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OMB APPROVAL  
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hours per response.....11  
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UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, DC 20549

SCHEDULE 13G

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

Isis Pharmaceuticals, Inc.

-----  
(Name of Issuer)

Common Stock, par value \$0.001 per share

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

464330109

-----  
(CUSIP Number)

February 9, 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 30 Pages  
Exhibit Index Found on Page 29

13G

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

-----  
NAMES OF REPORTING PERSONS

1 I.R.S. IDENTIFICATION NO. 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 ]\*\*

2

\*\* The reporting persons making this filing hold an aggregate of 3,696,828 Shares, which is 5.1% 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

CITIZENSHIP OR PLACE OF ORGANIZATION

4

California

SOLE VOTING POWER

5

NUMBER OF

-0-

SHARES

SHARED VOTING POWER

BENEFICIALLY OWNED BY

6

1,176,021 [See Preliminary Note]

EACH

SOLE DISPOSITIVE POWER

7

-0-

REPORTING PERSON WITH

SHARED DISPOSITIVE POWER

8

1,176,021 [See Preliminary Note]

AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

9

1,176,021 [See Preliminary Note]

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

10

[ ]

PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

11

1.6% [See Preliminary Note]

TYPE OF REPORTING PERSON (See Instructions)

12

PN

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

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY)

Farallon Capital Institutional 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

California

-----  
 SOLE VOTING POWER

5  
 NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-0-

-----  
 SHARED VOTING POWER

6  
 1,139,558 [See Preliminary Note]

-----  
 SOLE DISPOSITIVE POWER

7  
 -0-

-----  
 SHARED DISPOSITIVE POWER

8  
 1,139,558 [See Preliminary Note]

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

1,139,558 [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)

1.6% [See Preliminary Note]

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

PN

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

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NO. 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

256,723 [See Preliminary Note]

EACH

7

SOLE DISPOSITIVE POWER

-----  
 REPORTING  
 PERSON WITH

-0-

8

SHARED DISPOSITIVE POWER

256,723 [See Preliminary Note]

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

256,723 [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)

0.4% [See Preliminary Note]

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

PN

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

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NO. 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 SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-0-

-----  
 6 SHARED VOTING POWER

256,223 [See Preliminary Note]

-----  
 7 SOLE DISPOSITIVE POWER

-0-

-----  
 8 SHARED DISPOSITIVE POWER

256,223 [See Preliminary Note]

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

256,223 [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)

0.4% [See Preliminary Note]

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

PN

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

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NO. 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

-0-

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

400

EACH

-----  
 7 SOLE DISPOSITIVE POWER

REPORTING PERSON WITH

-0-

-----  
 8 SHARED DISPOSITIVE POWER

400

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

400

-----  
 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 NO. 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

-0-

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

9,200

EACH

-----  
 7 SOLE DISPOSITIVE POWER

REPORTING PERSON WITH

-0-

-----  
 8 SHARED DISPOSITIVE POWER

9,200

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

9,200

-----  
 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 NO. 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 BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

5 -0-

-----  
6 SHARED VOTING POWER

837,046 [See Preliminary Note]

-----  
7 SOLE DISPOSITIVE POWER

7 -0-

-----  
8 SHARED DISPOSITIVE POWER

837,046 [See Preliminary Note]

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

837,046 [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)

1.2% [See Preliminary Note]

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

PN



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

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NO. 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

-----  
 SOLE VOTING POWER

5  
 NUMBER OF -0-

-----  
 SHARED VOTING POWER

6  
 SHARES BENEFICIALLY OWNED BY 21,657

-----  
 SOLE DISPOSITIVE POWER

7  
 EACH REPORTING PERSON WITH -0-

-----  
 SHARED DISPOSITIVE POWER

8  
 21,657

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

21,657

-----  
 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 NO. 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

-----  
 6 SHARED VOTING POWER

3,675,171 [See Preliminary Note]

-----  
 7 SOLE DISPOSITIVE POWER

-0-

-----  
 8 SHARED DISPOSITIVE POWER

3,675,171 [See Preliminary Note]

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

3,675,171 [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)

5.0% [See Preliminary Note]

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

00

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

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NO. 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

-----  
 SOLE VOTING POWER

5

NUMBER OF

-0-

-----  
 SHARES  
 BENEFICIALLY  
 OWNED BY

6

SHARED VOTING POWER

3,696,828 [See Preliminary Note]

