QuickLinks -- Click here to rapidly navigate through this document

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): **September 16, 2002**

ISIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware
(State or Other Jurisdiction of Incorporation)

000-19125	**33-0336973**
(Commission File No.)	(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 September 16, 2002, Isis Pharmaceuticals, Inc. announced it had settled litigation pending against Sequitur, Inc. ("Sequitur). Isis had sued Sequitur, in three separate lawsuits, for alleged infringement of U.S. Patent Nos. 6,001,653; 6,326,199; 6,096,543; 5,959,097; and 5,958,773.

Isis and Sequitur reached a mutually agreeable business resolution that resulted in the dismissal of the three lawsuits and all counterclaims. Isis has granted Sequitur a license to certain Isis patents for target validation and functional genomics using first generation antisense oligonucleotides (also known as phosporothioate and/or phosphodiester deoxy antisense oligonucleotides) in exchange for undisclosed payments from Sequitur. Subject to a limited right to conclude existing customer contracts, Sequitur has agreed that it will not practice in the field of "second generation" or "next generation" antisense oligonucleotides, also known as chimeric antisense oligonucleotides.

Item 7. Exhibits.

10.1*	Settlement, Release, and License Grant Agreement dated September 6, 2002 between Isis Pharmaceuticals, Inc. and Sequitur, Inc.
99.1	Press Release dated September 16, 2002 regarding Sequitur, 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: September 16, 2002

By: /s/ B. LYNNE PARSHALL

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

INDEX TO EXHIBITS

10.1*	Settlement, Release, and License Grant Agreement dated September 6, 2002 between Isis Pharmaceuticals, Inc. and Sequitur, Inc.
99.1	Press Release dated September 16, 2002 regarding Sequitur, 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.

Exhibit 10.1

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

SETTLEMENT, RELEASE, AND LICENSE GRANT AGREEMENT

This **SETTLEMENT, RELEASE, AND LICENSE GRANT AGREEMENT** (hereinafter the "Agreement") is made and entered into effective on September 6, 2002, by and between Isis Pharmaceuticals, Inc. on the one hand and Sequitur, Inc. on the other hand.

Whereas, Isis Pharmaceuticals, Inc. is the owner of all rights, title and interest to United States Patent Number 6,001,653, 6,326,199, 5,959,097, 5,958,773, 6,043,090 and 6,096,543;

Whereas, on July 9, 2001, Isis Pharmaceuticals, Inc. instituted suit against Sequitur, Inc. in the United States District Court for the Southern District of California, Case No. 01 CV 1223 B JFS (hereinafter the "First Action"), seeking injunctive relief and damages against Sequitur, Inc. based on the allegation that Sequitur, Inc. was infringing U.S. Patent No. 6,001,653;

Whereas, Sequitur, Inc. denied all allegations of infringement in the First Action and Sequitur, Inc. further filed a counterclaim alleging that it was entitled to declaratory judgment of non-infringement, invalidity and/or unenforceability, and alleging claims of breach of contract, unfair competition under the Lanham Act, Antitrust Violations and unfair competition under California Law (the "Counterclaim");

Whereas, Isis Pharmaceuticals, Inc. denied all allegations of breach of contract, unfair competition and antitrust violations in the Counterclaim;

Whereas, on December 12, 2001, Isis Pharmaceuticals, Inc. instituted suit against Sequitur, Inc. in the United States District Court for the Southern District of California, Case No. 01 CV 2286 B JFS (hereinafter the "Second Action"), seeking injunctive relief and damages against Sequitur, Inc. based on the allegation that Sequitur, Inc. was infringing U.S. Patent No. 6,326,199;

Whereas, Sequitur, Inc. denied all allegations of infringement in the Second Action;

Whereas, on May 2, 2001, Isis Pharmaceuticals, Inc. instituted suit against Sequitur, Inc. in the United States District Court for the Southern District of California, Case No. 02 CV 0842 B JFS (hereinafter the "Third Action"), seeking injunctive relief and damages against Sequitur, Inc. based on the allegation that Sequitur, Inc. was infringing U.S. Patent Nos. 5,959,097, 5,958,773, 6,043,090 and 6,096,543;

Whereas, Sequitur, Inc. denied all allegations of infringement in the Third Action; and

Whereas, the parties to this Agreement deny any and all liability to one another, but desire to fully compromise and resolve all of the claims between them arising from or in any way related to the First Action, Second Action, Third Action and the Counterclaim ("the Lawsuit");

Now, Therefore, to reconcile their differences and in consideration of the promises and covenants and agreements contained herein, the parties agree as follows:

1. Definitions.

1.1 Antisense Oligonucleotides. As used herein, the term "Antisense Oligonucleotides" means a sequence of nucleotides which is designed to be complementary to and bind to a specific sequence of nucleotides in an mRNA target to inhibit production of the protein encoded by the target mRNA.

