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OMB APPROVAL  
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hours per response...14.5  
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UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, DC 20549

SCHEDULE 13G

Under the Securities Exchange Act of 1934  
(Amendment No. 1)\*

Isis Pharmaceuticals, Inc.

-----  
(Name of Issuer)

Common Stock, par value \$0.001 per share

-----  
(Title of Class of Securities)

464330109

-----  
(CUSIP Number)

December 31, 2006

-----  
(Date of Event which Requires Filing of this Statement)

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

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

\* 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.

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).

(Continued on following pages)  
Page 1 of 28 Pages

13G

=====  
CUSIP No. 464330109  
=====

-----  
NAMES OF REPORTING PERSONS  
1 I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Farallon Capital Partners, L.P.  
-----

CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
(b) [ X ]\*\*

\*\* The reporting persons making this filing hold an aggregate of 729,779 Shares, which is 1.0% of the class of securities. The reporting person on this cover page, however, is a beneficial owner only of the securities reported by it on this cover page. [See Preliminary Note]

3 SEC USE ONLY

CITIZENSHIP OR PLACE OF ORGANIZATION

4 California

SOLE VOTING POWER

5 NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH -0-

SHARED VOTING POWER

6 233,529 [See Preliminary Note]

SOLE DISPOSITIVE POWER

7 -0-

SHARED DISPOSITIVE POWER

8 233,529 [See Preliminary Note]

AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

9 233,529 [See Preliminary Note]

10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) [ ]

PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

11 0.3% [See Preliminary Note]

TYPE OF REPORTING PERSON (See Instructions)

12 PN

13G

=====  
CUSIP No. 464330109  
=====

NAMES OF REPORTING PERSONS

1 I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Farallon Capital Institutional Partners, L.P.

CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

2 (a) [ ]  
(b) [ X ]\*\*

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3 SEC USE ONLY

4

California

		SOLE VOTING POWER
5		
NUMBER OF	5	-0-
SHARES		
BENEFICIALLY	6	SHARED VOTING POWER
OWNED BY		226,231 [See Preliminary Note]
EACH		
REPORTING	7	SOLE DISPOSITIVE POWER
PERSON WITH		-0-
	8	SHARED DISPOSITIVE POWER
		226,231 [See Preliminary Note]
9		AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON
		226,231 [See Preliminary Note]
10		CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) [ ]
11		PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)
		0.3% [See Preliminary Note]
12		TYPE OF REPORTING PERSON (See Instructions)
		PN

=====  
 CUSIP No. 464330109  
 =====

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Farallon Capital Institutional Partners II, L.P.

-----  
 2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
 (b) [ X ]\*\*

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-----  
 3 SEC USE ONLY

-----  
 4 CITIZENSHIP OR PLACE OF ORGANIZATION

California

-----  
 SOLE VOTING POWER

5

NUMBER OF

-0-

-----  
 SHARES  
 BENEFICIALLY  
 OWNED BY

6

SHARED VOTING POWER

51,085 [See Preliminary Note]

EACH

7

SOLE DISPOSITIVE POWER

REPORTING  
 PERSON WITH

-0-

8

SHARED DISPOSITIVE POWER

51,085 [See Preliminary Note]

-----  
 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

51,085 [See Preliminary Note]

-----  
 10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES  
 CERTAIN SHARES (See Instructions) [ ]

-----  
 11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

0.1% [See Preliminary Note]

-----  
 12 TYPE OF REPORTING PERSON (See Instructions)

PN

=====  
CUSIP No. 464330109  
=====

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Farallon Capital Institutional Partners III, L.P.

-----  
2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)  
(a) [ ]  
(b) [ X ]\*\*

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-----  
3 SEC USE ONLY

-----  
4 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

		5	SOLE VOTING POWER
NUMBER OF			-0-
-----			
		6	SHARED VOTING POWER
SHARES			51,085 [See Preliminary Note]
BENEFICIALLY			
OWNED BY			
-----			
		7	SOLE DISPOSITIVE POWER
EACH			-0-
-----			
		8	SHARED DISPOSITIVE POWER
REPORTING			51,085 [See Preliminary Note]
PERSON WITH			

-----  
9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  
51,085 [See Preliminary Note]

-----  
10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES  
CERTAIN SHARES (See Instructions) [ ]

-----  
11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)  
0.1% [See Preliminary Note]

-----  
12 TYPE OF REPORTING PERSON (See Instructions)  
PN

=====  
CUSIP No. 464330109  
=====

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Tinicum Partners, L.P.

