ISIS PHARMACEUTICALS INC Form SC 13G/A February 06, 2006

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UNITED STATES SECURITIES AND EXCHANGE COMMISSION Washington, D.C. 20549

SCHEDULE 13G

Under the Securities Exchange Act of 1934 (Amendment No. 2)*

Isis Pharmaceuticals, Inc.
(Name of Issuer)
Common Stock
(Title of Class of Securities)
464330-1-09
(CUSIP Number)
May 23, 2005
(Date of Event Which Requires Filing of this Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

- o Rule 13d-1(b)

 b Rule 13d-1(c)
- o Rule 13d-1(d)

The information required in the remainder of this cover page shall not be deemed to be filed for the purpose of Section 18 of the Securities Exchange Act of 1934 (Act) or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

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 control number.

^{*} The remainder of this cover page shall be filled out for a reporting person s initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter the disclosures provided in a prior cover page.

CUSIP No. 5 464330-1-09 Page 2 of NAMES OF REPORTING PERSONS: Eli Lilly and Company 1 I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY): 35-0470950 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (SEE INSTRUCTIONS): 2 (a) o (b) o Not Applicable SEC USE ONLY: 3 CITIZENSHIP OR PLACE OF ORGANIZATION: 4 Indiana **SOLE VOTING POWER:** 5 NUMBER OF 2,500,000 **SHARES** SHARED VOTING POWER: 6 BENEFICIALLY OWNED BY None **EACH** SOLE DISPOSITIVE POWER: 7 REPORTING **PERSON** 2,500,000 WITH: SHARED DISPOSITIVE POWER: 8 None

AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON:

9

2,500,000

CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS):

o Not Applicable

PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9):

11

3.5%

TYPE OF REPORTING PERSON (SEE INSTRUCTIONS):

12

CO

2

Item 1(a). Name of Issuer: Isis Pharmaceuticals, Inc. Item 1(b). Address of Issuer s Principal **Executive Offices:** 2292 Faraday Avenue Carlsbad, CA 92008 Item 2(a). Name of Person Filing: Eli Lilly and Company Item 2(b). Address of Principal Business Office or, if None, Residence: Lilly Corporate Center Indianapolis, IN 46285 Item 2(c). Citizenship: Indiana Title of Class of Securities: Item 2(d). Common Stock Item 2(e). **CUSIP** Number: 464330-1-09 Item 3. If this statement is filed pursuant to Rule 13d-1(b), or 13d-2(b) or (c), check whether the person filing is Not applicable (a)-(j)If this statement is filed pursuant to Rule 13d-1(c), check this box. [X] Page 3 of 5 Pages

Item 4.	Ownership.			
	(a)) Amount Beneficially Owned:		
		2,500,000		
	(b) Percent of Class:			
		3.5%		
	(c) Number of shares as to which the person has:		the person has:	
		Sole voting power	2,500,000	
		Shared voting power	None	
		Sole dispositive power	2,500,000	
		Shared dispositive power	None	
Item 5.	Ow	Ownership of Five Percent or Less of a Class. [X]		
Item 6.	Ow	Ownership of More Than Five Percent on Behalf of Another Person.		
	Not applicable			
Item 7.	Identification and Classification of the Subsidiary which Acquired the Security Being Reported on by the Parent Holding Company.			
	Not applicable			
Item 8.	Identification and Classification of Members of the Group.			
	Not applicable			
Item 9.	Notice of Dissolution of Group.			
	Not applicable Page 4 of 5 Pages			

Item 10. Certifications.

By signing below, I certify that, to the best of my knowledge and belief, the securities referred to above were not acquired and are not held for the purpose of or with the effect of changing or influencing control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect.

SIGNATURE

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

ELI LILLY AND COMPANY

By: /s/ Charles E. Golden
Charles E. Golden
Executive Vice President and Chief
Financial Officer

Date: February 6, 2006

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