1.2 Change of Control. As used herein, the term "Change in Control" shall be deemed to occur upon (i) the acquisition of all or substantially all of the assets of Sequitur, Inc. or (ii) an acquisition of Sequitur, Inc. by another corporation or entity by consolidation, merger or other reorganization in a transaction (or series of transactions) in which the holders of Sequitur, Inc.'s outstanding voting stock immediately prior to such transaction (or series of transactions) own, immediately after such transaction (or series of transactions), securities representing less than fifty percent (50%) of the voting power of the corporation or other entity surviving such transaction (or series of transactions).

1.3 Existing Customer. As used herein, the term "Existing Customer" means a customer of Sequitur's Target Validation Program, whether inside or outside the U.S., to whom Sequitur has supplied or used on their behalf Antisense Oligonucleotides prior to June 30, 2002, as set forth in Exhibit A attached hereto.

1.4 First Generation Oligonucleotides. As used herein, the term "First Generation Oligonucleotides" means Antisense Oligonucleotides having: phosphorothioate, phosphodiester, or mixed phosphorothiote/phosphodiester backbones; unmodified Adenine, Cytosine, Thymine, Guanine, bases; and, unmodified deoxy sugars. First Generation Oligos may contain fluorescent dyes or other non-nucleotide end-blocks incorporated at either or both the 3' and 5' ends.

1.5 Isis. As used herein, the term "Isis" shall mean Isis Pharmaceuticals, Inc., and its successors in interest.

1.6 Isis First Generation Oligonucleotide Patents. As used herein, the term "Isis First Generation Oligonucleotide Patents" means Patents owned by Isis on the Effective Date, including U.S. Patent No. 6,001,653, which have claims which read on First Generation Oligonucleotides. Isis First Generation Oligonucleotide Patents does not include Isis Patents that claim specific nucleotide sequences, or Patents claiming oligonucleotides designed to inhibit specific genes identified in the patent, or methods of using such oligonucleotides.

1.7 Next Generation Oligonucleotides. As used herein, the term "Next Generation Oligonucleotides" means Antisense Oligonucleotides with a combination of 2' hydrogen and 2' modified sugars that elicit RNase H cleavage as a mechanism of action.

1.8 Patents. As used herein, the term "Patents" means all U.S. patents and patent applications, divisions, continuations, reissues, re-examinations, extensions, supplementary protection, and any provisional applications, of any such patents or patent applications, and any foreign or international equivalent of any of the foregoing. The term Patents includes the claim of any continuation-in-part, and any foreign or international equivalents of such continuation-in-part, only to the extent that such claim is to an embodiment that does not include new matter.

1.9 Provide. As used herein, the term "Provide" will mean that Sequitur may supply Existing Customers with Next Generation Oligonucleotides, which are presently in the possession of Sequitur.

1.10 Resupply. As used herein, the term "Resupply" will mean that Sequitur can have Trilink or another supplier make an additional quantity of Next Generation Oligonucleotides to provide not more than 10mg of such Next Generation Oligonucleotides to an Existing Customer.

1.11 Sequitur. As used herein, the term "Sequitur" shall mean Sequitur, Inc.

1.12 Sequitur's Target Validation Program. As used herein, "Sequitur's Target Validation Program" shall mean internal use by Sequitur, and/or provision by Sequitur to its customers (for internal use only, and not for resale), of Antisense Oligonucleotides, wherein such use or provision of Antisense Oligonucleotides by Sequitur or use by its customers is for the purposes of

performing research regarding the validation or functionalization of gene targets or confirmation of such function.

2. Releases

2.1 Isis hereby releases, acquits and forever discharges Sequitur and each of its predecessors, successors, receivers, assigns, affiliated entities, parent and subsidiary entities, past or present owners, shareholders, partners, investors, employees, agents, representatives, consultants, officers, directors, managers, and any other person, firm or corporation acting by, through, under or in concert with it, from any and all claims, demands, actions, causes of action, suits, obligations, damages, restitution, promises, controversies, contracts, agreements, expenses, costs, fees, and losses or liabilities of any type or nature whatsoever, in equity or at law, by statute or common law, whether or not now known, suspected, disclosed, or claimed, whether or not now known, suspected, disclosed, or claimed, which Isis ever had, now has or claims to have against Sequitur, up to and including the Effective Date of this Agreement, including but not limited to all claims for attorney's fees and costs. Isis also releases, acquits, and forever discharges Sequitur customers from claims of patent infringement based on the use of oligonucleotides purchased from Sequitur under Sequitur's Target Validation Program that Isis ever had, now has or claims to have against such customers, up to and including the Effective Date of this Agreement.

