

| OMB APPROVAL | |
|--|-----------|
| OMB Number: | 3235-0287 |
| Estimated average burden hours per response: | 0.5 |

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

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

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

| | | | | | | | | |
|---|---------|----------|---|--|--|--|--|--|
| 1. Name and Address of Reporting Person* GABRIELI CHRISTOPHER | | | 2. Issuer Name and Ticker or Trading Symbol ISIS PHARMACEUTICALS INC [ISIS] | | | 5. Relationship of Reporting Person(s) to Issuer (Check all applicable) <input checked="" type="checkbox"/> Director 10% Owner Officer (give title below) Other (specify below) | | |
| (Last) | (First) | (Middle) | 3. Date of Earliest Transaction (Month/Day/Year) 05/14/2004 | | | 6. Individual or Joint/Group Filing (Check Applicable Line) <input checked="" type="checkbox"/> Form filed by One Reporting Person Form filed by More than One Reporting Person | | |
| 1865 PALMER AVE, SUITE 104 | | | 4. If Amendment, Date of Original Filed (Month/Day/Year) | | | | | |
| (Street) LARCHMONT NY 10538 | | | | | | | | |
| (City) (State) (Zip) | | | | | | | | |

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

| 1. Title of Security (Instr. 3) | 2. Transaction Date (Month/Day/Year) | 2A. Deemed Execution Date, if any (Month/Day/Year) | 3. Transaction Code (Instr. 8) | | 4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5) | | | 5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4) | 6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 7. Nature of Indirect Beneficial Ownership (Instr. 4) |
|---------------------------------|--------------------------------------|--|--------------------------------|---|---|------------|---------|---|--|---|
| | | | Code | V | Amount | (A) or (D) | Price | | | |
| Common Stock | 05/14/2004 | 05/14/2004 | M | | 20,000 ⁽¹⁾ | A | \$6.375 | 175,431 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 1,000 | D | \$6.82 | 174,431 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 1,000 | D | \$6.8 | 173,431 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 1,000 | D | \$6.79 | 172,431 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 2,500 | D | \$6.78 | 169,931 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 1,100 | D | \$6.77 | 168,831 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 2,700 | D | \$6.75 | 166,131 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 200 | D | \$6.74 | 165,931 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 1,000 | D | \$6.73 | 164,931 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 2,000 | D | \$6.72 | 162,931 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 1,000 | D | \$6.71 | 161,931 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 500 | D | \$6.7 | 161,431 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 1,000 | D | \$6.65 | 160,431 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 1,500 | D | \$6.63 | 158,931 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 1,800 | D | \$6.62 | 157,131 | D | |
| Common Stock | 05/14/2004 | 05/14/2004 | S | | 1,700 | D | \$6.61 | 155,431 | D | |
| Common Stock | | | | | | | | 740 | I | Footnote ⁽²⁾ |

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

| 1. Title of Derivative Security (Instr. 3) | 2. Conversion or Exercise Price of Derivative Security | 3. Transaction Date (Month/Day/Year) | 3A. Deemed Execution Date, if any (Month/Day/Year) | 4. Transaction Code (Instr. 8) | | 5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) | | 6. Date Exercisable and Expiration Date (Month/Day/Year) | | 7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4) | | 8. Price of Derivative Security (Instr. 5) | 9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4) | 10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 11. Nature of Indirect Beneficial Ownership (Instr. 4) |
|--|--|--------------------------------------|--|--------------------------------|---|--|-----|--|-----------------|---|----------------------------|--|--|---|--|
| | | | | Code | V | (A) | (D) | Date Exercisable | Expiration Date | Title | Amount or Number of Shares | | | | |
| Employee Stock Option (right to buy) | \$6.375 | 05/14/2004 | 05/14/2004 | M | | 20,000 ⁽¹⁾ | | 05/16/1999 | 05/15/2004 | Common Stock | 20,000 | \$0 | 0 | D | |

Explanation of Responses:

1. Acquired as a result of exercising a stock option that was scheduled to expire on 5-15-04.

2. Owned indirectly by the Gabrieli Family Foundation, a charitable foundation. The reporting person may be deemed to be a beneficial owner of such shares by virtue of his position as Trustee, but disclaims beneficial ownership.

Remarks:

Christopher F. O. Gabrieli

05/18/2004

** Signature of Reporting Person

Date

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

* 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.