FORM 4

## UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB APPROVAL								
OMB Number:	3235-0287							
Expires:	December 31, 2014							
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0.5

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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 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporting Person* WENDER JOSEPH H					2. Issuer Name and Ticker or Trading Symbol ISIS PHARMACEUTICALS INC [ ISIS ]								onship o	on(s) to Issu	er			
WENDER JOSEPH H													X	Director		10% Owner		ner
(Last)	ast) (First) (Middle)				3. Date of Earliest Transaction (Month/Day/Year) 07/01/2003								Officer ( below)	give title	Other (spe below)		pecify	
Street)					4. If Amendment, Date of Original Filed (Month/Day/Year)							6. Individual or Joint/Group Filing (Check Applicable Line)						
(Ou ool)													X	Form fil	ed by One	Repo	rting Person	·
(City)	(Si	ate)	(Zip)											Form filed by More than One Reporting Person				
	Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned																	
1. Title of Security (Instr. 3)  2. Transa Date (Month/D				•	2A. Deemed Execution Date of any (Month/Day/Ye		Date	e, Transaction Dis Code (Instr. 5)		4. Securities Acquired (A) Disposed Of (D) (Instr. 3, 4 5)			and Securitie Beneficia Owned F		s Illy ollowing	Form	: Direct I Indirect I str. 4)	7. Nature of Indirect Beneficial Ownership
								Code V		Amount	(A) or (D)	Price	, l		orted saction(s) tr. 3 and 4)		(	(Instr. 4)
	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)	erivative   Conversion   Date   Execution Date,   Tr ecurity   or Exercise   (Month/Day/Year)   if any   Co				ansaction of ode (Instr. Derivative			Expiration Date (Month/Day/Year)			7. Title and Amo of Securities Underlying Derivative Secu (Instr. 3 and 4)		De Se	8. Price of Derivative Security (Instr. 5)	9. Number derivative Securities Beneficial Owned Following Reported Transactio (Instr. 4)	illy D	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
				Code	v	(A)	(D)	Date Exercisable		xpiration vate	Title	Amour or Number of Shares	er					
Director Stock Option (right to buy)	5.17	07/01/2003	07/01/2003	A		10,000		07/01/2004 <sup>(1)</sup>	0	6/30/2013	Common Stock	10,00	00 :	\$5.17	10,000	0	D	

## **Explanation of Responses:**

1. Grant of 7-1-03 to reporting person of stock options under the Isis Pharmaceuticals, Inc. 2002 Non-Employee Directors' Stock Option Plan. The option vests and becomes exercisable in four equal annual installments, with the first installment vesting on 7-1-04. The option shall be fully vested and exercisable on 7-1-07. The option is exercisable as to 0 shares on 7-1-03.

B. Lynne Parshall, by Power of Attorney

07/02/2003

\*\* 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.