FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

OMB	APPROVAL
CIVID	AFFRUVAL

3235-0287

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

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

OMB Number: Estimated average burden hours per response: 0.5

Name and Address of Reporting Person* KLEIN JOSEPH III —————————————————————————————————					2. Issuer Name and Ticker or Trading Symbol ISIS PHARMACEUTICALS INC [ISIS] 5. Relationship of Reporting Person (Check all applicable) X Director Officer (give title									1	o Issuei 0% Owi other (sp	ner	
	,	First) ACEUTICALS, I DURT	(Middle)			e of Earlie /2012	st Transact	ion (Month/Day	//Year)			below)	nvo uuc		elow)	Cony	
(Street)	BAD (CA CA	92010		4. If Ar	mendment	, Date of O	riginal Filed (M	lonth/Day/Ye	ar)		Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person Form filed by More than One Reporting Person					
(City)	()	State)	(Zip)														
						_											
1. Title of S	Security (Ins	tr. 3)		2. Transa Date (Month/D	action 2A. Deemed Execution Date, if any (Month/Day/Year)			3. 4. Securities Acquired (A) of Disposed Of (D) (Instr. 3, 4			4 and 5)	and 5) Securities Beneficially (Following Reported		. Ownersh form: Dire D) or Indir) (Instr. 4)	ect E	. Nature of ndirect seneficial ownership nstr. 4)	
			Table II - I	Dorivat	tivo S	ocuritie	s Acqui	red Dispo	Amount	(D)	Price	(Instr. 3 and					
Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) 1. Title of 2. 3. Transaction 3A. Deemed 4. 5. Number of 6. Date Exercisable and 7. Title and Amount 8. Price of 9. Number of 10. 11. Nature																	
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	Table II - Do (e 3A. Deemed Execution Date, if any (Month/Day/Year) 01/04/2012 01/04/2012 01/04/2012		action (Instr.	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 derivative Securities Beneficiall Owned Following	Ow For Dire	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		Reported Transactio (Instr. 4)		,		
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	

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.		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	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		Reported Transaction(s) (Instr. 4)		
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⁾		07/01/2011	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

Explanation of Responses:

- $1. \ The \ reporting \ person \ transferred \ options \ to \ trusts \ for \ his \ three \ children \ who \ share \ the \ reporting \ person's \ household$
- 2. Grant of 7/1/08 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 7/1/09. The option shall be fully vested and exercisable on 7-1-12. The option was exercisable as to 11,250 shares on 1/4/12.
- 3. Grant of 7/1/09 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 7/1/10. The option shall be fully vested and exercisable on 7-1-13. The option was exercisable as to 7,500 shares on 1/4/12.
- 4. Grant of 7/1/10 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 7/1/11. The option shall be fully vested and exercisable on 7-1-14. The option was exercisable as to 3,750 shares on 1/4/12.

Remarks:

/s/B. Lynne Parshall, Attorney-01/05/2012 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.