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

OMB Number: 3235-0287

OMB APPROVAL

Expires: January 31, 2005 Estimated average burden hours per response. . .0.5

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 Filed By Romeo & Dye's Instant Form 4 Filer 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) (Last) (First) (Middle) 3. I.R.S. Identification Number 4. Statement for Month/Day/Year of Reporting Person, 2292 Faraday Avenue if an entity (voluntary) 10/28/02 Vice President 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 (City) (State) (Zip) Table I — Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned 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 Owned Followor Indirect (I) lif anv Code Amount (A) Price Year) (Month/Day ing Reported Transactions(s) (Instr. 4) or (Instr. 3 & 4) (D) 10/28/02 10/28/02 Common Stock M 1269 10/28/02 10/28/02 $S^{(1)}$ 1269 D \$9.7341 Common Stock 10/28/02 10/28/02 1510 Common Stock M Α \$8.375 Common Stock 10/28/02 10/28/02 s(2)1510 D \$9,7341 178 D

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

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB control number

FORM 4 (continued) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) 7. Title and Amount 8. Price of 1. Title of 2. Conver-3. Trans-3A. 5. Number of Derivative 6. Date 9. Number of 10. 11. Nature Derivative action Deemed Trans-Securities Acquired (A) or Exercisable of Underlying Derivative Derivative Ownerof Indirect lsion or ship Security Exercise Date Execution action Disposed of (D) and Expiration Securities Security Securities Beneficial Date, Price of 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/ Reported **(8**) lative Year) Transaction(s)|Security: (Instr. 4) Direct (D) Title Code (A) Date Expira-Amount (D) tion Exeror cisable Date Number Indirect lof (I)Shares (Instr. 4) Employee Stock \$6.81 10/28/02 10/28/02 M 1269 (3). 1/5/10 Common 1269 1631 Ι by wife Option (right to Stock buv) Employee Stock \$8.375 10/28/02 10/28/02 1510 (4) 1/31/10 Common 1510 990 М ī by wife Option (right to Stock buy)

Explanation of Responses:

- (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, 1,269 shares subject to the option were vested and
- (4) On July 31, 2002, the spouse of the reporting person terminated her employment with the Issuer. On such date, 1,510 shares subject to the option were vested and exercisable.

^{*} 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.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.