-----  
2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
(b) [ X ]\*\*

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-----  
3 SEC USE ONLY

-----  
4 CITIZENSHIP OR PLACE OF ORGANIZATION

New York

-----  
5 SOLE VOTING POWER

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-----  
-0-

-----  
6 SHARED VOTING POWER

-----  
-0-

-----  
7 SOLE DISPOSITIVE POWER

-----  
-0-

-----  
8 SHARED DISPOSITIVE POWER

-----  
-0-

-----  
9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

-0-

-----  
10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)

[ ]

-----  
11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

0.0%

-----  
12 TYPE OF REPORTING PERSON (See Instructions)

PN  
-----

=====  
CUSIP No. 464330109  
=====

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Farallon Capital Offshore Investors II, L.P.

-----  
2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
(b) [ X ]\*\*

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-----  
3 SEC USE ONLY

-----  
4 CITIZENSHIP OR PLACE OF ORGANIZATION

Cayman Islands

-----  
5 SOLE VOTING POWER

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-----  
6 SHARED VOTING POWER

-----  
7 SOLE DISPOSITIVE POWER

-----  
8 SHARED DISPOSITIVE POWER

-----  
9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

-0-

-----  
10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)

[ ]

-----  
11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

0.0%

-----  
12 TYPE OF REPORTING PERSON (See Instructions)

PN  
-----

=====  
 CUSIP No. 464330109  
 =====

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Farallon Special Situation Partners II, L.P.

-----  
 2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
 (b) [ X ]\*\*

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-----  
 3 SEC USE ONLY

-----  
 4 CITIZENSHIP OR PLACE OF ORGANIZATION

Cayman Islands

-----  
 5 SOLE VOTING POWER

NUMBER OF SHARES -0-

-----  
 6 SHARED VOTING POWER

SHARES BENEFICIALLY OWNED BY EACH 167,849 [See Preliminary Note]

-----  
 7 SOLE DISPOSITIVE POWER

REPORTING PERSON WITH -0-

-----  
 8 SHARED DISPOSITIVE POWER

167,849 [See Preliminary Note]

-----  
 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

167,849 [See Preliminary Note]

-----  
 10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)

[ ]

-----  
 11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

0.2% [See Preliminary Note]

-----  
 12 TYPE OF REPORTING PERSON (See Instructions)

PN



=====  
 CUSIP No. 464330109  
 =====

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Farallon Capital Management, L.L.C.

-----  
 2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
 (b) [ X ]\*\*

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-----  
 3 SEC USE ONLY

-----  
 4 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

-----  
 5 SOLE VOTING POWER

NUMBER OF  
 SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-----  
 6 SHARED VOTING POWER

-----  
 7 SOLE DISPOSITIVE POWER

-----  
 8 SHARED DISPOSITIVE POWER

-0-

-----  
 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

-0-

-----  
 10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)

[ ]

-----  
 11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

0.0%

-----  
 12 TYPE OF REPORTING PERSON (See Instructions)

IA, 00  
 -----

=====  
 CUSIP No. 464330109  
 =====

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Farallon Partners, L.L.C.

