

SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

SCHEDULE 13D

Under the Securities Exchange Act of 1934 (Amendment No. \_\_\_)\*

ISIS PHARMACEUTICALS, INC.

-----  
(Name of Issuer)

Common Stock  
Warrant  
Convertible Promissory Note

-----  
(Title of Class of Securities)

464330-1-09

-----  
(CUSIP Number)

Elan Corporation, plc  
Lincoln House  
Lincoln Place  
Dublin 2  
Ireland

Attention: General Counsel

-----  
Copy to:

Brock Silverstein LLC  
800 Third Avenue  
21st Floor  
New York, New York 10022  
Attn: David Robbins/Kim Lefkowitz

-----  
(Name, Address and Telephone Number of Person Authorized to  
Receive Notices and Communications)

December 20, 2000

-----  
(Date of Event which Requires Filing of this Statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition which is the subject of this Schedule 13D, and is filing this schedule because of ss.ss. 240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box.    / /

Note: Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See ss. 240.13d-7(b) for other parties to whom copies are to be sent.

\*The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

SCHEDULE 13D

CUSIP No. 82123D 30 9

PAGE 2 OF 8 PAGES

(1) Names of Reporting Persons

I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Elan Corporation, plc

(2) CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (A) / /  
(SEE INSTRUCTIONS) (B) / /

(3) SEC USE ONLY

(4) SOURCE OF FUNDS (SEE INSTRUCTIONS)

WC

(5) CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO  
ITEMS 2(d) or 2(e) / /

(6) CITIZENSHIP OR PLACE OF ORGANIZATION

Ireland

NUMBER OF SHARES

(7) SOLE VOTING POWER

BENEFICIALLY OWNED

2,150,405 shares (assumes conversion of  
convertible promissory notes into 712,061  
shares of Common Stock as at December 20,  
2000)

BY EACH REPORTING

PERSON WITH

(8) SHARED VOTING POWER

-0-

(9) SOLE DISPOSITIVE POWER

2,150,405 shares (assumes conversion of  
convertible promissory notes into 712,061  
shares of Common Stock as at December 20,  
2000)

(10) SHARED DISPOSITIVE POWER

-0-

(11) AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

2,150,405 (assumes conversion of convertible promissory notes into 712,061  
shares of Common Stock and conversion of warrants to purchase up to 229,880  
shares of Common Stock)

(12) CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN / /  
SHARES (SEE INSTRUCTIONS)

(13) PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11)

5.24% (based on 40,119,564 shares of Common Stock of the Issuer outstanding  
as of January 12, 2001, as reported on the Issuer's Form 10K, dated  
February 26, 2001, plus the conversion of the convertible promissory notes  
into 712,061 shares of Common Stock and warrants to purchase up to 229,880  
shares of Common Stock)

(14) TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)

CO

ITEM 1. SECURITY AND ISSUER.

- (a) 1,208,463 shares of Common Stock, par value \$0.001 per share (the "Common Stock");
- (b) Convertible Promissory Note for up to \$18,400,000 principal amount outstanding ("Note 1")
- (c) Convertible Promissory Note for up to \$12,015,000 principal amount outstanding ("Note 2");
- (d) Warrant to purchase up to 215,000 shares of Common Stock ("Warrant 1");
- (e) Warrant to purchase up to 14,881 shares of Common Stock ("Warrant 2");
- (f) 120,150 shares of Series A Convertible Exchangeable Preferred Stock par value \$0.001; and
- (g) 12,015 shares of Series B Convertible Exchangeable Preferred Stock par value \$0.001.

ISIS Pharmaceuticals, Inc.  
2292 Faraday Avenue  
Carlsbad, California 92008

ITEM 2. IDENTITY AND BACKGROUND.

