

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

SCHEDULE 13G

UNDER THE SECURITIES EXCHANGE ACT OF 1934
(AMENDMENT NO. 2)*

Isis Pharmaceuticals, Inc.

(Name of Issuer)

Common Stock

(Title of Class of Securities)

464330-1-09

(CUSIP Number)

December 31, 2000

(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).

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

Salomon Smith Barney 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	6,709,761*
OWNED BY		
EACH	(7) SOLE DISPOSITIVE POWER	0
REPORTING		
PERSON	(8) SHARED DISPOSITIVE POWER	6,709,761*
WITH:		

 (9) AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 6,709,761*

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

 (11) PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 17.2%*

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

 * Includes shares for which the reporting person disclaims beneficial ownership. See Item 4(a).

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

Salomon Brothers Holding Company 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	6,709,761*
OWNED BY		
EACH	(7) SOLE DISPOSITIVE POWER	0
REPORTING		
PERSON	(8) SHARED DISPOSITIVE POWER	6,709,761*
WITH:		

 (9) AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 6,709,761*

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

 (11) PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 17.2%*

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

 * Includes shares for which the reporting person disclaims beneficial ownership. See Item 4(a).

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

Salomon Smith Barney 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	8,182,011*
OWNED BY		
EACH	(7) SOLE DISPOSITIVE POWER	0
REPORTING		
PERSON	(8) SHARED DISPOSITIVE POWER	8,182,011*
WITH:		

 (9) AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 8,182,011*

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

 (11) PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 21.0%*

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

 * Includes shares for which the reporting person disclaims beneficial ownership. See Item 4(a).

 (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	8,186,141*
OWNED BY		**
EACH	(7) SOLE DISPOSITIVE POWER	0
REPORTING		
PERSON	(8) SHARED DISPOSITIVE POWER	8,186,141*
WITH:		**

 (9) AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 8,186,141*
**

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

 (11) PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9) 21.0%*
**

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

 * Includes shares for which the reporting person disclaims beneficial ownership. See Item 4(a).

** 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:
Salomon Smith Barney Inc. ("SSB")
Salomon Brothers Holding Company Inc ("SBHC")
Salomon Smith Barney Holdings Inc. ("SSB Holdings")
Citigroup Inc. ("Citigroup")
- Item 2(b). Address or Principal Office or, if none, Residence:
The address of the principal office of each of
SSB, SBHC and SSB 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:
SSB and SSB Holdings are New York corporations.
SBHC and Citigroup are Delaware corporations.
- Item 2(d). Title of Class of Securities:
Common Stock
- Item 2(e). Cusip Number:
464330-1-09

- 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) 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) 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, 2000)

- (a) Amount beneficially owned: See item 9 of cover pages
(Includes shares for which the reporting person disclaims beneficial ownership.)
- (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

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.

SBHC is the sole stockholder of SSB; SSB Holdings is the sole stockholder of SBHC; and Citigroup is the sole stockholder of SSB Holdings.

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

Not Applicable.

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 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: January 29, 2001

SALOMON SMITH BARNEY INC.

By: /s/ Howard M. Darmstadter

Name: Howard M. Darmstadter
Title: Assistant Secretary

SALOMON BROTHERS HOLDING COMPANY INC

By: /s/ Howard M. Darmstadter

Name: Howard M. Darmstadter
Title: Assistant Secretary

SALOMON SMITH BARNEY HOLDINGS INC.

By: /s/ Howard M. Darmstadter

Name: Howard M. Darmstadter
Title: Assistant Secretary

CITIGROUP INC.

By: /s/ Joseph B. Wollard

Name: Joseph B. Wollard
Title: Assistant Secretary

EXHIBIT INDEX TO SCHEDULE 13G

EXHIBIT 1

Agreement among SSB, SBHC, SSB Holdings and Citigroup as to joint filing of
Schedule 13G

EXHIBIT 1

AGREEMENT AS TO JOINT FILING OF SCHEDULE 13G

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: January 29, 2001

SALOMON SMITH BARNEY INC.

By: /s/ Howard M. Darmstadter

Name: Howard M. Darmstadter
Title: Assistant Secretary

SALOMON BROTHERS HOLDING COMPANY INC

By: /s/ Howard M. Darmstadter

Name: Howard M. Darmstadter
Title: Assistant Secretary

SALOMON SMITH BARNEY HOLDINGS INC.

By: /s/ Howard M. Darmstadter

Name: Howard M. Darmstadter
Title: Assistant Secretary

CITIGROUP INC.

By: /s/ Joseph B. Wollard

Name: Joseph B. Wollard
Title: Assistant Secretary