-----  
 2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
 (b) [ X ]\*\*

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-----  
 3 SEC USE ONLY

-----  
 4 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

-----  
 5 SOLE VOTING POWER

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-0-

-----  
 6 SHARED VOTING POWER

729,779 [See Preliminary Note]

-----  
 7 SOLE DISPOSITIVE POWER

-0-

-----  
 8 SHARED DISPOSITIVE POWER

729,779 [See Preliminary Note]

-----  
 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

729,779 [See Preliminary Note]

-----  
 10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)

[ ]

-----  
 11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

1.0% [See Preliminary Note]

-----  
 12 TYPE OF REPORTING PERSON (See Instructions)

00

=====  
CUSIP No. 464330109  
=====

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Chun R. Ding

-----  
2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)  
(a) [ ]  
(b) [ X ]\*\*

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-----  
3 SEC USE ONLY

-----  
4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

-----  
5 SOLE VOTING POWER  
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH  
-0-  
-----  
6 SHARED VOTING POWER  
729,779 [See Preliminary Note]  
-----  
7 SOLE DISPOSITIVE POWER  
-0-  
-----  
8 SHARED DISPOSITIVE POWER  
729,779 [See Preliminary Note]

-----  
9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  
729,779 [See Preliminary Note]

-----  
10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) [ ]

-----  
11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)  
1.0% [See Preliminary Note]

-----  
12 TYPE OF REPORTING PERSON (See Instructions)  
IN

=====  
CUSIP No. 464330109  
=====

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

William F. Duhamel

-----  
2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
(b) [ X ]\*\*

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-----  
3 SEC USE ONLY

-----  
4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

-----  
5 SOLE VOTING POWER

NUMBER OF

-0-

-----  
6 SHARED VOTING POWER  
SHARES BENEFICIALLY OWNED BY

729,779 [See Preliminary Note]

EACH

-----  
7 SOLE DISPOSITIVE POWER

REPORTING PERSON WITH

-0-

-----  
8 SHARED DISPOSITIVE POWER

729,779 [See Preliminary Note]

-----  
9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

729,779 [See Preliminary Note]

-----  
10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) [ ]

-----  
11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

1.0% [See Preliminary Note]

-----  
12 TYPE OF REPORTING PERSON (See Instructions)

IN

=====  
CUSIP No. 464330109  
=====

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Charles E. Ellwein [See Preliminary Note]

-----  
2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

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(b) [ X ]\*\*

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-----  
3 SEC USE ONLY

-----  
4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

-----  
5 SOLE VOTING POWER

NUMBER OF SHARES BENEFICIALLY OWNED BY

5  
-0-

-----  
6 SHARED VOTING POWER

6  
-0-

-----  
8 SHARED DISPOSITIVE POWER

8  
0-

-----  
9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

-0-

-----  
10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) [ ]

-----  
11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

-0-

-----  
12 TYPE OF REPORTING PERSON (See Instructions)

IN

=====  
 CUSIP No. 464330109  
 =====

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Richard B. Fried

-----  
 2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
 (b) [ X ]\*\*

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-----  
 3 SEC USE ONLY

-----  
 4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

-----  
 5 SOLE VOTING POWER

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-----  
 6 SHARED VOTING POWER

729,779 [See Preliminary Note]

-----  
 7 SOLE DISPOSITIVE POWER

-0-

-----  
 8 SHARED DISPOSITIVE POWER

729,779 [See Preliminary Note]

-----  
 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

729,779 [See Preliminary Note]

-----  
 10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)

[ ]

-----  
 11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

1.0% [See Preliminary Note]

-----  
 12 TYPE OF REPORTING PERSON (See Instructions)

IN

=====  
CUSIP No. 464330109  
=====

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Monica R. Landry  
-----

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
(b) [ X ]\*\*

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3 SEC USE ONLY  
-----

4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States  
-----

5 SOLE VOTING POWER

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

6 SHARED VOTING POWER

729,779 [See Preliminary Note]

7 SOLE DISPOSITIVE POWER

-0-

8 SHARED DISPOSITIVE POWER

729,779 [See Preliminary Note]

9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

729,779 [See Preliminary Note]

10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)

[ ]

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

1.0% [See Preliminary Note]

12 TYPE OF REPORTING PERSON (See Instructions)

IN  
-----

=====  
CUSIP No. 464330109  
=====

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

William F. Mellin

-----  
2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
(b) [ X ]\*\*

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-----  
3 SEC USE ONLY

-----  
4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

-----  
5 SOLE VOTING POWER

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-----  
6 SHARED VOTING POWER

