by Orasense to Elan in accordance with the terms of this Agreement. Orasense shall remain responsible for all acts and omissions of any sub-licensee, as if they were acts and omissions by Orasense. Rights of permitted third party sublicensees in and to the Elan Intellectual Property shall survive the termination of the license and sublicense

agreements granting said intellectual property rights to Orasense; and Orasense and Elan shall in good faith agree upon the form most advantageous to Elan in which the rights of the sublicensor under any such sublicenses are to be held (which form may include continuation of Orasense solely as the holder of such licenses or assignment of such rights to a third party or parties, including an assignment to Elan).

2.7. Orasense will use its reasonable commercial endeavours to exploit the Elan Intellectual Property, the Isis Intellectual Property and Orasense Technology in accordance with this Agreement, the Isis License Agreement and the Plan. Orasense shall employ diligent efforts to research, develop, register, and Commercialize the Products in the Territory. Orasense shall employ or have employed on its behalf a level of advertising, sales, marketing, and promotion efforts in each country in the Territory where Marketing Authorization for Product has been obtained which is: (i) commensurate with that used by other pharmaceutical manufacturers for products of similar market potential in that country in the Territory, and (ii) sufficient with respect to the potential for that country to fully exploit the market potential for the Product as depicted in the Plan and as determined by the Management Committee in accordance with the Development Agreement.

2.8. Orasense will be solely responsible for ensuring that it or its sublicensees manufacture and Commercialize the Products within each country of the Territory strictly in accordance with all the legal and regulatory requirements of each country of the Territory.

2.9. Upon the request of Orasense and with the consent of Elan, Elan shall grant to Orasense during the Term a non-exclusive royalty free license in the Territory, solely for use in connection with the sale of the Products, to use one or more Trademark, on the following terms:

2.9.1 Orasense shall as soon as it becomes aware of any infringement give to Elan in writing full particulars of any use or proposed use by any other person, firm or company of a trade name or trademark or promotional or advertising activity which may constitute infringement.

2.9.2 If Orasense becomes aware that any other person, firm or company alleges that such Trademark is invalid or that the use of such Trademark infringes any rights of another party or that the Trademark is otherwise attacked or attackable, Orasense shall immediately give to Elan full particulars in writing thereof and shall make no comment or admission to any third party in respect thereof.

2.9.3 Elan shall have the right to conduct all proceedings relating to such Trademark and shall in its sole discretion decide what action, if any, to take in respect of any infringement or alleged infringement of such Trademark or any other claim or counter-claim brought or threatened in respect of the use or registration of such Trademark. Any such proceedings shall be conducted at Elan's expense and for its own benefit.

2.9.4 Nothing contained in this Agreement shall grant to Orasense any right, title, or interest in or to such Trademark, whether or not specifically recognized or perfected under applicable laws, except for the non-exclusive license granted herein. At no time during or after the term of this Agreement shall Orasense challenge or assist others to challenge any such Trademark or the registration thereof or attempt to register any trademarks, marks, or trade names confusingly similar to any such trademark. All displays of any such Trademark that Orasense intends to adopt shall first be submitted to Elan for approval (which shall not be unreasonably withheld) of design, color, and other details, or shall be exact copies of those used by Elan. In addition, Orasense shall fully comply with all reasonable guidelines, if any, communicated by Elan concerning the use of any such Trademark as well as all rules and regulations of such use throughout the Territory.

2.9.5 The rights granted to Orasense under this Article 2.9 shall automatically terminate respect to a Product in a country in the Territory upon termination of Orasense's right to market such Product in any such country.

2.10. When packaged, and to the extent permitted by law, a product label shall include an acknowledgement that the Product is made under license from Elan. Such acknowledgement shall take into consideration regulatory requirements and Orasense's reasonable commercial requirements. Orasense shall wherever possible give due acknowledgement and recognition to Elan in all printed promotional and other material regarding the Product such as stating that the Product is under license from Elan and that the applicable Elan Intellectual Property has been applied to the Products. Orasense shall consult with and obtain the written approval of Elan as to the format and content of the promotional and other material insofar as it relates to a description of, or other reference to, the application of the Elan Intellectual Property, such approval not to be unreasonably withheld or delayed. The further consent of Elan shall not be required where the format and content of such materials is substantively similar as the materials previously furnished to and approved in writing by Elan.

2.11 Notwithstanding anything contained in this Agreement to the contrary, Elan shall have [...***...]. Such [...***...] shall be exercised

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as follows:

2.11.1 If Orasense intends to [...***...], then Orasense immediately shall notify Elan in writing that Elan may elect to [...***...] referred to in this Article 2.11. Elan shall indicate its desire to [...***...] pursuant to this Article 2.11 by delivering written notice to Orasense within forty-five (45) days of Elan's receipt of the written notification from Orasense to Elan. If Elan elects to [...***...], the Parties shall [...***...].

2.11.2 If, despite such good faith negotiations, Elan and Orasense do not [...***...] within [...***...] from the notification in writing by Orasense to Elan, then Orasense shall be free to [...***...], which [...***...], as the case may be.

2.12. Elan shall have the first option to manufacture the Development Product for Orasense and meet its requirements, and Orasense shall agree to utilize Elan as its sole supplier, subject to the customary terms and conditions contained in a supply agreement to be executed by the parties at the price set forth in Clause 6.1.2 hereof. If, despite good faith negotiations, Elan and Orasense do not reach agreement on the terms of such manufacturing agreement within [...***...] from the Parties' commencement of discussion of such terms, then Orasense shall be free to offer a third party (other than a Technological Competitor of Elan unless consented to by Elan which consent may be withheld for any reason, and otherwise subject to the terms and conditions of this Agreement) terms to manufacture the Development Product in the Territory, which terms when taken as a whole, are more favorable to Orasense than the principal terms of the last written proposal offered to Orasense by Elan, or by Orasense to Elan, as the case may be. Subject to the foregoing rights of Elan with respect to the Development Product, Orasense shall not be permitted to contract the manufacture or Commercialization of any Product without the prior written consent of Elan and Isis, which consent will not be unreasonably withheld or delayed; provided that such reasonableness standard, in the case of Elan, shall not be applicable in the case of a proposed sublicense to any Technological Competitor of Elan and in the case of Isis, shall not be applicable in the case of a proposed sublicense to any Technological Competitor of Isis.

3. IMPROVEMENTS AND AFTER ACQUIRED TECHNOLOGY

3.1 Elan Improvements shall be deemed, immediately upon development, to be

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included in the license of the Elan Intellectual Property granted to Orasense hereunder.

3.2 The Elan License specifically excludes any right to use Elan Improvements outside of the Field.

3.3 If the inclusion of an Elan Improvement in the license of Elan Intellectual Property granted to Orasense hereunder is restricted or limited by a third party agreement, then Elan shall use reasonable commercial efforts to exclude, or where applicable, to minimize any such restriction or limitation.

3.4 All rights, title, and interest to any Elan Improvements developed by Orasense, Isis or any third party shall be the property of Elan. Orasense, Isis and any such third party shall execute and deliver documents, and take such other actions as Elan may reasonably request, to effect or evidence such ownership.

3.5 If Elan acquires know-how or patent rights relating to the Field, or if Elan acquires or merges with an Independent Third Party that has know-how or patent rights relating to the Field, then Elan shall offer to license such know-how and patent rights to Orasense (subject to existing contractual obligations), on such terms as would be offered to an Independent Third Party negotiating in good faith on an arms-length basis, and if the Management Committee determines that Orasense should not acquire such license, then Elan shall be free to fully exploit such know-how and patent rights, and to grant to third parties licenses and sublicenses with respect thereto.

4. DEVELOPMENT OF PRODUCTS

4.1 During the Research Term, Orasense will diligently pursue the research and development of the Elan Intellectual Property, Isis Intellectual Property and Orasense Technology in accordance with the Research and Development Program. The objectives of this initial phase of the Research and Development Program will be (a) to develop the Oral Platform, and (b) to develop the Development Product.

4.2 Orasense will diligently pursue the research, development and Commercialization of the Development Product and other Products in accordance with the Plan, this Agreement, the Isis License Agreement and the Development Agreement.

5 REGULATORY APPROVALS

5.1 Orasense shall, or shall cause its sublicensees, at its or their sole cost file and shall use its reasonable best efforts to prosecute to approval or cause its sublicensees to prosecute to approval, the Marketing Authorizations for the Products in the Territory in accordance with the Plan. During any Marketing Authorization registration procedure, Orasense shall keep Elan promptly and fully advised of Orasense's registration activities, progress and procedures. Each Party shall inform the other Party and Isis of any dealings

such Party has with the FDA and any other Regulatory Authority. The Parties and Isis shall collaborate in relation to obtaining any approval of the FDA or Regulatory Authority for final approved labeling.

5.2 Subject to agreement to the contrary, any and all Marketing Authorizations filed hereunder for Products shall, to the extent owned by Orasense, remain the property of Orasense, provided that Orasense shall allow Elan access thereto to enable Elan to fulfill its obligations and exercise its rights under this Agreement and the Development Agreement. Orasense shall maintain or cause its sublicensees to maintain such Marketing Authorizations at its or their own cost.

5.3 Orasense shall indemnify and hold harmless Elan, its agents and employees from and against all claims, damages, losses, liabilities and expenses to which Elan, its agents, and employees may become subject related to or arising out of Orasense's bad faith, negligence or intentional misconduct in connection with the filing or maintenance of the Marketing Authorizations.

6 FINANCIAL PROVISIONS.

6.1 In consideration of the license to the Elan Patents, Orasense shall pay to Elan the following amounts:

6.1.1 Up Front License Fee Payment. [...***...]United States Dollars (US$[...***...]), simultaneously with the execution and delivery of this Agreement by both Parties; and

6.1.2 Development Product Fees and Royalties. Payments to Elan with respect to services rendered in connection with the Development Product shall be paid as provided below and net proceeds derived by Orasense from the Development Product shall be allocated as additional royalties in proportion to [...***...], as more particularly or as otherwise set forth below.

(a) Development Work - Research and development work performed during the Research Term pursuant to the Research and Development Program regarding the Oral Platform and the Development Candidate contracted by Orasense to Elan shall be payable by Orasense to Elan based on fully burdened actual costs at Elan's Full Time Equivalent Rate, with annual Cost of Living Increases. In the event Elan is required to perform additional research and development work beyond that contemplated during the Research Term (without any extensions thereto), Orasense shall pay to Elan [...***...].

(b) Milestone Payments - If any Independent Third Party shall make milestone payments (e.g., for NDA filing, approvals, etc.) to Orasense, Orasense shall pay to Elan and Isis an additional royalty in the amount of [...***...].

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(c) Royalties payable to Elan Upon Sales of the Development Product - Elan shall receive royalties of [...***...] of the In-market Net Sales of Development Products by Orasense or its sublicensees. Notwithstanding the foregoing, in no event shall royalties payable to Elan with respect to sales of the Development Product [...***...].

(d) Manufacturing Charges. In the event Elan exercises its option to manufacture the Development Products for Orasense, Orasense shall pay Elan a price equal to [...***...] for the manufacture of Development Products.

6.1.3 Isis Product Fees and Royalties. Payments to Elan with respect to services rendered in connection with Isis Products shall be paid as provided below and net proceeds derived by Orasense from Isis Products shall be allocated as additional royalties in proportion to [...***...], as more particularly or as otherwise set forth below.

(a) Development Work - Research and development work performed by Elan for Orasense related to Isis Products shall be payable to Elan by Orasense at [...***...].

(b) Milestone Payments - If any Independent Third party shall make milestone payments (e.g., for NDA filing, approvals, etc.) to Isis with respect to an Isis Product, then [...***...] of such milestone payment shall be paid to Orasense by Isis as an additional royalty and Orasense shall pay a royalty [...***...] to Elan; provided however, that development related milestone payments with respect to any Isis Product shall not be payable by Isis to Orasense or by Orasense to Elan except to the extent such payments exceed [...***...] with respect to such Isis Product (or, in the event the milestone is intended to be applied towards future work to be performed by Isis, in excess of [...***...].

(c) Elan Royalty Payments. Orasense shall pay to Elan a royalty of [...***...] of In-market Net Sales of any Isis Products. Any marketing and/or development agreement between Orasense and Isis with respect to Isis Products shall provide for a royalty payment to Orasense of [...***...] of In-market Net Sales of the Isis Products. At such time as royalty payments by Isis to Orasense shall equal [...***...] for the particular Isis Product subject to any such agreement, the royalty payable by Isis to Orasense with respect to In-market Net Sales of the Isis Product shall be [...***...] and the royalty payable by

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Orasense to Elan with respect to such Isis Product shall be [...***...] of In-market Net Sales of such Isis Product.

(d) Manufacturing Charges. In the event Elan agrees to provide manufacturing services for Products based on Isis Products (other than the Development Candidate), Elan shall be paid a price equal to [...***...].

6.1.4 Third Party Products. Payments to Elan with respect to services rendered in connection with Third Party Products shall be paid as provided below and net proceeds derived by Orasense from Third Party Products shall be allocated as additional royalties with [...***...] of such amount being paid to Elan and [...***...] to Isis, as more particularly or as otherwise set forth below set forth below; provided, however, that in the event [...***...] significantly contributes to the research and development work related to a Third Party Product, the Participants shall negotiate in good faith an appropriate adjustment to the allocation of such additional royalties to reflect their relative contributions to the development of such Third Party Product.

(a) Development Work - Research and development work performed by Elan for Orasense related to Third Party Products shall be payable to Elan at [...***...]. Orasense shall pay to Elan an additional fee equal to [...***...] of all amounts paid by an Independent Third Parties to Orasense for development work to the extent the amounts paid to Orasense for such work exceeds any charges by Elan and Isis; with the remaining [...***...] of such excess amount being payable to Isis.

(b) Royalty Payments to Elan - In the event Orasense contracts development work to Elan for any Third Party Product, Orasense shall pay Elan, a royalty equal to [...***...] of the royalties it receives with respect to such Product (with the remaining [...***...] of such royalties payable to Isis) until such time as Elan has been paid a sum equal to [...***...]. Thereafter, [...***...] of the royalties received by Orasense with respect to such Third Party Product shall be paid to Elan (with the balance payable to Isis).

(c) Milestone Payments - If any Independent Third Party shall make milestone payments (e.g., for NDA filing, approvals, etc.) to Orasense, then [...***...] of such milestone payment shall be paid by Orasense to Elan as an additional royalty and [...***...] shall be paid by Orasense to Isis as an additional royalty to Isis.

(d) Manufacturing and Supply of Products - In the event Orasense contracts with Elan to manufacture Third Party Products, Elan shall charge Orasense a price equal to [...***...].

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Orasense shall pay to Elan an additional fee equal to [...***...] of all amounts paid by an Independent Third Parties to Orasense for the manufacture of such Third Party Products to the extent such amounts exceed the amount previously charged by Elan; with the remaining [...***...] of such excess amount being payable to Isis.

6.2 Payment of royalties pursuant to Clauses 6.1.2-6.1.4, if any, shall be made quarterly in arrears within forty-five (45) days after the expiry of the calendar quarter. The method of payment shall be by wire transfer to an account specified by Elan and shall be nonrefundable to Orasense. Each payment made to Elan shall be accompanied by a true accounting of all Products sold by Orasense, its Affiliates and its permitted sublicensees, if any, during such quarter. Such accounting shall show, on a country-by-country and Product-by-Product basis, Net Sales or royalties received by Orasense (and the calculation thereof) and each calculation of royalties with respect thereto, including the calculation of all adjustments and currency conversions.

