

**STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP**

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

<b>1. Name and Address of Reporting Person*</b> <u>Geary Richard S</u>  (Last) (First) (Middle) <u>C/O ISIS PHARMACEUTICALS, INC.</u> <u>2855 GAZELLE COURT</u>  (Street) <u>CARLSBAD CA 92010</u>  (City) (State) (Zip)	<b>2. Issuer Name and Ticker or Trading Symbol</b> <u>ISIS PHARMACEUTICALS INC [ ISIS ]</u>	<b>5. Relationship of Reporting Person(s) to Issuer</b> (Check all applicable)  Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) <u>Senior Vice President</u>
	<b>3. Date of Earliest Transaction (Month/Day/Year)</b> <u>12/20/2011</u>	
<b>4. If Amendment, Date of Original Filed (Month/Day/Year)</b>		

**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	12/16/2011	12/16/2011	M <sup>(1)</sup>		1,000 <sup>(1)</sup>	A	\$5.8	5,278	D	
Common Stock	12/16/2011	12/16/2011	S <sup>(1)</sup>		1,000 <sup>(1)</sup>	D	\$6.79	4,278	D	
Common Stock	12/19/2011	12/19/2011	M <sup>(1)</sup>		118 <sup>(1)</sup>	A	\$5.8	4,396	D	
Common Stock	12/19/2011	12/19/2011	S <sup>(1)</sup>		118 <sup>(1)</sup>	D	\$6.9	4,278	D	
Common Stock	12/19/2011	12/19/2011	M <sup>(1)</sup>		982 <sup>(1)</sup>	A	\$5.8	5,260	D	
Common Stock	12/19/2011	12/19/2011	S <sup>(1)</sup>		982 <sup>(1)</sup>	D	\$6.82	4,278	D	
Common Stock	12/20/2011	12/20/2011	M <sup>(1)</sup>		1,500 <sup>(1)</sup>	A	\$5.8	5,778	D	
Common Stock	12/20/2011	12/20/2011	S <sup>(1)</sup>		1,500 <sup>(1)</sup>	D	\$6.82	4,278	D	
Common Stock	12/20/2011	12/20/2011	M <sup>(1)</sup>		300 <sup>(1)</sup>	A	\$5.8	4,578	D	
Common Stock	12/20/2011	12/20/2011	S <sup>(1)</sup>		300 <sup>(1)</sup>	D	\$6.92	4,278	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
Employee Stock Option (right to buy)	\$5.8	12/16/2011	12/16/2011	M		1,000		01/03/2009	01/02/2012	Common Stock	1,000	\$0	4,044	D	
Employee Stock Option (right to buy)	\$5.8	12/19/2011	12/19/2011	M		1,100		01/03/2009	01/02/2012	Common Stock	1,100	\$0	2,944	D	
Employee Stock Option (right to buy)	\$5.8	12/20/2011	12/20/2011	M		1,800		01/03/2009	01/02/2012	Common Stock	1,800	\$0	1,144	D	

**Explanation of Responses:**

1. Acquired as a result of exercising a stock option that was scheduled to expire on 1/2/12. The purchase and sale reported on this Form 4 was effected pursuant to a Rule 10b5-1 trading plan adopted by the reporting person on 2/3/09.

**Remarks:**

/s/B. Lynne Parshall, Attorney- 12/20/2011 in-Fact

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.

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