

INITIAL STATEMENT OF BENEFICIAL OWNERSHIP OF SECURITIES

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
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1. Name and Address of Reporting Person* Holmlund Jon T.		2. Date of Event Requiring Statement Month/Day/Year 04/02/03	4. Issuer Name and Ticker or Trading Symbol Isis Pharmaceuticals, Inc. (ISIS)	
(Last) (First) (Middle)	2292 Faraday Avenue (Street) Carlsbad, CA 92008 (City) (State) (Zip)	3. I.R.S. Identification Number of Reporting Person, if an entity (voluntary)	5. Relationship of Reporting Person(s) to Issuer (Check all applicable) <input type="checkbox"/> Director <input type="checkbox"/> 10% Owner <input checked="" type="checkbox"/> Officer <input type="checkbox"/> Other (give title below) (specify below) Vice President	
			6. If Amendment, Date of Original (Month/Day/Year) 04/02/03	
		7. Individual or Joint/Group Filing (Check Applicable Line) <input checked="" type="checkbox"/> Form filed by One Reporting Person <input type="checkbox"/> Form filed by More than One Reporting Person		
Table I — Non-Derivative Securities Beneficially Owned				
1. Title of Security (Instr. 4)	2. Amount of Securities Beneficially Owned (Instr. 4)	3. Ownership Form: Direct (D) or Indirect (I) (Instr. 5)		4. Nature of Indirect Beneficial Ownership (Instr. 5)
Common Stock	5,593	D		

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 5(b)(v).

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FORM 3 (continued)

Table II - Derivative Securities Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

1. Title of Derivative Security (Instr. 4)	2. Date Exercisable and Expiration Date (Month/Day/ Year)		3. Title and Amount of Securities Underlying Derivative Security (Instr. 4)		4. Conversion or Exercise Price of Derivative Security	5. Ownership Form of Derivative Security: Direct (D) or Indirect (I) (Instr. 5)	6. Nature of Indirect Beneficial Ownership (Instr. 5)
	Date Exercisable	Expiration Date	Title	Amount or Number of Shares			
Employee Stock Option (right to buy)	01/01/2002	12/31/2007	Common Stock	8,750	12.3125	D	
Employee Stock Option (right to buy)	01/01/2003	12/31/2008	Common Stock	10,000	12.9375	D	
Employee Stock Option (right to buy)	(1)	01/05/2010	Common Stock	30,000	6.8100	D	
Employee Stock Option (right to buy)	(2)	02/28/2010	Common Stock	5,000	16.0000	D	
Employee Stock Option (right to buy)	(3)	01/01/2011	Common Stock	8,000	9.6250	D	
Employee Stock Option (right to buy)	(4)	01/01/2012	Common Stock	6,000	21.0500	D	
Employee Stock Option (right to buy)	(5)	06/15/2012	Common Stock	25,000	7.4100	D	
Employee Stock Option (right to buy)	(6)	01/01/2013	Common Stock	9,000	6.8400	D	
Employee Stock Option (right to buy)	(2)	03/15/2013	Common Stock	10,000	4.1600	D	

Explanation of Responses:

- (1) 25% of the shares subject to the option vested and became exercisable on 01/06/2001. Thereafter, the remaining shares subject to the option vest and become exercisable in 36 equal monthly installments, at the rate of 7,500 shares per year. The option is exercisable as to 10,000 shares on 04/02/2003.
- (2) 25% of the shares subject to the option vested and became exercisable on 03/01/2001. Thereafter, the remaining shares subject to the option vest and become exercisable in 36 equal monthly installments, at the rate of 1,250 shares per year. The option is exercisable as to 3,854 shares on 04/02/2003.
- (3) 25% of the shares subject to the option vested and became exercisable on 01/02/2002. Thereafter, the remaining shares subject to the option vest and become exercisable in 36 equal monthly installments, at the rate of 2,000 shares per year . The option is exercisable as to 4,500 shares on 04/02/2003.
- (4) 25% of the shares subject to the option vested and became exercisable on 01/02/2003. Thereafter, the remaining shares subject to the option vest and become

exercisable in 36 equal monthly installments, at the rate of 1,500 shares per year. The option is exercisable as to 1,875 shares on 04/02/2003.

(5) 25% of the shares subject to the option vested and became exercisable on 06/16/2003. 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 04/02/2003.

(6) 25% of the shares subject to the option vested and became exercisable on 01/02/2004. Thereafter, the remaining shares subject to the option vest and become exercisable in 36 equal monthly installments, at the rate of 2,250 shares per year. The option is exercisable as to 0 shares on 04/02/2003.

(7) 25% of the shares subject to the option vested and became exercisable on 03/16/2004. Thereafter, the remaining shares subject to the option vest and become exercisable in 36 equal monthly installments, at the rate of 2,500 shares per year. The option is exercisable as to 0 shares on 04/02/2003.

By: /s/ **Jon T. Holmlund**

Jon T. Holmlund

**Signature of Reporting Person

04/28/2003

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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