### FORM 4

## UNITED STATES SECURITIES AND EXCHANGE COMMISSION Washington, D.C. 20549

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b)

# STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934, Section 17(a) of the Public Utility Holding Company Act of 1935 or Section 30(h) of the Investment Company Act of 1940

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OMB APPROVAL

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www.section16.net 1. Name and Address of Reporting Person\* 2. Issuer Name **and** Ticker or Trading Symbol 6. Relationship of Reporting Person(s) Isis Pharmaceuticals, Inc. (ISIS) to Issuer (Check all applicable) Director 10% Owner Levin Arthur A X Officer (give title below) \_ Other (specify below) 3. I.R.S. Identification Number (Last) (First) (Middle) 4. Statement for Month/Day/Year of Reporting Person, Vice President 2292 Faraday Avenue if an entity (voluntary) 10/31/02 5. If Amendment, 7. Individual or Joint/Group Filing (Check Applicable Line) (Street) Date of Original X Form filed by One Reporting Person Carlsbad, CA 92008 (Month/Day/Year) Form filed by More than One Reporting Person Table I — Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned (City) (State) (Zip) 2A. Deemed 3. Trans-4. Securities Acquired (A) or Disposed of (D) 5. Amount of 6. Owner-1. Title of Security 2. Trans-7. Nature of Indirect Execution action Code (Instr. 3, 4 & 5) ship Form: Beneficial Ownership (Instr. 3) action Securities Date Date. (Instr. 8) Beneficially Direct (D) (Instr. 4) (Month/ Day if anv Owned Followor Indirect (I) Code Amount (A) Price Year) (Month/Day ing Reported Transactions(s) (Instr. 4) or (Instr. 3 & 4) (D) 10/31/02 10/31/02 1125 Common Stock M

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

 $S^{(1)}$ 

M

s(2)

9.625 10/31/02 10/31/02

M

10/31/02

10/31/02

10/31/02

10/31/02

10/31/02

10/31/02

Common Stock

Common Stock

Common Stock

FORM 4 (continued)

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Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned

1125

1407

1407

D

Α

D

10.1616

9.625

10.1616

178

D

### (e.g., puts, calls, warrants, options, convertible securities) 1. Title of 2. Conver-3. Trans-3A. 5. Number of Derivative 6. Date 7. Title and Amount 8. Price of 9. Number of 10. 11. Nature Derivative sion or action Deemed Trans-Securities Acquired (A) or Exercisable of Underlying Derivative Derivative Ownerof Indirect Security Exercise Date Execution action Disposed of (D) and Expiration Securities Security Securities ship Beneficial Price of Date, Beneficially Form Ownership Code Date (Instr. 3 & 4) (Instr. 5) (Month/ Month/Day/ (Instr. 3) Derivative if any (Instr. 3, 4 & 5) Owned οf (Instr. 4) Day/ Year) (Month Security (Instr. Following Deriv-Year) Day/ ative **(8**) Reported Year) Transaction(s)|Security: (Instr. 4) Direct (D) Title Code (A) Date Expira-Amount (D) Exertion or cisable Date Number Indirect lof (I)Shares (Instr. 4) Employee Stock 9.625 10/31/02 10/31/02 M 1125 (3) 1/1/11 Common 1125 1875 Ι by wife

1407 (4)

Explanation of Responses:

Option (right to

Employee Stock

Option (right to

buv)

buy)

- (1) The sale reported in this Form 4 was effected pursuant to a Rule 10b5-1 trading plan adopted by the reporting person's wife on August 19, 2002.
- (2) The sale reported in this Form 4 was effected pursuant to a Rule 10b5-1 trading plan adopted by the reporting person's wife on August 19, 2002.
- (3) On July 31, 2002, the spouse of the reporting person terminated her employment with the Issuer. On such date, 1,125 shares subject to the option were vested and exercisable. Due to her termination, the remaining 1,875 unexercisable shares expired at the end of the day on October 31, 2002.
- (4) On July 31, 2002, the spouse of the reporting person terminated her employment with the Issuer. On such date, 1,407 shares subject to the option were vested and exercisable. Due to her termination, the remaining 2,343 u nexercisable shares expired at the end of the day on October 31, 2002.

1/1/11

Stock

Stock

Common

1407

2343

ī

by wife

<sup>\*</sup> If the form is filed by more than one reporting person, see Instruction 4(b)(v).

## \*\*Signature of Reporting Person

\*\*Intentional misstatements or omissions of facts constitute Federal Criminal Violations. See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, See Instruction 6 for procedure.

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