2.2 Sequitur hereby releases, acquits and forever discharges Isis, and each of its predecessors, successors, receivers, assigns, affiliated entities, parent and subsidiary entities, past or present owners, shareholders, partners, investors, employees, agents, representatives, consultants, officers, directors, managers, and any other person, firm or corporation acting by, through, under or in concert with it, from any and all claims, demands, actions, causes of action, suits, obligations, damages, restitution, promises, controversies, contracts, agreements, expenses, costs, fees, and losses or liabilities of any type or nature whatsoever, in equity or at law, by statute or common law, whether or not now known, suspected, disclosed, or claimed, which Sequitur ever had, now has or claims to have against Isis up to and including the Effective Date of this Agreement, including but not limited to all claims for attorney's fees and costs. Without limiting the generality of the foregoing, Sequitur expressly agrees to withdraw, release, acquit and forever discharge Isis, and each of its predecessors, successors, receivers, assigns, affiliated entities, parent and subsidiary entities, past or present owners, shareholders, partners, investors, employees, agents, representatives, consultants, officers, directors, managers, and any other person, firm or corporation acting by, through, under or in concert with it, from any and all claims for recovery of sanctions or contempt arising from or related to the Lawsuit.

2.3 Each Party understands and expressly waives any rights or benefits available under Section 1542 of the Civil Code of California, which provides:

> "A general release does not extend to claims which the creditor does not know or suspect to exist in his favor at the time of executing the release, which if known by him must have materially affected his settlement with the debtor."

3. Restrictions on Use

3.1 During the term of this Agreement,:

(a) Sequitur will not make, have made, use, sell or offer to sell Next Generation Oligonucleotides in the United States; Sequitur may or will, as indicated below, however, perform the following activities with regard to Next Generation Oligonucleotides as part of Sequitur's Target Validation Program and its obligations hereunder:

(i) Sequitur may Provide and Resupply to an Existing Customer any Next Generation Oligonucleotide ordered by Sequitur prior to January 6, 2002;

(ii) Sequitur may Provide and Resupply to an Existing Customer any Next Generation Oligonucleotide that was purchased by Sequitur for such Existing Customer or provided to such Existing Customer by Sequitur prior to June 30, 2002;

(iii) Sequitur may Provide and Resupply to an Existing Customer any Next Generation Oligonucleotide that is Provided to such Existing Customer from Sequitur's stock of approximately 38 Next Generation Oligonucleotides which were ordered by Sequitur between January 4th, 2002 and June 30, 2002. Resupply will be completed by December 31, 2002. Sequitur must inventory its Next Generation

Oligonucleotides on a first in, first out basis, and may only have additional quantities of Next Generation Oligonucleotides made for Resupply after it has depleted its currently on-hand stock of such Next Generation Oligonucleotides;

(iv) Sequitur will provide to an independent Third Party, at Sequitur's expense a list of the currently existing Next Generation Oligonucleotides referenced above, and a supplier of Sequitur's choice will confirm with such Third Party its ability to make such Next Generation Oligonucleotides for Sequitur;

(v) Sequitur's agreement regarding restrictions on making, having made, using, selling or offering to sell use of Next Generation Oligonucleotides under this Section will terminate 7 years from the Effective Date of this Agreement. After 7 years from the Effective Date of this Agreement, Isis will, from time to time, give Sequitur a list of all patents and applications certified by Isis' patent counsel to cover Next Generation Oligonucleotides, and Sequitur agrees that it will not infringe valid claims in issued patents covering Next Generation Oligonucleotides on such list;

(vi) With regard to Sequitur's use or provision of Next Generation Oligonucleotides outside of the U.S., Sequitur agrees that it will not infringe any valid issued claims of any Isis owned or controlled European patents covering Next Generation Oligonucleotides. If, in the opinion of Isis, Sequitur does infringe any such patents outside the U.S., Isis may pursue any available legal remedy, and will not be bound by the Dispute Resolution provision of Section 15; and

(vii) Sequitur will use reasonable efforts to avoid infringing any Isis Patents.

