

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): **January 7, 2002**

ISIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware

(State or Other Jurisdiction of Incorporation)

000-19125

(Commission File No.)

33-0336973

(IRS Employer Identification No.)

**2292 Faraday Avenue
Carlsbad, CA 92008**

(Address of Principal Executive Offices and Zip Code)

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

Item 5. Other Events.

On January 7, 2002, Isis Pharmaceuticals, Inc. announced an intellectual property licensing agreement with Eyetech Pharmaceuticals, Inc., a privately held company. Eyetech licensed Isis' patents necessary for Eyetech to develop, make and commercialize EYE001, a non-antisense Phase II/III product for the treatment of ophthalmic diseases. Under the multi-million dollar transaction, Eyetech will pay Isis an upfront fee of \$2,000,000, as well as milestone and royalty payments in exchange for non-exclusive, worldwide rights to the intellectual property licensed from Isis.

Item 7. Exhibits.

10.1* License Agreement dated December 31, 2001 between Isis Pharmaceuticals, Inc. and EyeTech Pharmaceuticals, Inc.
99.1 Press Release dated January 7, 2002 regarding EyeTech Pharmaceuticals, Inc. and Isis Pharmaceuticals, Inc.

* 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.

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Isis Pharmaceuticals, Inc.

Dated: January 04, 2002

By: /s/ B. LYNNE PARSHALL

B. Lynne Parshall
Executive Vice President, Chief
Financial Officer and Director

INDEX TO EXHIBITS

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[Item 5. Other Events.](#)

[Item 7. Exhibits.](#)

[SIGNATURE](#)

LICENSE AGREEMENT

This License Agreement (the "Agreement") is effective as of December 31, 2001 (the "Effective Date") between Isis Pharmaceuticals, Inc., a Delaware corporation having an address at 2292 Faraday Avenue, Carlsbad, CA ("Isis") and EyeTech Pharmaceuticals, Inc., a corporation having an address at 666 Fifth Avenue, 35th Floor, New York, NY 10103 ("EyeTech"). Isis and EyeTech may be referred to herein as the "Parties," or each individually as a "Party."

**ARTICLE 1
DEFINITIONS**

Capitalized terms used herein have the meaning set forth in Exhibit A.

**ARTICLE 2
SCOPE OF LICENSE**

2.1 *Grant.* Subject to the terms of this Agreement and during the Term, Isis grants to EyeTech a non-exclusive license under the Licensed Patent Rights to make, have made, use and sell EYE001 worldwide. The license is sublicensable.

**ARTICLE 3
LICENSE FEES AND ROYALTIES**

3.1 *Fees and Royalties.* EyeTech will pay to Isis the fees, milestones and royalties set forth in this Article 3.

3.1.1 *License Fees.* EyeTech will pay an initial, irrevocable and non-refundable license fee of \$2,000,000 (the "License Fee") to Isis, \$1,000,000 of which will be paid upon execution of this Agreement and \$1,000,000 of which will be paid upon the earlier of (i) the date of the AMD Completed Patient Enrollment, or (ii) July 31, 2002.

3.1.2 *Milestones.* EyeTech will pay the following milestones to Isis:

a. For the initial indication of age-related macular degeneration for EYE001:

[***]

b. For each additional therapeutic indication for EYE001:

[***]

3.1.3 *Royalties on EYE001.* EyeTech will pay Isis a royalty of [***] on Net Sales of EYE001 when the manufacture, use or sale of EYE001 would infringe the Licensed Patent Rights.

**ARTICLE 4
PAYMENTS AND REPORTS**

4.1 *Payment.* Royalty payments will be due every three (3) months beginning with the first commercial sale of EYE001 (each such 3-month period a "Reporting Period") and will be paid within sixty (60) days of the close of each Reporting Period. Each royalty payment will be accompanied by a statement of the amount of Net Sales and all adjustments thereto during such Reporting Period.

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4.2 *Mode of Payment.* EyeTech will make all payments required under this Agreement in U.S. Dollars. The payments due on the sale of EYE001 received outside the United States will be translated using exchange rates published in the Wall Street Journal on the last day of the Reporting Period in question.