6.3 Orasense shall maintain and keep clear, detailed, complete, accurate and separate records for a period of three (3) years following the completion of such records so: (i) as to enable any royalties which shall have accrued hereunder to be determined; and (ii) that any deductions made in arriving at the Net Sales can be determined.

6.4 All payments due hereunder shall be made in United States Dollars. Payments due on Net Sales of any Product or royalties received by Orasense with respect to any Product for each calendar quarter made in a currency other than United States Dollars shall first be calculated in the foreign currency and then converted to United States Dollars on the basis of the average exchange rate in effect for such quarter for the purchase of United States Dollars with such foreign currency quoted in the Wall Street Journal (or comparable publication if not quoted in the Wall Street Journal) with respect to the currency of the country of origin of such payment, determined by averaging the rates so quoted on each business day of such quarter.

6.5 If Orasense claims in good faith that one or more of its devices, products, parts or components thereof, compounds and/or drug products does not utilize, incorporate, apply or is not based on the Elan Intellectual Property, the Isis Intellectual Property and/or Orasense Technology, then Orasense shall immediately notify Elan in writing and establish same to Elan's reasonable satisfaction.

6.6 If, at any time, legal restrictions in the Territory prevent the prompt payment when due of royalties or any portion thereof, the Parties shall meet to discuss suitable and reasonable alternative methods of reimbursing Elan the amount of such royalties. In the event that Orasense is prevented from making any payment under this Agreement by virtue of the statutes, laws, codes or government regulations of the country from which the payment is to be made, then such payments may be paid by depositing them in the currency in which they accrue to Elan's account in a bank acceptable to Elan in the country the currency of which is involved or as otherwise agreed by the Parties.

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6.7 Elan and Orasense agree to co-operate in all respects necessary to take advantage of any double taxation agreements or similar agreements as may, from time to time, be available.

6.8 Any taxes payable by Elan on any payment made to Elan pursuant to this Agreement shall be for the account of Elan. If so required by applicable law, any payment made pursuant to this Agreement shall be made by Orasense after deduction of the appropriate withholding tax, in which event the Parties shall co-operate to obtain the appropriate tax clearance as soon as is practicable. On receipt of such clearance, Orasense shall forthwith procure that the amount so withheld is paid to Elan.

6.9 Orasense shall, not more than once in each calendar year, permit Elan or its duly authorized representatives upon reasonable notice and at any reasonable time during normal business hours to have access to inspect and audit the accounts and records of Orasense and any other book, record, voucher, receipt or invoice relating to the calculation of the royalty payments on Net Sales submitted to Elan. Any such inspection of Orasense's records shall be at the expense of Elan, except that if any such inspection reveals a deficiency in the amount of the royalty actually paid to Elan hereunder in any calendar quarter of five percent (5%) or more of the amount of any royalty actually due to Elan hereunder, then the expense of such inspection shall be borne solely by Orasense. Any amount of deficiency shall be paid promptly to Elan by Orasense. If such inspection reveals a surplus in the amount of royalties actually paid to Elan by Orasense, Elan shall reimburse Orasense the surplus within fifteen (15) days after determination.

6.10 In the event of any unresolved dispute regarding any alleged deficiency or overpayment of royalty payments hereunder, the matter will be subject to resolution in accordance with Clause 24.9 of the Development Agreement, which is incorporated by reference and shall for such purposes survive termination of the Development Agreement.

7 CONFIDENTIAL INFORMATION

7.1 The Parties acknowledge that it may be necessary, from time to time, to disclose to each other confidential and proprietary information, including without limitation, inventions, works of authorship, trade secrets, specifications, designs, data, know-how and other information relating to the Field, the Products, Elan Intellectual Property, Isis Intellectual Property or the Orasense Technology, as the case may be, processes, services and business of the disclosing Party. The foregoing shall be referred to collectively as "Confidential Information". Any Confidential Information revealed by a Party to another Party shall be used by the receiving Party exclusively for the purposes of fulfilling the receiving Party's obligations under this Agreement and the Development Agreement and for no other purpose.

7.2 Each Party agrees to disclose Confidential Information of another Party only to those employees, representatives and agents requiring knowledge thereof in connection with their duties directly related to the fulfilling of the Party's obligations under this

Agreement. Each Party further agrees to inform all such employees, representatives and agents of the terms and provisions of this Agreement and their duties hereunder and to obtain their consent hereto as a condition of receiving Confidential Information. Each Party agrees that it will exercise the same degree of care, but in no event less than a reasonable degree, and protection to preserve the proprietary and confidential nature of the Confidential Information disclosed by a Party, as the receiving Party would exercise to preserve its own proprietary and confidential information. Each Party agrees that it will, upon request of a Party, return all documents and any copies thereof containing Confidential Information belonging to or disclosed by, such Party.

7.3 Notwithstanding the above, each Party may use or disclose Confidential Information disclosed to it by another party to the extent such use or disclosure is reasonably necessary in filing or prosecuting patent applications, prosecuting or defending litigation, complying with patent applications, complying with applicable governmental regulations or otherwise submitting information to tax or other governmental authorities, conducting clinical trials, or making a permitted sub-license or otherwise exercising its rights hereunder, provided that if a Party is required to make any such disclosure of the other Party's Confidential Information, other than pursuant to a confidentiality agreement, such Party shall inform the recipient of the terms and provisions of this Agreement and their duties hereunder and to obtain their consent hereto as a condition of receiving Confidential Information.

7.4 Any breach of this Clause 7 by any of the Persons informed by one of the Parties is considered a breach by the Party itself.

7.5 Confidential Information shall not be deemed to include:

(i) information that is generally available to the public;

(ii) information which is made public by the disclosing Party;

(iii) information which is independently developed by a Party as evidenced by such Party's written records, without the aid, application or use of the disclosing Party's Confidential Information;

(iv) information that is published or otherwise becomes part of the public domain without any disclosure by a Party, or on the part of a Party's directors, officers, agents, representatives or employees;

(v) information that becomes available to a Party on a non-confidential basis, whether directly or indirectly, from a source other than a Party, which source did not acquire this information on a confidential basis;

(vi) information which the receiving Party is required to disclose pursuant to:

(A) a valid order of a court or other governmental body or any political subdivision thereof or otherwise required by law; or

(B) any other requirement of law;

provided that if the receiving Party becomes legally required to disclose any Confidential Information, the receiving Party shall give the disclosing Party prompt notice of such fact so that the disclosing Party may obtain a protective order or other appropriate remedy concerning any such disclosure. The receiving Party shall fully cooperate with the disclosing Party in connection with the disclosing Party's efforts to obtain any such order or other remedy. If any such order or other remedy does not fully preclude disclosure, the receiving Party shall make such disclosure only to the extent that such disclosure is legally required;

(v) information which was already in the possession of the receiving Party at the time of receiving such information, as evidenced by its written records, provided such information was not previously provided to the receiving Party from a source which was under an obligation to keep such information confidential; or

(vi) information that is the subject of a written permission to disclose, without restriction or limitation, by the disclosing Party.

7.6 The provisions relating to confidentiality in this Clause 7 shall remain in effect during the term of this Agreement, and for a period of seven (7) years following the expiration or earlier termination of this Agreement but shall not apply to any information which a Party is required to file or otherwise disclose in accordance with requirements which are legally binding on it.

7.7 The Parties agree that the obligations of this Clause 7 are necessary and reasonable in order to protect the Parties' respective businesses, and each Party expressly agrees that monetary damages would be inadequate to compensate a Party for any breach by the other Party of its covenants and agreements set forth herein. Accordingly, the Parties agree and acknowledge that any such violation or threatened violation will cause irreparable injury to a Party and that, in addition to any other remedies that may be available, in law and equity or otherwise, any Party shall be entitled to obtain injunctive relief against the threatened breach of the provisions of this Clause 7, or a continuation of any such breach by the other Party, specific performance and other equitable relief to redress such breach together with its damages and reasonable counsel fees and expenses to enforce its rights hereunder, without the necessity of proving actual or express damages.

8 WARRANTIES/INDEMNITIES

8.1 Elan represents and warrants to Orasense that:

(a) Elan is a corporation duly organized under the laws of its jurisdiction of organization and has all the requisite corporate power and authority to own

and lease its respective properties, to carry on its respective business as presently conducted and as proposed to be conducted and to carry out the transactions contemplated hereby;

(b) Elan has full corporate power and authority enter into this Agreement and to perform its obligations hereunder, which have been duly authorized by all requisite corporate action of Elan. This Agreement is the valid and binding obligation of Elan, enforceable against it in accordance with its terms, except as limited by applicable bankruptcy, insolvency, reorganization, moratorium and other laws of general application affecting the enforcement of creditors' rights generally, and by general equity principles and limitations on the availability of equitable relief, including specific performance;

(c) The execution, delivery and performance by Elan of this Agreement will not: (i) violate any provision of applicable law, statute, rule or regulation known by and applicable to Elan or any ruling, writ, injunction, order, judgment or decree of any court, arbitrator, administrative agency or other governmental body applicable to Elan or any of its properties or assets; or (ii) conflict with or result in any breach of any of the terms, conditions or provisions of, or constitute (with notice or lapse of time or both) a default (or give rise to any right of termination, cancellation or acceleration) under the charter or organizational documents of Elan to which Elan is a party, except where such violation, conflict or breach would not, individually or in the aggregate, have an adverse material effect on the business, assets, liabilities (contingent or otherwise), operations, condition (financial or otherwise), or prospects of Elan;

(d) To Elan's best knowledge, except as set forth on Schedule 3 hereto, (i) Elan has the right to grant the Elan License and any other rights granted herein, (ii) Schedule 1 contains primary examples of the Elan Intellectual Property existing as of the Effective Date, which listing is not necessarily exhaustive, (iii) there are no agreements between Elan and any third parties that conflict with the Elan License which would have a material adverse effect on the ability of Orasense to conduct its business as presently proposed to be conducted, (iv) Elan is the owner or licensee of all rights, title and interest in the Elan Intellectual Property; (v) Elan has no knowledge of any pending or threatened action, suit, proceeding or claim by others challenging Elan's rights in or to such Elan Intellectual Property as related to the Field, which would have a material adverse effect on the ability of Orasense to conduct its business as presently proposed to be conducted, and (vi) the Elan Intellectual Property constitutes all material intellectual property in Elan's Control reasonably applicable to the Project as it relates to Oral controlled release in the Field.

8.2 Orasense represents and warrants to Elan the following:

(a) Orasense is duly and validly existing in good standing in the jurisdiction of its incorporation and each other jurisdiction in which the conduct of its business requires such qualification (except where such failure to so qualify shall not have a material adverse affect on the business and assets of Orasense), and Orasense is in compliance with all applicable laws, rules, regulations or orders relating to its business and assets;

(b) Orasense has full corporate authority to execute and deliver this Agreement and to consummate the transactions contemplated hereby; this Agreement has been duly executed and delivered and constitutes the legal and valid obligations of Orasense and is enforceable against Orasense in accordance with its terms; and the execution, delivery and performance of this Agreement and the transactions contemplated hereby will not violate or result in a default under or creation of lien or encumbrance under Orasense's certificate of incorporation, by-laws or other organic documents, any material agreement or instrument binding upon or affecting Orasense, or its properties or assets or any applicable laws, rules, regulations or orders affecting Orasense or its properties or assets;

(c) Orasense is not in default of its charter or by-laws, any applicable laws or regulations or any material contract or agreement binding upon or affecting it or its properties or assets and the execution, delivery and performance of this Agreement and the transactions contemplated hereby will not result in any such violation;

(d) Orasense represents and warrants to Elan that the execution of this Agreement by Orasense and the full performance and enjoyment of the rights of Orasense under this Agreement will not breach the terms and conditions of any license, contract, understanding or agreement, whether express, implied, written or oral between Orasense and any third party.

8.3 Orasense represents and warrants to and covenants with Elan that it has the sole, exclusive and unencumbered right to grant the licenses and rights herein granted to Elan and that it has not granted and will not grant any option, license, right or interest in or to the Elan Intellectual Property, the Orasense Technology, or other property to any third party which would conflict with the rights granted by this Agreement and the Definitive Documents.

8.4 Orasense represents and warrants to and covenants and agrees with Elan that the Products shall be developed, manufactured, transported, stored, handled, packaged, marketed, promoted, distributed, offered for sale and sold in accordance with all regulations and requirements of the FDA and foreign regulatory authorities including, without limitation, cGCP, cGLP, cGMP regulations. The Products shall not be adulterated or misbranded as defined by the Federal Food, Drug and Cosmetic Act (or applicable foreign law) and shall not be a product which would violate any section of such Act if introduced in interstate commerce.

8.5 Orasense represents and warrants to Elan that it is fully cognizant of all applicable statutes, ordinances and regulations of the United States of America and countries in the Territory with respect to the manufacture of the Products including, but not limited to, the U.S. Federal Food, Drug and Cosmetic Act and regulations thereunder and similar statutes in countries outside of the United States. Orasense shall manufacture or procure the manufacture of the Products in conformity with the Marketing Authorizations and in a manner which fully complies with all United States of America and foreign statutes,

ordinances, regulations and practices.

8.6 In addition to any other indemnifications provided for herein, Elan shall indemnify and hold harmless Orasense and its Affiliates and their respective employees, agents, partners, officers and directors from and against any claims, losses, liabilities or damages (including reasonable attorney's fees and expenses) incurred or sustained by Orasense arising out of or in connection with any (a) breach of any representation, covenant, warranty or obligation by Elan hereunder, or (b) any act or omission on the part of Elan or any of its agents or employees in the performance of this Agreement.

8.7 In addition to any other indemnifications provided for herein, Orasense shall indemnify and hold harmless Elan and its Affiliates and their respective employees, agents, partners, officers and directors from and against any claims, losses, liabilities or damages (including reasonable attorney's fees and expenses) incurred or sustained by Elan arising out of or in connection with any (a) breach of any representation, covenant, warranty or obligation by Orasense hereunder, or (b) any act or omission on the part of Orasense or any of its agents or employees in the performance of this Agreement.

8.8 The Party seeking an indemnity shall:

8.8.1 fully and promptly notify the other Party of any claim or proceeding, or threatened claim or proceeding;

8.8.2 permit the indemnifying Party to take full care and control of such claim or proceeding;

8.8.3 cooperate in the investigation and defense of such claim or proceeding;

8.8.4 not compromise or otherwise settle any such claim or proceeding without the prior written consent of the other Party, which consent shall not be unreasonably withheld, conditioned or delayed; and

8.8.5 take all reasonable steps to mitigate any loss or liability in respect of any such claim or proceeding.

8.9 NOTWITHSTANDING ANYTHING TO THE CONTRARY IN THIS AGREEMENT, NEITHER ELAN NOR ORASENSE SHALL BE LIABLE TO THE OTHER PARTY, OTHER BY REASON OF ANY REPRESENTATION OR WARRANTY, CONDITION OR OTHER TERM OR ANY DUTY OF COMMON LAW, OR UNDER THE EXPRESS TERMS OF THIS AGREEMENT, OR FOR ANY CONSEQUENTIAL OR INCIDENTAL LOSS OR DAMAGE (WHETHER FOR LOSS OF PROFIT OR OTHERWISE) AND WHETHER OCCASIONED BY THE APPLICABLE PARTY'S NEGLIGENCE OR OF ITS EMPLOYEES OR AGENTS OR OTHERWISE

8.10 EXCEPT AS SET FORTH IN THIS CLAUSE 8, ELAN IS GRANTING THE

ELAN LICENSE HEREUNDER ON AN "AS IS" BASIS WITHOUT RECOURSE, REPRESENTATION OR WARRANTY WHETHER EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR INFRINGEMENT OF THIRD PARTY RIGHTS, AND ALL SUCH WARRANTIES ARE EXPRESSLY DISCLAIMED.