729,779 [See Preliminary Note]

-----  
7 SOLE DISPOSITIVE POWER

-0-

-----  
8 SHARED DISPOSITIVE POWER

729,779 [See Preliminary Note]

-----  
9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

729,779 [See Preliminary Note]

-----  
10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) [ ]

-----  
11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

1.0% [See Preliminary Note]

-----  
12 TYPE OF REPORTING PERSON (See Instructions)

IN



=====  
 CUSIP No. 464330109  
 =====

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Stephen L. Millham

-----  
 2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
 (b) [ X ]\*\*

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-----  
 3 SEC USE ONLY

-----  
 4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

-----  
 SOLE VOTING POWER

5  
 NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-0-

-----  
 SHARED VOTING POWER

6  
 729,779 [See Preliminary Note]

-----  
 SOLE DISPOSITIVE POWER

7  
 -0-

-----  
 SHARED DISPOSITIVE POWER

8  
 729,779 [See Preliminary Note]

-----  
 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

729,779 [See Preliminary Note]

-----  
 10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) [ ]

-----  
 11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

1.0% [See Preliminary Note]

-----  
 12 TYPE OF REPORTING PERSON (See Instructions)

IN

=====  
CUSIP No. 464330109  
=====

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Jason E. Moment

-----  
2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
(b) [ X ]\*\*

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-----  
3 SEC USE ONLY

-----  
4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

-----  
5 SOLE VOTING POWER

NUMBER OF

5

-0-

SHARES  
BENEFICIALLY  
OWNED BY

6

-----  
6 SHARED VOTING POWER

729,779 [See Preliminary Note]

EACH

7

-----  
7 SOLE DISPOSITIVE POWER

REPORTING  
PERSON WITH

8

-0-

-----  
8 SHARED DISPOSITIVE POWER

729,779 [See Preliminary Note]

-----  
9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

729,779 [See Preliminary Note]

-----  
10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES  
CERTAIN SHARES (See Instructions) [ ]

-----  
11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

1.0% [See Preliminary Note]

-----  
12 TYPE OF REPORTING PERSON (See Instructions)

IN

=====  
CUSIP No. 464330109  
=====

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Rajiv A. Patel

-----  
2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
(b) [ X ]\*\*

\*\* The reporting persons making this filing hold an aggregate of 729,779 Shares, which is 1.0% of the class of securities. The reporting person on this cover page, however, may be deemed a beneficial owner only of the securities reported by it on this cover page. [See Preliminary Note]

-----  
3 SEC USE ONLY

-----  
4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

-----  
5 SOLE VOTING POWER

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-----  
6 SHARED VOTING POWER

729,779 [See Preliminary Note]

-----  
7 SOLE DISPOSITIVE POWER

-0-

-----  
8 SHARED DISPOSITIVE POWER

729,779 [See Preliminary Note]

-----  
9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

729,779 [See Preliminary Note]

-----  
10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)

[ ]

-----  
11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

1.0% [See Preliminary Note]

-----  
12 TYPE OF REPORTING PERSON (See Instructions)

IN

=====  
 CUSIP No. 464330109  
 =====

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Derek C. Schrier

-----  
 2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
 (b) [ X ]\*\*

\*\* The reporting persons making this filing hold an aggregate of 729,779 Shares, which is 1.0% of the class of securities. The reporting person on this cover page, however, may be deemed a beneficial owner only of the securities reported by it on this cover page. [See Preliminary Note]

-----  
 3 SEC USE ONLY

-----  
 4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

-----  
 SOLE VOTING POWER

5  
 NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-----  
 6 SHARED VOTING POWER  
 729,779 [See Preliminary Note]

-----  
 SOLE DISPOSITIVE POWER

7  
 -0-

-----  
 SHARED DISPOSITIVE POWER

8  
 729,779 [See Preliminary Note]

-----  
 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

729,779 [See Preliminary Note]

-----  
 10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) [ ]

-----  
 11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

1.0% [See Preliminary Note]

-----  
 12 TYPE OF REPORTING PERSON (See Instructions)

