# FORM 4

to Section 16. Form 4 or Form 5

obligations may continue. See

Instruction 1(b).

Check this box if no longer subject

# UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

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## STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934, Section 17(a) of the Public Utility Holding Company Act of 1935 or Section 30(h) of the Investment Company Act of 1940

 Name and Address of Reporting Person\* 2. Issuer Name **and** Ticker or Trading Symbol Relationship of Reporting Person(s) Isis Pharmaceuticals, Inc. (ISIS) to Issuer (Check all applicable) X Director Parshall B. Lynne 10% Owner 3. I.R.S. Identification Number X Officer (give title below) Other (specify below) (Last) (First) (Middle) 4. Statement for of Reporting Person, Month/Day/Year 2/21/03 Executive Vice President 2292 Faraday Avenue if an entity (voluntary) (Street) 5. If Amendment, 7. Individual or Joint/Group Filing (Check Applicable Line) Date of Original X Form filed by One Reporting Person Carlsbad, CA 92008 Form filed by More than One Reporting Person (Month/Day/Year) (City) (State) (Zip) Table I — Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned 1. Title of Security 2. Trans-2A. Deemed 3. Trans-4. Securities Acquired (A) or Disposed of (D) 5. Amount of Owner-7. Nature of Indirect ship Form: Beneficial Ownership action Code (Instr. 3, 4 & 5) Securities (Instr. 3) action Execution Date Date, (Instr. 8) Beneficially Direct (D) Instr. 4) (Month/ Day if any Code Amount (A) Price Owned Followor Indirect (I) Year) (Month/Day/ ing Reported Transactions(s) (Instr. 4) or Year) (Instr. 3 & 4) (D)

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

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### FORM 4 (continued) Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

1. Title of	2. Conver-	3.	3A.	4.		5. Number of 1	Derivative	6. Date		7. Title an	d Amount	8. Price of	9. Number of	10.	11. Nature
Derivative	sion or	Trans-	Deemed	Trans	-	Securities Acq	uired (A) or	Exercisa	able	of Underly	ing	Derivative	Derivative	Owner-	of Indirect
Security	Exercise	action	Execution	action	ı	Disposed of (I	))	and Exp	iration	Securities	Ü	Security	Securities	ship	Beneficial
	Price of	Date	Date,	Code		-		Date		(Instr. 3 &	4)	(Instr. 5)	Beneficially	Form	Ownership
(Instr. 3)	Derivative		if any			(Instr. 3, 4 & 5	)	(Month/D	ay/	ľ			Owned	of	(Instr. 4)
	Security		(Month/	(Instr.	tr.			Year)					Following	Deriv-	
			Day/ Year)	8)									Reported	ative	
		,	- /									Transaction(s)	Security:		
				Code	V	(A)	(D)	Date	Expira-	Title	Amount		(Instr. 4)	Direct	
					П	` '			tion		or			(D)	
					П			cisable	Date		Number			or	
					П						of			Indirect	
					П						Shares			(I)	
					Ш									(Instr. 4)	
Employee Stock	\$6.8125	2-21-	2-21-03	$G^{(1)}$	$ \mathbf{v} $		20,000	1-2-02	1-5-10	Common	139,910		139,910	D	
Option (right to		03			П					Stock					
buy)					Ш										
Employee Stock	\$6.8125	2-21-	2-21-03	$G^{(1)}$	$ \mathbf{v} $	10,000		1-2-02	1-5-10	Common	15,045		15,045	I	By
Option (right to		03			П					Stock					daughter
buy)					П										
Employee Stock	\$6.8125	2-21-	2-21-03	G.(1)	$ \mathbf{v} $	10,000		1-2-02	1-5-10	Common	15,045		15,045	I	By
Option (right to		03								Stock					daughter
buy)															

**Explanation of Responses:** 

(1) The reporting person transferred the reported options to her two daughters, both minors who share reporting person's household, divided equally.

By: /s/ B. Lynne Parshall **B. Lynne Parshall** \*\*Signature of Reporting Person

\*\*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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2-21-03 Date

<sup>\*</sup> If the form is filed by more than one reporting person, see Instruction 4(b)(v).