

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

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).

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* COLE DOUGLAS L			2. Issuer Name and Ticker or Trading Symbol ISIS PHARMACEUTICALS INC [ISIS]			5. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) Vice President		
(Last)	(First)	(Middle)	3. Date of Earliest Transaction (Month/Day/Year) 05/09/2003			6. Individual or Joint/Group Filing (Check Applicable Line) <input checked="" type="checkbox"/> Form filed by One Reporting Person Form filed by More than One Reporting Person		
(Street)			4. If Amendment, Date of Original Filed (Month/Day/Year)					
(City)	(State)	(Zip)						

Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned

1. Title of Security (Instr. 3)	2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any (Month/Day/Year)	3. Transaction Code (Instr. 8)			4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5)			5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4)	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial Ownership (Instr. 4)
			Code	V	Amount	(A) or (D)	Price				

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

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transaction Code (Instr. 8)		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)	8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4)	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)	
				Code	V	(A)	(D)	Date Exercisable	Expiration Date						Title
Employee Stock Option (right to buy)	5.15	05/09/2003	05/09/2003	A		44,410 ⁽¹⁾		01/01/2004 ⁽¹⁾	12/31/2008	Common Stock	44,410	\$5.15	44,410	D	
Employee Stock Option (right to buy)	6.625	05/09/2003	05/09/2003	D		15,267 ⁽²⁾		10/01/1996	06/16/2003	Common Stock	15,267	\$6.625	0	D	
Employee Stock Option (right to buy)	6.75	05/09/2003	05/09/2003	D		20,000 ⁽²⁾		12/31/1998	12/30/2003	Common Stock	20,000	\$6.75	0	D	
Employee Stock Option (right to buy)	13.125	05/09/2003	05/09/2003	D		15,000 ⁽²⁾		01/01/2000	12/31/2005	Common Stock	15,000	\$13.125	0	D	
Employee Stock Option (right to buy)	18	05/09/2003	05/09/2003	D		8,500 ⁽²⁾		01/01/2001	12/31/2006	Common Stock	8,500	\$18	0	D	
Employee Stock Option (right to buy)	12.3125	05/09/2003	05/09/2003	D		10,000 ⁽²⁾		01/01/2002	12/31/2007	Common Stock	10,000	\$12.3125	0	D	
Employee Stock Option (right to buy)	12.9375	05/09/2003	05/09/2003	D		10,000 ⁽²⁾		01/01/2003	12/31/2008	Common Stock	10,000	\$12.9375	0	D	

Explanation of Responses:

1. These options were issued in connection with the Company's option exchange program. 33.34% of the shares subject to the option vest and become exercisable on 01/01/2004. Thereafter, the remaining shares subject to the option vest and become exercisable in 24 equal monthly installments, at the rate of 14,803 shares per year. The option is exercisable as to 0 shares on 05/09/2003.

2. These options were cancelled in connection with the Company's option exchange program

/s/Douglas L. Cole

05/13/2003

** Signature of Reporting Person

Date

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 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.