## 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 or Section 30(h) of the Investment Company Act of 1940

# OMB APPROVAL OMB Number: 3235-0287 Estimated average burden

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|                         | hours per response:      | 0.5 |

|               |                      |          | of Section So(ii) of the investment Company Act of 1940                          |                                                                            |                                |                     |  |  |  |
|---------------|----------------------|----------|----------------------------------------------------------------------------------|----------------------------------------------------------------------------|--------------------------------|---------------------|--|--|--|
|               | ess of Reporting Per | son*     | 2. Issuer Name and Ticker or Trading Symbol<br>ISIS PHARMACEUTICALS INC [ ISIS ] | 5. Relationship of Reporting Person(s) to Issuer<br>(Check all applicable) |                                |                     |  |  |  |
| LEVIN ART     | <u>HUR A</u>         |          |                                                                                  |                                                                            | Director                       | 10% Owner           |  |  |  |
|               |                      |          | ,                                                                                | x                                                                          | Officer (give title            | Other (specify      |  |  |  |
| (Last)        | (First)              | (Middle) | 3. Date of Earliest Transaction (Month/Day/Year)                                 |                                                                            | below)                         | below)              |  |  |  |
| C/O ISIS PHAI | RMACEUTICAL          | S, INC.  | 01/02/2007                                                                       |                                                                            | Vice Presi                     | dent                |  |  |  |
| 1896 RUTHER   | FORD ROAD            |          |                                                                                  |                                                                            |                                |                     |  |  |  |
|               |                      |          | 4. If Amendment, Date of Original Filed (Month/Day/Year)                         | 6. Indiv<br>Line)                                                          | idual or Joint/Group Filin     | g (Check Applicable |  |  |  |
| (Street)      | <b>C 1</b>           | 00000    |                                                                                  | X                                                                          | Form filed by One Rep          | porting Person      |  |  |  |
| CARLSBAD      | CA                   | 92008    |                                                                                  |                                                                            | Form filed by More that Person | an One Reporting    |  |  |  |
| (City)        | (State)              | (Zip)    |                                                                                  |                                                                            | 1 613011                       |                     |  |  |  |

#### Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned

| 1. Title of Security (Instr. 3) | 2. Transaction<br>Date<br>(Month/Day/Year) | 2A. Deemed<br>Execution Date,<br>if any<br>(Month/Day/Year) | n Date, Transa<br>Code (I |   | 4. Securities Acquired<br>Disposed Of (D) (Instr.<br>5) |               |       | 5. Amount of<br>Securities<br>Beneficially<br>Owned Following<br>Reported | 6. Ownership<br>Form: Direct<br>(D) or Indirect<br>(I) (Instr. 4) | 7. Nature of<br>Indirect<br>Beneficial<br>Ownership |
|---------------------------------|--------------------------------------------|-------------------------------------------------------------|---------------------------|---|---------------------------------------------------------|---------------|-------|---------------------------------------------------------------------------|-------------------------------------------------------------------|-----------------------------------------------------|
|                                 |                                            |                                                             | Code                      | v | Amount                                                  | (A) or<br>(D) | Price | Transaction(s)<br>(Instr. 3 and 4)                                        |                                                                   | (Instr. 4)                                          |

 Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

|                                                     |                                                                       |                                            | (- 5 )                                                      | -                            | · | -                                                                                               |                              | -                                                  |                    |                                                                       |                                        |                                                     |                                                                                                                            |                                                                          |                                                                    |
|-----------------------------------------------------|-----------------------------------------------------------------------|--------------------------------------------|-------------------------------------------------------------|------------------------------|---|-------------------------------------------------------------------------------------------------|------------------------------|----------------------------------------------------|--------------------|-----------------------------------------------------------------------|----------------------------------------|-----------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|--------------------------------------------------------------------|
| 1. Title of<br>Derivative<br>Security<br>(Instr. 3) | 2.<br>Conversion<br>or Exercise<br>Price of<br>Derivative<br>Security | 3. Transaction<br>Date<br>(Month/Day/Year) | 3A. Deemed<br>Execution Date,<br>if any<br>(Month/Day/Year) | 4.<br>Transa<br>Code (<br>8) |   | 5. Numb<br>of<br>Derivati<br>Securiti<br>Acquire<br>(A) or<br>Dispose<br>of (D) (II<br>3, 4 and | ve<br>es<br>d<br>ed<br>nstr. | 6. Date Exerci:<br>Expiration Dat<br>(Month/Day/Ye | e                  | 7. Title an<br>of Securiti<br>Underlyin<br>Derivative<br>(Instr. 3 ar | ies<br>g<br>Security                   | 8. Price of<br>Derivative<br>Security<br>(Instr. 5) | 9. Number of<br>derivative<br>Securities<br>Beneficially<br>Owned<br>Following<br>Reported<br>Transaction(s)<br>(Instr. 4) | 10.<br>Ownership<br>Form:<br>Direct (D)<br>or Indirect<br>(I) (Instr. 4) | 11. Nature<br>of Indirect<br>Beneficial<br>Ownership<br>(Instr. 4) |
|                                                     |                                                                       |                                            |                                                             | Code                         | v | (A)                                                                                             | (D)                          | Date<br>Exercisable                                | Expiration<br>Date | Title                                                                 | Amount<br>or<br>Number<br>of<br>Shares |                                                     |                                                                                                                            |                                                                          |                                                                    |
| Employee<br>Stock<br>Option<br>(right to<br>buy)    | \$11.12                                                               | 01/02/2007                                 | 01/02/2007                                                  | A                            |   | 36,145                                                                                          |                              | 01/02/2008 <sup>(1)</sup>                          | 01/01/2014         | Common<br>Stock                                                       | 36,145                                 | \$0                                                 | 36,145                                                                                                                     | D                                                                        |                                                                    |

#### Explanation of Responses:

1. Grant of 1-2-07 to reporting person of stock options under the Isis Pharmaceuticals, Inc. 1989 Stock Option Plan. 25% of the shares subject to the option will vest and become exercisable on 1-2-08. Thereafter, the remaining shares subject to the option vest and become exercisable in 36 equal monthly installments, at the rate of 9,036 shares per year. The option is exercisable as to 0 shares on 1-2-07.

#### **Remarks:**

#### /s/B. Lynne Parshall, Attorney-01/03/2007

in-Fact

\*\* Signature of Reporting Person Date

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

 $^{\ast}$  If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

\*\* 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.