EACH

7

SOLE DISPOSITIVE POWER

REPORTING  
 PERSON WITH

-0-

8

SHARED DISPOSITIVE POWER

3,696,828 [See Preliminary Note]

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

3,696,828 [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)

5.1% [See Preliminary Note]

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

IN

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

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NO. 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

-----  
 SOLE VOTING POWER

5

NUMBER OF

-0-

-----  
 SHARES  
 BENEFICIALLY  
 OWNED BY

6

SHARED VOTING POWER

3,696,828 [See Preliminary Note]

EACH

7

SOLE DISPOSITIVE POWER

-----  
 REPORTING  
 PERSON WITH

-0-

8

SHARED DISPOSITIVE POWER

3,696,828 [See Preliminary Note]

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

3,696,828 [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)

5.1% [See Preliminary Note]

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

IN

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

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY)

Charles E. Ellwein

-----  
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 SHARED VOTING POWER  
3,696,828 [See Preliminary Note]

EACH

-----  
7 SOLE DISPOSITIVE POWER

REPORTING  
PERSON WITH

-----  
8 SHARED DISPOSITIVE POWER

3,696,828 [See Preliminary Note]

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

3,696,828 [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)

5.1% [See Preliminary Note]

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

IN

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

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NO. 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

-----  
 SOLE VOTING POWER

5  
 NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

-0-

-----  
 SHARED VOTING POWER

6  
 3,696,828 [See Preliminary Note]

-----  
 SOLE DISPOSITIVE POWER

7  
 -0-

-----  
 SHARED DISPOSITIVE POWER

8  
 3,696,828 [See Preliminary Note]

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

3,696,828 [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)

5.1% [See Preliminary Note]

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

IN

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

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NO. 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

-----  
 SOLE VOTING POWER

5

NUMBER OF

-0-

-----  
 SHARES  
 BENEFICIALLY  
 OWNED BY

6

SHARED VOTING POWER

3,696,828 [See Preliminary Note]

EACH

7

SOLE DISPOSITIVE POWER

REPORTING  
 PERSON WITH

-0-

8

SHARED DISPOSITIVE POWER

3,696,828 [See Preliminary Note]

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

3,696,828 [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)

5.1% [See Preliminary Note]

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

IN

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

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NO. 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

3,696,828 [See Preliminary Note]

-----  
7 SOLE DISPOSITIVE POWER

-0-

-----  
8 SHARED DISPOSITIVE POWER

3,696,828 [See Preliminary Note]

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

3,696,828 [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)

5.1% [See Preliminary Note]

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

IN



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

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NO. 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

-----  
5 SOLE VOTING POWER

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH

5 -0-

-----  
6 SHARED VOTING POWER

3,696,828 [See Preliminary Note]

-----  
7 SOLE DISPOSITIVE POWER

7 -0-

-----  
8 SHARED DISPOSITIVE POWER

3,696,828 [See Preliminary Note]

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

3,696,828 [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)

5.1% [See Preliminary Note]

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

IN

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

-----  
1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY)

Jason E. Moment

-----  
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 3,696,828 Shares, which is 5.1% 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

-0-

-----  
6 SHARED VOTING POWER

3,696,828 [See Preliminary Note]

-----  
7 SOLE DISPOSITIVE POWER

-0-

-----  
8 SHARED DISPOSITIVE POWER

3,696,828 [See Preliminary Note]

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

3,696,828 [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)

5.1% [See Preliminary Note]

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

IN

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

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY)

Rajiv A. Patel

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

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

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-0-

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 SHARED VOTING POWER

6  
 3,696,828 [See Preliminary Note]

-----  
 SOLE DISPOSITIVE POWER

7  
 -0-

-----  
 SHARED DISPOSITIVE POWER

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 3,696,828 [See Preliminary Note]

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 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

3,696,828 [See Preliminary Note]

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

[ ]

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

5.1% [See Preliminary Note]

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 12 TYPE OF REPORTING PERSON (See Instructions)

IN

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

-----  
 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY)

Derek C. Schrier

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

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

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 4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

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 5 SOLE VOTING POWER

NUMBER OF

-0-

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 6 SHARED VOTING POWER  
 SHARES BENEFICIALLY OWNED BY

3,696,828 [See Preliminary Note]

