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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. ___)*

ISIS PHARMACEUTICALS, INC.

(Name of Issuer)

COMMON STOCK, PAR VALUE \$0.001 PER SHARE

(Title of Class of Securities)

464330109

(CUSIP Number)

SEPTEMBER 27, 2007

(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 disclosures provided in a prior cover page.

The information required on 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)

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CUSIP NO. 464330109

Schedule 13G

Page 2 of 18

1 NAMES OF REPORTING PERSON Symphony Capital Partners, L.P.
S.S OR I.R.S. IDENTIFICATION
NOS. OF ABOVE PERSONS (ENTITIES ONLY)

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(SEE INSTRUCTIONS) (a)
(b)

3 SEC USE ONLY

4 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

5 SOLE VOTING POWER

NUMBER OF 4,552,471

SHARES BENEFICIALLY 6 SHARED VOTING POWER

OWNED BY -0-

EACH 7 SOLE DISPOSITIVE POWER

REPORTING PERSON 4,552,471

8 SHARED DISPOSITIVE POWER

-0-

9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

4,552,471

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

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

5.1%

12 TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)

PN

1 NAMES OF REPORTING PERSON Symphony Capital GP, L.P.
S.S OR I.R.S. IDENTIFICATION
NOS. OF ABOVE PERSONS (ENTITIES ONLY)

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(SEE INSTRUCTIONS) (a)
(b)

3 SEC USE ONLY

4 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

5 SOLE VOTING POWER

NUMBER OF 4,552,471

SHARES BENEFICIALLY 6 SHARED VOTING POWER

OWNED BY -0-

EACH 7 SOLE DISPOSITIVE POWER

REPORTING PERSON 4,552,471

8 SHARED DISPOSITIVE POWER

-0-

9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

4,552,471

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

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

5.1%

12 TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)

PN

1 NAMES OF REPORTING PERSON Symphony GP, LLC
S.S OR I.R.S. IDENTIFICATION
NOS. OF ABOVE PERSONS (ENTITIES ONLY)

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(SEE INSTRUCTIONS) (a)
(b)

3 SEC USE ONLY

4 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

5 SOLE VOTING POWER

NUMBER OF 4,552,471

SHARES BENEFICIALLY 6 SHARED VOTING POWER

OWNED BY -0-

EACH 7 SOLE DISPOSITIVE POWER

REPORTING PERSON 4,552,471

8 SHARED DISPOSITIVE POWER

-0-

9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

4,552,471

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

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

5.1%

12 TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)

00

 1 NAMES OF REPORTING PERSON Symphony Strategic Partners, LLC
 S.S OR I.R.S. IDENTIFICATION
 NOS. OF ABOVE PERSONS (ENTITIES ONLY)

 2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
 (SEE INSTRUCTIONS) (a)
 (b)

 3 SEC USE ONLY

 4 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

 5 SOLE VOTING POWER

NUMBER OF 247,475

 SHARES BENEFICIALLY 6 SHARED VOTING POWER

OWNED BY -0-

 EACH 7 SOLE DISPOSITIVE POWER

REPORTING PERSON 247,475

 8 SHARED DISPOSITIVE POWER

-0-

 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

247,475

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

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

0.3%

 12 TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)

00

1 NAMES OF REPORTING PERSON Mark Kessel
S.S OR I.R.S. IDENTIFICATION
NOS. OF ABOVE PERSONS (ENTITIES ONLY)

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(SEE INSTRUCTIONS) (a)
(b)

3 SEC USE ONLY

4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

5 SOLE VOTING POWER

NUMBER OF

-0-

SHARES BENEFICIALLY

6 SHARED VOTING POWER

OWNED BY

4,799,946

EACH

7 SOLE DISPOSITIVE POWER

REPORTING PERSON

-0-

8 SHARED DISPOSITIVE POWER

4,799,946

9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

4,799,946

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

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

5.4%

12 TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)

IN

1 NAMES OF REPORTING PERSON Harri V. Taranto
S.S OR I.R.S. IDENTIFICATION
NOS. OF ABOVE PERSONS (ENTITIES ONLY)

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(SEE INSTRUCTIONS) (a)
(b)

3 SEC USE ONLY

4 CITIZENSHIP OR PLACE OF ORGANIZATION

United States

5 SOLE VOTING POWER

NUMBER OF

-0-

SHARES BENEFICIALLY

6 SHARED VOTING POWER

OWNED BY

4,799,946

EACH

7 SOLE DISPOSITIVE POWER

REPORTING PERSON

-0-

8 SHARED DISPOSITIVE POWER

4,799,946

9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

4,799,946

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

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

5.4%

12 TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)

IN

Item 1. (a) NAME OF ISSUER

Isis Pharmaceuticals, Inc. (the "Company").

