FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

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

0.5

hours per response:

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

| | | | | | 01 5 | ecuc | on 30(n) | or the r | nvesime | IL COI | прапу Аст | 01 194 | 40 | | | | | | |
|-----------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------|---------------------------------------------------|-----------------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------|----------|-----------------------------------|------------------------------------|----------|---------------------------------------------------------------|-------------------------------------------------------------------------------------------------|------------------|---------------------|---------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|-------------------------------------------------------------------|--------------------------------------------------------------------|
| 1. Name and Address of Reporting Person* <u>BENNETT C FRANK</u> | | | | | 2. Issuer Name and Ticker or Trading Symbol ISIS PHARMACEUTICALS INC [ISIS] | | | | | | | | | Check all | ship of Reportir applicable) rector | ng Pei | 10% O | wner | |
| (Last) (First) (Middle) C/O ISIS PHARMACEUTICALS, INC. 1896 RUTHERFORD ROAD | | | | | 3. Date of Earliest Transaction (Month/Day/Year) 07/28/2011 | | | | | | | | | | X Officer (give title below) Oth below Senior Vice President | | | | specify |
| (Street) CARLSBAD CA 92008 (City) (State) (Zip) | | | | | 4. If Amendment, Date of Original Filed (Month/Day/Year) | | | | | | | | | | ne) X F | ual or Joint/Group Filing (Check Applicable Form filed by One Reporting Person Form filed by More than One Reporting Person | | | |
| | | Tabl | e I - Nor | -Deriv | ative | Se | curitie | s Acc | quired, | Dis | posed o | f, or | Bene | eficia | ally Ow | ned | | | |
| 1. Title of Security (Instr. 3) 2. Transac Date (Month/Date) | | | | Day/Year) if | | 2A. Deemed Execution Date, if any (Month/Day/Year) | | Transaction Di Code (Instr. 5) | | Disposed | 4. Securities Acquired (A Disposed Of (D) (Instr. 3, 5) | | (A) or 3, 4 a | nd Sed Bei Ow | Securities Beneficially | | 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 | Tra | nsaction(s) tr. 3 and 4) | | | (111511.4) |
| Common Stock 07/28 | | | | 07/28/2011 | | S ⁽¹⁾ | | 1,000(1) | | D | \$8 | .6 | 305 | | D | | | | |
| | 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 E if any (Month/Day | Date, Transaction Code (Ins | | | | | 6. Date E Expiratio (Month/D | n Date | | 7. Title and Amount of Securities Underlying Derivative Security (Inst and 4) | | str. 3 | 8. Price Derivativ Security (Instr. 5) | | , | Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 11. Nature of Indirect Beneficial Ownership (Instr. 4) |
| | | | | | Code | | (A) | (D) | Date Exercisa | | Expiration Date | Title | or Nun of | ount nber | | | | | |

Explanation of Responses:

 $1. \ The sale reported in this Form 4 was effected pursuant to a Rule 10b5-1 trading plan adopted by the reporting person on <math>6/23/11$.

Remarks:

/s/C. Frank Bennett

07/29/2011

** 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.