

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

SCHEDULE 13G

Under the Securities Exchange Act of 1934

(Amendment No. 1)*

ISIS PHARMACEUTICALS, INC.

(Name of Issuer)

COMMON STOCK

(Title of Class of Securities)

464330109

(CUSIP Number)

December 31, 2005

(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).

CUSIP No. 464330109

1. Names of Reporting Persons.
I.R.S. Identification Nos. of above persons (entities only). Federated Investors, 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: Pennsylvania

Number of 5. Sole Voting Power 9,980,130

Shares Bene- 6. Shared Voting Power

ficially by

Owned by Each Reporting Person With: 7. Sole Dispositive Power 9,980,130
8. Shared Dispositive Power

9. Aggregate Amount Beneficially Owned by Each Reporting Person 9,980,130

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)

11. Percent of Class Represented by Amount in Row (9) 13.60%

12. Type of Reporting Person (See Instructions) HC

1. Names of Reporting Persons.
I.R.S. Identification Nos. of above persons (entities only). Voting Shares Irrevocable Trust

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: Pennsylvania

Number of Shares Beneficially Owned by Each Reporting Person With: 5. Sole Voting Power 9,980,130
6. Shared Voting Power
7. Sole Dispositive Power 9,980,130
8. Shared Dispositive Power

9. Aggregate Amount Beneficially Owned by Each Reporting Person 9,980,130

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)

11. Percent of Class Represented by Amount in Row (9) 13.60%

12. Type of Reporting Person (See Instructions) 00

1. Names of Reporting Persons.
I.R.S. Identification Nos. of above persons (entities only).
John F. Donahue

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

Number of Shares Beneficially Owned by Each Reporting Person With: 5. Sole Voting Power
6. Shared Voting Power 9,980,130
7. Sole Dispositive Power
8. Shared Dispositive Power 9,980,130

9. Aggregate Amount Beneficially Owned by Each Reporting Person 9,980,130

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)

11. Percent of Class Represented by Amount in Row (9) 13.60%

12. Type of Reporting Person (See Instructions) IN

1. Names of Reporting Persons.

I.R.S. Identification Nos. of above persons (entities only).

Rhodora J. Donahue

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

Number of Shares Beneficially by Owned by Each Reporting Person With:

5. Sole Voting Power

6. Shared Voting Power 9,980,130

7. Sole Dispositive Power

8. Shared Dispositive Power 9,980,130

9. Aggregate Amount Beneficially Owned by Each Reporting Person 9,980,130

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)

11. Percent of Class Represented by Amount in Row (9) 13.60%

12. Type of Reporting Person (See Instructions) IN

1. Names of Reporting Persons.

I.R.S. Identification Nos. of above persons (entities only).

J. Christopher Donahue

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

Number of Shares Beneficially by Owned by Each Reporting Person With:

5. Sole Voting Power

6. Shared Voting Power 9,980,130

7. Sole Dispositive Power

8. Shared Dispositive Power 9,980,130

9. Aggregate Amount Beneficially Owned by Each Reporting Person 9,980,130

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions)

11. Percent of Class Represented by Amount in Row (9) 13.60%

12.

Type of Reporting Person (See Instructions) IN

INSTRUCTIONS FOR SCHEDULE 13G

Instructions for Cover Page

- (1) Names and I.R.S. Identification Numbers of Reporting Persons--Furnish the full legal name of each person for whom the report is filed--i.e., each person required to sign the schedule itself--including each member of a group. Do not include the name of a person required to be identified in the report but who is not a reporting person. Reporting persons that are entities are also requested to furnish their I.R.S. identification numbers, although disclosure of such numbers is voluntary, not mandatory (see "SPECIAL INSTRUCTIONS FOR COMPLYING WITH SCHEDULE 13G" below).
- (2) If any of the shares beneficially owned by a reporting person are held as a member of a group and that membership is expressly affirmed, please check row 2(a). If the reporting person disclaims membership in a group or describes a relationship with other persons but does not affirm the existence of a group, please check row 2(b) [unless it is a joint filing pursuant to Rule 13d-1(k)(1) in which case it may not be necessary to check row 2(b)].
- (3) The third row is for SEC internal use; please leave blank.
- (4) Citizenship or Place of Organization--Furnish citizenship if the named reporting person is a natural person. Otherwise, furnish place of organization.
- (5)-(9), (11) Aggregate Amount Beneficially Owned By Each Reporting Person, Etc.--Rows (5) through (9) inclusive, and (11) are to be completed in accordance with the provisions of Item 4 of Schedule 13G. All percentages are to be rounded off to the nearest tenth (one place after decimal point).
- (10) Check if the aggregate amount reported as beneficially owned in row (9) does not include shares as to which beneficial ownership is disclaimed pursuant to Rule 13d-4 (17 CFR 240.13d-4] under the Securities Exchange Act of 1934.
- (12) Type of Reporting Person--Please classify each "reporting person" according to the following breakdown (see Item 3 of Schedule 13G) and place the appropriate symbol on the form:

Category	Symbol
Broker Dealer	BD
Bank	BK
Insurance Company	IC
Investment Company	IV
Investment Adviser	IA
Employee Benefit Plan, Pension Fund, or Endowment Fund	EP
Parent Holding Company/Control Person	HC
Savings Association	SA
Church Plan	CP
Corporation	CO
Partnership	PN
Individual	IN
Other	OO

Notes:

Attach as many copies of the second part of the cover page as are needed, one reporting person per page.