9. INTELLECTUAL PROPERTY OWNERSHIP RIGHTS

9.1 Subject to the terms and conditions of this Agreement, including, without limitation Section 11 below, Orasense shall own the legal and equitable title to the Orasense Technology.

9.2 Elan shall own the legal and equitable title to the Elan Intellectual Property, including without limitation, Elan Improvements.

9.3 Orasense shall permanently mark or otherwise use reasonable efforts to cause any third party to permanently mark all Products and/or the packaging therefor with such license or patent notices to comply with the laws of the country of sale or otherwise to generally communicate the existence of any Elan Patents for the countries of the Territory and in such manner as Elan may reasonably request in writing prior to the sale or commercial use thereof.

9.4 Elan, at its expense, shall make a good faith effort (i) to secure the grant of any material patent applications within the Elan Patents that relate to the Field; (ii) to file and prosecute patent applications on material patentable inventions and discoveries within the Elan Improvements that relate to the Field; (iii) to defend all such applications against third party oppositions; and (iv) to maintain in force any material issued letters patent within the Elan Patents that relate to the Field (including any letters patent that may issue covering any such Elan Improvements that relate to the Field). Elan shall have the right in its discretion to control such filing, prosecution, defense and maintenance provided that Orasense and Isis at their request shall be provided with copies of all documents relating to such filing, prosecution, defense and maintenance in sufficient time to review such documents and comment thereon prior to filing.

9.5 In the event that Elan informs the Orasense and Isis that it does not intend to file patent applications on patentable inventions and discoveries within the Elan Intellectual Property that relate to the Field in one or more countries in the Territory or fails to file such an application within a reasonable period of time, Orasense shall have the option at its expense to file and prosecute such patent application(s) in the joint names of Orasense and Elan. Upon written request from Orasense, Elan shall execute all documents, forms and declarations and to do all things as shall be reasonably necessary to enable Orasense to exercise such option.

9.6 Orasense, Isis and Elan shall promptly inform each other in writing of any alleged infringement of any patents within the Elan Patents or any alleged misappropriation

of trade secrets within the Elan Intellectual Property by a third party of which it becomes aware and provide the others with any available evidence of such infringement or misappropriation insofar as such infringements or misappropriation relate solely to the Field.

9.7 Orasense shall have the right to prosecute at its own expense and for its own benefit any infringements of the Elan Patents or misappropriation of the Elan Intellectual Property, insofar as such infringements or misappropriation relate solely to the Field. In the event that Orasense takes such action, Orasense shall do so at its own cost and expense. At Orasense's request, Elan shall cooperate with such action. Any recovery remaining after the deduction by Orasense of the reasonable expenses (including attorney's fees and expenses) incurred in relation to such infringement proceeding [...***...]. Should Orasense decide not to pursue such infringers, within a reasonable period but in any event within twenty (20) days after receiving written notice of such alleged infringement or misappropriation Elan may in its discretion initiate such proceedings in its own name, at its expense and for its own benefit, and at Elan's request, Orasense shall cooperate with such action. Alternatively, the Participants may agree to institute such proceedings in their joint names and shall reach agreement as to the proportion in which they shall share the proceeds of any such proceedings, and the expense of any costs not recovered, or the costs or damages payable to the third party. If the infringement of the Elan Patents affects both the Field as well as other products being developed or commercialized by Elan or its commercial partners outside the Field, Orasense and Elan shall endeavor to agree as to the manner in which the proceedings should be instituted and as to the proportion in which they shall share the proceeds of any such proceedings, and the expense of any costs not recovered, or the costs or damages payable to the third party.

9.8 Orasense shall indemnify, defend and hold harmless Elan, against all actions, losses, claims, demands, damages, costs and liabilities (including reasonable attorneys fees) relating directly or indirectly to all such claims or proceedings referred to herein, provided that Elan, shall not acknowledge to the third party or to any other person the validity of any claims of such a third party, and shall not compromise or settle any claim or proceedings relating thereto without the prior written consent to Orasense, not to be unreasonably withheld or delayed. At its option, Elan or Isis, as the case may be, may elect to take over the conduct of such proceedings from Orasense provided that Orasense's indemnification obligations shall continue; the costs of defending such claim shall be borne by Elan or Isis, as the case may be and such Participant shall not compromise or settle any such claim or proceeding without the prior written consent of Orasense, such consent not to be unreasonably withheld or delayed.

10. RIGHTS EXPLOITATION OUTSIDE THE FIELD

10.1 Licenses to Elan Program Technology. Orasense hereby grants to Elan a perpetual, exclusive, royalty free and sublicensable license to Elan Program Technology outside of the Field.

10.2 Licenses for Orasense Program Technology Outside the Field. Orasense

*CONFIDENTIAL TREATMENT REQUESTED

hereby grants to Elan a perpetual exclusive license for the use of Orasense Program Technology in all fields other than (i) the Field or (ii) in connection with Isis proprietary drug products. The terms of such license for the use of Orasense Program Technology shall be decided by the unanimous decision of the Management Committee on such terms and conditions as the Management Committee shall approve after good faith negotiations with Elan.

11. NON-COMPETITION

11.1. During the Research Term (and any extension thereto), Elan shall not develop or Commercialize, or assist in the development or Commercialization of Oligonucleotide Drugs in the Field or develop or Commercialize, or assist in the development or Commercialization of an Oral Platform for systemic and topical delivery of Oligonucleotide Drugs, except (a) for or on behalf of Orasense, or (b) with the prior written, unanimous consent of the Management Committee. In no event, however, shall the foregoing non-competition restrictions apply to the entities listed in Section 1.16(b) above. Nothing contained herein shall be construed as (i) limiting the activities of an existing third party licensee of Elan from developing Oligonucleotide Drugs utilizing Elan Intellectual Property to the extent such rights have been previously granted by Elan, provided Elan does not provide any active support to any such activities in excess of its existing contractual obligations or (ii) prohibiting Elan from licensing Elan Intellectual Property to an Independent Third Party or limiting the activities of any such future Independent Third Party licensee of Elan from developing Oligonucleotide Drugs utilizing Elan Intellectual Property; provided that the primary purpose of any such license is not the development of an Oral Platform for Oligonucleotide Drugs and Elan does not provide any active support to any such activities.

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12. TERM AND TERMINATION OF AGREEMENT

12.1. The term of this Agreement and the term of the Licenses granted hereunder with respect to a Product utilizing or based on the Licensed Technologies shall commence as of the Effective Date and continue, on a Product-by-Product basis and country by country basis, for the life of the patent rights upon which such Product is based on or utilizes in such country (the "Term"); provided, however, that all royalty and fee obligations contained herein shall survive for the greater of (i) the Term or (ii) 15 years from the first commercial sale of such Product.

12.2. Nothing contained herein shall obligate or restrict any party from utilizing public, non-proprietary information which is not subject to the protection of applicable patent laws.

12.3. If either party breaches any material provision of this Agreement and if such breach is (i) not capable of being cured or (ii) is capable of being cured but is not corrected within sixty (60) days after the non-breaching party gives written notice of the breach to the

breaching party, the non-breaching party may terminate this Agreement immediately by giving notice of the termination, effective on the date of the notice, provided, however, that (x) if any such curable breach is not capable of being cured within such sixty (60) day period, so long as the breaching party commences to cure the breach promptly after receiving notice of the breach from the non-breaching party and thereafter diligently prosecutes the cure to completion as soon as is practicable, the non-breaching Party may not terminate this Agreement so long as the breaching party is acting in good faith to rectify such breach or (y) the default involves a good faith dispute regarding the amount of any required payment, provided any undisputed amount is paid, such default shall be stayed and the remainder may be withheld for a reasonable period during which a good faith resolution of the amount owed is being pursued.

12.4. In the event that a Competitive Change of Control Event shall occur, at the sole option of Elan and upon written notice to Isis and Orasense, the Elan License shall be immediately terminated. Upon written notice from Isis to Elan of a proposed Competitive Change of Control Event or the occurrence of a Competitive Change of Control Event, Elan shall have thirty (30) days from such notice to Isis to provide written notice to Isis as to whether it intends to terminate the Elan License. In the event Elan does not provide written notice to Isis during such thirty (30) day period of its intention to terminate the Elan License, such termination right shall be deemed waived with respect to such occurrence.

12.5. In the event that the Isis License Agreement shall be terminated, at the sole option of Elan and upon written notice to Isis and Orasense, the Elan License shall be immediately terminated.

12.6. Upon the occurrence of an Event of Bankruptcy with respect to Orasense or Elan, the other Party may, upon written notice to Isis and the Party with respect to which such Event of Bankruptcy has occurred, immediately terminate the Elan License. As used in this Clause 12.6, the term "Event of Bankruptcy" relating to either Orasense or Elan shall mean:

12.6.1. the appointment of a liquidator, receiver, administrator, examiner, trustee or similar officer of either Party of it or over all or a substantial part of its assets under the law of any applicable jurisdiction, including without limit, Bermuda, the United States of America or Ireland; or

12.6.2 an application or petition for bankruptcy, corporate re-organization, composition, administration, examination, arrangement or any other procedure similar to any of the foregoing under the law of any applicable jurisdiction, including without limit, Bermuda, the United States of America or Ireland (other than as part of a bona fide restructuring or reorganization), is filed, and is not discharged within forty-five (45) days, or if either Party applies for or consents to the appointment of a receiver, administrator, examiner or similar officer of it or of all or a material part of its assets, rights or revenues or the assets and/or the business of either Party are for any reason seized, confiscated or condemned.

12.7. Upon exercise of those rights of termination as specified in Clause 12.1 to Clause 12.6 inclusive or elsewhere within this Agreement, this Agreement shall, subject to the other provisions of this Agreement, automatically terminate forthwith and be of no further legal force or effect.

12.8. Upon expiration or termination of the Agreement:

12.8.1 any sums that were due from Orasense to Elan with respect to license granted hereunder, including without limitation on Net Sales, in the Territory or in such particular country or countries in the Territory (as the case may be) prior to the expiration or termination of this Agreement as set forth herein shall be paid in full within sixty (60) days after the expiration or termination of this Agreement for the Territory or for such particular country or countries in the Territory (as the case may be);

12.8.2 any provisions clearly meant to survive termination or expiration of this Agreement, including without limitation Clause 7, shall remain in full force and effect;

12.8.3 all representations, warranties and indemnities shall insofar as are appropriate remain in full force and effect;

12.8.4 the rights of inspection and audit set out in Clause 6 shall continue in force for a period of one year;

12.8.5 termination of this Agreement for any reason shall not release any Party hereto from any liability which, at the time of such termination, has already accrued to the other Party or which is attributable to a period prior to such termination nor preclude either Party from pursuing all rights and remedies it may have hereunder or at law or in equity with respect to any breach of this Agreement;

12.8.6 the Elan Intellectual Property and all rights, licenses and sublicenses granted by Elan in and pursuant to this Agreement shall cease for the Territory or for such particular country or countries in the Territory (as the case may be) and shall immediately revert to Elan and all Elan Program Technology shall be deemed immediately transferred and assigned to Elan. Following such expiration or termination, Orasense may not thereafter use in the Territory or in such particular country or countries in the Territory (as the case may be) (a) any valid and unexpired Elan Patents, (b) any Elan Intellectual Property that remains confidential or otherwise proprietary to Elan, and/or (c) Trademarks. All rights to Orasense Technology (other than Elan Program Technology and Isis Program Technology) shall be transferred to and jointly owned by Elan and Isis and may only be utilized by such parties royalty-free, consistent with the other restriction contained in Section 10 of this Agreement and the comparable section of the Isis License Agreement regarding the limitation of such rights outside the Field. Rights of permitted Independent Third Party sublicensees in and to the Elan Intellectual Property shall survive the termination of the license and sublicense agreements granting said intellectual property rights to Orasense; and Orasense, Elan and Isis shall in good faith agree upon the form most advantageous to Elan and Isis in which the

rights of the sublicensor under any such sublicenses are to be held (which form may include continuation of Orasense solely as the holder of such licenses or assignment of such rights to a third party or parties, including an assignment to both Elan and Isis). Any sublicense agreement between Orasense and such permitted sublicensee shall permit an assignment of rights by Orasense to Elan and shall contain additional reasonable confidentiality protections which an assignee shall reasonably require. Upon any such assignment, Elan and Isis shall enter into good faith negotiations with respect to additional reasonable confidentiality protections which either party shall reasonably require.

13. IMPOSSIBILITY OF PERFORMANCE - FORCE MAJEURE

13.1. Neither Party to this Agreement shall be liable for delay in the performance of any of its obligations hereunder if such delay results from causes beyond its reasonable control, including, without limitation, acts of God, fires, strikes, acts of war, or intervention of a government authority, non availability of raw materials, but any such delay or failure shall be remedied by such Party as soon as practicable.

14. SETTLEMENT OF DISPUTES; GOVERNING LAW

14.1. Any dispute between the Parties arising out of or relating to this Agreement will be subject to resolution in accordance with Clause 24.9 of the Development Agreement, which is incorporated by reference and shall for such purposes survive termination of the Development Agreement.

14.2. This Agreement is construed under and ruled by the laws of the State of New York, without regard to the conflict of law principles.

15. ASSIGNMENT

15.1. This Agreement may not be assigned by either Party without the prior written consent of the other, which consent shall not be unreasonably withheld, conditioned or delayed, save that (i) either Party may assign this Agreement to its Affiliate without such consent, provided that such assignment does not have any adverse tax consequences on the other Party, and (ii) Elan may assign its rights and obligations hereunder in connection with a sale of all or substantially all of the business of Elan to which the Transaction Documents relate, whether by merger, sale of stock, sale of assets or otherwise (provided that, in the event of such transaction, no intellectual property rights of any third party that is the acquiring corporation in such transaction shall be included in the Elan Intellectual Property licensed hereunder). Elan and Orasense will discuss any assignment by either Party to an Affiliate prior to its implementation in order to avoid or reduce any additional tax liability to the other Party resulting solely from different tax law provisions applying after such assignment to an Affiliate. For the purpose hereof, an additional tax liability shall be deemed to have occurred if either Party would be subject to a higher net tax on payments made hereunder after taking into account any applicable tax treaty and available tax credits than such Party was subject to before the proposed assignment. Notwithstanding any assignment

hereof to an Affiliate, each Party will remain fully liable hereunder.

16. NOTICES

16.1. Any notice to be given under this Agreement shall be sent in writing in English by registered airmail or telefaxed to the following addresses:

If to Orasense at:	Orasense Ltd. c/o Isis Pharmaceuticals, Inc. 2292 Faraday Avenue Carlsbad, California 92008 Attention: Ms. Lynne Parshall Telephone: (760) 603-2460 Telefax: (760) 931-9639
If to Isis to:	Isis Pharmaceuticals, Inc. 2292 Faraday Avenue Carlsbad, California 92008 Attention: Ms Lynne Parshall Telephone: (760) 603-2460 Telefax: (760) 931-9639
with a copy to:	Cooley Godward LLP 4365 Executive Drive Suite 1100 San Diego, CA 91212 Attention: L. Kay Chandler Telephone: (619) 550-6000 Telefax: (619) 453-3555
If to Elan at:	Elan Corporation plc Lincoln House, Lincoln Place, Dublin 2, Ireland Attention: Vice President, General Counsel, Elan Pharmaceutical Technologies, a division of Elan Corporation, plc Telephone: + 353 1 709 4000 Telefax: + 353 1 709 4124
with a copy to:	Cohen & Tauber LLP 1350 Avenue of the Americas 26th Floor New York, New York 10019 Attention: Laurence S. Tauber Telephone: (212) 519-5195

Telefax: (212) 262-1766

or to such other address(es) and telefax numbers as may from time to time be notified by either Party to the other hereunder.