(b) Sequitur will not advertise Next Generation Oligonucleotides, or promote Sequitur's services with data generated through the use of Next Generation Oligonucleotides after June 30, 2002;

(c) Sequitur's Existing Customers may use Next Generation Oligonucleotides Provided and Resupplied by Sequitur hereunder as part of Sequitur's Target Validation Program as expressly provided herein. Sequitur's Existing Customers may use Next Generation Oligonucleotides that were provided by Sequitur prior to June 30, 2002 at any time. Sequitur's Existing Customers may use Next Generation Oligonucleotides Provided or Resupplied by Sequitur after June 30, 2002 until June 30, 2003.

3.2 If Isis licenses any supplier to provide Next Generation Oligonucleotides to functional genomics service providers without restriction on resale (or to Sequitur specifically), Sequitur may buy Next Generation Oligonucleotides from such supplier.

4. Mutual Covenants

4.1 Isis and Sequitur each agree that it will not, and that its executive officers will not, disparage the other, the other's products or patents, or act as an advisor or expert witness for third parties against the other at any time.

4.2 Except as provided in Section 8.3, Isis and Sequitur each agree that for the period of 5 years from the Effective Date it will not, and that its executive officers will not, discuss or characterize the First Action, Counterclaim, Second Action, Third Action or the subject matter thereof, in whole or in part, other than by stating that "the litigation between the parties was settled on mutually satisfactory terms."

5. License Grants / Change of Control

5.1 Subject to the limitations and restrictions of Section 3.1, Isis hereby grants to Sequitur a non-exclusive, non-sublicensable, non-transferable, license under Isis First Generation Oligonucleotide Patents, to make, have made, use, sell, or offer to sell, First Generation Oligonucleotides solely for use in Sequitur's Target Validation Program. (For purposes of clarification, Sequitur's clients can use First Generation Oligonucleotides provided by Sequitur for the purposes of performing research regarding the validation or functionalization of gene targets or confirmation of such function.) The license granted pursuant to this Section extends to the termination of the last to expire licensed Patent, unless earlier terminated as provided herein. In the event of a Change of Control, the license granted in this Section 5.1 may be transferred to the successor entity who assumes all of Sequitur's rights and obligations hereunder.

5.2 In the event of a Change of Control:

a) the successor entity may maintain the Section 5.1 license by making the payments required in Section 6.1;

b) the successor entity may complete the Section 3.1 concessions in accordance with their terms; and

c) the Section 15 agreement to mediate will terminate.

6. Consideration

6.1 In consideration of (i) the releases and covenants set forth above, (ii) Isis' concessions regarding Sequitur's use of certain Next Generation Oligonucleotides as set forth in Section 3.1, (iii) the license granted in Section 5.1, (iv) the right granted to Sequitur to transfer the Section 5.1 license to the successor entity upon a Change of Control event, and (v) the agreement to mediate in Section 15.1 and the agreement to delay mediation in Section 15.2 below, Sequitur will pay Isis the amount of [***].

6.2 If Sequitur fails to make any [***] payment, the Section 5.1 license and the Section 15 agreement to mediate will terminate.

7. Statement of Confirmation

7.1 Isis confirms that Integrated DNA Technologies, Inc. does not as of the Effective Date have a license or right from Isis to supply Sequitur with Next Generation Oligonucleotides for use in Sequitur's Target Validation Program, and that Isis has not committed to provide such a license or right in the future.

8. Confidentiality and Publicity

8.1 Isis and Sequitur will not disclose to any third parties the terms and conditions of this Agreement without the prior written consent of all parties hereto except as otherwise provided herein.

8.2 The parties shall be permitted to disclose this Agreement as required by law. Should discovery of this Agreement be sought in a separate civil litigation, the parties shall be permitted to disclose this Agreement to certain qualified persons consented to by the non-producing party (either Sequitur or Isis) and identified in a protective order entered in the separate action.

8.3 The parties shall be free to disclose that Isis and Sequitur have reached a mutually agreeable business solution which settles the formerly disputed claims in the Lawsuit and Counterclaim, as set forth in the press release attached hereto as Exhibit B.

8.4 In the event that a third party requests due diligence on this Agreement, Sequitur may show the third party a version of this Agreement with Section 6 redacted, under a Confidential Disclosure Agreement.

8.5 The parties shall be permitted to disclose the terms of this agreement to such of their employees who have a need to know the terms hereof and who are bound by written obligation of confidentiality to the disclosing party. The parties may also disclose the terms of this agreement to their customers under the terms of written confidentiality agreements. Section 6 will be redacted in any event of disclosure under this Section 8.5 and, in the case of Isis, Section 15.2 will also be redacted.