IN

=====  
 CUSIP No. 464330109  
 =====

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Thomas F. Steyer

-----  
 2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
 (b) [ X ]\*\*

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-----  
 3 SEC USE ONLY

-----  
 4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

-----  
 SOLE VOTING POWER

NUMBER OF	5	-0-
SHARES		
BENEFICIALLY	6	729,779 [See Preliminary Note]
OWNED BY		

-----  
 SOLE DISPOSITIVE POWER

EACH	7	-0-
REPORTING		
PERSON WITH	8	729,779 [See Preliminary Note]

-----  
 SHARED DISPOSITIVE POWER

-----  
 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

729,779 [See Preliminary Note]

-----  
 10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions) [ ]

-----  
 11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

1.0% [See Preliminary Note]

-----  
 12 TYPE OF REPORTING PERSON (See Instructions)

IN

=====  
 CUSIP No. 464330109  
 =====

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY)

Mark C. Wehrly

-----  
 2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)

(a) [ ]  
 (b) [ X ]\*\*

\*\* The reporting persons making this filing hold an aggregate of 729,779 Shares, which is 1.0% of the class of securities. The reporting person on this cover page, however, may be deemed a beneficial owner only of the securities reported by it on this cover page. [See Preliminary Note]

-----  
 3 SEC USE ONLY

-----  
 4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

-----  
 SOLE VOTING POWER

5  
 NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-0-

-----  
 SHARED VOTING POWER

6  
 729,779 [See Preliminary Note]

-----  
 SOLE DISPOSITIVE POWER

7  
 -0-

-----  
 SHARED DISPOSITIVE POWER

8  
 729,779 [See Preliminary Note]

-----  
 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

729,779 [See Preliminary Note]

-----  
 10 CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)

[ ]

-----  
 11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

1.0% [See Preliminary Note]

-----  
 12 TYPE OF REPORTING PERSON (See Instructions)

IN

This Amendment No. 1 to Schedule 13G amends and restates in its entirety the Schedule 13G initially filed on February 21, 2005 (collectively, with all amendments thereto, the "Schedule 13G").

Preliminary Note: The Reporting Persons are filing this Schedule 13G with respect to the Common Shares, par value \$0.001 per share (the "Shares"), of Isis Pharmaceuticals, Inc. (the "Company"). Certain of the Reporting Persons own, in aggregate, (i) 0 Shares and (ii) warrants exercisable for 729,779 Shares (the "Warrants") issued by the Company, each Warrant being currently exercisable at an exercise price of \$5.2395 per Share (subject to adjustment pursuant to the terms of the Warrants). All numbers and percentages contained in this Schedule 13G represent Shares and not Warrants unless stated otherwise. For information regarding the Warrants, see the Company's Current Report on Form 8-K filed with the Securities and Exchange Commission on August 25, 2005.

This Schedule 13G reports that effective as of April 3, 2006, Mr. Ellwein resigned as a managing member of FPLLC and Mr. Ellwein may therefore no longer be deemed a beneficial owner of the Issuer's securities reported herein.

Item 1. Issuer

(a) Name of Issuer:

Isis Pharmaceuticals, Inc.

(b) Address of Issuer's Principal Executive Offices:

1896 Rutherford Road, Carlsbad, California 92008

Item 2. Identity And Background

Title Of Class Of Securities And CUSIP Number (Item 2(d) and (e))

This statement relates to Shares of Common Stock, par value \$0.001 per share (the "Shares"), of the Company. The CUSIP number of the Shares is 464330109.

Name Of Persons Filing, Address Of Principal Business Office And  
Citizenship (Item 2(a), (b) and (c))

This statement is filed by the entities and persons listed below, all of whom together are referred to herein as the "Reporting Persons."

