

**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

OMB APPROVAL	
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1. Name and Address of Reporting Person * <u>Geary Richard S</u>  (Last) (First) (Middle) C/O ISIS PHARMACEUTICALS, INC. 2855 GAZELLE COURT  (Street) CARLSBAD CA 92010  (City) (State) (Zip)	2. Issuer Name and Ticker or Trading Symbol <u>ISIS PHARMACEUTICALS INC [ ISIS ]</u>	5. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) <u>SVP, Development</u>
	3. Date of Earliest Transaction (Month/Day/Year) <u>07/05/2013</u>	
		6. Individual or Joint/Group Filing (Check Applicable Line) <input checked="" type="checkbox"/> Form filed by One Reporting Person <input type="checkbox"/> Form filed by More than One Reporting Person

**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	07/05/2013	07/05/2013	s <sup>(1)</sup>		1,625 <sup>(1)</sup>	D	\$29.25	3,446	D	
Common Stock	07/05/2013	07/05/2013	M <sup>(2)</sup>		16,960 <sup>(2)</sup>	A	\$14.47	20,406	D	
Common Stock	07/05/2013	07/05/2013	s <sup>(2)</sup>		16,960 <sup>(2)</sup>	D	\$30.015	3,446	D	
Common Stock	07/05/2013	07/05/2013	M <sup>(2)</sup>		2,220 <sup>(2)</sup>	A	\$11.27	5,666	D	
Common Stock	07/05/2013	07/05/2013	s <sup>(2)</sup>		2,220 <sup>(2)</sup>	D	\$30.015	3,446	D	
Common Stock	07/05/2013	07/05/2013	M <sup>(3)</sup>		5,000 <sup>(3)</sup>	A	\$19.08	8,446	D	
Common Stock	07/05/2013	07/05/2013	s <sup>(3)</sup>		5,000 <sup>(3)</sup>	D	\$30.015	3,446	D	
Common Stock	07/08/2013	07/08/2013	M <sup>(2)</sup>		5,007 <sup>(2)</sup>	A	\$11.27	8,453	D	
Common Stock	07/08/2013	07/08/2013	s <sup>(2)</sup>		5,007 <sup>(2)</sup>	D	\$30.026	3,446	D	
Common Stock	07/08/2013	07/08/2013	M <sup>(2)</sup>		17,933 <sup>(2)</sup>	A	\$11.27	21,379	D	
Common Stock	07/08/2013	07/08/2013	s <sup>(2)</sup>		17,933 <sup>(2)</sup>	D	\$30.09	3,446	D	
Common Stock	07/08/2013	07/08/2013	M <sup>(2)</sup>		7,060 <sup>(2)</sup>	A	\$10.29	10,506	D	
Common Stock	07/08/2013	07/08/2013	s <sup>(2)</sup>		7,060 <sup>(2)</sup>	D	\$30.09	3,446	D	
Common Stock	07/09/2013	07/09/2013	M <sup>(2)</sup>		10,358 <sup>(2)</sup>	A	\$10.29	13,804	D	
Common Stock	07/09/2013	07/09/2013	s <sup>(2)</sup>		10,358 <sup>(2)</sup>	D	\$30.043	3,446	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 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					
Employee Stock Option (right to buy)	\$14.47	07/05/2013	07/05/2013	M			16,960	01/02/2013	01/01/2016	Common Stock	16,960	\$0	0	D
Employee Stock Option (right to buy)	\$11.27	07/05/2013	07/05/2013	M			2,220	01/04/2014	01/03/2017	Common Stock	2,220	\$0	30,420	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 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)	\$19.08	07/05/2013	07/05/2013	M			5,000	08/16/2012	08/15/2015	Common Stock	5,000	\$0	0	D	
Employee Stock Option (right to buy)	\$11.27	07/08/2013	07/08/2013	M			22,940	01/04/2014	01/03/2017	Common Stock	22,940	\$0	7,480	D	
Employee Stock Option (right to buy)	\$10.29	07/08/2013	07/08/2013	M			7,060	01/03/2015	01/02/2018	Common Stock	7,060	\$0	26,384	D	
Employee Stock Option (right to buy)	\$10.29	07/09/2013	07/09/2013	M			10,358	01/03/2013	01/02/2018	Common Stock	10,358	\$0	16,026	D	

**Explanation of Responses:**

- The sale reported in this Form 4 was effected pursuant to a Rule 10b5-1 trading plan adopted by the reporting person on 2/12/13.
- Acquired as a result of exercising a stock option pursuant to a Rule 10b5-1 Trading Plan. The purchase and sale reported on this Form 4 was effective pursuant to a Rule 10b5-1 Trading Plan adopted by the reporting person on 2/12/13.
- Acquired as a result of exercising a stock option pursuant to a Rule 10b5-1 Trading Plan. The purchase and sale reported on this Form 4 was effective pursuant to a Rule 10b5-1 Trading Plan adopted by the reporting person on 10/14/10.

**Remarks:**

/s/Richard S. Geary                      07/09/2013  
 \*\* 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.