FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL

OMB Number: 3235-0287 Estimated average burden hours per response: 0.5

10% Owner

5. Relationship of Reporting Person(s) to Issuer (Check all applicable)

X Director

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

1. Name and Address of Reporting Person*

CROOKE STANLEY T

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

ISIS PHARMACEUTICALS INC [ISIS]

2. Issuer Name **and** Ticker or Trading Symbol

(Last) (First) (Middle) C/O ISIS PHARMACEUTICALS, INC. 2855 GAZELLE COURT							3. Date of Earliest Transaction (Month/Day/Year) 06/27/2013								X Officer (give title Other (specify below) Chairman and CEO					
(Street)	Street) CARLSBAD CA 92010						4. If Amendment, Date of Original Filed (Month/Day/Year)								dividual or Joint/Group Filing (Check Applicable Form filed by One Reporting Person Form filed by More than One Reporting Person					
		Tal	ole I - No	n-Deriv	/ativ	e Se	curit	ties Ac	guired,	Dis	posed o	f, or Be	neficia	lly C	wned					
1. Title of Security (Instr. 3) 2. Transac Date (Month/Date)						ar)	if any	emed ion Date, /Day/Year)	Code (Transaction Code (Instr.		4. Securities Acquired (A) Disposed Of (D) (Instr. 3, 4			5. Amount of Securities Beneficially Owned Following Reported		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect Beneficial Ownership	
									Code	v	Amount	(A) oi (D)	Price	- 1	Reported Transact (Instr. 3 a	ion(s)			(Instr. 4)	
Common	Stock			06/27	7/2013	/2013		06/27/2013			10,000	(1) A	\$6.	81	11,661			D		
Common	Stock			06/27	7/2013		06/27/2013		S ⁽¹⁾		10,000	(1) D	\$28	3.3	1,661		D			
Common Stock (06/27	6/27/2013		06/27/2013		M ⁽¹⁾		10,000	(1) A	\$6.	81	11,661		D			
Common Stock 06/2					27/2013		06/27/2013		S ⁽¹⁾		10,000	(1) D	\$27	\$27.4		1,661		D		
Common Stock 06/28/					/2013		06/28/2013		M ⁽¹⁾		10,000	(1) A	\$6.	81	11,661		D			
Common Stock 06/2					28/2013		06/28/2013		S ⁽¹⁾		10,000	(1) D	\$27.	\$27.07		1,661		D		
Common Stock 06/28					3/2013		06/28/2013		M ⁽²⁾		4,725	2) A	\$6.	\$6.81		4,899		I	By Wife	
Common Stock 06/28/					3/2013	2013 0		8/2013	S ⁽²⁾		4,725	2) D	\$27.	.31	174			I	By Wife	
Common Stock 06/28/3					3/2013	2013 06/2		8/2013	M ⁽²⁾		5,958 ⁽²	2) A	\$11.	.12	6,132		I I		By Wife	
Common Stock 06/28/2					3/2013	2013 06/28/2		8/2013	S ⁽²⁾		5,958 ⁽²	2) D	\$27.	\$27.31		174		I :	By Wife	
Common Stock 07/01/2					/2013	2013 07/01/2		1/2013	S ⁽³⁾		10,000	(3) D	\$28	.17	775	,391		I .	By Trust	
			Table II -								osed of, convertil				vned					
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	3A. Deeme Execution if any (Month/Da	ed Date,	4. Transactior Code (Instr 8)		5. Number of		6. Date Exercis Expiration Date (Month/Day/Yea		able and	7. Title and Amour of Securities Underlying Derivative Security (Instr. 3 and 4)		t 8. F Dei	Price of rivative curity str. 5)	9. Number derivative Securities Beneficial Owned Following Reported Transactio (Instr. 4)	ily	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownershij (Instr. 4)	
					Code	de V		(D)	Date Exercisal		Expiration Date	Title	Amoun or Numbe of Shares	r						
Employee Stock Option (right to buy)	\$6.81	06/27/2013	06/27/2	5/27/2013			20,000		01/02/20	08	01/01/2014	Common Stock	20,000	ס	\$0 10,000)	D		
Employee Stock Option (right to buy)	\$6.81	06/28/2013	06/28/2	2013	M		10,0		01/02/20	08	01/01/2014	Common Stock	10,000	0	\$0	0		D		
Employee Stock Option (right to buy)	\$6.81	06/28/2013	06/28/2	06/28/2013				4,725	01/02/2008		01/14/2014 Common Stock		4,725		\$0 0			I	By wife	
Employee Stock Option (right to buy)	\$11.12	06/28/2013	06/28/2013		M	Л		5,958	01/02/20	08	01/01/2014	Common Stock	5,958		\$0		I		By wife	
	n of Respon	505:										<u> </u>								

reporting person on 6/27/12.

- 2. Acquired as a result of exercising a stock option that was scheduled to expire on 1/1/14. The purchase and sale reported on this Form 4 was effective pursuant to a Rule 10b5-1 Trading Plan adopted by the reporting person's wife on 6/27/12.
- 3. The sale was a result of shares owned. The sale reported on this Form 4 was effective pursuant to a Rule 10b5-1 Trading Plan adopted by the reporting person on 2/4/2013.

Remarks:

/s/B. Lynne Parshall, attorney-07/01/2013 in-fact

** 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.