

**STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP**

<b>OMB APPROVAL</b>	
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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

<p>1. Name and Address of Reporting Person*</p> <p><b>PARSHALL B LYNNE</b></p> <p>(Last) (First) (Middle)</p> <p><b>C/O ISIS PHARMACEUTICALS, INC.</b></p> <p><b>1896 RUTHERFORD ROAD</b></p> <p>(Street)</p> <p><b>CARLSBAD CA 92008</b></p> <p>(City) (State) (Zip)</p>	<p>2. Issuer Name and Ticker or Trading Symbol</p> <p><b>ISIS PHARMACEUTICALS INC [ ISIS ]</b></p> <p>3. Date of Earliest Transaction (Month/Day/Year)</p> <p><b>01/01/2008</b></p> <p>4. If Amendment, Date of Original Filed (Month/Day/Year)</p>	<p>5. Relationship of Reporting Person(s) to Issuer (Check all applicable)</p> <p><input checked="" type="checkbox"/> Director 10% Owner</p> <p><input checked="" type="checkbox"/> Officer (give title below) Other (specify below)</p> <p style="text-align: right;"><b>Director, COO</b></p> <p>6. Individual or Joint/Group Filing (Check Applicable Line)</p> <p><input checked="" type="checkbox"/> Form filed by One Reporting Person</p> <p><input type="checkbox"/> Form filed by More than One Reporting Person</p>
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**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	01/01/2008	01/01/2008	J <sup>(1)</sup>	V	876 <sup>(1)</sup>	A	\$8.3045	6,569	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)	\$15.38	01/02/2008	01/02/2008	A	V	91,520		01/02/2009 <sup>(2)</sup>	01/01/2015	Common Stock	91,520	\$0	91,520	D	
Employee Stock Option (right to buy)	\$5.8	01/03/2008	01/03/2008	G <sup>(3)</sup>			20,000 <sup>(3)</sup>	01/03/2006 <sup>(4)</sup>	01/02/2012	Common Stock	20,000	\$0	10,263	D	
Employee Stock Option (right to buy)	\$5.8	01/03/2008	01/03/2008	G <sup>(3)</sup>	V	10,000 <sup>(3)</sup>		01/03/2008	01/02/2012	Common Stock	10,000	\$0	10,000	I	By daughter
Employee Stock Option (right to buy)	\$5.8	01/03/2008	01/03/2008	G <sup>(3)</sup>	V	10,000 <sup>(3)</sup>		01/03/2008	01/02/2012	Common Stock	10,000	\$0	10,000	I	By daughter

**Explanation of Responses:**

- Reporting 876 shares acquired under the Isis Pharmaceuticals, Inc. 2000 Employee Stock Purchase Plan on January 1, 2008.
- Grant of 1-2-08 to reporting person of stock options under the Isis Pharmaceuticals, Inc. 1989 Stock Option Plan. 25% of the shares subject to the option will vest and become exercisable on 1-2-09. Thereafter, the remaining shares subject to the option vest and become exercisable in 36 equal monthly installments, at the rate of 22,880 shares per year. The option is exercisable as to 0 shares on 1-2-08.
- The reporting person transferred options to her two daughters (one is a minor) who share reporting person's household, divided equally.
- Stock option under the Isis Pharmaceuticals, Inc. 1989 Stock Option Plan. 25% of the shares subject to the option vested and became exercisable on 1-3-06. Thereafter, the remaining shares subject to the option vest and become exercisable in 36 equal monthly installments, at the rate of 7,565 shares per year. The option was exercisable as to 22,698 shares on 1-3-08 prior to the reported transfer.

**Remarks:**

/s/B. Lynne Parshall                      01/04/2008  
 \*\* 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 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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