16.2. Any notice sent by mail shall be deemed to have been delivered within seven (7) working days after dispatch and any notice sent by telex or telefax shall be deemed to have been delivered within twenty four (24) hours of the time of the dispatch. Notice of change of address shall be effective upon receipt.

17. MISCELLANEOUS CLAUSES

17.1. No waiver of any right under this Agreement shall be deemed effective unless contained in a written document signed by the Party charged with such waiver, and no waiver of any breach or failure to perform shall be deemed to be a waiver of any other breach or failure to perform or of any other right arising under this Agreement.

17.2. If any provision in this Agreement is agreed by the Parties to be, or is deemed to be, or becomes invalid, illegal, void or unenforceable under any law that is applicable hereto, (i) such provision will be deemed amended to conform to applicable laws so as to be valid and enforceable or, if it cannot be so amended without materially altering the intention of the Parties, it will be deleted, with effect from the date of such agreement or such earlier date as the Parties may agree, and (ii) the validity, legality and enforceability of the remaining provisions of this Agreement shall not be impaired or affected in any way.

17.3. The Parties shall use their respective reasonable endeavors to ensure that the Parties and any necessary third party shall execute and perform all such further deeds, documents, assurances, acts and things as any of the Parties hereto may reasonably require by notice in writing to the other Party or such third party to carry the provisions of this Agreement.

17.4. This Agreement shall be binding upon and inure to the benefit of the Parties hereto, their successors and permitted assigns and sub-licenses. Isis shall be a third party beneficiary to this Agreement and shall have the right to cause Orasense to enforce Orasense's rights against Elan.

17.5. No provision of this Agreement shall be construed so as to negate, modify or affect in any way the provisions of any other agreement between the Parties unless specifically referred to, and solely to the extent provided, in any such other agreement. In the event of a conflict between the provisions of this Agreement and the provisions of the Development Agreement, the terms of the Development Agreement shall prevail unless this Agreement specifically provides otherwise.

17.6. No amendment, modification or addition hereto shall be effective or binding on either Party unless set forth in writing and executed by a duly authorized representative of

each Party. Amendments hereto shall be subject to the prior approval of Isis, which approval shall not be unreasonably withheld or delayed.

17.7. This Agreement may be executed in any number of counterparts, each of which when so executed shall be deemed to be an original and all of which when taken together shall constitute this Agreement.

17.8. Each of the Parties undertakes to do all things reasonably within its power which are necessary or desirable to give effect to the spirit and intent of this Agreement.

17.9. Each of the Parties hereby acknowledges that in entering into this Agreement it has not relied on any representation or warranty save as expressly set out herein or in any document referred to herein.

17.10. Nothing contained in this Agreement is intended or is to be construed to constitute Elan, Isis and Orasense as partners, or Elan as an employee of Orasense and Isis, or Orasense and Isis as an employee of Elan. Neither Party hereto shall have any express or implied right or authority to assume or create any obligations on behalf of or in the name of

the other Party or to bind the other Party to any contract, agreement or undertaking with any third party.

IN WITNESS WHEREOF, the Parties hereto have executed this Agreement as of the date first set forth above.

ELAN PHARMACEUTICAL TECHNOLOGIES,
A DIVISION OF ELAN CORPORATION, PLC

By: /s/ KEVIN INSLEY

Kevin Insley
Authorized Signatory

ORASENSE LTD.

By: /s/ B. LYNNE PARSHALL

B. Lynne Parshall
President

AGREED TO:

ISIS PHARMACEUTICAL, INC.

By: /s/ B. LYNNE PARSHALL

B. Lynne Parshall
Executive Vice President

[ELAN LICENSE AGREEMENT EXECUTION PAGE]

EXHIBIT A

DESCRIPTION OF DEVELOPMENT CANDIDATE

[...***...]

*CONFIDENTIAL TREATMENT REQUESTED

EXHIBIT 10.8

***TEXT OMITTED AND FILED SEPARATELY
CONFIDENTIAL TREATMENT REQUESTED
UNDER 17 C.F.R. SECTIONS 200.80(b)(4),
200.83 AND 240.24B-2

LICENSE AGREEMENT

BY AND BETWEEN

ORASENSE LTD

A BERMUDA LIMITED COMPANY

AND

ISIS PHARMACEUTICALS, INC.

A DELAWARE CORPORATION

APRIL 20, 1999

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LICENSE AGREEMENT dated as of March 31, 1999 between Orasense Ltd,. a Bermuda limited company, and Isis Pharmaceuticals, Inc., a Delaware corporation.

RECITALS:

A. Contemporaneously herewith, Elan and Isis (capitalized terms used herein are defined below) propose to enter into the Development Agreement for the purpose of recording the terms and conditions of a joint venture and of regulating their relationship with each other and certain aspects of the affairs of and their dealings with Orasense.

B. Isis is beneficially entitled to the use of certain know-how and certain patents that have been granted or are pending in relation to the development and production of various drug delivery technologies and drug products.

C. Orasense desires to enter into this Agreement with Isis so as to permit Orasense to utilize the Isis Intellectual Property in the research, development, manufacture, distribution and sale of the Products in the Field and in the Territory.

D. Elan, EIS and Isis entered into a letter agreement dated March 31, 1999 (the "Letter Agreement") pursuant to which they agreed to enter into definitive documents, including this Agreement, and the Elan License Agreement relating to Orasense's use of the Elan Intellectual Property.

NOW THEREFORE IT IS HEREBY AGREED AS FOLLOWS:

1. DEFINITIONS; INTERPRETATION.

A. Definitions. In this Agreement, the following definitions shall apply:

1.1. "Affiliate" shall mean, with respect to Elan or Isis, any corporation or entity other than Orasense (and entities controlled by it) controlling, controlled or under the common control of Elan or Isis, as the case may be, and, with respect to Orasense, any corporation or entity under control of Orasense. A corporation or non-corporate entity shall be regarded as in control of another corporation if it owns or directly or indirectly controls at least fifty percent (50%) of the voting stock of the other corporation or (a) in the absence of the ownership of at least fifty percent (50%) of the voting stock of a corporation or (b) in the case of a non-corporate entity, the power to direct or cause the direction of the management and policies of such corporation or non-corporate entity, as applicable.

1.2. "Agreement" shall mean this agreement (which expression shall be deemed to include the Recitals and the Schedules hereto);

1.3. "cGCP", "cGLP" and "cGMP" shall mean current Good Clinical Practices, current Good Laboratory Practices and current Good Manufacturing Practices respectively;

1.4. "Change of Control" shall mean, with respect to a Party, the acquisition of

fifty percent (50%) or more of its voting securities, the ability, by contract or otherwise, to control the board of directors or management of any such entity, or a sale of all or substantially all of the business of such Party to which the Definitive Documents relate, whether by merger, sale of stock, sale of assets or otherwise;

1.5. "Commercialization" shall mean the manufacture, promotion, distribution, marketing and sale of the Products;

1.6. "Competitive Change of Control Event" shall mean that a Primary Technological Competitor of Elan acquires directly or indirectly voting stock or equivalent securities in Isis or Orasense representing [...***...] percent or more of the stock which carries entitlement to vote, or a Primary Technological Competitor of Elan acquires by all or substantially all of the business of Isis or Orasense to which the Definitive Documents relate, whether by merger, sale of stock, sale of assets or otherwise;

1.7. "Control" shall mean the ability to grant a license or sublicense as contemplated herein without violating the terms of any agreement with any third party;

1.8. "Cost of Living Increase" shall mean, with respect to any year of the Term, any increase in the Consumer Price Index published by the Bureau of Labor Statistics of the United States Department of Labor, All Urban Consumers, United States City Average, All Items (1982/84=100);

1.9. "Definitive Documents" shall have the same meaning as given to the term "Transaction Documents" in the Development Agreement;

1.10. "Development Agreement" shall mean the Joint Development and Operating Agreement of even date entered into among Isis, Elan, EIS and Orasense;

1.11. "Development Candidate" shall mean [...***...] antisense inhibitor of TNF-(alpha), as more specifically detailed in Exhibit A hereto;

1.12. "Development Product" shall mean any product containing as an active ingredient the Development Candidate (or a Substituted Development Candidate) in an Oral formulation for humans;

1.13. "Effective Date" shall mean the date of execution and delivery of the Definitive Documents;

1.14. "EIS" shall mean Elan International Services, Ltd., a Bermuda limited company;

1.15. "Elan" shall mean Elan Pharmaceutical Technologies, a division of Elan Corporation, plc, a public limited company incorporated under the laws of Ireland, its, successors and permitted assigns;

*CONFIDENTIAL TREATMENT REQUESTED

1.16. "Elan Improvements" shall mean any improvements to the Elan Patents and Elan Know-How developed by Elan (other than pursuant to the Research and Development Program). Subject to contractual restrictions, Elan Improvements shall be deemed part of and shall be included in the term "Elan Intellectual Property" and shall be deemed, immediately upon development by Elan, to be included in the license of the Elan Intellectual Property hereunder. If the inclusion of an Elan Improvement in the license of Elan Intellectual Property is restricted or limited by a third party agreement, Elan shall use reasonable commercial efforts to exclude or where applicable minimize any such restriction or limitation;

1.17. "Elan Intellectual Property" shall mean the Elan Know-How, the Elan Patent Rights and/or the Elan Improvements. Examples of the Elan Intellectual Property existing as of the Effective Date include, but are not limited to, technology related to the modification of the solubility, intrinsic dissolution, stability and/or permeability of a drug or modification of the surface(s) of particles, pharmaceutical formulation excipient technology, formulation, scale-up and manufacturing know-how. Schedule 1 to the Elan License Agreement shall contain, by way of illustration but not limitation, examples of Elan Intellectual Property. For the avoidance of doubt, Elan Intellectual Property shall consist of Oral drug delivery technology Controlled by Elan doing business as Elan Pharmaceutical Technologies and shall exclude (a) the Excluded Elan Technology, as such term is defined in the Elan License Agreement, (b) inventions, patents and know-how Controlled by all other affiliates or subsidiaries of Elan, including, but not limited to the Elan Pharmaceuticals division which incorporates Athena Neurosciences, Inc., Carnrick Laboratories, Targon Corporation and Neurex Corporation and (c) inventions, patents and know-how that are subject to contractual obligations of Elan to third parties as of the Effective Date to the extent the licensing of such inventions, patents and know-how is restricted or limited;

1.18. "Elan Know-How" shall mean any and all rights Controlled by Elan as of the Effective Date to any discovery, invention (whether or not patentable), know-how, substances, data, techniques, processes, systems, formulations and designs relating to Oral drug delivery;

1.19. "Elan License" shall have the meaning set forth in Section 2.1 of the Elan License Agreement;

1.20. "Elan License Agreement" shall mean that certain license agreement, of even date herewith, entered into between Elan and Orasense;

1.21. "Elan Patents" shall mean any and all patents and patent applications Controlled by Elan, existing and/or pending as of the Effective Date or hereafter filed or obtained relating to Oral drug delivery technology Controlled by Elan on the Effective Date. Elan Patent Rights shall also include all extensions, continuations, continuations-in-part,

divisionals, patents-of-additions, re-examinations, re-issues, supplementary protection certificates and foreign counterparts of such patents and patent applications and any patents issuing thereon and extensions of any patents licensed hereunder;

1.22. "Elan Program Technology" shall mean all Program Technology solely conceived or made by Elan and/or its agents;

1.23. "Excluded Isis Technology" shall mean any Isis [...***...] technology including, without limitation, [...***...];

1.24. "FDA" shall mean the United States Food and Drug Administration or any successors or agency the approval of which is necessary to market a product in the United States of America;

1.25. "Field" shall mean the research, development and Commercialization of in an Oral Platform for delivery of Oligonucleotide Drugs;

1.26. "Full Time Equivalent Rate" shall mean, for the services proposed to be rendered by Isis, $[...***...] for developmental chemistry (including pharmaceutics) and $[...***...] for all other services (including pharmacology, toxicology, clinical work, etc.);

1.27. "Independent Third Party" shall mean any person other than Orasense, Isis, Elan or any of their respective Affiliates;

1.28. "In market" shall mean sales of Products whether by Orasense or its Affiliates, or where applicable by a sublicensee, to an Independent Third Party being a wholesaler, distributor, managed care organization, hospital, pharmacy and/or the like;

1.29. "Isis" shall mean Isis Pharmaceuticals, Inc., a Delaware corporation;

1.30. "Isis Delivery Know-How" shall mean any and all rights Controlled by Isis as of the Effective Date to any discovery, invention (whether or not patentable), know-how, substances, data, techniques, processes, systems, formulations and designs relating to Oral Oligonucleotide drug delivery;

1.31. "Isis Delivery Patents" shall mean any and all patents and patent applications Controlled by Isis, existing and/or pending as of the Effective Date or hereafter filed or obtained relating to Oral drug delivery technology Controlled by Isis on the Effective Date. Isis Delivery Patents shall also include all extensions, continuations, continuations-in-part, continuing prosecution applications divisionals, patents-of-additions, re-examinations, re-issues, supplementary protection certificates and foreign counterparts of such patents and patent applications and any patents issuing thereon and extensions of any patents licensed hereunder;

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1.32. "Isis Delivery Technology" shall mean Isis Delivery Patents, Isis Delivery Know-How and Isis Improvements with respect thereto. Schedule 1A contains by way of illustration but not limitation, examples of existing Isis Delivery Technology;

1.33. "Isis Development Candidate Know-How" shall mean any and all rights Controlled by Isis to any discovery, invention (whether or not patentable), know-how, substances, data, techniques, processes, systems, formulations and designs which are necessary or useful for the manufacture or Commercialization of the Development Product;

1.34. "Isis Development Candidate Patents" shall mean any and all patents and patent applications Controlled by Isis, existing and/or currently pending as of the Effective Date or hereafter filed or obtained relating to the Development Candidate, or, if applicable, the Substituted Development Candidate, Controlled by Isis on the Effective Date which are necessary or useful for the manufacture or Commercialization of the Development Product. Isis Development Candidate Patents shall also include all extensions, continuations, continuations-in-part, continuing prosecution applications divisionals, patents-of-additions, re-examinations, re-issues, supplementary protection certificates and foreign counterparts of such patents and patent applications and any patents issuing thereon and extensions of any patents licensed hereunder;

1.35. "Isis Development Candidate Technology" shall mean Isis Development Candidate Patents, Isis Development Candidate Know-How and Isis Improvements with respect thereto. Schedule 1B contains by way of illustration but not limitation, examples of existing Isis Development Candidate Technology;

1.36. "Isis Improvements" shall mean any improvements to the Isis Delivery Technology and Isis Development Candidate Technology developed by Isis (other than pursuant to the Research and Development Program). Isis Improvements shall be deemed part of and shall be included in the term "Isis Intellectual Property" and shall be deemed, immediately upon development by Isis, to be included in the license of the Isis Delivery Technology and Isis Development Candidate Technology hereunder;

1.37. "Isis Intellectual Property" shall mean the Isis Delivery Technology and the Isis Development Candidate Technology. For the avoidance of doubt, Isis Intellectual Property shall exclude the Excluded Isis Technology.