4.3 *Records Retention.* EyeTech and its sublicensees will keep complete and accurate records pertaining to the sale of EYE001 and covering all transactions from which the Net Sales are derived for a period of thirty-six (36) months after the year in which such Net Sales were received, and in sufficient detail to permit Isis to confirm the accuracy of royalty calculations hereunder.

4.4 *Audit Request.* No more than once each calendar year and at the request of Isis, EyeTech will permit an independent, certified public accountant appointed by Isis and acceptable to EyeTech, at reasonable times and upon reasonable notice, to examine those records and all other material documents relating to or relevant to Net Sales in the possession or control of EyeTech, for a period of two (2) years after such royalties have accrued, as may be necessary to: (a) determine the correctness of any report or payment made under this Agreement; or (b) obtain information as to the royalties payable for any Reporting Period in the case of EyeTech's failure to report or pay pursuant to this Agreement. Said accountant will not disclose to Isis any information other than information relating to said reports, royalties, and payments and will disclose such information in a format agreed upon by the parties that will ensure that no confidential information of EyeTech is disclosed. Results of any such examination will be made available to both parties. The fees charged by the public accountant conducting the audit will be paid for by Isis, provided that, if the audit determines that the additional royalties payable by EyeTech for an audited period exceed [***] of the royalties actually paid for such period, then EyeTech will pay the fees and expenses charged by such accounting firm.

**ARTICLE 5
PATENTS, INFRINGEMENT AND ENFORCEMENT**

5.1 *Patent Prosecution and Maintenance.* Isis will have the right and responsibility to prosecute and/or maintain the Licensed Patent Rights in any country at its own expense. If ISIS decides to discontinue the prosecution or maintenance of any Licensed Patent Right entirely or in a particular country, it will inform EyeTech thereof with sufficient time for EyeTech to assume the prosecution or maintenance of such Licensed Patent Right, and EyeTech may assume such prosecution or maintenance if such Licensed Patent Right provides a substantial competitive advantage to EyeTech with respect to EYE001 in the applicable country. If Isis has granted similar rights to third parties, EyeTech's rights under this section 5.1 will be shared equally with such third parties.

ARTICLE 6 REPRESENTATIONS AND WARRANTIES

6.1 *Isis Representation and Warranty.* Isis warrants that it has the lawful right to grant the license made the subject of this Agreement. Except as expressly stated in this section, Isis makes no other representations of any kind or nature whatsoever. ISIS MAKES NO WARRANTIES OR REPRESENTATIONS, EXPRESS OR IMPLIED, INCLUDING BUT NOT LIMITED TO, WARRANTIES OF FITNESS FOR A PARTICULAR PURPOSE OR MERCHANTABILITY OR NONINFRINGEMENT REGARDING OR WITH RESPECT TO THE LICENSED PATENTS. Without limiting the generality of the foregoing, nothing in this Agreement will be construed as (a) a warranty or representation by Isis as to validity or scope of the Licensed Patent Rights or (b) a warranty or representation that anything made, used, sold or otherwise disposed of under the license is or will be free from infringement of third party rights.

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6.2 *EyeTech Representations and Warranties.* EyeTech represents and warrants to Isis that EyeTech has the power and authority to execute, deliver and perform this Agreement, and this Agreement is a valid and binding obligation of EyeTech, enforceable in accordance with its terms.

ARTICLE 7 INDEMNITY

7.1 EyeTech agrees to indemnify, hold harmless and defend Isis, its officers, directors, employees and agents, from and against any and all claims, suits, losses, damages, costs, fees and expenses (collectively, "Claims") resulting from or arising out of (a) the development, manufacture, storage, sale or other distribution or any other use of EYE001 by EyeTech, its affiliates, sublicensees, agents and representatives or use by end users and other third parties of EYE001; and (b) EyeTech's breach of any representation or warranty herein.

7.2 In all cases where Isis seeks indemnification from EyeTech under this Article 7, Isis will promptly notify EyeTech of receipt of any claim or lawsuit covered by such indemnification obligation and will cooperate fully with EyeTech in connection with the investigation and defense of such claim or lawsuit. EyeTech will have the right to control the defense, with counsel of its choice, provided that Isis will have the right to be represented by advisory counsel at its own expense. Neither party will settle or dispose of the matter in any matter that could negatively and materially affect the rights or liability of the other party without the prior written consent of such party, which will not be unreasonably withheld or delayed.

