

**INITIAL STATEMENT OF BENEFICIAL OWNERSHIP OF SECURITIES**

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

OMB APPROVAL	
OMB Number:	3235-0104
Estimated average burden hours per response:	0.5

<b>1. Name and Address of Reporting Person*</b> <u>HOUGEN ELIZABETH L.</u>  (Last) (First) (Middle) C/O ISIS PHARMACEUTICALS, INC. 2855 GAZELLE COURT  (Street) CARLSBAD CA 92010  (City) (State) (Zip)	<b>2. Date of Event Requiring Statement</b> (Month/Day/Year) 01/01/2013	<b>3. Issuer Name and Ticker or Trading Symbol</b> <u>ISIS PHARMACEUTICALS INC [ ISIS ]</u>	<b>5. If Amendment, Date of Original Filed (Month/Day/Year)</b>
		<b>4. Relationship of Reporting Person(s) to Issuer</b> (Check all applicable) Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) SVP, Finance and CFO	<b>6. Individual or Joint/Group Filing (Check Applicable Line)</b> <input checked="" type="checkbox"/> Form filed by One Reporting Person 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)
No securities are beneficially owned	0	D	

**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: Direct (D) or Indirect (I) (Instr. 5)	6. Nature of Indirect Beneficial Ownership (Instr. 5)
	Date Exercisable	Expiration Date				
Employee Stock Option (right to buy)	01/02/2008	01/01/2014	Common Stock 5,040	6.81	D	
Employee Stock Option (right to buy)	01/01/2011	12/31/2013	Common Stock 4,792	11.12	D	
Employee Stock Option (right to buy)	01/02/2011	01/01/2014	Common Stock 9,584	11.12	D	
Employee Stock Option (right to buy)	01/02/2012	01/01/2015	Common Stock 18,230	15.38	D	
Employee Stock Option (right to buy)	01/02/2013 <sup>(1)</sup>	01/01/2016	Common Stock 22,500	14.47	D	
Employee Stock Option (right to buy)	01/04/2014 <sup>(2)</sup>	01/03/2017	Common Stock 20,000	11.27	D	
Employee Stock Option (right to buy)	01/03/2015 <sup>(3)</sup>	01/02/2018	Common Stock 22,000	10.29	D	
Employee Stock Option (right to buy)	01/03/2016 <sup>(4)</sup>	01/02/2019	Common Stock 19,500	7.25	D	
Restricted Stock Units	(5)	(5)	Common Stock 2,166	(6)	D	

**Explanation of Responses:**

- Grant of 1/2/09 to reporting person of stock options under the Isis Pharmaceuticals, Inc. 1989 Stock Option Plan. 25% of the shares subject to the option vested and became exercisable on 1/2/10. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments, at the rate of 5,625 shares per year. The option is exercisable as to 22,031 on 1/1/13.
- Grant of 1/4/10 to reporting person of stock options under the Isis Pharmaceuticals, Inc. 1989 Stock Option Plan. 25% of the shares subject to the option vested and became exercisable on 1/4/11. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments, at the rate of 5,000 shares per year. The option is exercisable as to 14,583 on 1/1/13.
- Grant of 1/3/11 to reporting person of stock options under the Isis Pharmaceuticals, Inc. 1989 Stock Option Plan. 25% of the shares subject to the option vested and became exercisable on 1/3/12. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments, at the rate of 5,500 shares per year. The option is exercisable as to 10,541 on 1/1/13.
- Grant of 1/3/12 to reporting person of stock options under the Isis Pharmaceuticals, Inc. 1989 Stock Option Plan. 25% of the shares subject to the option vested and became exercisable on 1/3/13. Thereafter, the remaining shares subject to the option vested and became exercisable in 36 equal monthly installments, at the rate of 4,875 shares per year. The option is exercisable as to 0 on 1/1/13.
- The restricted stock units vest in four equal annual installments, the first installment vesting on 1/15/13. Upon vesting, the restricted stock units will be paid out in whole shares of Isis common stock or cash as may be determined by the Company. The restricted stock unit will be fully vested on 1/15/16. The restricted stock unit is vested as to 0 shares on 1/1/13.
- Each restricted stock unit represents a contingent right to receive one share of Isis common stock or its equivalent cash value.

**Remarks:**

/s/Elizabeth L. Hougen

\*\* Signature of Reporting Person

01/02/2013

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 5 (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.

POWER OF ATTORNEY

Know all by these presents, that the undersigned hereby constitutes and appoints each of Stanley T. Crooke and B. Lynne Parshall, signing individually, the undersigned (1) execute for and on behalf of the undersigned, an officer, director or holder of 10% or more of a registered class of securities of Isis Pharmaceuticals, Inc. (Isis) (2) do and perform any and all acts for and on behalf of the undersigned that may be necessary or desirable to complete and execute such Form 3, 4 or 5, complete and (3) take any other action of any nature whatsoever in connection with the foregoing which, in the opinion of such attorney-in-fact, may be of benefit, in the best interest of the undersigned. The undersigned hereby grants to each such attorney-in-fact full power and authority to do and perform any and every act and thing whatsoever requisite, necessary, and proper that may be required to carry out the foregoing. This Power of Attorney shall remain in full force and effect until the earliest to occur of (a) the undersigned is no longer required to file Forms 3, 4 and 5 with the SEC.

IN WITNESS WHEREOF, the undersigned has caused this Power of Attorney to be executed as of this 1st day of January, 2013.

/s/Elizabeth L. Hougen