1.38. "Isis License" shall have the meaning set forth in Section 2.2 hereof;

1.39. "Isis Oligonucleotide" shall mean any Oligonucleotide Drug Controlled by Isis other than the Development Candidate;

1.40. "Isis Products" shall mean Products based upon Isis Oligonucleotides that are made, designed, or otherwise created by or on behalf of Isis or any of its Affiliates after the

date hereof pursuant to the Project using the Orasense Technology and/or the Licensed Technologies;

1.41. "Isis Program Technology" shall mean all Program Technology solely conceived by Isis and/or its agents.

1.42. "Licensed Technologies" shall mean the Elan Intellectual Property and the Isis Intellectual Property;

1.43. "Licenses" shall mean the Elan License and the Isis License;

1.44. "Lien" shall mean any and all liens, security interests, restrictions, claims, encumbrances or rights of third parties of every kind and nature;

1.45. "Management Committee" shall have the meaning given to such term in the Development Agreement;

1.46. "Marketing Authorization" shall mean the procurement of registrations and permits required by applicable government authorities in a country in the Territory for the marketing, sale, and distribution of a Product in such country;

1.47. "Net Sales" shall mean the amount billed, invoiced and/or received on sales of a Product sold by Orasense or its Affiliates or sublicensees to an Independent Third Party, less, to the extent included in such invoice price the total of: (1) ordinary and customary trade quantity or cash discounts and nonaffiliated brokers' or agents' commissions actually allowed, including government managed care and other contract rebates, pharmacy incentive programs, including chargebacks of pharmacy or hospital performance incentive programs or similar programs; (2) credits, rebates and returns (including, but not limited to, wholesaler and retailer returns); (3) freight, postage and duties paid for and separately identified on the invoice or other documentation maintained in the ordinary course of business, and (4) import, export and sales taxes, excise taxes, other consumption taxes, customs duties, tariffs and compulsory payments to governmental authorities actually paid and separately identified on the invoice or other documentation maintained in the ordinary course of business and based on sales or turnover or delivery of the Products. Net Sales shall also include the amount or fair market value of all other consideration received by Orasense or its Affiliates or sublicensees in respect of Products, whether such consideration is payment in kind, exchange or another form. If a Product is provided to an Independent Third Party by Orasense or its Affiliates or sublicensees without charge or provision of invoice and used by such Independent Third Party, then Orasense or its Affiliates or sublicensees shall be treated as having sold such Product to such Independent Third Party for an amount equal to the fair market value of such Product. Sales between or among Orasense and its respective Affiliates or authorized licensees shall be excluded from the computation of Net Sales. A "sale" of a Product is deemed to occur upon the earlier of invoicing, shipment or transfer of title in the Product to an Independent Third Party. For avoidance of doubt, Net Sales shall include

royalties received by Orasense or its Affiliates from any Independent Third Party in respect of Products;

1.48. "Oligonucleotide Drug" shall mean any single stranded, [...***...] oligonucleotide including those [...***...] used as a human therapeutic and/or prophylactic compound containIng between [...***...] nucleotides and/or nucleosides including oligonucleotide analogs which may include [...***...]. For purposes of this agreement, Oligonucleotide Drug shall specifically exclude oligonucleotides used in [...***...], oligonucleotides used as [...***...] an oligonucleotide, oligonucleotides used as [...***...] or oligonucleotides used as adjuvants. Oligonucleotide Drug shall also specifically exclude polymers in which the [...***...] but shall not exclude [...***...]. Should Isis develop [...***...] oligonucleotides or should Elan independently discover drug delivery technology it believes to be potentially applicable to [...***...] oligonucleotides, then the Participants shall discuss in good faith whether such oligonucleotides can be formulated for Oral delivery using the Oral Platform, and whether such formulation appears feasible without requiring a significant further investment in developing or enhancing the Oral Platform; if such formulation appears feasible, the Participants shall discuss in good faith the inclusion of such oligonucleotides as Oligonucleotide Drugs;

1.49. "Oral" shall mean administration by way of the mouth for the purpose of topical or systemic delivery by way of the alimentary canal;

1.50. "Oral Delivery Devices" shall mean devices for delivering an active agent orally such as those employing [...***...] technologies;

1.51. "Oral Platform" shall mean formulation and excipient systems and technologies including [...***...] and including the use of [...***...], which can be employed to develop dosage forms of Oligonucleotide Drugs, deliver said dosage forms to the alimentary canal and facilitate and promote the systemic and topical delivery of Oligonucleotide Drugs;

1.52. "Orasense" shall mean Orasense, Ltd., a Bermuda limited company;

1.53. "Orasense Program Technology" shall mean all Program Technology other than Elan Program Technology and Isis Program Technology;

1.54. "Orasense Technology" shall mean all Program Technology and all technology licensed or acquired by Orasense or developed by Orasense whether or not

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pursuant to the Research and Development Program, excluding, however, Isis Intellectual Property and Elan Intellectual Property;

1.55. "Participant" shall mean Elan or Isis, as the case may be. "Participants" shall mean both Elan and Isis;

1.56. "Parties" shall mean Isis and Orasense;

1.57. "Person" shall mean an individual, partnership, corporation, limited liability company, business trust, joint stock company, trust, unincorporated association, joint venture, or other entity of whatever nature;

1.58. "Plan" shall mean the business plan and program of development agreed to by Elan and Isis within sixty (60) days of the date hereof, with respect to the research, development, prosecution and commercialization of the Products, which Plan shall be reviewed and mutually agreed to in writing by Elan and Isis on an annual basis;

1.59. "Primary Technological Competitor of Elan" shall have the meaning given to such term in the Elan License Agreement;

1.60. "Project" shall mean all activity as undertaken by Elan, Isis and Orasense to develop the Products in accordance with the Plan;

1.61. "Product" shall mean any Oligonucleotide Drug under development or developed by or on behalf of Orasense in an Oral formulation for administration to humans;

1.62. "Program Technology" shall mean all technology developed by or on behalf of Orasense, whether by Elan, Isis, a third party or jointly by any combination thereof, pursuant to the Research and Development Program;

1.63. "Regulatory Authority" shall mean any regulatory authority outside the United States of America, the approval of which is necessary to market a Product;

1.64. "Research and Development Program" shall have the same meaning as ascribed to such term in the Development Agreement;

1.65. "Research Term" shall mean the period commencing on the Effective Date and continuing for a period of [...***...] thereafter, unless extended by the mutual writTen agreement of Elan and Isis; provided, however, that if a Participant shall be prevented by (i) events beyond the Participants' control, or (ii) by such Participant's delay or negligent act or omission, from performing its obligations under the Definitive Documents within said [...***...], then the other Participant at its option, may extend the duration of the Research Term by a term equal in length to the period during which the first Participant was unable to perform its obligations hereunder;

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1.66. "Technological Competitor of Elan" shall have the meaning given to such term in the Elan License Agreement;

1.67. "Technological Competitor of Isis" shall mean any entity listed on Schedule 2 hereto, subject to amendment from time to time upon mutual written agreement of Orasense, Isis and Elan;

1.66. "Term" shall have the meaning given to it in Clause 12 below;

1.67. "Territory" shall mean all the countries of the world;

1.68. "Third Party Oligonucleotide Drug" shall mean any Oligonucleotide Drug Controlled by an Independent Third Party, other than an Isis Oligonucleotide Drug;

1.69. "Third Party Product" shall mean Products based upon Third Party Oligonucleotide Drug that are made, designed, or otherwise created by or on behalf of an Independent Third Party after the date hereof pursuant to the Project using the Orasense Technology and/or the Licensed Technologies. For avoidance of doubt, any Product based upon an Oligonucleotide Drug jointly developed by an Independent Third Party and Isis other than pursuant of the Program shall be deemed to be an Isis Product;

1.70. "Trademark" shall mean the trademark(s) belonging to Isis as may be selected by Orasense or its permitted sub-licensees, with Isis's consent, for use in connection with the Products.

1.71. "United States Dollar" and "US$" shall mean the lawful currency for the time being of the United States of America;

B. Interpretation. In this Agreement the following shall apply:

1.1 The singular includes the plural and vice versa, the masculine includes the feminine and vice versa.

1.2. Any reference to a Clause or Schedule shall, unless otherwise specifically provided, be to a Clause or Schedule of this Agreement.

1.3. The headings of this Agreement are for ease of reference only and shall not affect its construction or interpretation.

2. GRANT OF RIGHTS

2.1. Subject to the terms and conditions contained herein and, in consideration of the payments specified in Clause 6.1(i), Isis hereby grants to Orasense for the Term a non-

exclusive license, including the limited right to grant sublicenses pursuant to Clause 2.6 hereof, to the Isis Delivery Technology within the Field for the Territory, solely to research, develop, manufacture, have manufactured, and Commercialize the Products in the Territory, subject to any contractual obligations of Isis to Independent Third Parties as of the Effective Date and, unless prohibited by the paragraph below titled Non Competition, contractual obligations to Independent Third Parties that Isis may enter into after the Effective Date.

2.2. Subject to the terms and conditions contained herein and, in consideration of the payments specified in Clause 6.1(i), Isis hereby grants to Orasense for the Term an exclusive license in the Territory of Isis's rights in the Isis Development Candidate Technology to manufacture and Commercialize the Development Candidate, or if applicable, the Substituted Development Candidate, in an Oral formulation for administration to humans, subject to any contractual obligations of Isis to Independent Third Parties as of the Effective Date. The licenses granted by Isis pursuant to Sections 2.1 and 2.2 are hereafter referred to as the "Isis License".

2.3. In the event, as of the Effective Date, the Isis License granted to Orasense hereunder is restricted or limited by any contractual obligations of Isis to Independent Third Parties, then Isis shall use reasonable commercial efforts to exclude or, where applicable, to minimize any such restriction or limitation. Except as expressly provided herein, all proprietary rights and rights of ownership with respect to the Isis Intellectual Property shall at all times remain solely with Isis. Isis shall disclose to Orasense inventions made by or on behalf of Isis in connection with the performance of the Project, any patentable inventions and discoveries within the Isis Intellectual Property that relate to the Field and any patentable Isis Improvements developed by or on behalf of Isis.

2.4. To the extent royalty or other compensation obligations to Independent Third Parties that are payable with respect to Isis Intellectual Property would be triggered by a proposed use of Isis Intellectual Property in connection with the Project, Isis will inform Orasense and Elan of such royalty or compensation obligation. If Orasense decides to utilize such Isis Intellectual Property in connection with the Project, Orasense will be responsible for the payment of such royalty or other compensation obligations relating thereto.

2.5. Notwithstanding anything contained in this Agreement to the contrary, Isis shall have the right, and subject to the paragraph below titled Non-Competition, to fully exploit and grant licenses and sublicenses with respect to the Isis Delivery Technology. Isis's rights to exploit and grant licenses referred to in the immediately preceding sentence shall include the right to research, develop, manufacture, license or Commercialize products.

2.6. Orasense shall not be permitted to (a) encumber any of its rights under the Licenses or the Orasense Technology without the prior written consent of Isis; (b) assign or sublicense any of its rights under the licenses for the Licensed Technologies and the Orasense Technology without the prior written consent of Isis, which consent may be withheld in Isis's sole discretion. Any agreement between Orasense and any permitted third party for the

development or exploitation of the Isis Intellectual Property shall require such third party to maintain the confidentiality of all information concerning the Isis Intellectual Property and shall provide that any Isis Improvements shall belong to Isis and shall permit an assignment of rights by Orasense to Isis in accordance with the terms of this Agreement. Orasense shall remain responsible for all acts and omissions of any sub-licensee, as if they were acts and omissions by Orasense. Rights of permitted third party sublicensees in and to the Isis Intellectual Property shall survive the termination of the license and sublicense agreements granting said intellectual property rights to Orasense; and Orasense and Isis shall in good faith agree upon the form most advantageous to Isis in which the rights of the sublicensor under any such sublicenses are to be held (which form may include continuation of Orasense solely as the holder of such licenses or assignment of such rights to a third party or parties, including an assignment to Isis).

2.7. Orasense will use its reasonable commercial endeavours to exploit the Elan Intellectual Property, the Isis Intellectual Property and Orasense Technology in accordance with this Agreement, the Elan License Agreement and the Plan. Orasense shall employ diligent efforts to research, develop, register, and Commercialize the Products in the Territory. Orasense shall employ or have employed on its behalf a level of advertising, sales, marketing, and promotion efforts in each country in the Territory where Marketing Authorization for Product has been obtained which is: (i) commensurate with that used by other pharmaceutical manufacturers for products of similar market potential in that country in the Territory, and (ii) sufficient with respect to the potential for that country to fully exploit the market potential for the Product as depicted in the Plan and as determined by the Management Committee in accordance with the Development Agreement.

2.8. Orasense will be solely responsible for ensuring that it or its sublicensees manufacture and Commercialize the Products within each country of the Territory strictly in accordance with all the legal and regulatory requirements of each country of the Territory.

2.9. Upon the request of Orasense and with the consent of Isis, Isis shall grant to Orasense during the Term a non-exclusive royalty free license in the Territory, solely for use in connection with the sale of the Products, to use one or more Trademark, on the following terms:

2.9.1 Orasense shall as soon as it becomes aware of any infringement give to Isis in writing full particulars of any use or proposed use by any other person, firm or company of a trade name or trademark or promotional or advertising activity which may constitute infringement.

2.9.2 If Orasense becomes aware that any other person, firm or company alleges that such Trademark is invalid or that the use of such Trademark infringes any rights of another party or that the Trademark is otherwise attacked or attackable, Orasense shall immediately give to Isis full particulars in writing thereof and shall make no comment or admission to any third party

in respect thereof.

2.9.3 Isis shall have the right to conduct all proceedings relating to such Trademark and shall in its sole discretion decide what action, if any, to take in respect of any infringement or alleged infringement of such Trademark or any other claim or counter-claim brought or threatened in respect of the use or registration of such Trademark. Any such proceedings shall be conducted at Isis's expense and for its own benefit.

2.9.4 Nothing contained in this Agreement shall grant to Orasense any right, title, or interest in or to such Trademark, whether or not specifically recognized or perfected under applicable laws, except for the non-exclusive license granted herein. At no time during or after the term of this Agreement shall Orasense challenge or assist others to challenge any such Trademark or the registration thereof or attempt to register any trademarks, marks, or trade names confusingly similar to any such trademark. All displays of any such Trademark that Orasense intends to adopt shall first be submitted to Isis for approval (which shall not be unreasonably withheld) of design, color, and other details, or shall be exact copies of those used by Isis. In addition, Orasense shall fully comply with all reasonable guidelines, if any, communicated by Isis concerning the use of any such Trademark as well as all rules and regulations of such use throughout the Territory.

2.9.5 The rights granted to Orasense under this Article 2.9 shall automatically terminate respect to a Product in a country in the Territory upon termination of Orasense's right to market such Product in any such country.

2.10. When packaged, and to the extent permitted by law, a product label shall include an acknowledgement that the Product is made under license from Isis. Such acknowledgement shall take into consideration regulatory requirements and Orasense's reasonable commercial requirements. Orasense shall wherever possible give due acknowledgement and recognition to Isis in all printed promotional and other material regarding the Product such as stating that the Product is under license from Isis and that the applicable Isis Intellectual Property has been applied to the Products. Orasense shall consult with and obtain the written approval of Isis as to the format and content of the promotional and other material insofar as it relates to a description of, or other reference to, the application of the Isis Intellectual Property, such approval not to be unreasonably withheld or delayed. The further consent of Isis shall not be required where the format and content of such materials is substantively similar as the materials previously furnished to and approved in writing by Isis.