ARTICLE 8 TERM AND TERMINATION

8.1 *Term.* This Agreement will commence as of the Effective Date and continue until the last Licensed Patent Rights expire (the "Term").

8.2 *Termination for Breach.* Notwithstanding anything to the contrary herein, a party may terminate this Agreement in the event that the other party (the "Defaulting Party") materially breaches its obligations hereunder and fails to cure such breach within [***] days of receipt of written notice thereof (which notice will specify the breach in reasonable detail and demand it be cured) (or, if such breach cannot be cured in such ninety [***] day period, if the Defaulting Party does not commence and diligently continue (until completed) actions to cure such default). Such termination will be without prejudice to the non-Defaulting Party's other rights under this Agreement, or any of its other rights or remedies available to it by law or in equity.

8.3 *Termination by EyeTech.* Notwithstanding anything contained herein to the contrary, EyeTech has the right to terminate this Agreement at any time in its sole discretion by giving [***] days advance written notice to ISIS; *provided*, that at the time of such termination EyeTech is not conducting (and does not intend to conduct) itself in a manner that would, but for the license granted in Article 2 of this Agreement, infringe the Licensed Patent Rights. In the event of such termination by EyeTech, EyeTech will still be obligated to pay any amounts due to Isis hereunder which, but for the lapse of time, will be owed to Isis, including the unpaid portion of the License Fee. Notwithstanding Section 3.1.1 above, any unpaid portion of the License Fee will be immediately due and payable upon such termination.

8.3 *Effect of Termination.* Upon the termination of this Agreement for any reason, all rights licensed to EyeTech will revert to Isis.

8.4 *Accrued Rights, Surviving Rights and Obligations.* Termination or expiration of this Agreement for any reason will be without prejudice to any rights that will have accrued to the benefit of either party prior to such termination or expiration. Such termination or expiration will not relieve either

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party from obligations that are expressly indicated to survive termination or expiration of this Agreement including, without limitation, EyeTech's obligation to pay all royalties that will have accrued hereunder. Without limiting the foregoing, the parties' rights and obligations under Articles 4, 6 and 7, and section 8.3 will likewise survive termination or expiration of this Agreement.

ARTICLE 9 MISCELLANEOUS

9.1 *Relationship of the Parties.* Nothing in this Agreement is intended to create, or creates, a partnership or joint venture relationship between the parties. The relationship between the parties hereunder is that of independent contractors.

9.2 *Successors and Assigns.* Except as otherwise provided herein, this Agreement may not be assigned by a party without the prior written consent of the other, provided, however, that either party may assign this Agreement to any successor by merger or to the purchaser of all or substantially all of its assets provided that the party will remain liable and responsible for the performance and observance of all of its duties and obligations hereunder. Nothing in this

Agreement, express or implied, is intended to confer upon any party other than the parties hereto or their respective permitted successors and assigns any rights, remedies, obligations or liabilities under this Agreement.

9.3 *Governing Law.* This Agreement will be governed by and construed under the laws of the State of Delaware without giving effect to its conflict of laws rules.

9.4 *Counterparts.* This Agreement may be executed in two or more counterparts, each of which will be deemed an original, but all of which together will constitute one and the same instrument.

9.5 *Compliance With Laws.* Both parties will comply with all applicable laws, rules and regulations pertaining to the development, testing, manufacture, marketing and import or export of EYE001 and will, as appropriate, include similar provisions in any sublicense agreements requiring sublicensees to do the same.

9.6 *Notices.* Unless otherwise provided, any notice required or permitted under this Agreement will be given in writing and will be deemed effectively given upon personal delivery to the party to be notified or five (5) days after upon deposit with the United States Post Office by registered or certified

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mail, postage prepaid or through a major courier (such as Federal Express, DHL or UPS), or sent by facsimile, and addressed to the party to be notified at the address set forth below.

To Isis: Isis Pharmaceuticals, Inc.
292 Faraday Avenue
Carlsbad, CA 92008
Attn: Executive Vice President
Fax: 760-931-3861
Phone: 760-603-2707

with copies to: General Counsel
Fax: 760-603-3820

To EyeTech: EyeTech Pharmaceuticals, Inc.
666 Fifth Avenue
35th Floor
New York, NY 10103
Attn: Chief Executive Officer
Fax: 212-582-2645
Phone: 212-582-8376

with copies to: General Counsel

9.7 *Amendments and Waivers.* Any term of this Agreement may be amended and the observance of any term of this Agreement may be waived (either generally or in a particular instance and either retroactively or prospectively), only with the written consent of Isis and EyeTech. The waiver by either of the parties of any breach of any provision hereof by the other party shall not be construed to be a waiver of any succeeding breach of such provision or a waiver of the provision itself.