EACH

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 7 SOLE DISPOSITIVE POWER

REPORTING PERSON WITH

-0-

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 8 SHARED DISPOSITIVE POWER

3,696,828 [See Preliminary Note]

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3,696,828 [See Preliminary Note]

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

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

5.1% [See Preliminary Note]

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 12 TYPE OF REPORTING PERSON (See Instructions)

IN

=====  
CUSIP No. 464330109  
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1 NAMES OF REPORTING PERSONS  
I.R.S. IDENTIFICATION NO. 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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4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

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5 SOLE VOTING POWER

NUMBER OF

-0-

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6 SHARED VOTING POWER  
SHARES BENEFICIALLY OWNED BY

3,696,828 [See Preliminary Note]

EACH

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7 SOLE DISPOSITIVE POWER

REPORTING PERSON WITH

-0-

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3,696,828 [See Preliminary Note]

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9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

3,696,828 [See Preliminary Note]

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

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

5.1% [See Preliminary Note]

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

IN

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

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 1 NAMES OF REPORTING PERSONS  
 I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY)

Mark C. Wehrly

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

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

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

[ ]

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

5.1% [See Preliminary Note]

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

IN

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) 2,967,049 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.

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, 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 Shares and 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 Shares and 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 Shares and 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 Shares and Warrants);
- (v) Tincum Partners, L.P., a New York limited partnership ("Tincum"), with respect to the Shares held by it;
- (vi) Farallon Capital Offshore Investors II, L.P., a Cayman Islands exempted limited partnership ("FCOI II"), with respect to the Shares held 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 Shares and 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.

The Farallon Managing Members  
-----

- (ix) The following persons who are 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: Chun R. Ding ("Ding"), William F. Duhamel ("Duhamel"), Charles E. Ellwein ("Ellwein"), 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, Ellwein, 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.

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 Shares reported hereby for the Farallon Funds are owned directly by the Farallon Funds and those reported by the Management Company on behalf of the Managed Account are owned directly by the Managed Account. 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

Not Applicable.

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  
-----

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

-----

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: February 21, 2006

/s/ Monica R. Landry

-----

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 Monica R. Landry,  
Managing Member

/s/ Monica R. Landry

-----

FARALLON CAPITAL MANAGEMENT, L.L.C.  
By Monica R. Landry,  
Managing Member

/s/ Monica R. Landry

-----

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

The Powers of Attorney executed by Duhamel, Fried, Mellin, Millham, Steyer and Wehrly authorizing Landry to sign and file this Schedule 13G on each person's behalf, which were filed with Amendment No. 2 to the Schedule 13D filed with the Securities and Exchange Commission on July 16, 2003, by such Reporting Persons with respect to the Common Stock of New World Restaurant Group, Inc., are hereby incorporated by reference. The Powers of Attorney executed by Ding and Schrier authorizing Landry 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 Powers of Attorney executed by Ellwein and Patel authorizing Landry to sign and file this Schedule 13G on each person's behalf, which were filed with Amendment No. 4 to the Schedule 13G filed with the Securities and Exchange Commission on January 8, 2004, by such Reporting Persons with respect to the Common Stock of Catalytica Energy Systems, Inc., are hereby incorporated by reference. The Power of Attorney executed by Moment authorizing Landry 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.

EXHIBIT INDEX

EXHIBIT 1

Joint Acquisition Statement Pursuant to  
Section 240.13d-1(k)

JOINT ACQUISITION STATEMENT  
PURSUANT TO SECTION 240.13d-1(k)  
-----

The undersigned acknowledge and agree that the foregoing statement on Schedule 13G is filed on behalf of each of the undersigned and that all subsequent amendments to this statement on Schedule 13G shall be filed on behalf of each of the undersigned without the necessity of filing additional joint acquisition statements. The undersigned acknowledge that each shall be responsible for the timely filing of such amendments, and for the completeness and accuracy of the information concerning him, her or it contained therein, but shall not be responsible for the completeness and accuracy of the information concerning the other entities or persons, except to the extent that he, she or it knows or has reason to believe that such information is inaccurate.

Dated: February 21, 2006

/s/ Monica R. Landry  
-----

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 Monica R. Landry,  
Managing Member

/s/ Monica R. Landry  
-----

FARALLON CAPITAL MANAGEMENT, L.L.C.  
By Monica R. Landry,  
Managing Member

/s/ Monica R. Landry  
-----

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