FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Washington, D.C. 20	7549

OMB APPROVAL OMB Number: Estimated average burden hours per response: 0.5

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

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* BROWN RICHARD K				2. Issuer Name and Ticker or Trading Symbol ISIS PHARMACEUTICALS INC [ISIS]									eck all applic Directo Officer	r	g Person(s) to Issu 10% Ow Other (sp				
(Last) (First) (Middle) C/O ISIS PHARMACEUTICALS, INC. 1896 RUTHERFORD ROAD				3. Date of Earliest Transaction (Month/Day/Year) 03/03/2006									below) Vice President						
(Street) CARLSBAD CA 92008 (City) (State) (Zip)						4. If Amendment, Date of Original Filed (Month/Day/Year)								. Individual or Joint/Group Filing (Check Applicable ine) X Form filed by One Reporting Person Form filed by More than One Reporting Person					
	Tab	le I - Nor	า-Deriv	ative S	ecurit	ties Acq	uired,	Dis	posed o	f, or I	3en	eficiall	y Owned						
			2. Transaction Date (Month/Day/Year)		2A. Deemed Execution Date, if any (Month/Day/Year)		Code (Instr.		Disposed Of (D) (Instr. 3,			(A) or 3, 4 and	Securitie Benefici Owned F	5. Amount of Securities Beneficially Owned Following		: Direct C Indirect E str. 4)	7. Nature of Indirect Beneficial Ownership		
								v	Amount	(A (C	() or ()	Price	Transact	Transaction(s) (Instr. 3 and 4)			Instr. 4)		
Common Stock				03/03/2006		03/03/2006			1,008	3	A	\$6.84	1 3,	3,356		D			
Common Stock				03/03/2006		03/03/2006			1,000	(1)	D	\$8.2	2,356			D			
Common Stock			03/03	/03/2006		03/03/2006			8(1)		D	\$8.20	5 2,	2,348		D			
	1												Owned						
		ransactio ode (Inst	n of Deri Sec Acq (A) of Disp of (I	piration Date			(Instr. 3 and 4)		Amount	8. Price of Derivative Security (Instr. 5)	derivative Securities Beneficial Owned Following Reported	ly		11. Nature of Indirect Beneficial Ownership (Instr. 4)					
	S PHARMA JTHERFOR BAD CA (Si Security (Inst Stock Stock Stock Stock Conversion or Exercise Price of Derivative	BAD CA (State) Tab Security (Instr. 3) Stock Stock Stock Conversion or Exercise Price of Derivative (Month/Day/Year)	S PHARMACEUTICALS, INC. JTHERFORD ROAD BAD CA 92008 (State) (Zip) Table I - Nor Security (Instr. 3) Stock Stock Stock Stock Table II - Conversion or Exercise Price of Derivative (Month/Day/Year) I Stock Stock A Jac Deeme Execution if any (Month/Day/Year) Conversion or Exercise Price of Derivative (Month/Day/Year)	S PHARMACEUTICALS, INC. JTHERFORD ROAD Security (Instr. 3) Security (Instr. 3) Stock Sto	SPHARMACEUTICALS, INC.	SPHARMACEUTICALS, INC.	S PHARMACEUTICALS, INC. JTHERFORD ROAD A. If Amendment, Date of Table I - Non-Derivative Securities Acquired (State) (Zip) Table I - Non-Derivative Securities Acquired (Month/Day/Year) 2. Transaction Date (Month/Day/Year) A Stock 03/03/2006 03/03/2006 03/03/2006 03/03/2006 03/03/2006 03/03/2006 03/03/2006 03/03/2006 03/03/2006 5. Number of Conversion Or Exercise Price of Derivative (Month/Day/Year) 3. Transaction Date (Month/Day/Year) 3. Transaction Date (Month/Day/Year) 3. Transaction Date (Month/Day/Year) 4. Transaction Code (Instr. 8) 5. Number of Derivative Securities Code (Instr. 8) 5. Number of Derivative Securities Acquired (Instr. 8)	S PHARMACEUTICALS, INC. D3/03/2006	S PHARMACEUTICALS, INC.	O3/03/2006 O3/	03/03/2006 03/	Security (Instr. 3) 2. Transaction Date (Month/Day/Year) 2. Transaction (Month/Day/Year) 2. Transaction Date (Month/Day/Year) 2. Transaction Date (Date (Month/Day/Year) 2. Transaction Date (Month/Day/Year) 2. Transaction (Month/Day/Year) 2. Transaction (Month/Day/Year) 2. Transaction Date (e.g., puts, calls, warrants, options, convertible security (Instr. 3) 3. Transaction Date (e.g., puts, calls, warrants, options, convertible security (Instr. 3) 3. Transaction Date (Month/Day/Year) 3. Transacti	(First) (Middle) S PHARMACEUTICALS, INC. 3. Date of Earliest Transaction (Month/Day/Year) 03/03/2006 4. If Amendment, Date of Original Filed (Month/Day/Year) 5. Inc. Code V Amount (A) or (D)	Security (Instr. 3) 2. Transaction 2. Transaction	(First) (Middle) 3. Date of Earliest Transaction (Month/Day/Year) (Month/Day/Year) (Month/Day/Year) (S. Individual or Joint/Group Line) (State) (Zip) (Month/Day/Year) (Month/Day/Ye	Security (Instr. 3) 2. Transaction 2. Transaction	Security (Instr. 3)		

Explanation of Responses:

\$6.84

1. The sale reported in this Form 4 was effected pursuant to a Rule 10b5-1 trading plan adopted by the reporting person on 2-16-06.

03/03/2006

2. Stock option under the Isis Pharmaceuticals, Inc. 2000 Broad-Based Equity Incentive Plan. 25% of the shares subject to the option vested and became 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 4,125 shares per year. The option was exercisable as to 5,778 shares on 3-3-06 prior to the reported exercise.

Date

Exercisable

01/02/2004(2)

(A) (D)

1,008

Expiration Date

05/24/2006

Title

Stock

Remarks:

Employee Stock Option

(right to buy)

/s/B. Lynne Parshall

03/06/2006

Date

4,770

D

** Signature of Reporting Person

1,008

\$<mark>0</mark>

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).

03/03/2006

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

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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.