

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

<p>1. Name and Address of Reporting Person*</p> <p><u>KLEIN JOSEPH III</u></p> <hr/> <p>(Last) (First) (Middle)</p> <p>C/O ISIS PHARMACEUTICALS, INC.</p> <p>2855 GAZELLE COURT</p> <hr/> <p>(Street)</p> <p>CARLSBAD CA 92010</p> <hr/> <p>(City) (State) (Zip)</p>	<p>2. Issuer Name and Ticker or Trading Symbol</p> <p><u>ISIS PHARMACEUTICALS INC [ISIS]</u></p> <hr/> <p>3. Date of Earliest Transaction (Month/Day/Year)</p> <p>01/04/2012</p> <hr/> <p>4. If Amendment, Date of Original Filed (Month/Day/Year)</p>	<p>5. Relationship of Reporting Person(s) to Issuer (Check all applicable)</p> <p><input checked="" type="checkbox"/> Director 10% Owner</p> <p>Officer (give title below) Other (specify below)</p> <hr/> <p>6. Individual or Joint/Group Filing (Check Applicable Line)</p> <p><input checked="" type="checkbox"/> Form filed by One Reporting Person</p> <p>Form filed by More than One Reporting Person</p>
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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	Amount or Number of Shares				
Employee Stock Option (right to buy)	\$9.77	01/04/2012	01/04/2012	G ⁽¹⁾			12,500 ⁽¹⁾	07/02/2011	07/01/2017	Common Stock	12,500	\$0	0	D	
Employee Stock Option (right to buy)	\$13.88	01/04/2012	01/04/2012	G ⁽¹⁾			11,250 ⁽¹⁾	07/01/2012 ⁽²⁾	06/30/2018	Common Stock	11,250	\$0	3,750	D	
Employee Stock Option (right to buy)	\$16.32	01/04/2012	01/04/2012	G ⁽¹⁾			7,500 ⁽¹⁾	07/01/2013 ⁽³⁾	06/30/2019	Common Stock	7,500	\$0	7,500	D	
Employee Stock Option (right to buy)	\$9.22	01/04/2012	01/04/2012	G ⁽¹⁾			3,750 ⁽¹⁾	07/01/2014 ⁽⁴⁾	06/30/2020	Common Stock	3,750	\$0	11,250	D	
Employee Stock Option (right to buy)	\$9.77	01/04/2012	01/04/2012	G ⁽¹⁾			4,166 ⁽¹⁾	07/02/2011	07/01/2017	Common Stock	4,166	\$0	4,166	I	By Trust
Employee Stock Option (right to buy)	\$13.88	01/04/2012	01/04/2012	G ⁽¹⁾			3,750 ⁽¹⁾	07/01/2009	06/30/2018	Common Stock	3,750	\$0	3,750	I	By Trust
Employee Stock Option (right to buy)	\$16.32	01/04/2012	01/04/2012	G ⁽¹⁾			2,500 ⁽¹⁾	07/01/2011	06/30/2019	Common Stock	2,500	\$0	2,500	I	By Trust
Employee Stock Option (right to buy)	\$9.22	01/04/2012	01/04/2012	G ⁽¹⁾			1,250 ⁽¹⁾	07/01/2011	06/30/2020	Common Stock	1,250	\$0	1,250	I	By Trust
Employee Stock Option (right to buy)	\$9.77	01/04/2012	01/04/2012	G ⁽¹⁾			4,167 ⁽¹⁾	07/02/2011	07/01/2017	Common Stock	4,167	\$0	4,167	I	By Trust
Employee Stock Option (right to buy)	\$13.88	01/04/2012	01/04/2012	G ⁽¹⁾			3,750 ⁽¹⁾	07/01/2010	06/30/2018	Common Stock	3,750	\$0	3,750	I	By Trust

