FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

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| STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP | - 11 | ı |
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| | OMB APPROVAL | | | | | | | | | | |
|--------------------------|---------------------|-----------|--|--|--|--|--|--|--|--|--|
| | OMB Number: | 3235-0287 | | | | | | | | | |
| Estimated average burden | | | | | | | | | | | |
| | hours per response: | 0.5 | | | | | | | | | |

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

| (Last) (First) (Middle) C/O ISIS PHARMACEUTICALS, INC. 2855 GAZELLE COURT (Street) CARLSBAD CA 92010 Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned (Month/Day/Year) 1. Title of Security (Instr. 3) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried (Month/Day/Year) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried (Month/Day/Year) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, countried) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warr | Name and Address of Reporting Person* Monia Brett P | | | | | | 2. Issuer Name and Ticker or Trading Symbol ISIS PHARMACEUTICALS INC [ISIS] | | | | | | | | (Check | all app Direc | olicable) | g Person(s) to I: 10% (| |
|--|---|--|--|--|--|--------------------------|--|---------------------|-------------|--|------|----------------------|-------------------|--|--|--|---------------------------------|--|------------|
| Carlibration Carl | C/O ISIS | | | | | | | | | | X | belov | N) . | below |) | | | | |
| Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned 1. Title of Security (Instr. 3) 2. Transaction Date (Month/Day/Year) 3. Transaction Date (Instr. 3, 4 and 5) 3. Transaction (Dodg (Instr. 3, 4 and 5) 4. Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 5. Amount (A) or Price (D) or Indirect (D) | (Street) | | | | | 4. If | 4. If Amendment, Date of Original Filed (Month/Day/Year) | | | | | | | | X Form filed by One Reporting Person Form filed by More than One Reporting | | | | |
| 1. Title of Security (Instr. 3) 2. Transaction Date (Month/Day/Year) 2. Transaction Code (Instr. 4) 2. Transaction Date (Month/Day/Year) 2. Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) 1. Title of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) 3. Transaction Date (I) (Instr. 4) 4. Transaction Date (Month/Day/Year) 3. Transaction Date (I) (Instr. 4) 4. Transaction Date (Month/Day/Year) 5. Number of Derivative Securities Date (Month/Day/Year) 6. Ownership Form: Direct (D) or Indirect (D) or In | (City) | (St | | | D i | | 0 | | - 4 - | | L D: | | f | 6 | -: | 0 | | | |
| Date (Month/Day/Year) Price (Month/Day/Yea | | | | | | | | | | | | | | | | | | | |
| Common Stock O7/01/2014 O7/01/2014 J(I) V T6 A \$30.2005 1,892 D | Date | | | | | Execut (/Year) if any | | ecution Date, ny | | Transaction Code (Instr. | | | | | Securities Beneficially Owned Following | | Form: Direct (D) or Indirect | of Indirect Beneficial Ownership | |
| 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) 1. Title of Derivative Security (Instr. 3) 2. Conversion or Exercise Price of Derivative Security (Instr. 3) 2. Conversion or Exercise Price of Derivative Security (Instr. 3) 3. Transaction Date Execution Date (Month/Day/Year) 4. Transaction Ode (Instr. 8) 5. Number of Operivative Securities (Month/Day/Year) Conversion Ode (Instr. 8) 4. Transaction Date (Month/Day/Year) Ownership Form: Direct (D) Owners (Instr. 4) Ownership Form: Direct (D) Or Indirect (I) (Instr. 4) Ownership Form: Direct (D) Or Indirect (I) (Instr. 4) Amount or Amount or Amount or | | | | | | | | | | Code V | | Amount | (A) or (D) Price | | е | Transaction(s) | | | (111511.4) |
| 1. Title of Derivative Security (Instr. 3) 1. Title of Derivative Security (Security Security Securities Securities Securities Securities Securities Securities Securities Securities Securitie | Common Stock 07/01/20 | | | | | | 014 07/01/2 | | 014 | J ⁽¹⁾ | V | 76 | A \$30 | | .2005 | 05 1,892 | | D | |
| Derivative Security (Instr. 3) Price of Derivative Security (Security (Instr. 3) Price of Derivative Security (Instr. 4) Price of Derivative Security (Instr. 5) Price of Derivative Security (Instr. 4) Price of Derivative Security (Instr. 5) Price of Derivative Security (Instr. 4) Price of Derivative Security (Instr. 4) Price of Derivative Security (Instr. 5) Price of Derivative Security (Instr. 4) Price of Derivative Security (Instr. 5) Price of Derivative Security (Instr. 4) Price of Derivative Security (Instr. 5) Price of Derivative Security (Instr. 4) Price of Derivative Security (Instr. 5) Price of Derivative Security (Instr. 5) Price of Derivative Security (Instr. 4) Price | | | | | | | | | | | | | | | | | | | |
| Number Date Expiration Of | Derivative Security | Conversion or Exercise (Month/Day/Year) Execution Date, if any (Month/Day/Year) (Month/Day/Year) (Month/Day/Year) 8) | | | 5. Number of Expiration Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 | | | | ate ear) | Amount of Securities Underlying Derivative Security (Instr. and 4) | | Deri Sec (Inst | curity str. 5) | derivative Securities Beneficially Owned Following Reported Transaction(| Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 11. Nature of Indirect Beneficial Ownership (Instr. 4) | | | |

Explanation of Responses:

1. Reporting 76 shares acquired under the Isis Pharmaceuticals, Inc. Amended and Restated 2000 Employee Stock Purchase Plan on July 1, 2014. These 76 shares may not be sold until January 2, 2015.

Remarks:

/s/B. Lynne Parshall, attorneyin-fact 07/01/2014

** 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.