This Form 13-D is filed by Elan Corporation, plc, an Irish public limited company ("Elan"), located at Lincoln House, Lincoln Place, Dublin 2, Ireland. Elan is the parent company of Elan International Services, Ltd., a Bermuda exempted limited liability company ("EIS"), located at 102 St. James Ct., Flatts Smith Partsh, Bermuda FL 04. Elan is the sole beneficial owner of Elan Pharmaceutical Investments Ltd., a Bermuda exempted limited liability company ("EPIL"), of 102 St. James Court, Parish, Bermuda FL 04 and Elan Pharmaceutical Investments II, Ltd., a Bermuda exempted limited liability company ("EPIL II"), located at 102 St. James Court, Flatts, Smiths Parish, Bermuda, Fl 04. During the last five years, none of the persons named above in this Item 2: (i) has been convicted in a criminal proceeding (excluding traffic violations or similar misdemeanors); or (ii) was a party to a civil proceeding of a judicial or administrative body of competent jurisdiction, as a result of which proceeding it was or is subject to a judgment, decree or final order enjoining future violations of, or prohibiting or mandating activities subject to, United States federal or state securities laws, or finding any violation with respect to such laws.

ITEM 3. SOURCE AND AMOUNT OF FUNDS OR OTHER CONSIDERATION.

On April 20, 1999, pursuant to the terms of a securities purchase agreement dated April 20, 1999 ("SPA 1") among EIS on the one hand, and Isis Pharmaceuticals Inc., a Delaware corporation (the "Issuer"), on the other hand, EIS acquired: (a) 910,844 shares of Common Stock; (b) Warrant 1, to purchase up to 215,000 shares of Common Stock (exercisable at any time); (c) 120,150 shares of Series A Convertible Exchangeable Preferred Stock (convertible into Common Stock after March 31, 2002); and (d) Note 1, for up to an aggregate principal amount outstanding of \$18,400,000, which is convertible on five days' written notice into shares of Common Stock. Note 1 bears interest at 12% per annum, compounding semi annually.

The Series A Convertible Exchangeable Preferred Stock is convertible into Common Stock at any time and from time to time after March 31, 2002. The Series A Convertible Exchangeable Preferred Stock is not convertible prior to March 31, 2002 unless there is: (a) an event of reorganization, merger or consolidation where the original shareholders of the Issuer prior to the event no

longer hold 50% of the voting power of the Issuer; (b) an acquisition of all outstanding capital stock of the Issuer; (c) a sale of all or substantially all of the Issuer's assets; or (d) a liquidation or winding down of the Issuer's business. The Series A Convertible Exchangeable Preferred Stock bears an annual mandatory dividend equal to 5.0% per year of \$100 per share payable to issuances of additional Common Stock or conversion.

On June 29, 1999, pursuant to an Asset Transfer Agreement dated June 29, 1999 ("Transfer Agreement 1") EIS transferred to EPIL its right, title and interest to: (a) 910,844 shares of Common Stock; (b) Warrant 1 (the right to purchase up to 215,000 shares of Common Stock); and (c) 120,150 shares of the Issuers Series A Convertible Exchangeable Preferred Stock. The rights to Note 1 (for up to an aggregate principal amount of \$18,400,000) remained with EIS.

On January 14, 2000, pursuant to a securities purchase agreement dated January 14, 2000 ("SPA 2") among EIS on the one hand and the Issuer on the other hand, EIS acquired (a) \$7,500,000 worth of Common Stock (which amounted to 297,619 shares of Common Stock); (b) Warrant 2, to purchase 5% of the number of the shares of Common Stock acquired by EIS under Securities Purchase Agreement 2 (which amounted to 14,881 shares of Common Stock) (exercisable at any time); (c) 12,015 shares of Series B Convertible Exchangeable Preferred Stock (not convertible into Common Stock until after June 30, 2002) and (d) Note 2, for up to an aggregate principal amount outstanding of \$12,015,000 which is convertible on five days' written notice into shares of Common Stock. Note 2 bears interest at 12% per annum, compounding semi annually.

The Series B Convertible Exchangeable Preferred Stock is convertible into Common Stock at any time and from time to time after June 30, 2002. The Series B Convertible Exchangeable Preferred Stock is not convertible prior to June 30, 2002 unless there is (a) an event of reorganization, merger or consolidation where the original shareholders of the Issuer no longer hold 50% of the voting power of the Issuer; (b) an acquisition of all outstanding capital stock of the Issuer; (c) a sale of all or substantially all of the Issuer's assets; or (d) a liquidation or winding down of the Issuer's business. The Series B Convertible Exchangeable Preferred Stock bears an annual mandatory dividend equal to 5.0% per year of \$1,000 per share payable to issuances of additional Common Stock or conversion.