2.11. Isis shall have the first option to manufacture the active ingredient of the

Development Product for Orasense and meet its requirements, and Orasense shall agree to utilize Isis as its sole supplier, subject to the customary terms and conditions contained in a supply agreement to be executed by the parties at a price equal to [...***...]. If, despite good faith negotiations, Isis and Orasense do not reach agreement on the terms of such manufacturing agreement within [...***...] from the Parties' commencement of discussion of such terms, then Orasense shall be free to offer a third party (other than a Technological Competitor of Isis unless consented to by Isis which consent may be withheld for any reason, and otherwise subject to the terms and conditions of this Agreement) terms to manufacture the active ingredient of the Development Product in the Territory, which terms when taken as a whole, are more favorable to Orasense than the principal terms of the last written proposal offered to Orasense by Isis, or by Orasense to Isis, as the case may be. Subject to the foregoing rights of Isis with respect to the Development Product, Orasense shall not be permitted to contract the manufacture or Commercialization of any Product without the prior written consent of Elan and Isis, which consent will not be unreasonably withheld or delayed; provided that such reasonableness standard, in the case of Elan, shall not be applicable in the case of a proposed sublicense to any Technological Competitor of Elan and in the case of Isis, shall not be applicable in the case of a proposed sublicense to any Technological Competitor of Isis.

3. IMPROVEMENTS AND AFTER ACQUIRED TECHNOLOGY

3.1 Isis Improvements shall be deemed, immediately upon development, to be included in the license of the Isis Intellectual Property granted to Orasense hereunder.

3.2 The Isis License specifically excludes any right to use Isis Improvements outside of the Field.

3.3 If the inclusion of an Isis Improvement in the license of Isis Intellectual Property granted to Orasense hereunder is restricted or limited by a third party agreement, then Isis shall use reasonable commercial efforts to exclude, or where applicable, to minimize any such restriction or limitation.

3.4 All rights, title, and interest to any Isis Improvements developed by Orasense, Isis or any third party shall be the property of Isis. Orasense, Isis and any such third party shall execute and deliver documents, and take such other actions as Isis may reasonably request, to effect or evidence such ownership.

3.5 If Isis acquires know-how or patent rights relating to the Field, or if Isis acquires or merges with an Independent Third Party that has know-how or patent rights relating to the Field, then Isis shall offer to license such know-how and patent rights to Orasense (subject to existing contractual obligations), on such terms as would be offered to an Independent Third Party negotiating in good faith on an arms-length basis, and if the Management Committee determines that Orasense should not acquire such license, then Isis

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shall be free to fully exploit such know-how and patent rights, and to grant to third parties licenses and sublicenses with respect thereto.

4. DEVELOPMENT OF PRODUCTS

4.1 During the Research Term, Orasense will diligently pursue the research and development of the Elan Intellectual Property, Isis Intellectual Property and Orasense Technology in accordance with the Research and Development Program. The objectives of this initial phase of the Research and Development Program will be (a) to develop the Oral Platform, and (b) to develop the Development Product.

4.2 The results of Orasense's research pursuant to the Research and Development Program shall be shared with Isis and, in the event Isis utilizes such data in connection with a product based upon the Development Candidate in a non-Oral formulation and includes such data in any regulatory submission and the use of such data substantially enhances such application, and a product which is the subject of such application is Commercialized, Isis agrees to negotiate in good faith reasonable compensation to Orasense for the use of such data.

4.3 Isis agrees to provide at Orasense's cost such amounts of the Isis Oligonucleotide Drugs designated by Isis as [...***...] and [...***...] as Orasense shall require for testing and research purposes only; provided however, that no clinical studies on humans may be performed utilizing [...***...].

4.4 Orasense will diligently pursue the research, development and Commercialization of the Development Product and other Products in accordance with the Plan, this Agreement, the Elan License Agreement and the Development Agreement.

4.5 In the event the Management Committee, by unanimous vote of its members, shall determine that preclinical toxicology or pharmacology studies indicate that clinical trials of the Development Candidate should not be undertaken, or the Management Committee determines that development of the Development Candidate is not economically viable, Isis in good faith shall offer, and the Management Committee, by unanimous vote of its members shall approve, an Isis Oligonucleotide in pre-clinical development that it deems economically viable as a Substituted Development Candidate, subject to the agreement of the Participants, negotiating in good faith, to changes concerning the budget, Plan and funding of Orasense.

4.6 Except as otherwise provided herein, upon designation of an Isis Oligonucleotide as a Substituted Development Candidate, (i) all rights to the Development Candidate shall revert to Isis and (ii) all provisions contained herein other than in the preceding clause (i) relating to the Development Candidate shall be deemed to apply to the Substituted Development Candidate as if it were the Development Candidate.

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5 REGULATORY APPROVALS

5.1 Orasense shall, or shall cause its sublicensees, at its or their sole cost file and shall use its reasonable best efforts to prosecute to approval or cause its sublicensees to prosecute to approval, the Marketing Authorizations for the Products in the Territory in accordance with the Plan. During any Marketing Authorization registration procedure, Orasense shall keep Isis promptly and fully advised of Orasense's registration activities, progress and procedures. Each Party shall inform the other Party and Isis of any dealings such Party has with the FDA and any other Regulatory Authority. The Parties and Elan shall collaborate in relation to obtaining any approval of the FDA or Regulatory Authority for final approved labeling.

5.2 Subject to agreement to the contrary, any and all Marketing Authorizations filed hereunder for Products shall, to the extent owned by Orasense, remain the property of Orasense, provided that Orasense shall allow Isis access thereto to enable Isis to fulfill its obligations and exercise its rights under this Agreement and the Development Agreement. Orasense shall maintain or cause its sublicensees to maintain such Marketing Authorizations at its or their own cost.

5.3 Orasense shall indemnify and hold harmless Isis, its agents and employees from and against all claims, damages, losses, liabilities and expenses to which Isis, its agents, and employees may become subject related to or arising out of Orasense's bad faith, negligence or intentional misconduct in connection with the filing or maintenance of the Marketing Authorizations.

6 FINANCIAL PROVISIONS

6.1 In consideration of the license to the Isis Patents, Orasense shall pay to Isis, and, in consideration for license to Isis of Orasense Technology in connection with the Commercialization of Isis Products, Isis shall pay to Orasense, the following amounts:

6.1.1 Development Product Fees and Royalties. Payments to Isis with respect to services rendered in connection with the Development Product shall be paid as provided below and net proceeds derived by Orasense from the Development Product shall be allocated as additional royalties in proportion to [...***...], as more particularly or as otherwise set forth below.

(a) Development Work - Research and development work performed during the Research Term pursuant to the Research and Development Program regarding the Oral Platform and the Development Candidate contracted by Orasense to Isis shall be payable by Orasense to Isis based on [...***...] at Isis's Full Time Equivalent Rate, with annual Cost of Living Increases. In the event Isis is required to perform additional research and development work beyond that

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contemplated during the Research Term (without any extensions thereto), Orasense shall pay to Isis [...***...].

(b) Milestone Payments - If any Independent Third Party shall make milestone payments (e.g., for NDA filing, approvals, etc.) to Orasense, Orasense shall pay to Elan and Isis an additional royalty in the amount of [...***...].

(c) Royalties payable to Isis Upon Sales of the Development Product - Isis shall receive royalties of [...***...] of the In-market Net Sales of Development Products by OraseNse or its sublicensees. Notwithstanding the foregoing, in no event shall royalties payable to [...***...] with respect to sales of the Development Product [...***...].

6.1.2 Isis Product Fees and Royalties. Net proceeds derived by Orasense from Isis Products shall be allocated between the Participants as additional royalties in proportion to [...***...], as more particularly or as otherwise set forth below.

(a) Milestone Payments - If any Independent Third party shall make milestone payments (e.g., for NDA filing, approvals, etc.) to Isis with respect to an Isis Product, then [...***...] of such milestone payment shall be paid to Orasense by Isis as an additional royalty and Orasense shall pay a royalty equal in such amount to Elan; provided however, that development related milestone payments with respect to any Isis Product shall not be payable by Isis to Orasense or by Orasense to Elan except to the extent such payments exceed [...***...] with respect to such Isis Product (or, in the event the milestone is intended to be applied towards future work to be performed by Isis, in excess of [...***...].

(c) Royalty Payments. Any marketing and/or development agreement between Orasense and Isis with respect to Isis Products shall provide for a royalty payment by Isis to Orasense of [...***...] of In-market Net Sales of the Isis Products. At such time as royalty payments by Isis to Orasense shall equal [...***...] for the particular Isis Product subject to any such agreement, the royalty payable by Isis to Orasense with respect to In-market Net Sales of the Isis Product shall be [...***...] and the royalty payable by Orasense to Elan with respect to such Isis Product shall be [...***...] of In-market Net Sales of such Isis Product.

6.1.3 Third Party Products. Payments to Isis with respect to services

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rendered in connection with Third Party Products shall be paid as provided below and net proceeds derived by Orasense from Third Party Products shall be allocated as additional royalties with [...***...] of such amount being paid to Elan and [...***...] to Isis, as more particularly or as otherwise set forth below set forth below; provided, however, that in the event [...***...] significantly contributes to the research And development work related to a Third Party Product, the Participants shall negotiate in good faith an appropriate adjustment to the allocation of such additional royalties to reflect their relative contributions to the development of such Third Party Product.

(a) Development Work - Research and development work performed by Isis for Orasense related to Third Party Products shall be payable Isis at [...***...]. Orasense shall Pay to Isis an additional fee equal to [...***...] of all amounts paid by an Independent Third Parties to Orasense for development work to the extent the amounts paid to Orasense for such work exceeds any charges by Elan and Isis; with the remaining [...***...] of such excess amount being payable to Elan.

(b) Royalty Payments - In the event Orasense contracts development work to Elan for any Third Party Product, Orasense shall pay Isis, a royalty equal to [...***...] of the royalties it receives with respect to such Product (with the remaining [...***...] of such royalties payable to Elan) until such time as Elan has been paid a sum equal to [...***...] paid to it. Thereafter, [...***...] of the royalties received by Orasense With respect to such Third Party Product shall be paid to Isis (with the balance payable to Elan).

(c) Milestone Payments - If any Independent Third Party shall make milestone payments (e.g., for NDA filing, approvals, etc.) to Orasense, then [...***...] of such milestone payment shall be paid by Orasense to Elan as an additional royalty and [...***...] shall be paid by Orasense to Isis as an additional royalty to Isis.

(d) Manufacturing and Supply of Products - In the event Orasense contracts with Elan to manufacture Third Party Products, Orasense shall pay to Isis an additional fee equal to [...***...] of all amounts paid by an Independent Third Parties to Orasense for the manufacture of such Third Party Products to the extent such amounts exceed the amount previously charged by Elan; with the remaining [...***...] of such excess amount being payable to Elan.

6.2 Payment of royalties pursuant to Clauses 6.1.2-6.1.4, if any, shall be made quarterly in arrears within forty-five (45) days after the expiry of the calendar quarter. The method of payment shall be by wire transfer to an account specified by Isis and shall be

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nonrefundable to Orasense. Each payment made to Isis shall be accompanied by a true accounting of all Products sold by Orasense, its Affiliates and its permitted sublicensees, if any, during such quarter. Such accounting shall show, on a country-by-country and Product-by-Product basis, Net Sales or royalties received by Orasense (and the calculation thereof) and each calculation of royalties with respect thereto, including the calculation of all adjustments and currency conversions.

6.3 Orasense shall maintain and keep clear, detailed, complete, accurate and separate records for a period of three (3) years following the completion of such records so: (i) as to enable any royalties which shall have accrued hereunder to be determined; and (ii) that any deductions made in arriving at the Net Sales can be determined.

6.4 All payments due hereunder shall be made in United States Dollars. Payments due on Net Sales of any Product or royalties received by Orasense with respect to any Product for each calendar quarter made in a currency other than United States Dollars shall first be calculated in the foreign currency and then converted to United States Dollars on the basis of the average exchange rate in effect for such quarter for the purchase of United States Dollars with such foreign currency quoted in the Wall Street Journal (or comparable publication if not quoted in the Wall Street Journal) with respect to the currency of the country of origin of such payment, determined by averaging the rates so quoted on each business day of such quarter.

6.5 If Orasense claims in good faith that one or more of its devices, products, parts or components thereof, compounds and/or drug products does not utilize, incorporate, apply or is not based on the Elan Intellectual Property, the Isis Intellectual Property and/or Orasense Technology, then Orasense shall immediately notify Isis in writing and establish same to Isis's reasonable satisfaction.

6.6 If, at any time, legal restrictions in the Territory prevent the prompt payment when due of royalties or any portion thereof, the Parties shall meet to discuss suitable and reasonable alternative methods of reimbursing Isis the amount of such royalties. In the event that Orasense is prevented from making any payment under this Agreement by virtue of the statutes, laws, codes or government regulations of the country from which the payment is to be made, then such payments may be paid by depositing them in the currency in which they accrue to Isis's account in a bank acceptable to Isis in the country the currency of which is involved or as otherwise agreed by the Parties.

6.7 Isis and Orasense agree to co-operate in all respects necessary to take advantage of any double taxation agreements or similar agreements as may, from time to time, be available.

6.8 Any taxes payable by Isis on any payment made to Isis pursuant to this Agreement shall be for the account of Isis. If so required by applicable law, any payment made pursuant to this Agreement shall be made by Orasense after deduction of the appropriate withholding tax, in which event the Parties shall co-operate to obtain the

appropriate tax clearance as soon as is practicable. On receipt of such clearance, Orasense shall forthwith procure that the amount so withheld is paid to Isis.

6.9 Orasense shall, not more than once in each calendar year, permit Isis or its duly authorized representatives upon reasonable notice and at any reasonable time during normal business hours to have access to inspect and audit the accounts and records of Orasense and any other book, record, voucher, receipt or invoice relating to the calculation of the royalty payments on Net Sales submitted to Isis. Any such inspection of Orasense's records shall be at the expense of Isis, except that if any such inspection reveals a deficiency in the amount of the royalty actually paid to Isis hereunder in any calendar quarter of five percent (5%) or more of the amount of any royalty actually due to Isis hereunder, then the expense of such inspection shall be borne solely by Orasense. Any amount of deficiency shall be paid promptly to Isis by Orasense. If such inspection reveals a surplus in the amount of royalties actually paid to Isis by Orasense, Isis shall reimburse Orasense the surplus within fifteen (15) days after determination.

6.10 In the event of any unresolved dispute regarding any alleged deficiency or overpayment of royalty payments hereunder, the matter will be subject to resolution in accordance with Clause 24.9 of the Development Agreement, which is incorporated by reference and shall for such purposes survive termination of the Development Agreement.

7 CONFIDENTIAL INFORMATION

7.1 The Parties acknowledge that it may be necessary, from time to time, to disclose to each other confidential and proprietary information, including without limitation, inventions, works of authorship, trade secrets, specifications, designs, data, know-how and other information relating to the Field, the Products, Elan Intellectual Property, Isis Intellectual Property or the Orasense Technology, as the case may be, processes, services and business of the disclosing Party. The foregoing shall be referred to collectively as "Confidential Information". Any Confidential Information revealed by a Party to another Party shall be used by the receiving Party exclusively for the purposes of fulfilling the receiving Party's obligations under this Agreement and the Development Agreement and for no other purpose.

