FORM 4

## UNITED STATES SECURITIES AND EXCHANGE COMMISSION

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OMB APPE	ROVAL							
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Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

## STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

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

1. Name and Address of Reporting Person* PARSHALL B LYNNE					2. Issuer Name and Ticker or Trading Symbol ISIS PHARMACEUTICALS INC [ ISIS ]							(Che	Relationship of Reporting Person(s) to Issuer (Check all applicable)     X Director 10% Owner				
(Last) 2292 FA	( RADAY A	First) VENUE	(Middle)		3. Date of Earliest Transaction (Month/Day/Year) 09/30/2004							C Officer (give title Other (specify below)  Executive Vice President				pecify	
(Street) CARLSBAD CA 92008  (City) (State) (Zip)					4. If Amendment, Date of Original Filed (Month/Day/Year)						Line)	Individual or Joint/Group Filing (Check Applicable ne)  X Form filed by One Reporting Person Form filed by More than One Reporting Person					
(5.5)			able I - Non-	-Deriva	tive S	ecuriti	es Acc	nuired	Disi	nosed of	or Bene	ficially	Owned				
1. Title of Security (Instr. 3)  2. Trans. Date				2. Transac	action 2A. Deemed Execution Date,		3. Transa Code (	3. 4. Securities Disposed Of Code (Instr.		s Acquired	(A) or	5. Amount of Securities Beneficially Owned Following		Form: Direct (D) or Indirect (I) (Instr. 4)	t B	7. Nature of Indirect Beneficial Ownership	
								Code	v	Amount	(A) or (D)	Price	Reported Transactio (Instr. 3 ar			(Instr. 4)	
			Table II - D							osed of, o onvertibl			wned				
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security		3A. Deemed Execution Date if any (Month/Day/Yea	Code	saction Derivative E			6. Date Exercisable and Expiration Date (Month/Day/Year)  7. Title and Ar of Securities Underlying Derivative Sec (Instr. 3 and 4)			es g Security	8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially Owned Following Reported	Owne	t (D) lirect	Beneficial Ownership (Instr. 4)	
				Code	e V	(A)	(D)	Date Exercisa	able	Expiration Date	Title	Amount or Number of Shares		Transaction(s (Instr. 4)		;)   	
Employee Stock Option (right to buy)	\$5.15	09/30/2004	09/30/2004	G <sup>(1)</sup>	v		30,000	01/01/20	)06 <sup>(2)</sup>	12/31/2008	Common Stock	56,466	\$0	26,466	,	)	
Employee Stock Option (right to buy)	\$5.15	09/30/2004	09/30/2004	G <sup>(1)</sup>	v	15,000		09/30/2	2004	12/31/2008	Common Stock	15,000	\$0	15,000		I	By daughter
Employee Stock Option (right to buy)	\$5.15	09/30/2004	09/30/2004	G <sup>(1)</sup>	v	15,000		09/30/2	2004	12/31/2008	Common Stock	15,000	\$0	15,000		ſ	By daughter

## **Explanation of Responses:**

- 1. The reporting person transferred options to her two daughters, both minors who share reporting person's household, divided equally.
- 2. 33.34% of the option vested and became exercisable on 1/1/04. Thereafter, the remaining shares subject to the option vest and become exercisable in 24 equal monthly installments, at the rate of 18,822 shares per year. The option is exercisable as to 31,370 shares on 9/30/04.

## Remarks:

B. Lynne Parshall

09/30/2004

\*\* Signature of Reporting Person

Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- $^{\star}$  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.