9. Disposition of Pending Lawsuits and Allocation of Costs

9.1 Isis and Sequitur agree, promptly upon execution of this Agreement, to execute and cause to be filed a Stipulation of Dismissal of the Lawsuit, in the form attached hereto as Exhibit C. All parties' claims and counterclaims are dismissed with prejudice.

9.2 Each party will bear its own costs, expenses, expert witness fees, and attorneys' fees in connection with the Lawsuit and with this Agreement.

9.3 This Agreement shall be governed by, and construed in accordance with, the laws of the State of California.

9.4 The parties consent to the jurisdiction and venue of the United States District Court for the Southern District of California should any dispute arise between or among the parties concerning the interpretation and enforcement of this Agreement or the license grants hereunder not otherwise to be resolved by binding mediation pursuant to Section 15. The parties agree to file a joint stipulated Order consenting to jurisdiction with the Court in the form of Exhibit D hereto within ten (10) days of the Effective Date.

9.5 If the wording of Exhibits C and D cannot be agreed to by the Parties, Judge Stiven will resolve the differences.

10. Term and Termination

10.1 Term:

a) the releases and covenants in this Agreement will not terminate;

b) the Section 3.1 concessions will terminate in accordance with their terms;

c) the section 5.1 license will terminate with the last to expire Patent or in accordance with the terms of Section 6; and

d) the Section 15 agreement to mediate will terminate in accordance with the terms of Sections 5.2 and 6.2.

10.2 Except as expressly provided herein, mediation (rather than termination) shall be the sole remedy for a breach of this Agreement.

11. Agreement Binding On Successors

11.1 The provisions of this Agreement shall be binding upon and inure to the benefit of the parties hereto, their permitted heirs, administrators, successors and assigns, as noted below.

12. Nonassignability

12.1 The parties agree this Agreement imposes personal obligations on Isis and Sequitur. Sequitur shall not assign any rights under this Agreement, except in the event of a Change of Control, without the written consent of Isis. Isis may not assign its rights hereunder without the written consent of Sequitur. However, the releases and covenants are assigned to any successor in interest of either party.

13. Notices

13.1 Any notice or other communication required or permitted hereunder shall be in writing and shall be deemed given if: (i) delivered personally to an officer of the party to be notified; (ii) sent by facsimile transmission to the facsimile number set forth below; or (iii) sent by overnight courier or United States registered or certified mail, postage prepaid, return receipt requested, to the address set forth below:

If to Isis:

Isis Pharmaceuticals, Inc.
2292 Faraday Avenue
Carlsbad, California 92008
Attention: Executive Vice President
Facsimile: (760) 603-4650

with a copy to:

Attention: General Counsel
Facsimile: (760) 268-4922

If to Sequitur:

Sequitur, Inc.
14 Tech Circle
Natick, Massachusetts 01760
Attention: President
Facsimile: (508) 655-1625

or such other address or facsimile number as may be designated by any party hereto by written notice to the other as herein above provided.

14. Right to Review Records

14.1 From the date of execution of this Agreement until the end of the Term, Sequitur shall maintain records sufficient to reflect its purchase, manufacture, use and sales of Antisense Oligonucleotides. The records shall be kept by Sequitur for a period of at least 2 years following the calendar year to which they pertain. Isis will have the right to review these records as described below, solely for purposes of determining Sequitur's compliance with Section 3.1 of this Agreement regarding Next Generation Oligonucleotides.

14.2 Upon the written request of Isis, which shall be limited to no more than once per calendar year, Sequitur agrees to provide to an independent reviewer designated by Isis and reasonably agreed to by Sequitur records sufficient to determine Sequitur's compliance with the Restrictions on Use set forth in Section 3.1 of this Agreement. Sequitur shall not charge to produce the records, but Isis shall bear the costs for such review of records provided by Sequitur as provided above, unless the results of such review establish a violation by Sequitur of Section 3.1 of this Agreement, in which case Sequitur shall bear the cost of such review.

14.3 All such records produced pursuant to a request in accord with Section 14.1 or 14.2 shall be considered and maintained as confidential and shall not be disclosed to anyone except as provided herein. Records produced by Sequitur in response to a request by Isis pursuant to this Section 14 shall not be disclosed to anyone other than Isis's independent reviewer. If Isis' reviewer determines that a violation by Sequitur of Section 3.1 has occurred, records sufficient to establish such violation may be disclosed to a mediator pursuant to the Dispute Resolution provision of Section 15. Mediation regarding any violation discovered according to the review of this Section will proceed immediately, and will not be subject to the provision of Section 15 requiring 45 days of negotiation by the business principals of Isis and Sequitur.

