

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

SCHEDULE 13G

UNDER THE SECURITIES EXCHANGE ACT OF 1934  
(AMENDMENT NO. 7)\*

Isis Pharmaceuticals, Inc.

-----  
(Name of Issuer)

Common Stock

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

464330-10-9

-----  
(CUSIP Number)

December 31, 2004

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

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

/X/ 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).

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CUSIP NO. 464330-10-9

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

Citigroup Global Markets Inc.

-----  
(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

New York

-----

NUMBER OF	(5) SOLE VOTING POWER	0
SHARES		
BENEFICIALLY	(6) SHARED VOTING POWER	3,370,624
OWNED BY		
EACH	(7) SOLE DISPOSITIVE POWER	0
REPORTING		
PERSON	(8) SHARED DISPOSITIVE POWER	3,370,624
WITH:		
(9) AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON		3,370,624

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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) 5.9%

(12) TYPE OF REPORTING PERSON (SEE INSTRUCTIONS) BD

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

Citigroup Financial Products Inc.

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(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

-----

NUMBER OF	(5) SOLE VOTING POWER	0
SHARES		
BENEFICIALLY	(6) SHARED VOTING POWER	3,371,184
OWNED BY		
EACH	(7) SOLE DISPOSITIVE POWER	0
REPORTING		
PERSON	(8) SHARED DISPOSITIVE POWER	3,371,184
WITH:		
(9) AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON		3,371,184

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

-----  
(11) PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 5.9%

-----  
(12) TYPE OF REPORTING PERSON (SEE INSTRUCTIONS) CO

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

Citigroup Global Markets Holdings Inc.

-----  
(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 New York

-----  
NUMBER OF (5) SOLE VOTING POWER 0  
SHARES  
BENEFICIALLY (6) SHARED VOTING POWER 5,140,388  
OWNED BY  
EACH (7) SOLE DISPOSITIVE POWER 0  
REPORTING  
PERSON (8) SHARED DISPOSITIVE POWER 5,140,388  
WITH:

-----  
(9) AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 5,140,388

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

-----  
(11) PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 9.0%

-----  
(12) TYPE OF REPORTING PERSON (SEE INSTRUCTIONS) HC

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

Citigroup Inc.

-----  
 (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

NUMBER OF	(5) SOLE VOTING POWER	0
SHARES		
BENEFICIALLY	(6) SHARED VOTING POWER	5,204,195*
OWNED BY		
EACH	(7) SOLE DISPOSITIVE POWER	0
REPORTING		
PERSON	(8) SHARED DISPOSITIVE POWER	5,204,195*
WITH:		

-----  
 (9) AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 5,204,195\*

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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) 9.1%\*

-----  
 (12) TYPE OF REPORTING PERSON (SEE INSTRUCTIONS) HC

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 \* Includes shares held by the other reporting persons.

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:  
 Citigroup Global Markets Inc. ("CGM")

Item 2(b). Address of Principal Office or, if none, Residence:

The address of the principal office of each of  
CGM, CFP and CGM Holdings is:

388 Greenwich Street  
New York, NY 10013

The address of the principal office of Citigroup is:

399 Park Avenue  
New York, NY 10043

Item 2(c). Citizenship or Place of Organization:

CGM and CGM Holdings are New York corporations.

CFP and Citigroup are Delaware corporations.

Item 2(d). Title of Class of Securities:

Common Stock

Item 2(e). CUSIP Number:

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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 a(n):

- (a)  [X] Broker or dealer registered under Section 15 of the  
Act (15 U.S.C. 78o);
- (b)  [ ] Bank as defined in Section 3(a)(6) of the Act  
(15 U.S.C. 78c);
- (c)  [ ] Insurance company as defined in Section 3(a)(19) of  
the Act (15 U.S.C. 78c);
- (d)  [ ] Investment company registered under Section 8 of the  
Investment Company Act of 1940 (15 U.S.C. 80a-8);
- (e)  [ ] Investment adviser in accordance with Section  
240.13d-1(b)(1)(ii)(E);
- (f)  [ ] Employee benefit plan or endowment fund in accordance  
with Section 240.13d-1(b)(1)(ii)(F);
- (g)  [X] Parent holding company or control person in accordance  
with Section 240.13d-1(b)(1)(ii)(G);
- (h)  [ ] Savings association as defined in Section 3(b) of the  
Federal Deposit Insurance Act (12 U.S.C. 1813);
- (i)  [ ] Church plan that is excluded from the definition of an  
investment company under Section 3(c)(14) of the  
Investment Company Act of 1940 (15 U.S.C. 80a-3);
- (j)  [ ] Group, in accordance with Section 240.13d-1(b)(1)(ii)(J).

Item 4. Ownership. (as of December 31, 2004)

- (a) Amount beneficially owned: See item 9 of cover pages
- (b) Percent of Class: See item 11 of cover pages
- (c) Number of shares as to which the person has:
  - (i) Sole power to vote or to direct the vote:
  - (ii) Shared power to vote or to direct the vote:

(iii) Sole power to dispose or to direct the disposition of:

(iv) Shared power to dispose or to direct the disposition of:

See Items 5-8 of cover pages

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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 person has ceased to be the beneficial owner of more than five percent of the class of securities, check the following [ ].

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.

CFP is the sole stockholder of CGM. CGM Holdings is the sole stockholder of CFP. Citigroup is the sole stockholder of CGM Holdings.

Item 8. Identification and Classification of Members of the Group.

Not Applicable.

Item 9. Notice of Dissolution of Group.

Not Applicable.

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Item 10. Certification.

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired and are held in the ordinary course of business and 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.

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.

Dated: February 4, 2005

CITIGROUP GLOBAL MARKETS INC.

By: /s/ David C. Goldberg

-----  
Name: David C. Goldberg  
Title: Assistant Secretary

CITIGROUP FINANCIAL PRODUCTS INC.

By: /s/ David C. Goldberg

-----

Name: David C. Goldberg  
Title: Assistant Secretary

CITIGROUP GLOBAL MARKETS HOLDINGS INC.

By: /s/ David C. Goldberg

-----  
Name: David C. Goldberg  
Title: Assistant Secretary

CITIGROUP INC.

By: /s/ David C. Goldberg

-----  
Name: David C. Goldberg  
Title: Assistant Secretary

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EXHIBIT INDEX TO SCHEDULE 13G

EXHIBIT 1  
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Agreement among CGM, CFP, CGM Holdings and Citigroup as to joint filing of  
Schedule 13G

EXHIBIT 1

-----

AGREEMENT AS TO JOINT FILING OF SCHEDULE 13G

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Each of the undersigned hereby affirms that it is individually eligible to use Schedule 13G, and agrees that this Schedule 13G is filed on its behalf.

Date: February 4, 2005

CITIGROUP GLOBAL MARKETS INC.

By: /s/ David C. Goldberg

-----  
Name: David C. Goldberg  
Title: Assistant Secretary

CITIGROUP FINANCIAL PRODUCTS INC.

By: /s/ David C. Goldberg

-----  
Name: David C. Goldberg  
Title: Assistant Secretary

CITIGROUP GLOBAL MARKETS HOLDINGS INC.

By: /s/ David C. Goldberg

-----  
Name: David C. Goldberg  
Title: Assistant Secretary

CITIGROUP INC.

By: /s/ David C. Goldberg

-----  
Name: David C. Goldberg  
Title: Assistant Secretary