

INITIAL STATEMENT OF BENEFICIAL OWNERSHIP OF SECURITIES

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. 1896 RUTHERFORD ROAD (Street) CARLSBAD CA 92008 (City) (State) (Zip)			2. Date of Event Requiring Statement (Month/Day/Year) 08/16/2008	3. Issuer Name and Ticker or Trading Symbol (Check all applicable) <u>ISIS PHARMACEUTICALS INC [ISIS]</u>
4. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) Senior Vice President		5. If Amendment, Date of Original Filed (Month/Day/Year) 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		

Table I - Non-Derivative Securities Beneficially Owned

1. Title of Security (Instr. 4)	2. Amount of Securities Beneficially Owned (Instr. 4)	3. Ownership Form: Direct (D) or Indirect (I) (Instr. 5)	4. Nature of Indirect Beneficial Ownership (Instr. 5)
No securities are beneficially owned	0	D	

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

1. Title of Derivative Security (Instr. 4)	2. Date Exercisable and Expiration Date (Month/Day/Year)		3. Title and Amount of Securities Underlying Derivative Security (Instr. 4)		4. Conversion or Exercise Price of Derivative Security	5. Ownership Form: Direct (D) or Indirect (I) (Instr. 5)	6. Nature of Indirect Beneficial Ownership (Instr. 5)
	Date Exercisable	Expiration Date	Title	Amount or Number of Shares			
Employee Stock Option (right to buy)	01/02/2005	01/01/2011	Common Stock	8,480	9.625	D	
Employee Stock Option (right to buy)	01/02/2006	01/01/2012	Common Stock	8,000	21.05	D	
Employee Stock Option (right to buy)	08/01/2004	07/31/2010	Common Stock	5,000	11.5625	D	
Employee Stock Option (right to buy)	01/02/2008	01/01/2014	Common Stock	1,049	6.81	D	
Employee Stock Option (right to buy)	01/03/2009 ⁽¹⁾	01/02/2012	Common Stock	5,044	5.8	D	
Employee Stock Option (right to buy)	01/03/2007 ⁽²⁾	01/02/2013	Common Stock	11,686	5.25	D	
Employee Stock Option (right to buy)	01/02/2008 ⁽³⁾	01/01/2014	Common Stock	19,042	11.12	D	
Employee Stock Option (right to buy)	01/02/2009 ⁽⁴⁾	01/01/2015	Common Stock	24,000	15.38	D	
Employee Stock Option (right to buy)	01/01/2009 ⁽⁵⁾	12/31/2014	Common Stock	10,000	15.75	D	

Explanation of Responses:

- Grant of 1-3-05 to reporting person of stock options under the Isis Pharmaceuticals, Inc. 1989 Stock Option Plan. The option is exercisable as to 3,362 shares on 8-16-08. The remaining shares subject to the option vest and become exercisable at the rate of 336.4 shares per month.
- Grant of 1-3-06 to reporting person of stock options under the Isis Pharmaceuticals, Inc. 1989 Stock Option Plan. The option is exercisable as to 4,328 shares on 8-16-08. The remaining shares subject to the option vest and become exercisable at the rate of 432.84 shares per month.
- Grant of 1-2-07 to reporting person of stock options under the Isis Pharmaceuticals, Inc. 1989 Stock Option Plan. The option is exercisable as to 7,538 shares on 8-16-08. The remaining shares subject to the option vest and become exercisable at the rate of 396.69 shares per month.
- Grant of 1-2-08 to reporting person of stock options under the Isis Pharmaceuticals, Inc. 2000 Broad-Based Equity Incentive Plan. 25% of the shares subject to the option will vest and become exercisable on 1-2-09. The remaining shares subject to the option vest and become exercisable at the rate of 500 shares per month. The option is exercisable as to 0 shares on 8-16-08.
- Grant of 1-1-08 to reporting person of stock options under the Isis Pharmaceuticals, Inc. 2000 Broad-Based Equity Incentive Plan. 25% of the shares subject to the option will vest and become exercisable on 1-1-09. The remaining shares subject to the option vest and become exercisable at the rate of 208.33 shares per month. The option is exercisable as to 0 shares on 8-16-08.

Remarks:

/s/Richard S. Geary

08/19/2008

** 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 5 (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.

POWER OF ATTORNEY

Know all by these presents, that the undersigned hereby constitutes and appoints each of Stanley T. Crooke and B. Lynne Parshall, signing individually, the undersigned (1) execute for and on behalf of the undersigned, an officer, director or holder of 10% or more of a registered class of securities of Isis Pharmaceuticals, Inc. (Isis), (2) do and perform any and all acts for and on behalf of the undersigned that may be necessary or desirable to complete and execute such Form 3, 4 or 5, complete and file such Form 3, 4 or 5, (3) take any other action of any nature whatsoever in connection with the foregoing which, in the opinion of such attorney-in-fact, may be of benefit, in the best interest of Isis. The undersigned hereby grants to each such attorney-in-fact full power and authority to do and perform any and every act and thing whatsoever requisite, necessary, convenient or proper in the premises, and which may in anywise relate to the foregoing, and to execute the same. This Power of Attorney shall remain in full force and effect until the earliest to occur of (a) the undersigned is no longer required to file Forms 3, 4 and 5 with the SEC.

IN WITNESS WHEREOF, the undersigned has caused this Power of Attorney to be executed as of this 8th day of August, 2008.

/S/Richard S. Geary