15. Dispute Resolution

15.1 Isis and Sequitur agree that any real or perceived violations of this Settlement Agreement or other alleged future infringement of patents or future disputes regarding actions contemplated by this Agreement will be addressed in a face-to-face meeting of business principals of each company who will attempt to resolve any such issue. Isis and Sequitur agree to negotiate in good faith for a period of up to 45 days the nature of the violation and/or infringement and the magnitude of damages (if any). If Isis and Sequitur fail to reach agreement, the parties will submit to binding mediation to resolve the dispute. The mediator will be able to reasonably request documents from each Party to enable decision-making and will decide the claim scope and validity of any patents (only in regard to Sequitur). If the mediator determines that Sequitur or Isis is infringing it will immediately stop infringing. Notwithstanding the foregoing, if Sequitur has complied with Section 3.1 (vii) and, nevertheless, has infringed an Isis Patent, as long as Sequitur agrees to cease such infringement immediately, there will be no damages for infringement that occurs within 120 days of issuance of the patent, or use of oligonucleotides synthesized prior to 120 days after the patent issuance. The mediator cannot impose a license. The mediator will be selected mutually by the parties at a mutually agreed location. Such mutual agreement must be reached within two weeks. The mediator will be instructed that the parties desire to have the mediation process as inexpensive and rapid as possible consistent with achieving an accurate result and informed decision. Any mediator must have no affiliation in the past or present with any party or their employees. The mediator will decide what discovery if any is needed (and the time to comply with such discovery) and will have authority to obtain that discovery and impose penalties for non-compliance. All requests to the mediator will be made in letter format with no formal requirements except that a copy must be sent to the other party. The parties submit to the authority of the mediator in the place of any court and will be bound by all decisions of the mediator without recourse to any court or appeal therefrom. The mediator's decisions are final and if not followed may be enforced by a court of competent jurisdiction with all cost and attorney fees for such enforcement being paid by the losing party.

15.2 [***]

16. Integration

16.1 The provisions contained herein constitute the entire understanding between the parties with respect to the subject matter hereof, and revoke or supersede all prior Agreements between the parties with respect to the subject matter hereof, and is intended as a final expression of their

Agreement. This Agreement shall take precedence over any other documents that may be in conflict with said Agreement.

17. Effect of Headings

17.1 The headings and subheadings of the sections of this Agreement are inserted for convenience of reference only and shall not control or affect the meaning or construction of any of the Agreements, terms, covenants and conditions of this Agreement in any manner.

18. Severability

18.1 If any term or provisions of this Agreement shall be found to be void or contrary to law, such term or provision shall, but only to the extent necessary to bring this Agreement within the requirements of law, be deemed to be severable from the other terms and provisions hereof, and the remainder of this Agreement shall be given effect as if the parties had not included the severed term herein.

19. Amendments

19.1 No provision of this Agreement may be modified, waived or amended except by written instrument duly executed by each of the parties hereto and specifically referring to this Agreement. Any such modifications, waivers or amendments shall not require additional consideration to be effective.

20. Interpretation.

20.1 This Agreement, including the Exhibits hereto, is the result of bilateral negotiations between the parties and shall be construed without regard to the party or parties responsible for its preparation. In resolving any ambiguity or uncertainty existing herein, the parties agree that no consideration or weight shall be given to the identity of the party drafting this Agreement.

21. Counterparts

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

The parties have duly authorized and caused this Agreement to be executed as follows:

Dated: September 6, 2002 By: /s/ Grantland E. Bryce,
VP, Legal and General Counsel

Isis Pharmaceuticals, Inc.

Dated: September 6, 2002 By: /s/ Tod Woolf, President

Sequitur, Inc.

Exhibit A

Sequitur's Existing Customers

[***]

Exhibit B

Press Release (attached as Exhibit 99.1 to 8-K)

Exhibit C
Stipulated Dismissal and Proposed Order Thereon (attached)

STEPHEN P. SWINTON (106398)
KENT M. WALKER (173700)
COOLEY GODWARD LLP
4401 Eastgate Mall
San Diego, CA 92121-1909
Telephone: (858) 550-6000
Facsimile: (858) 550-6420

JOSEPH LUCCI (admitted *pro hac vice*)
WOODCOCK WASHBURN LLP
1 Liberty Place, 46th Floor
Philadelphia, PA 19103

Telephone: (215) 568-3100
Facsimile: (215) 568-3439

Attorneys for Plaintiff and Counterclaim Defendant
ISIS PHARMACEUTICALS, INC.