(b) ADDRESS OF ISSUER'S PRINCIPAL EXECUTIVE OFFICES

1896 Rutherford Road, Carlsbad, California 92008.

Item 2. (a) NAMES OF PERSONS FILING

This Statement is being filed on behalf of each of the following persons (collectively, the "Reporting Persons")

(i) Symphony Capital Partners, L.P. ("SCP")

(ii) Symphony Capital GP, L.P. ("Symphony Capital GP")

(iii) Symphony GP, LLC ("Symphony GP")

(iv) Symphony Strategic Partners, LLC ("SSP")

(v) Mark Kessel

(vi) Harri V. Taranto

(b) ADDRESS OF PRINCIPAL BUSINESS OFFICE

The address of the principal business offices of the Reporting Persons is 875 Third Avenue, 18th Floor, New York, NY 10022

(c) CITIZENSHIP

- (i) SCP - a Delaware limited partnership
- (ii) Symphony Capital GP - a Delaware limited partnership
- (iii) Symphony GP - a Delaware limited liability company
- (iv) SSP - a Delaware limited liability company
- (v) Mark Kessel - a citizen of the United States
- (vi) Harri V. Taranto - a citizen of the United States

(d) TITLE OF CLASS OF SECURITIES

Common Stock, par value \$0.001 per share (the "Common Stock" or "Shares")

(e) CUSIP NUMBER

464330109

Item 3. This statement is not being filed pursuant to either Rule 13d-1(b) or 13d-2(b) or (c).

Item 4. OWNERSHIP.

(a) (i) Each of SCP, Symphony Capital GP and Symphony GP may be deemed to beneficially own an aggregate of 4,552,471 Shares (including 2,535,689 Shares issuable upon exercise of currently exercisable warrants).

(ii) SSP may be deemed to beneficially own an aggregate of 247,475 Shares (including 137,842 Shares issuable upon exercise of currently exercisable warrants).

(iii) Each of Mark Kessel and Harri V. Taranto may be deemed to beneficially own an aggregate of 4,799,946 Shares (including 2,673,531 Shares issuable upon exercise of currently exercisable warrants).

(b) Based on calculations made in accordance with Rule 13d-3(d), and there being 86,174,309 Shares outstanding after giving effect to the issuance of 3,383,651 Shares on September 27, 2007, (i) each of SCP, Symphony Capital GP and Symphony GP may be deemed to own approximately 5.1% of the outstanding Common Stock, (ii) SSP may be deemed to own approximately 0.3% of the outstanding Common Stock, and (iii) each of Mark Kessel and Harri V. Taranto may be deemed to beneficially own approximately 5.4% of the outstanding Common Stock.

(c) (i) Each of SCP, Symphony Capital GP, Symphony GP may be deemed to have sole power to direct the voting and disposition of 4,552,471 Shares (including 2,535,689 Shares issuable upon exercise of currently exercisable warrants).

(ii) SSP may be deemed to have sole power to direct the voting and disposition of 247,475 Shares (including 137,842 Shares issuable upon exercise of currently exercisable warrants).

(iii) Each of Mark Kessel and Harri V. Taranto may be deemed to have shared power to direct the voting and disposition of 4,799,946 Shares (including 2,673,531 Shares issuable upon exercise of currently exercisable warrants).

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 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

See Item 2.

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.

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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 as of October 4, 2007

SYMPHONY CAPITAL PARTNERS, L.P.

By: Symphony Capital GP, L.P.
its general partner

By: Symphony GP, LLC
its general partner

By: /s/ Mark Kessel

Name: Mark Kessel
Title: Managing Member

SYMPHONY STRATEGIC PARTNERS, LLC

By: /s/ Mark Kessel

Name: Mark Kessel
Title: Managing Member

SYMPHONY CAPITAL GP, L.P.

By: Symphony GP, LLC
its general partner

By: /s/ Mark Kessel

Name: Mark Kessel
Title: Managing Member

SYMPHONY GP, LLC

By: /s/ Mark Kessel

Name: Mark Kessel
Title: Managing Member

MARK KESSEL

By: /s/ Mark Kessel

Name: Mark Kessel
Title: Managing Member

HARRI V. TARANTO

By: /s/ Harri V. Tarranto

Name: Harri V. Taranto
Title: Managing Member

EXHIBIT INDEX

Exhibit 1. Joint Filing Agreement as required by Rule 13d-1(k)(1) under the Securities Exchange Act of 1934, as amended.

JOINT FILING AGREEMENT PURSUANT TO RULE 13d-1(k)(1)

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 filing 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 herein, 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 as of October 4, 2007

SYMPHONY CAPITAL PARTNERS, L.P.

By: Symphony Capital GP, L.P.
its general partner

By: Symphony GP, LLC
its general partner

By: /s/ Mark Kessel

Name: Mark Kessel
Title: Managing Member

SYMPHONY STRATEGIC PARTNERS, LLC

By: /s/ Mark Kessel

Name: Mark Kessel
Title: Managing Member

SYMPHONY CAPITAL GP, L.P.

By: Symphony GP, LLC
its general partner

By: /s/ Mark Kessel

Name: Mark Kessel
Title: Managing Member

SYMPHONY GP, LLC

By: /s/ Mark Kessel

Name: Mark Kessel
Title: Managing Member

MARK KESSEL

By: /s/ Mark Kessel

Name: Mark Kessel
Title: Managing Member

HARRI V. TARANTO

By: /s/ Harri V. Tarranto

Name: Harri V. Taranto
Title: Managing Member