9.8 *Severability.* If one or more provisions of this Agreement are held to be unenforceable under applicable law, such provision will be excluded from this Agreement and the balance of the Agreement will be interpreted as if such provision were so excluded and will be enforceable in accordance with its terms.

9.9 *Force Majeure.* No party will be deemed to be in default of this Agreement to the extent the performance of its obligations or attempts to cure any breach are delayed or prevented by reason of any act of God, war, fire, natural disaster, accident, act of government, or any other cause beyond the reasonable control of such party, if the party affected will give prompt notice of any such event to the other party. In the event of such a force majeure event, the time for performance or cure will be extended for the period equal to the duration of such force majeure event but not in excess of six (6) months.

9.10 *Entire Agreement.* This Agreement is the entire agreement of the parties with respect to the subject matter hereof, and any previous agreements, discussions or understandings, whether written or oral, are hereby merged herein.

9.11 *Press Release.* EyeTech and Isis agree that each Party may issue a press release. The Parties will confer on such press releases, to review and comment and incorporate the other Party's reasonable comments and suggestions prior to issuance of such press release.

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IN WITNESS WHEREOF, the parties have executed this Agreement as of the Effective Date.

Isis Pharmaceuticals, Inc.

By: /s/ B. Lynne Parshall

Name: B. Lynne Parshall

Title: Executive Vice President

EyeTech Pharmaceuticals, Inc.

By: /s/ David Guyer

Name: David Guyer

Title: CEO

**EXHIBIT A
DEFINITIONS**

1. "AMD Completed Patient Enrollment" means the completion of enrollment of that number of patients in EyeTech's Pivotal Phase II/III clinical trial program that is necessary to gain Food and Drug Administration regulatory approval of EYE001 for the treatment of the wet form of age-related macular degeneration.
2. "Major Market" means Canada, any European Community member country, Japan or the United States.
3. "Manufacturing Process" means the process steps [***] set forth in master batch records for EYE001 in the version existing as of the Effective Date, including reasonable minor variants and extensions of process steps thereof.
4. "Net Sales" will mean the gross invoice price of EYE001 sold by EyeTech, its affiliates and sublicensees to a third party less the following items: (i) trade discounts, credits or allowances, (ii) credits or allowances additionally granted upon returns, rejections or recalls (except where any such recall arises out of EyeTech's or sublicensee's gross negligence, willful misconduct or fraud), (iii) freight, shipping and insurance charges, (iv) taxes, duties or other governmental tariffs (other than income taxes) and (v) government-mandated rebates. EyeTech, its affiliates or sublicensees will be treated as having sold EYE001 for an amount equal to the fair market value of EYE001 if: (a) EYE001 is used by EyeTech, its affiliates or sublicensees without charge or provision of invoice, or (b) EYE001 is provided to a third party by EyeTech, its affiliates or sublicensees without charge or provision of invoice and used by such third party.
5. "EYE001" means EyeTech's EYE001 NX1838 non-antisense therapeutic product (or any product containing EyeTech's EYE001 NX1838 non-antisense therapeutic product for the treatment of ophthalmic conditions. EYE001 will also include any minor chemical modification to EYE001 NX1838.
6. "Patent" or "Patents" means (a) patent applications (including provisional applications and applications for certificates of invention); (b) any patents issuing from such patent applications (including certificates of invention); (c) all patents and patent applications based on, corresponding to, or claiming the priority date(s) of any of the foregoing; and (d) any substitutions, extensions (including supplemental protection certificates), registrations, confirmations, reissues, divisionals, continuations, re-examinations, renewals and foreign counterparts thereof.
7. "Licensed Patent Rights" means all Patents owned by Isis or controlled by Isis through the Term which Isis has the right to sublicense and such sublicense does not create any obligation to any third party, which claim or cover [***]
8. "Reporting Period" has the meaning set forth in Section 4.1.
9. "Term" has the meaning set forth in Section 8.1.