On June 20, 2000, pursuant to an Asset Transfer Agreement dated June 20, 2000, ("Transfer Agreement 2") EIS transferred to EPIL II its right, title and interest to: (a) 297,619 shares of the Common Stock; (b) Warrant 2 (the right to purchase up to 14,881 shares of Common Stock); (c) 12,015 shares of Series B Convertible Exchangeable Preferred Stock; and (d) the amounts currently outstanding to the Issuer under Notes 1 and 2 (\$5,062,805 excluding accumulated interest for Note 1 and Nil for Note 2 respectively). The remaining rights to Note 1 and Note 2 remained with EIS.

#### ITEM 4. PURPOSE OF TRANSACTION.

Elan acquired the Securities for investment purposes.

Except as set forth above, Elan does not have a plan or proposal which relates to or would result in:

(a) The acquisition by any person of additional securities of the Issuer, or the disposition of securities of the Issuer;

(b) An extraordinary corporate transaction such as a merger, reorganization or liquidation involving the Issuer or any of its subsidiaries;

(c) A sale or transfer of a material amount of assets of the Issuer or any of its subsidiaries;

(d) Any change in the present Board of Directors or management of the Issuer, including any plans or proposals to change the number of or term of Directors or to fill any existing vacancies on the Board;

(e) Any material change in the present capitalization or dividend policy of the Issuer;

(f) Any other material change in the Issuer's business or corporate structure;

(g) Changes in the Issuer's charter, by-laws, or instruments corresponding thereto or other actions which may impede the acquisition of control of the Issuer by any person;

(h) Causing the Common Stock to cease to be authorized to be traded on the Nasdaq National Stock Market.

(i) To have the Common Stock terminated from registration under the Securities Act of 1933; or

(j) Any action similar to any of those enumerated above.

ITEM 5. INTEREST IN THE SECURITIES OF THE ISSUER.

(a) 2,150,405 shares (or rights to convert into shares) of Common Stock representing 5.24% of the Issuer's Common Stock (based on 40,119,564 shares of Common Stock of the Issuer outstanding as of January 12, 2001, as reported on the Issuer's Form 10K, dated February 26, 2001 plus the conversion of the convertible promissory notes into 712,061 shares of Common Stock and warrants to purchase up to 229,880 shares of Common Stock).

(b) sole power to vote: 2,150,405  
shares shared power to vote: -0-  
sole power to dispose: 2,150,405  
shared power to dispose: -0-

(c) None.

(d) None.

(e) Not Applicable.

ITEM 6. CONTRACTS, ARRANGEMENTS, UNDERSTANDINGS OR RELATIONSHIPS WITH RESPECT TO SECURITIES OF THE ISSUER.

Not Applicable.

ITEM 7. MATERIAL TO BE FILED AS EXHIBITS.

EXHIBIT INDEX

1. Securities Purchase Agreement, dated as of April 20, 1999, as filed as exhibit 10.2 to the Issuer's Form 8-K as filed on May 3, 1999.

2. Convertible Promissory Note dated April 20, 1999, as filed as exhibit 10.3 to the Issuer's Form 8-K as filed on May 3, 1999.
3. Warrant to purchase shares of Common Stock dated April 20, 1999, as filed as exhibit 10.4 to the Issuer's Form 8-K as filed on May 3, 1999.
4. Securities Purchase Agreement, dated January 14, 2000, as filed as exhibit 10.2 to the Issuer's Form 8-K as filed on January 14, 2000.
5. Convertible Promissory Note, dated January 14, 2000, as filed as exhibit 10.3 to the Issuer's Form 8-K as filed on January 14, 2000.
6. Form of Warrant to purchase shares of Common Stock, of contingent date, as filed as exhibit 10.4 to the Issuer's Form 8-K as filed on January 14, 2000.

SIGNATURES

After reasonable inquiry and to the best of my knowledge and belief, the undersigned certifies that the information set forth in this statement is true, complete and correct.

Date: April 12, 2001

Elan Corporation, plc.

By: /s/ Liam Daniel

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Name: Liam Daniel  
Title: Group Vice President,  
Finance and Controller

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