FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL

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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, 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 and Dye's Section 16 Filer www.section16.net

1. Name and Address of Repor	2 Is	suer	Name and Ticker	or Tradi	ng Symbol	6. Relationship of Reporting Person(s)						
Traine una ridaress of respon			rmaceuticals, Inc.		116 07 111001	to Issuer (Check all applicable)						
Parshall B. Lynne				(1010)		X Director 10% Owner						
(Last) (First) (- 1		Identification Num		4. Statement for	\overline{X} Officer (give title below)	Other (specify below)					
2292 Faraday Avenue			1 1 9 1			Month/Day/Year 1/29/03	Executive Vice President, CFO, Secretary					
(Street)					5. If Amendment, Date of Original	7. Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person						
Carlsbad, CA 92008					(Month/Day/Year) 1/2/03	Form filed by More than One Reporting Person						
(City) (State)		Table I — Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned						wned				
			ode	4. Securities Acqui (Instr. 3, 4 & 5)	red (A)	· · · · · · · · · · · · · · · · · · ·	5. Amount of Securities Beneficially		7. Nature of Indirect Beneficial Ownership (Instr. 4)			
(Month/ Day/ Year)	if any (Month/Day/ Year)	Code	V	Amount	(A) or (D)	Price	Owned Follow- ing Reported Transactions(s) (Instr. 3 & 4)	or Indirect (I) (Instr. 4)				
Common Stock 1/1/03	1/2/03	J	V	3213 ⁽¹⁾	A	\$5.6015	6458	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 Deri	vative	6. Date		7. Title an	d Amount	8. Price of	9. Number of	10.	11. Nature
Derivative	sion or	Trans-	Deemed	Trans-	Securities Acquire	d (A) or	Exercis	able	of Underly	ying	Derivative	Derivative	Owner-	of Indirect
Security	Exercise	action	Execution	action	Disposed of (D)		and Exp	iration	Securities		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/				Owned	of	(Instr. 4)
	Security		(Month/	(Instr.			Year)					Following	Deriv-	
		Day/ Year)	Day/ Year)	8)								Reported	ative	
		" /	'									Transaction(s)	Security:	
				Code	(A)	(D)	Date	Expira-	Title	Amount	1	(Instr. 4)	Direct	
				1 1		` ′	1	tion	1	or			(D)	
				1 1			cisable	Date		Number			or	
				1 1						of			Indirect	
				1 1						Shares			(I)	
													(Instr. 4)	
Employee Stock	\$6.84	1-2-	1-2-03	A	25,000		<u>(2)</u>	1-1-13	Common	25,000		25,000	D	
Option (right to		03		1					Stock					
buy)				1										1

Explanation of Responses:

(1) The purpose of this amendment is to report an additional 1,335 shares for a total of 3,213 shares acquired under the Isis Pharmaceuticals, Inc. 2000 Employee Stock Purchase Plan on January 1, 2003. Due to a misstatement in the confirmation of purchase notice regarding this transaction, the reporting person was unaware of these additional shares until 1-29-03.

(2) 25% of the shares subject to the option will vest and become exercisable on 1-2-04. Thereafter, the remaining shares subject to the option vest and become exercisable in 36 equal monthly installments, at the rate of 6,250 shares per year. The option is exercisable as to 0 shares on 1-2-03.

> By: /s/ B. Lynne Parshall **B.** Lynne Parshall

1-29-03 Date

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