7.2 Each Party agrees to disclose Confidential Information of another Party only to those employees, representatives and agents requiring knowledge thereof in connection with their duties directly related to the fulfilling of the Party's obligations under this Agreement. Each Party further agrees to inform all such employees, representatives and agents of the terms and provisions of this Agreement and their duties hereunder and to obtain their consent hereto as a condition of receiving Confidential Information. Each Party agrees that it will exercise the same degree of care, but in no event less than a reasonable degree, and protection to preserve the proprietary and confidential nature of the Confidential Information disclosed by a Party, as the receiving Party would exercise to preserve its own proprietary and confidential information. Each Party agrees that it will, upon request of a Party, return all

documents and any copies thereof containing Confidential Information belonging to or disclosed by, such Party.

7.3 Notwithstanding the above, each Party may use or disclose Confidential Information disclosed to it by another party to the extent such use or disclosure is reasonably necessary in filing or prosecuting patent applications, prosecuting or defending litigation, complying with patent applications, complying with applicable governmental regulations or otherwise submitting information to tax or other governmental authorities, conducting clinical trials, or making a permitted sub-license or otherwise exercising its rights hereunder, provided that if a Party is required to make any such disclosure of the other Party's Confidential Information, other than pursuant to a confidentiality agreement, such Party shall inform the recipient of the terms and provisions of this Agreement and their duties hereunder and to obtain their consent hereto as a condition of receiving Confidential Information.

7.4 Any breach of this Clause 7 by any of the Persons informed by one of the Parties is considered a breach by the Party itself.

7.5 Confidential Information shall not be deemed to include:

(i) information that is generally available to the public;

(ii) information which is made public by the disclosing Party;

(iii) information which is independently developed by a Party as evidenced by such Party's written records, without the aid, application or use of the disclosing Party's Confidential Information;

(iv) information that is published or otherwise becomes part of the public domain without any disclosure by a Party, or on the part of a Party's directors, officers, agents, representatives or employees;

(v) information that becomes available to a Party on a non-confidential basis, whether directly or indirectly, from a source other than a Party, which source did not acquire this information on a confidential basis;

(vi) information which the receiving Party is required to disclose pursuant to:

(A) a valid order of a court or other governmental body or any political subdivision thereof or otherwise required by law; or

(B) any other requirement of law;

provided that if the receiving Party becomes legally required to disclose any Confidential

Information, the receiving Party shall give the disclosing Party prompt notice of such fact so that the disclosing Party may obtain a protective order or other appropriate remedy concerning any such disclosure. The receiving Party shall fully cooperate with the disclosing Party in connection with the disclosing Party's efforts to obtain any such order or other remedy. If any such order or other remedy does not fully preclude disclosure, the receiving Party shall make such disclosure only to the extent that such disclosure is legally required;

(v) information which was already in the possession of the receiving Party at the time of receiving such information, as evidenced by its written records, provided such information was not previously provided to the receiving Party from a source which was under an obligation to keep such information confidential; or

(vi) information that is the subject of a written permission to disclose, without restriction or limitation, by the disclosing Party.

7.6 The provisions relating to confidentiality in this Clause 7 shall remain in effect during the term of this Agreement, and for a period of seven (7) years following the expiration or earlier termination of this Agreement but shall not apply to any information which a Party is required to file or otherwise disclose in accordance with requirements which are legally binding on it.

7.7 The Parties agree that the obligations of this Clause 7 are necessary and reasonable in order to protect the Parties' respective businesses, and each Party expressly agrees that monetary damages would be inadequate to compensate a Party for any breach by the other Party of its covenants and agreements set forth herein. Accordingly, the Parties agree and acknowledge that any such violation or threatened violation will cause irreparable injury to a Party and that, in addition to any other remedies that may be available, in law and equity or otherwise, any Party shall be entitled to obtain injunctive relief against the threatened breach of the provisions of this Clause 7, or a continuation of any such breach by the other Party, specific performance and other equitable relief to redress such breach together with its damages and reasonable counsel fees and expenses to enforce its rights hereunder, without the necessity of proving actual or express damages.

8 WARRANTIES/INDEMNITIES

8.1 Isis represents and warrants to Orasense that:

(a) Isis is a corporation duly organized under the laws of its jurisdiction of organization and has all the requisite corporate power and authority to own and lease its respective properties, to carry on its respective business as presently conducted and as proposed to be conducted and to carry out the transactions contemplated hereby;

(b) Isis has full corporate power and authority enter into this Agreement and to perform its obligations hereunder, which have been duly authorized by

all requisite corporate action of Isis. This Agreement is the valid and binding obligation of Isis, enforceable against it in accordance with its terms, except as limited by applicable bankruptcy, insolvency, reorganization, moratorium and other laws of general application affecting the enforcement of creditors' rights generally, and by general equity principles and limitations on the availability of equitable relief, including specific performance;

(c) The execution, delivery and performance by Isis of this Agreement will not: (i) violate any provision of applicable law, statute, rule or regulation known by and applicable to Isis or any ruling, writ, injunction, order, judgment or decree of any court, arbitrator, administrative agency or other governmental body applicable to Isis or any of its properties or assets; or (ii) conflict with or result in any breach of any of the terms, conditions or provisions of, or constitute (with notice or lapse of time or both) a default (or give rise to any right of termination, cancellation or acceleration) under the charter or organizational documents of Isis to which Isis is a party, except where such violation, conflict or breach would not, individually or in the aggregate, have an adverse material effect on the business, assets, liabilities (contingent or otherwise), operations, condition (financial or otherwise), or prospects of Isis;

(d) To Isis best knowledge, except as set forth on Schedule 3 hereto, (i) Isis has the right to grant the Isis License and any other rights granted herein, (ii) Schedule 1 contains primary examples of the Isis Intellectual Property existing as of the Effective Date, which listing is not necessarily exhaustive, (iii) there are no agreements between Isis and any third parties that conflict with the Isis License which would have a material adverse effect on the ability of Orasense to conduct its business as presently proposed to be conducted, (iv) Isis is the owner or licensee of all rights, title and interest in the Isis Intellectual Property; and (v) Isis has no knowledge of any pending or threatened action, suit, proceeding or claim by others challenging Isis`s rights in or to such Isis Intellectual Property as related to the Field, which would have a material adverse effect on the ability of Orasense to conduct its business as presently proposed to be conducted.

8.2 Orasense represents and warrants to Isis the following:

(a) Orasense is duly and validly existing in good standing in the jurisdiction of its incorporation and each other jurisdiction in which the conduct of its business requires such qualification (except where such failure to so qualify shall not have a material adverse affect on the business and assets of Orasense), and Orasense is in compliance with all applicable laws, rules, regulations or orders relating to its business and assets;

(b) Orasense has full corporate authority to execute and deliver this Agreement and to consummate the transactions contemplated hereby; this Agreement has been duly executed and delivered and constitutes the legal and valid obligations of Orasense and is enforceable against Orasense in accordance with its terms; and the execution, delivery and performance of this Agreement and the transactions contemplated hereby will not violate

or result in a default under or creation of lien or encumbrance under Orasense's certificate of incorporation, by-laws or other organic documents, any material agreement or instrument binding upon or affecting Orasense, or its properties or assets or any applicable laws, rules, regulations or orders affecting Orasense or its properties or assets;

(c) Orasense is not in default of its charter or by-laws, any applicable laws or regulations or any material contract or agreement binding upon or affecting it or its properties or assets and the execution, delivery and performance of this Agreement and the transactions contemplated hereby will not result in any such violation;

(d) Orasense represents and warrants to Elan that the execution of this Agreement by Orasense and the full performance and enjoyment of the rights of Orasense under this Agreement will not breach the terms and conditions of any license, contract, understanding or agreement, whether express, implied, written or oral between Orasense and any third party.

8.3 Orasense represents and warrants to and covenants with Isis that it has the sole, exclusive and unencumbered right to grant the licenses and rights herein granted to Isis and that it has not granted and will not grant any option, license, right or interest in or to the Isis Intellectual Property, the Orasense Technology, or other property to any third party which would conflict with the rights granted by this Agreement and the Definitive Documents.

8.4 Orasense represents and warrants to and covenants and agrees with Isis that the Products shall be developed, manufactured, transported, stored, handled, packaged, marketed, promoted, distributed, offered for sale and sold in accordance with all regulations and requirements of the FDA and foreign regulatory authorities including, without limitation, cGCP, cGLP, cGMP regulations. The Products shall not be adulterated or misbranded as defined by the Federal Food, Drug and Cosmetic Act (or applicable foreign law) and shall not be a product which would violate any section of such Act if introduced in interstate commerce.

8.5 Orasense represents and warrants to Isis that it is fully cognizant of all applicable statutes, ordinances and regulations of the United States of America and countries in the Territory with respect to the manufacture of the Products including, but not limited to, the U.S. Federal Food, Drug and Cosmetic Act and regulations thereunder and similar statutes in countries outside of the United States. Orasense shall manufacture or procure the manufacture of the Products in conformity with the Marketing Authorizations and in a manner which fully complies with all United States of America and foreign statutes, ordinances, regulations and practices.

8.6 In addition to any other indemnifications provided for herein, Isis shall indemnify and hold harmless Orasense and its Affiliates and their respective employees, agents, partners, officers and directors from and against any claims, losses, liabilities or damages (including reasonable attorney's fees and expenses) incurred or sustained by

Orasense arising out of or in connection with any (a) breach of any representation, covenant, warranty or obligation by Isis hereunder, or (b) any act or omission on the part of Isis or any of its agents or employees in the performance of this Agreement.

8.7 In addition to any other indemnifications provided for herein, Orasense shall indemnify and hold harmless Isis and its Affiliates and their respective employees, agents, partners, officers and directors from and against any claims, losses, liabilities or damages (including reasonable attorney's fees and expenses) incurred or sustained by Isis arising out of or in connection with any (a) breach of any representation, covenant, warranty or obligation by Orasense hereunder, or (b) any act or omission on the part of Orasense or any of its agents or employees in the performance of this Agreement.

8.8 The Party seeking an indemnity shall:

8.8.1 fully and promptly notify the other Party of any claim or proceeding, or threatened claim or proceeding;

8.8.2 permit the indemnifying Party to take full care and control of such claim or proceeding;

8.8.3 cooperate in the investigation and defense of such claim or proceeding;

8.8.4 not compromise or otherwise settle any such claim or proceeding without the prior written consent of the other Party, which consent shall not be unreasonably withheld, conditioned or delayed; and

8.8.5 take all reasonable steps to mitigate any loss or liability in respect of any such claim or proceeding.

8.9 NOTWITHSTANDING ANYTHING TO THE CONTRARY IN THIS AGREEMENT, NEITHER ISIS NOR ORASENSE SHALL BE LIABLE TO THE OTHER PARTY, OTHER BY REASON OF ANY REPRESENTATION OR WARRANTY, CONDITION OR OTHER TERM OR ANY DUTY OF COMMON LAW, OR UNDER THE EXPRESS TERMS OF THIS AGREEMENT, OR FOR ANY CONSEQUENTIAL OR INCIDENTAL LOSS OR DAMAGE (WHETHER FOR LOSS OF PROFIT OR OTHERWISE) AND WHETHER OCCASIONED BY THE APPLICABLE PARTY'S NEGLIGENCE OR OF ITS EMPLOYEES OR AGENTS OR OTHERWISE

8.10 EXCEPT AS SET FORTH IN THIS CLAUSE 8, ISIS IS GRANTING THE ISIS LICENSE HEREUNDER ON AN "AS IS" BASIS WITHOUT RECOURSE, REPRESENTATION OR WARRANTY WHETHER EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR INFRINGEMENT OF THIRD PARTY RIGHTS, AND ALL SUCH WARRANTIES ARE EXPRESSLY DISCLAIMED.

9. INTELLECTUAL PROPERTY OWNERSHIP RIGHTS

9.1 Subject to the terms and conditions of this Agreement, including, without limitation Section 11 below, Orasense shall own the legal and equitable title to the Orasense Technology.

9.2 Isis shall own the legal and equitable title to the Isis Intellectual Property, including without limitation, Isis Improvements.

9.3 Orasense shall permanently mark or otherwise use reasonable efforts to cause any third party to permanently mark all Products and/or the packaging therefor with such license or patent notices to comply with the laws of the country of sale or otherwise to generally communicate the existence of any Isis Delivery Patents or Isis Development Candidate Patents for the countries of the Territory and in such manner as Isis may reasonably request in writing prior to the sale or commercial use thereof.

9.4 Isis, at its expense, shall make a good faith effort (i) to secure the grant of any material patent applications within the Isis Delivery Patents that relate to the Field and the Isis Development Candidate Patents; (ii) to file and prosecute patent applications on material patentable inventions and discoveries within the Isis Improvements that relate to the Field or the Isis Development Candidate Patents; (iii) to defend all such applications against third party oppositions; and (iv) to maintain in force any material issued letters patent within the Isis Delivery Patents that relate to the Field and the Isis Development Candidate Patents (including any letters patent that may issue covering any such Isis Improvements that relate to the Field or the Development Candidate). Isis shall have the right in its discretion to control such filing, prosecution, defense and maintenance provided that Orasense and Elan at their request shall be provided with copies of all documents relating to such filing, prosecution, defense and maintenance in sufficient time to review such documents and comment thereon prior to filing.

9.5 In the event that Isis informs the Orasense and Elan that it does not intend to file patent applications on patentable inventions and discoveries within the Isis Intellectual Property that relate to the Field in one or more countries in the Territory or fails to file such an application within a reasonable period of time, Orasense shall have the option at its expense to file and prosecute such patent application(s) in the joint names of Orasense and Isis. Upon written request from Orasense, Isis shall execute all documents, forms and declarations and to do all things as shall be reasonably necessary to enable Orasense to exercise such option.

9.6 Orasense, Isis and Elan shall promptly inform each other in writing of any alleged infringement of any patents within the Isis Patents or any alleged misappropriation of trade secrets within the Isis Intellectual Property by a third party of which it becomes aware and provide the others with any available evidence of such infringement or misappropriation

insofar as such infringements or misappropriation relate solely to the Field.

9.7 Orasense shall have the right to prosecute at its own expense and for its own benefit any infringements of the Isis Patents or misappropriation of the Isis Intellectual Property, insofar as such infringements or misappropriation relate solely to the Field. In the event that Orasense takes such action, Orasense shall do so at its own cost and expense. At Orasense's request, Isis shall cooperate with such action. Any recovery remaining after the deduction by Orasense of the reasonable expenses (including attorney's fees and expenses) incurred in relation to such infringement proceeding [...***...]. Should Orasense decide not to pursue such infringers, within a reasonable period but in any event within twenty (20) days after receiving written notice of such alleged infringement or misappropriation Isis may in its discretion initiate such proceedings in its own name, at its expense and for its own benefit, and at Isis's request, Orasense shall cooperate with such action. Alternatively, the Participants may agree to institute such proceedings in their joint names and shall reach agreement as to the proportion in which they shall share the proceeds of any such proceedings, and the expense of any costs not recovered, or the costs or damages payable to the third party. If the infringement of the Isis Patents affects both the Field as well as other products being developed or commercialized by Isis or its commercial partners outside the Field, Orasense and Isis shall endeavor to agree as to the manner in which the proceedings should be instituted and as to the proportion in which they shall share the proceeds of any such proceedings, and the expense of any costs not recovered, or the costs or damages payable to the third party.