RICHARD WARBURG (155223)
ARTHUR A. WELLMAN, JR. (178309)
FOLEY & LARDNER
402 W. Broadway, 23rd Floor
San Diego, CA 92101-3542
Telephone: (619) 234-6655
Facsimile: (619) 234-3510

Attorneys for Defendant and Counterclaimant
SEQUITUR, INC.

UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF CALIFORNIA

ISIS PHARMACEUTICALS, INC., a Delaware corporation,

Plaintiff,

v.

SEQUITUR, INC., a Delaware corporation,

Defendant.

And Related Counterclaims.

No. 01 CV 1223, 01 CV 2286, and 02 CV 0842 B (JFS)

Stipulated Dismissal and [Proposed] Order thereon

Plaintiff and Counterclaim Defendant Isis Pharmaceuticals, Inc. and Defendant and Counterclaimant Sequitur, Inc., through their respective undersigned counsel, hereby stipulate that all

claims and counterclaims in the above-captioned actions are to be dismissed with prejudice, the parties bearing their own costs and fees of the actions.

Dated: September , 2002

Respectfully submitted,

COOLEY GODWARD LLP
STEPHEN P. SWINTON (106398)
KENT M. WALKER (173700)

By: _____
Kent M. Walker

Attorneys for Plaintiff and Counterclaim Defendant, ISIS PHARMACEUTICALS, INC.

Dated: September , 2002

FOLEY & LARDNER
RICHARD WARBURG (155223)
ARTHUR A. WELLMAN, JR. (178309)

By: _____
Richard Warburg
Arthur A. Wellman, Jr.

Attorneys for Defendant and Counterclaimant SEQUITUR, INC.

ORDER

Based on the stipulation of the parties, and good cause being shown, IT IS HEREBY ORDERED that all claims and counterclaims in the above-captioned actions are dismissed with prejudice, the parties bearing their own costs and fees of the actions.

IT IS SO ORDERED.

Dated: September , 2002

Judge Rudi M. Brewster

Exhibit D
Stipulated Consent to Jurisdiction and Proposed Order Thereon (attached)

STEPHEN P. SWINTON (106398)
KENT M. WALKER (173700)
COOLEY GODWARD LLP
4401 Eastgate Mall
San Diego, CA 92121-1909
Telephone: (858) 550-6000
Facsimile: (858) 550-6420

JOSEPH LUCCI (admitted *pro hac vice*)
WOODCOCK WASHBURN LLP
1 Liberty Place, 46th Floor
Philadelphia, PA 19103
Telephone: (215) 568-3100
Facsimile: (215) 568-3439

Attorneys for Plaintiff and Counterclaim Defendant
ISIS PHARMACEUTICALS, INC.

RICHARD WARBURG (155223)
ARTHUR A. WELLMAN, JR. (178309)
FOLEY & LARDNER
402 W. Broadway, 23rd Floor
San Diego, CA 92101-3542
Telephone: (619) 234-6655
Facsimile: (619) 234-3510

Attorneys for Defendant and Counterclaimant
SEQUITUR, INC.

UNITED STATES DISTRICT COURT

SOUTHERN DISTRICT OF CALIFORNIA

ISIS PHARMACEUTICALS, INC., a Delaware corporation,

Plaintiff,

v.

SEQUITUR, INC., a Delaware corporation,

Defendant.

And Related Counterclaims.

No. 01 CV 1223, 01 CV 2286, and 02 CV 0842 B (JFS)

Stipulated Consent to Jurisdiction and [Proposed] Order thereon

Whereas Plaintiff and Counterclaim Defendant Isis Pharmaceuticals, Inc. and Defendant and Counterclaimant Sequitur, Inc. executed a Settlement, Release, and License Grant Agreement ("the Agreement") whereby the parties stipulated that all claims and counterclaims in the above-captioned actions are to be dismissed with prejudice, the parties bearing their own costs and fees of the actions.

Whereas in the Agreement the parties consented to the jurisdiction and venue of the United States District Court for the Southern District of California should any dispute arise between or among the parties concerning the interpretation and enforcement of the Agreement or the license grants in the Agreement not otherwise to be resolved by binding mediation pursuant to Section 15 of the Agreement.

Therefore, the parties, by and through their respective attorneys of record, hereby stipulate to the following:

1. The United States District Court for the Southern District of California shall retain continuing jurisdiction over, and venue will be proper in, any dispute that may arise between or among the parties concerning the specific interpretation and enforcement of the Agreement and the license grants in the Agreement not otherwise to be resolved by binding mediation pursuant to Section 15 of the Agreement.