**CONFIDENTIAL TREATMENT REQUESTED
UNDER 17 C.F.R. §§ 200.80(b)4, AND 240.24b-2**

**ISIS PHARMACEUTICALS AND EYETECH PHARMACEUTICALS
SIGN INTELLECTUAL PROPERTY LICENSE AGREEMENT**

Carlsbad, CA—January 7—Isis Pharmaceuticals, Inc. (NASDAQ: ISIP) announced today that it has entered into an intellectual property licensing agreement with Eyetech Pharmaceuticals, Inc. Eyetech, which is a privately held company, has licensed Isis' patents necessary for Eyetech to develop, make and commercialize EYE001, a non-antisense compound for the treatment of ophthalmic diseases.

EYE001 is an aptamer that inhibits vascular endothelial growth factor (VEGF). The aptamer is an oligonucleotide that acts like a high affinity antibody to VEGF. This anti-VEGF aptamer blocks blood vessel growth and inhibits neovascularization in preclinical models.

Eyetech will pay Isis upfront fees, milestone and royalty payments in the multi-million dollar transaction in exchange for non-exclusive, worldwide rights to the intellectual property licensed from Isis.

"We are very pleased to be supportive of the exciting work Eyetech is doing in ophthalmic disease. Our relationship with Eyetech is consistent with our overall business strategy to continually leverage the value of our patent portfolio, which we have systematically built over the course of the company's 12-year history," said B. Lynne Parshall, Isis' Executive Vice President. "Our chemistry patent portfolio is the product of broad-based basic research that is relevant to drug discovery and extends beyond the realm of antisense therapeutics and functional genomics. We are actively creating opportunities for the industry to access our portfolio to help create drugs for patients in need."

Isis' chemistry suite of patents represents a subset of Isis' overall intellectual property estate of nearly 900 issued patents that Isis owns or exclusively licenses, covering RNA-based drug discovery and development. More specifically, the estate covers the use of

RNA/DNA oligonucleotides, or antisense inhibitors, in gene functionalization and target validation, including: chemistries; antisense inhibitor designs called "motifs;" methods of use of antisense inhibitors; and mechanisms of action by which antisense inhibitors inactivate an RNA target.

Eyetech Pharmaceuticals, Inc. is a privately-held, New York based biopharmaceutical company dedicated to developing and commercializing novel drugs to reduce and prevent vision loss caused by eye disease. The company is also focused on developing new technologies to deliver drugs safely to the back of the eye. Additional information about Eyetech is available at www.eyetk.com.

Isis Pharmaceuticals, Inc. is exploiting its expertise in RNA to discover and develop novel human therapeutic drugs. The company has commercialized its first product, Vitravene® (fomivirsen), to treat CMV-induced retinitis in AIDS patients. In addition, Isis has 13 products in its development pipeline with two in Phase III and seven in Phase II human clinical trials. ISIS 3521, an inhibitor of PKC-alpha, is in Phase III trials for non-small cell lung cancer, and alicaforsen (ISIS 2302), an ICAM-1 inhibitor, is also in Phase III trials for Crohn's disease. Isis has a broad patent estate as the owner or exclusive licensee of nearly 900 issued patents worldwide. Isis' GeneTrove™ division uses antisense to assist pharmaceutical industry partners in validating and prioritizing potential gene targets through customized services and access to an extensive gene function database. Ibis Therapeutics™ is a division focused on the discovery of small molecule drugs that bind to RNA. Additional information about Isis is available at www.isip.com.

This press release contains forward-looking statements concerning the intellectual property position of Isis Pharmaceuticals, Inc. and the company's relationship with Eyetech Pharmaceuticals, Inc. and the potential of EYE001. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics and financing such activities. Actual results could differ materially from those projected in this release. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' research and development programs are described in

additional detail in the Company's Quarterly Report on Form 10Q, for the period ended September 30, 2001, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the company.

Vitravene® (fomivirsen) is a trademark of Novartis AG.
GeneTrove™ and Ibis Therapeutics™ are trademarks of Isis Pharmaceuticals, Inc.

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[EXHIBIT 99.1](#)
[ISIS PHARMACEUTICALS AND EYETECH PHARMACEUTICALS SIGN INTELLECTUAL PROPERTY LICENSE AGREEMENT](#)