FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION Washington, D.C. 20549

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

OMB Number: 3235-0287

OMB APPROVAL

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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 Filed By Romeo & Dye's Instant Form 4 Filer

2. Issuer Name **and** Ticker or Trading Symbol 6. Relationship of Reporting Person(s) 1. Name and Address of Reporting Person* Isis Pharmaceuticals, Inc. (ISIS) to Issuer (Check all applicable) Dorr F. Andrew Director 10% Owner X Officer (give title below) Other (specify below) (Last) (First) (Middle) 3. I.R.S. Identification Number 4. Statement for of Reporting Person, Month/Day/Year 2292 Faraday Avenue if an entity (voluntary) 10/23/02 Vice President 5. If Amendment, 7. Individual or Joint/Group Filing (Check Applicable Line) (Street) Date of Original X Form filed by One Reporting Person Carlsbad, CA 92008 (Month/Day/Year) Form filed by More than One Reporting Person (City) (State) (Zip) Table I — Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned 2A. Deemed 3. Trans-4. Securities Acquired (A) or Disposed of (D) 5. Amount of 1. Title of Security 2. Trans-6. Owner-7. Nature of Indirect action Code (Instr. 3, 4 & 5) ship Form: Beneficial Ownership (Instr. 3) action Execution Securities Date Date. (Instr. 8) Beneficially Direct (D) (Instr. 4) (Month/ Day Owned Followor Indirect (I) lif anv Code Amount (A) Price Year) (Month/Day/ ing Reported Transactions(s) (Instr. 4) or (ear) (Instr. 3 & 4) (D) Common Stock 10/23/02 10/23/02 M 11000 \$6.81 10/23/02 10/23/02 $S^{(1)}$ 11000 D 38 D Common Stock \$9,1368

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. Trans-	3A.	4.	5	5. Number	of Derivative	6. Date		7. Title an	d	8. Price of	9. Number of	10.	11. Nature
Derivative	sion or	action	Deemed	Trans-	.	Securities Acquired (A) or		Exercisable		Amount of		Derivative	Derivative	Owner-	of Indirect
Security	Excercise	Date	Execution	action	1	Disposed of (D)		and Expiration		Underlying		Security	Securities	ship	Beneficial
	Price of		Date,	Code				Date		Securities		(Instr. 5)	Beneficially	Form	Ownership
(Instr. 3)	Derivative Security	(Month/ Day/ Year)	if any			(Instr. 3, 4 & 5)		(Month/Day/		(Instr. 3 & 4)			Owned	of	(Instr. 4)
			(Month/	(Instr.				Year)					Following	Deriv-	
		/	Day/ Year)	8)									Reported	ative	
			_										Transaction(s)	Security:	
				Code	v	(A)	(D)	Date	Expira-	Title	Amount	1	(Instr. 4)	Direct	
				1 1		` ′	,		tion		or			(D)	
				ll				cisable	Date		Number			or	
				1 1							of			Indirect	
				ll							Shares			(I)	
														(Instr. 4)	
Employee Stock	\$6.81	10/23/02	10/23/02	M	T		11000	1/1/02	12/31/02	Common	11000		15253	D	
Option (right to				ıl						Stock					
buy)				ıl											1

Explanation of Responses:

(1) The sale reported in this Form 4 was effected pursuant to a Rule 10b5-1 trading plan adopted by the reporting person on March 19, 2002.

By: /s/ F. Andrew Dorr F. Andrew Dorr

**Signature of Reporting Person

10/24/02

Date

**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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^{*} If the form is filed by more than one reporting person, see Instruction 4(b)(v).