Dated: September , 2002

Respectfully submitted,

COOLEY GODWARD LLP
STEPHEN P. SWINTON (106398)
KENT M. WALKER (173700)
By:

Kent M. Walker

Attorneys for Plaintiff and Counterclaim Defendant, ISIS PHARMACEUTICALS, INC.

Dated: September , 2002

FOLEY & LARDNER
RICHARD WARBURG (155223)
ARTHUR A. WELLMAN, JR. (178309)

By:

Richard Warburg
Arthur A. Wellman, Jr.

Attorneys for Defendant and Counterclaimant SEQUITUR, INC.

ORDER

Based on the stipulation of the parties, and good cause being shown, IT IS HEREBY ORDERED that the United States District Court for the Southern District of California shall retain continuing jurisdiction over, and venue will be proper in, any dispute that may arise between or among the parties concerning the specific interpretation and enforcement of the Agreement and the license grants in the Agreement not otherwise to be resolved by binding mediation pursuant to Section 15 of the Agreement.

IT IS SO ORDERED.

Dated: September , 2002

Judge Rudi M. Brewster

QuickLinks -- Click here to rapidly navigate through this document

Exhibit 99.1

Contact: Kristina Peterson
(760) 603-2521

ISIS PHARMACEUTICALS AND SEQUITUR SETTLE PATENT INFRINGEMENT LAW SUIT

Sequitur Licenses Isis' Intellectual Property for Functional Genomics

Carlsbad, CA, September 16, 2002—Isis Pharmaceuticals, Inc. ("Isis") (NASDAQ:ISIS) announced today it has settled litigation pending against Sequitur, Inc. ("Sequitur). Isis had sued Sequitur, in three separate lawsuits, for alleged infringement of U.S. Patent Nos. 6,001,653; 6,326,199; 6,096,543; 5,959,097; and 5,958,773.

Isis and Sequitur reached a mutually agreeable business resolution that resulted in the dismissal of the three lawsuits and all counterclaims. Isis has granted Sequitur a license to certain Isis patents for target validation and functional genomics using first generation antisense oligonucleotides (also known as phosporothioate and/or phosphodiester deoxy antisense oligonucleotides) in exchange for undisclosed payments from Sequitur. Subject to a limited right to conclude existing customer contracts, Sequitur has agreed that it will not practice in the field of "second generation" or "next generation" antisense oligonucleotides, also known as chimeric antisense oligonucleotides.

"We are pleased with the favorable and expeditious end to this matter, as the settlement terms underscore the importance of Isis' intellectual property position in antisense technology," said B. Lynne Parshall, Isis Executive Vice President and CFO. "We are deriving value from our investment in innovation as we have licensed our patents to several industry partners who perform antisense-based functional genomics as part of internal drug discovery programs."

Isis owns a broad intellectual property estate of nearly 1000 issued patents that covers RNA-based drug discovery and development. The patent portfolio covers the use of antisense inhibitors as drugs, 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. Isis' patent estate also covers the use of antisense inhibitors as tools for gene functionalization and target validation. Isis builds its intellectual property position through internal scientific innovation and by licensing 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 antisense products in its development pipeline with two in late-stage development and six in Phase II human clinical trials. Affinitac™, 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 in a Phase III trial in Crohn's disease. Isis has a broad patent estate as the owner or exclusive licensee of nearly 1000 issued patents worldwide. Isis' GeneTrove™ division uses antisense to assist pharmaceutical industry partners in validating and prioritizing potential gene targets through customized services. 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.isispharm.com*.

This press release contains forward-looking statements concerning Isis Pharmaceuticals and the potential of the company's intellectual property position. Any statement describing a goal, expectation, intention or belief of the Company is a forward-looking statement and should be considered an at-risk statement. 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, the reader is 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 Annual Report on Form 10K, for the period ended

---

December 31, 2001, which is on file with the U.S. Securities and Exchange Commission, copies of which are available from the Company.

Affinitac™, a trademark of Eli Lilly and Company, is an investigational cancer compound being developed through an alliance between Lilly and Isis Pharmaceuticals, Inc. and marketed globally by Lilly. GeneTrove™ and Ibis Therapeutics™ are trademarks of Isis Pharmaceuticals, Inc. Vitravene® is a registered trademark of Novartis AG.

QuickLinks

ISIS PHARMACEUTICALS AND SEQUITUR SETTLE PATENT INFRINGEMENT LAW SUIT