9.8 Orasense shall indemnify, defend and hold harmless Isis, against all actions, losses, claims, demands, damages, costs and liabilities (including reasonable attorneys fees) relating directly or indirectly to all such claims or proceedings referred to herein, provided that Isis shall not acknowledge to the third party or to any other person the validity of any claims of such a third party, and shall not compromise or settle any claim or proceedings relating thereto without the prior written consent to Orasense, not to be unreasonably withheld or delayed. At its option, Elan or Isis, as the case may be, may elect to take over the conduct of such proceedings from Orasense provided that Orasense's indemnification obligations shall continue; the costs of defending such claim shall be borne by Elan or Isis, as the case may be and such Participant shall not compromise or settle any such claim or proceeding without the prior written consent of Orasense, such consent not to be unreasonably withheld or delayed.

10. RIGHTS EXPLOITATION OUTSIDE THE FIELD

10.1 Licenses to Isis Program Technology. Orasense hereby grants to Isis a perpetual, exclusive, royalty free and sublicensable license to Isis Program Technology outside of the Field.

10.2 Licenses for Orasense Program Technology Outside the Field. Orasense hereby grants to Isis a perpetual exclusive license for the use of Orasense Program

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Technology outside the Field in the Territory solely for use in connection with Isis proprietary drug products (including drug products discovered or developed in collaborative partnerships). The terms of such license for the use of Orasense Program Technology shall be decided by the unanimous decision of the Management Committee on such terms and conditions as the Management Committee shall approve after good faith negotiations with Isis.

11. NON-COMPETITION

11.1. During the Research Term (and any extension thereto), Isis shall not develop or Commercialize, or assist in the development or Commercialization of Oligonucleotide Drugs in the Field or develop or Commercialize, or assist in the development or Commercialization of an Oral Platform for systemic and topical delivery of Oligonucleotide Drugs, except (a) for or on behalf of Orasense, or (b) with the prior written, unanimous consent of the Management Committee. During the Term and provided that Orasense is maintaining an active program for the development and Commercialization of the Development Candidate in the Field, Isis shall not develop or Commercialize or assist in the development for Commercialization of an Oral TNF-(alpha) inhibitor, or, if a Substituted Development Candidate is selected, an Oral inhibitor of the Substituted Development Candidate. Nothing contained herein shall be construed as (i) limiting the activities of an existing third party licensee of Isis from developing Oligonucleotide Drugs utilizing Isis Delivery Technology to the extent such rights have been previously granted by Isis, provided Isis does not provide any active support to any such activities in excess of its existing contractual obligations or (ii) prohibiting Isis from licensing Isis Delivery Technology to an Independent Third Party or limiting the activities of any such future Independent Third Party licensee of Isis from developing Oligonucleotide Drugs utilizing Isis Delivery Technology; provided that the primary purpose of any such license is not the development of an Oral Platform for Oligonucleotide Drugs and Isis does not provide any active support to any such activities.

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12. TERM AND TERMINATION OF AGREEMENT

12.1. The term of this Agreement and the term of the Licenses granted hereunder with respect to a Product utilizing or based on the Licensed Technologies shall commence as of the Effective Date and continue, on a Product-by-Product basis and country by country basis, for the life of the patent rights upon which such Product is based on or utilizes in such country (the "Term"); provided, however, that all royalty and fee obligations contained herein shall survive for the greater of (i) the Term or (ii) 15 years from the first commercial sale of such Product.

12.2. Nothing contained herein shall obligate or restrict any party from utilizing public, non-proprietary information which is not subject to the protection of applicable patent laws.

12.3. If either party breaches any material provision of this Agreement and if such breach is (i) not capable of being cured or (ii) is capable of being cured but is not corrected within sixty (60) days after the non-breaching party gives written notice of the breach to the breaching party, the non-breaching party may terminate this Agreement immediately by giving notice of the termination, effective on the date of the notice, provided, however, that (x) if any such curable breach is not capable of being cured within such sixty (60) day period, so long as the breaching party commences to cure the breach promptly after receiving notice of the breach from the non-breaching party and thereafter diligently prosecutes the cure to completion as soon as is practicable, the non-breaching Party may not terminate this Agreement so long as the breaching party is acting in good faith to rectify such breach or (y) the default involves a good faith dispute regarding the amount of any required payment, provided any undisputed amount is paid, such default shall be stayed and the remainder may be withheld for a reasonable period during which a good faith resolution of the amount owed is being pursued.

12.4. In the event that the Elan License Agreement shall be terminated, at the sole option of Isis and upon written notice to Elan and Orasense, the Isis License shall be immediately terminated.

12.5. Upon the occurrence of an Event of Bankruptcy with respect to Orasense or Elan, the other Party may, upon written notice to Isis and the Party with respect to which such Event of Bankruptcy has occurred, immediately terminate the Elan License. As used in this Clause 12.5, the term "Event of Bankruptcy" relating to either Orasense or Elan shall mean:

12.5.1.the appointment of a liquidator, receiver, administrator, examiner, trustee or similar officer of either Party of it or over all or a substantial part of its assets under the law of any applicable jurisdiction, including without limit, Bermuda, the United States of America or Ireland; or

12.5.2 an application or petition for bankruptcy, corporate re-organization, composition, administration, examination, arrangement or any other procedure similar to any of the foregoing under the law of any applicable jurisdiction, including without limit, Bermuda, the United States of America or Ireland (other than as part of a bona fide restructuring or reorganization), is filed, and is not discharged within forty-five (45) days, or if either Party applies for or consents to the appointment of a receiver, administrator, examiner or similar officer of it or of all or a material part of its assets, rights or revenues or the assets and/or the business of either Party are for any reason seized, confiscated or condemned.

12.6. Upon exercise of those rights of termination as specified in Clause 12.1 to Clause 12.5 inclusive or elsewhere within this Agreement, this Agreement shall, subject to the other provisions of this Agreement, automatically terminate forthwith and be of no further legal force or effect.

12.7. Upon expiration or termination of the Agreement:

12.7.1 any sums that were due from Orasense to Isis with respect to license granted hereunder, including without limitation on Net Sales, in the Territory or in such particular country or countries in the Territory (as the case may be) prior to the expiration or termination of this Agreement as set forth herein shall be paid in full within sixty (60) days after the expiration or termination of this Agreement for the Territory or for such particular country or countries in the Territory (as the case may be);

12.7.2 any provisions clearly meant to survive termination or expiration of this Agreement, including without limitation Clause 7, shall remain in full force and effect;

12.7.3 all representations, warranties and indemnities shall insofar as are appropriate remain in full force and effect;

12.7.4 the rights of inspection and audit set out in Clause 6 shall continue in force for a period of one year;

12.7.5 termination of this Agreement for any reason shall not release any Party hereto from any liability which, at the time of such termination, has already accrued to the other Party or which is attributable to a period prior to such termination nor preclude either Party from pursuing all rights and remedies it may have hereunder or at law or in equity with respect to any breach of this Agreement;

12.7.6 the Isis Intellectual Property and all rights, licenses and sublicenses granted by Isis in and pursuant to this Agreement shall cease for the Territory or for such particular country or countries in the Territory (as the case may be) and shall immediately revert to Isis and all Isis Program Technology shall be deemed immediately transferred and assigned to Elan. Following such expiration or termination, Orasense may not thereafter use in the Territory or in such particular country or countries in the Territory (as the case may be) (a) any valid and unexpired Isis Patents, (b) any Isis Intellectual Property that remains confidential or otherwise proprietary to Isis, and/or (c) Trademarks. All rights to Orasense Technology (other than Elan Program Technology and Isis Program Technology) shall be transferred to and jointly owned by Elan and Isis and may only be utilized by such parties royalty-free, consistent with the other restriction contained in Section 10 of this Agreement and the comparable section of the Elan License Agreement regarding the limitation of such rights outside the Field. Rights of permitted Independent Third Party sublicensees in and to the Isis Intellectual Property shall survive the termination of the license and sublicense agreements granting said intellectual property rights to Orasense; and Orasense, Elan and Isis

shall in good faith agree upon the form most advantageous to Elan and Isis in which the rights of the sublicensor under any such sublicenses are to be held (which form may include continuation of Orasense solely as the holder of such licenses or assignment of such rights to a third party or parties, including an assignment to both Elan and Isis). Any sublicense agreement between Orasense and such permitted sublicensee shall permit an assignment of rights by Orasense to Isis and shall contain additional reasonable confidentiality protections which an assignee shall reasonably require. Upon any such assignment, Elan and Isis shall enter into good faith negotiations with respect to additional reasonable confidentiality protections which either party shall reasonably require.

13. IMPOSSIBILITY OF PERFORMANCE - FORCE MAJEURE

13.1. Neither Party to this Agreement shall be liable for delay in the performance of any of its obligations hereunder if such delay results from causes beyond its reasonable control, including, without limitation, acts of God, fires, strikes, acts of war, or intervention of a government authority, non availability of raw materials, but any such delay or failure shall be remedied by such Party as soon as practicable.

14. SETTLEMENT OF DISPUTES; GOVERNING LAW

14.1. Any dispute between the Parties arising out of or relating to this Agreement will be subject to resolution in accordance with Clause 24.9 of the Development Agreement, which is incorporated by reference and shall for such purposes survive termination of the Development Agreement.

14.2. This Agreement is construed under and ruled by the laws of the State of New York, without regard to the conflict of law principles.

15. ASSIGNMENT

15.1. This Agreement may not be assigned by either Party without the prior written consent of the other, which consent shall not be unreasonably withheld, conditioned or delayed, save that (i) either Party may assign this Agreement to its Affiliate without such consent, provided that such assignment does not have any adverse tax consequences on the other Party, and (ii) subject to the rights of Elan under the Development Agreement upon the occurrence of a Change of Control and the rights of Elan under the Elan License Agreement upon the occurrence of a Competitive Change of Control Event, Isis may assign its rights and obligations hereunder in connection with a sale of all or substantially all of the business of Isis to which the Transaction Documents relate, whether by merger, sale of stock, sale of assets or otherwise (provided that, in the event of such transaction, no intellectual property rights of any third party that is the acquiring corporation in such transaction shall be included in the Isis Intellectual Property licensed hereunder). Isis and Orasense will discuss any assignment by either Party to an Affiliate prior to its implementation in order to avoid or reduce any additional tax liability to the other Party resulting solely from different tax law

provisions applying after such assignment to an Affiliate. For the purpose hereof, an additional tax liability shall be deemed to have occurred if either Party would be subject to a higher net tax on payments made hereunder after taking into account any applicable tax treaty and available tax credits than such Party was subject to before the proposed assignment. Notwithstanding any assignment hereof to an Affiliate, each Party will remain fully liable hereunder.

16. NOTICES

16.1. Any notice to be given under this Agreement shall be sent in writing in English by registered airmail or telefaxed to the following addresses:

If to Orasense at:	Orasense Ltd. c/o Isis Pharmaceuticals, Inc. 2292 Faraday Avenue Carlsbad, California 92008 Attention: Ms. Lynne Parshall Telephone: (760) 603-2460 Telefax: (760) 931-9639
If to Isis to:	Isis Pharmaceuticals, Inc. 2292 Faraday Avenue Carlsbad, California 92008 Attention: Ms Lynne Parshall Telephone: (760) 603-2460 Telefax: (760) 931-9639
with a copy to:	Cooley Godward LLP 4365 Executive Drive Suite 1100 San Diego, CA 91212 Attention: L. Kay Chandler Telephone: (619) 550-6000 Telefax: (619) 453-3555
If to Elan at:	Elan Corporation plc Lincoln House, Lincoln Place, Dublin 2, Ireland Attention: Vice President, General Counsel, Elan Pharmaceutical Technologies, a division of Elan Corporation, plc Telephone: + 353 1 709 4000 Telefax: + 353 1 709 4124

with a copy to: Cohen & Tauber LLP
1350 Avenue of the Americas
26th Floor
New York, New York 10019
Attention: Laurence S. Tauber
Telephone: (212) 519-5195
Telefax: (212) 262-1766

or to such other address(es) and telefax numbers as may from time to time be notified by either Party to the other hereunder.

16.2. Any notice sent by mail shall be deemed to have been delivered within seven (7) working days after dispatch and any notice sent by telex or telefax shall be deemed to have been delivered within twenty four (24) hours of the time of the dispatch. Notice of change of address shall be effective upon receipt.

17. MISCELLANEOUS CLAUSES

17.1. No waiver of any right under this Agreement shall be deemed effective unless contained in a written document signed by the Party charged with such waiver, and no waiver of any breach or failure to perform shall be deemed to be a waiver of any other breach or failure to perform or of any other right arising under this Agreement.

17.2. If any provision in this Agreement is agreed by the Parties to be, or is deemed to be, or becomes invalid, illegal, void or unenforceable under any law that is applicable hereto, (i) such provision will be deemed amended to conform to applicable laws so as to be valid and enforceable or, if it cannot be so amended without materially altering the intention of the Parties, it will be deleted, with effect from the date of such agreement or such earlier date as the Parties may agree, and (ii) the validity, legality and enforceability of the remaining provisions of this Agreement shall not be impaired or affected in any way.

17.3. The Parties shall use their respective reasonable endeavors to ensure that the Parties and any necessary third party shall execute and perform all such further deeds, documents, assurances, acts and things as any of the Parties hereto may reasonably require by notice in writing to the other Party or such third party to carry the provisions of this Agreement.

17.4. This Agreement shall be binding upon and inure to the benefit of the Parties hereto, their successors and permitted assigns and sub-licenses. Elan shall be a third party beneficiary to this Agreement and shall have the right to cause Orasense to enforce Orasense's rights against Isis.

17.5. No provision of this Agreement shall be construed so as to negate, modify or affect in any way the provisions of any other agreement between the Parties unless

specifically referred to, and solely to the extent provided, in any such other agreement. In the event of a conflict between the provisions of this Agreement and the provisions of the Development Agreement, the terms of the Development Agreement shall prevail unless this Agreement specifically provides otherwise.

17.6. No amendment, modification or addition hereto shall be effective or binding on either Party unless set forth in writing and executed by a duly authorized representative of each Party. Amendments hereto shall be subject to the prior approval of Isis, which approval shall not be unreasonably withheld or delayed.

17.7. This Agreement may be executed in any number of counterparts, each of which when so executed shall be deemed to be an original and all of which when taken together shall constitute this Agreement.

17.8. Each of the Parties undertakes to do all things reasonably within its power which are necessary or desirable to give effect to the spirit and intent of this Agreement.

17.9. Each of the Parties hereby acknowledges that in entering into this Agreement it has not relied on any representation or warranty save as expressly set out herein or in any document referred to herein.

17.10. Nothing contained in this Agreement is intended or is to be construed to constitute Elan, Isis and Orasense as partners, or Isis as an employee of Orasense and Elan, or Orasense and Elan as an employee of Isis. Neither Party hereto shall have any express or implied right or authority to assume or create any obligations on behalf of or in the name of

the other Party or to bind the other Party to any contract, agreement or undertaking with any third party.

IN WITNESS WHEREOF, the Parties hereto have executed this Agreement as of the date first set forth above.

ISIS PHARMACEUTICAL, INC.

By: /s/ B. LYNNE PARSHALL

B. Lynne Parshall
Executive Vice President

ORASENSE LTD.

By: /s/ B. LYNNE PARSHALL

B. Lynne Parshall
President

AGREED TO:

ELAN PHARMACEUTICAL TECHNOLOGIES,
A DIVISION OF ELAN CORPORATION, PLC

By: /s/ KEVIN INSLEY

Kevin Insley
Authorized Signatory

[ISIS LICENSE AGREEMENT EXECUTION PAGE]

EXHIBIT A

DESCRIPTION OF DEVELOPMENT CANDIDATE

[...***...]

*CONFIDENTIAL TREATMENT REQUESTED