The Farallon Funds

- (i) Farallon Capital Partners, L.P., a California limited partnership ("FCP"), with respect to the Shares beneficially owned by it (through its ownership of Warrants);
- (ii) Farallon Capital Institutional Partners, L.P., a California limited partnership ("FCIP"), with respect to the Shares beneficially owned by it (through its ownership of Warrants);
- (iii) Farallon Capital Institutional Partners II, L.P., a California limited partnership ("FCIP II"), with respect to the Shares beneficially owned by it (through its ownership of Warrants);
- (iv) Farallon Capital Institutional Partners III, L.P., a Delaware limited partnership ("FCIP III"), with respect to the Shares beneficially owned by it (through its ownership of Warrants);
- (v) Tincum Partners, L.P., a New York limited partnership ("Tincum"), with respect to the Shares beneficially owned by it;
- (vi) Farallon Capital Offshore Investors II, L.P., a Cayman Islands exempted limited partnership ("FCOI II"), with respect to the Shares beneficially owned by it; and
- (vii) Farallon Special Situation Partners II, L.P., a Cayman Islands exempted limited partnership ("FSSP II"), with respect to the Shares beneficially owned by it (through its ownership of Warrants).

FCP, FCIP, FCIP II, FCIP III, Tincum, FCOI II and FSSP II are together referred to herein as the "Farallon Funds."

The Management Company

- (vii) Farallon Capital Management, L.L.C., a Delaware limited liability company (the "Management Company"), with respect to the Shares beneficially owned by a certain account managed by the Management Company (the "Managed Account").

The Farallon General Partner

- (viii) Farallon Partners, L.L.C., a Delaware limited liability company which is the general partner of each of the Farallon Funds (the "Farallon General Partner"), with respect to the Shares beneficially owned by each of the Farallon Funds (through their ownership of Warrants).



The Farallon Managing Members  
-----

- (ix) The following persons who are, or solely with respect to Charles Ellwein were, managing members of both the Farallon General Partner and the Management Company, with respect to the Shares beneficially owned by the Farallon Funds and the Managed Account (through their ownership of Warrants): Chun R. Ding ("Ding"), William F. Duhamel ("Duhamel"), Richard B. Fried ("Fried"), Monica R. Landry ("Landry"), William F. Mellin ("Mellin"), Stephen L. Millham ("Millham"), Jason E. Moment ("Moment"), Rajiv A. Patel ("Patel"), Derek C. Schrier ("Schrier"), Thomas F. Steyer ("Steyer") and Mark C. Wehrly ("Wehrly").

Ding, Duhamel, Fried, Landry, Mellin, Millham, Moment, Patel, Schrier, Steyer and Wehrly are together referred to herein as the "Farallon Individual Reporting Persons."

The citizenship of each of the Farallon Funds, the Management Company and the Farallon General Partner is set forth above. Each of the Farallon Individual Reporting Persons is a citizen of the United States. The address of the principal business office of each of the Reporting Persons other than FSSP II and FCOI II is c/o Farallon Capital Management, L.L.C., One Maritime Plaza, Suite 1325, San Francisco, California 94111. The address of the principal business office of FSSP II is c/o Walker House, Mary Street, P.O. Box 908 GT, George Town, Grand Cayman, Cayman Islands. The address of the principal business office of FCOI II is Harbour Centre, P.O. Box 896, George Town, Grand Cayman, Cayman Islands.

Item 3. If This Statement Is Filed Pursuant To Sections 240.13d-1(b) or 240.13d-2(b) or (c), Check Whether The Person Filing Is An Entity Specified In (a) - (j):  
-----

Not Applicable.

If This Statement Is Filed Pursuant To Section 240.13d-1(c), Check This Box.   
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Item 4. Ownership  
-----

The information required by Items 4(a) - (c) and set forth in Rows 5 through 11 of the cover page for each Reporting Person hereto is incorporated herein by reference for each such Reporting Person.

The Warrants in respect of which certain of the Farallon Funds and the Managed Account (as reported by the Management Company) are deemed to beneficially own Shares are owned directly by the stated Farallon Funds and the Managed Account. The Farallon General Partner, as general partner to the Farallon Funds, may be deemed to be the beneficial owner of all such Shares beneficially owned by the Farallon Funds. The Management Company, as investment adviser to the Managed Account, may be deemed to be the beneficial owner of all such Shares beneficially owned by the Managed Account. The Farallon Individual Reporting Persons, as managing members of both the Farallon General Partner and the Management Company with the power to exercise investment discretion, may each be deemed to be the beneficial owner of all

such Shares beneficially owned by the Farallon Funds and the Managed Account. Each of the Management Company, the Farallon General Partner and the Farallon Individual Reporting Persons hereby disclaims any beneficial ownership of any such Shares.

Item 5. Ownership Of Five Percent Or Less Of A Class  
-----

If this statement is being filed to report the fact that as of the date hereof the Reporting Persons have ceased to be the deemed beneficial owner of more than five percent of the class of securities, check the following [ X ].

Item 6. 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  
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The Reporting Persons are filing this Schedule 13G pursuant to Section 240.13d-1(c). Consistent with Item 2 of the cover page for each Reporting Person above, the Reporting Persons neither disclaim nor affirm the existence of a group among them.

Item 9. Notice Of Dissolution Of Group  
-----

Not Applicable.

Item 10. Certification  
-----

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 the 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.

SIGNATURES

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

Dated: January \_\_, 2007

-----  
FARALLON PARTNERS, L.L.C.,  
On its own behalf and  
as the General Partner  
of FARALLON CAPITAL PARTNERS, L.P.,  
FARALLON CAPITAL INSTITUTIONAL PARTNERS, L.P.,  
FARALLON CAPITAL INSTITUTIONAL PARTNERS II, L.P.,  
FARALLON CAPITAL INSTITUTIONAL PARTNERS III, L.P.,  
TINICUM PARTNERS, L.P.,  
FARALLON CAPITAL OFFSHORE INVESTORS II, L.P. and  
FARALLON SPECIAL SITUATION PARTNERS II, L.P.  
By Mark C. Wehrly,  
Managing Member

-----  
FARALLON CAPITAL MANAGEMENT, L.L.C.  
By Mark C. Wehrly,  
Managing Member

-----  
Mark C. Wehrly, individually and as attorney-in-fact for  
each of Chun R. Ding, William F. Duhamel, Charles E. Ellwein,  
Richard B. Fried, Monica R. Landry, William F. Mellin, Stephen  
L. Millham, Jason E. Moment, Rajiv A. Patel, Derek C. Schrier  
and Thomas F. Steyer

The Powers of Attorney executed by Ding and Schrier authorizing Wehrly to sign and file this Schedule 13G on each person's behalf, which were filed with Amendment No. 1 to the Schedule 13D filed with the Securities and Exchange Commission on July 2, 2003, by such Reporting Persons with respect to the Common Stock of Salix Pharmaceuticals, Ltd., are hereby incorporated by reference. The Power of Attorney executed by Ellwein and Patel authorizing Wehrly to sign and file this Schedule 13G on his behalf, which was filed with Amendment No. 4 to the Schedule 13G filed with the Securities and Exchange Commission on January 8, 2004, by such Reporting Person with respect to the Common Stock of Catalytica Energy Systems, Inc., is hereby incorporated by reference. The Power of Attorney executed by Mittal authorizing Wehrly to sign and file this Schedule 13G on his behalf, which was filed with Amendment No. 6 to the Schedule 13G filed with the Securities and Exchange Commission on October 5, 2005, by such

Reporting Person with respect to the Common Stock of Catalytica Energy Systems, Inc., is hereby incorporated by reference. The Power of Attorney executed by Moment authorizing Wehrly to sign and file this Schedule 13G on his behalf, which was filed with the Schedule 13D filed with the Securities and Exchange Commission on January 9, 2006, by such Reporting Person with respect to the Common Stock of Vintage Petroleum, Inc., is hereby incorporated by reference. The Powers of Attorney executed by Duhamel, Fried, Landry, Mellin, Millham and Steyer authorizing Wehrly to sign and file this Schedule 13G on each person's behalf, which were filed with Amendment No. 2 to the Schedule 13G filed with the Securities and Exchange Commission on January 13, 2006, by such Reporting Persons with respect to the Common Stock of Arbor Realty Trust, Inc., are hereby incorporated by reference.