Filing persons may, in order to avoid unnecessary duplication, answer items on the schedules (Schedule 13D, 13G or 14D-1) by appropriate cross references to an item or items on the cover page(s). This approach may only be used where the cover page item or items provide all the disclosure required by the schedule item. Moreover, such a use of a cover page item will result in the item becoming a part of the schedule and accordingly being considered as "filed" for purposes of Section 18 of the Securities Exchange Act or otherwise subject to the liabilities of that section of the Act.

Reporting persons may comply with their cover page filing requirements by filing either completed copies of the blank forms available from the Commission, printed or typed facsimiles, or computer printed facsimiles, provided the documents filed have identical formats to the forms prescribed in the Commission's regulations and meet existing Securities Exchange Act rules as to

such matters as clarity and size (Securities Exchange Act Rule 12b-12).

SPECIAL INSTRUCTIONS FOR COMPLYING WITH SCHEDULE 13G

Under Sections 13(d), 13(g), and 23 of the Securities Exchange Act of 1934 and the rules and regulations thereunder, the Commission is authorized to solicit the information required to be supplied by this schedule by certain security holders of certain issuers.

Disclosure of the information specified in this schedule is mandatory, except for I.R.S. identification numbers, disclosure of which is voluntary. The information will be used for the primary purpose of determining and disclosing the holdings of certain beneficial owners of certain equity securities. This statement will be made a matter of public record. Therefore, any information given will be available for inspection by any member of the public.

Because of the public nature of the information, the Commission can use it for a variety of purposes, including referral to other governmental authorities or securities self-regulatory organizations for investigatory purposes or in connection with litigation involving the Federal securities laws or other civil, criminal or regulatory statutes or provisions. I.R.S. identification numbers, if furnished, will assist the Commission in identifying security holders and, therefore, in promptly processing statements of beneficial ownership of securities.

Failure to disclose the information requested by this schedule, except for I.R.S. identification numbers, may result in civil or criminal action against the persons involved for violation of the Federal securities laws and rules promulgated thereunder.

GENERAL INSTRUCTIONS

- A. Statements filed pursuant to Rule 13d-1(b) containing the information required by this schedule shall be filed not later than February 14 following the calendar year covered by the statement or within the time specified in Rules 13d-1(b)(2) and 13d-2(c). Statements filed pursuant to Rule 13d-1(c) shall be filed within the time specified in Rules 13d-1(c), 13d-2(b) and 13d-2(d). Statements filed pursuant to Rule 13d-1(d) shall be filed not later than February 14 following the calendar year covered by the statement pursuant to Rules 13d-1(d) and 13d-2(b).
- B. Information contained in a form which is required to be filed by rules under section 13(f) (15 U.S.C. 78m(f)) for the same calendar year as that covered by a statement on this schedule may be incorporated by reference in response to any of the items of this schedule. If such information is incorporated by reference in this schedule, copies of the relevant pages of such form shall be filed as an exhibit to this schedule.
- C. The item numbers and captions of the items shall be included but the text of the items is to be omitted. The answers to the items shall be so prepared as to indicate clearly the coverage of the items without referring to the text of the items. Answer every item. If an item is inapplicable or the answer is in the negative, so state.

Item 1.

(a) Name of Issuer

ISIS PHARMACEUTICALS, INC.

(b) Address of Issuer's Principal Executive Offices

1896 Rutherford Road

Carlsbad, CA 92008-7208

Item 2.

(a) Name of Person Filing

(b) Address of Principal Business Office or, if none, Residence

Federated Investors Tower, Pittsburgh, PA 15222-3779

(c) Citizenship

(d) Title of Class of Securities

Common Stock

(e) CUSIP Number

464330109

Item 3. If this statement is filed pursuant to ss.ss.240.13d-1(b) or 240.13d-2(b) or (c), check whether the person filing is a:

- (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) An investment adviser in accordance with ss.240.13d-1(b)(1)(ii)(E);
- (f) An employee benefit plan or endowment fund in accordance with ss.240.13d-1(b)(1)(ii)(F);
- (g) A parent holding company or control person in accordance with ss. 240.13d-1(b)(1)(ii)(G);
- (h) A savings associations as defined in Section 3(b) of the Federal Deposit Insurance Act (12 U.S.C. 1813);
- (i) A 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 ss.240.13d-1(b)(1)(ii)(J).

Item 4. Ownership.

Provide the following information regarding the aggregate number and percentage of the class of securities of the issuer identified in Item 1.

A. Federated Investors, Inc. (See Footnote 1, next page)

- (a) Amount beneficially owned: 9,980,130
- (b) Percent of class: 13.60%
- (c) Number of shares as to which the person has:
 - (i) Sole power to vote or to direct the vote 9,980,130
 - (ii) Shared power to vote or to direct the vote -0-
 - (iii) Sole power to dispose or to direct the disposition of 9,980,130
 - (iv) Shared power to dispose or to direct the disposition of -0-

B. Voting Shares Irrevocable Trust

- (a) Amount beneficially owned: 9,980,130
- (b) Percent of class: 13.60%
- (c) Number of shares as to which the person has:
 - (i) Sole power to vote or to direct the vote 9,980,130
 - (ii) Shared power to vote or to direct the vote -0-
 - (iii) Sole power to dispose or to direct the disposition of 9,980,130
 - (iv) Shared power to dispose or to direct the disposition of -0-

C. John F. Donahue

- (a) Amount beneficially owned: 9,980,130
- (b) Percent of class: 13.60%

- (c) Number of shares as to which the person has:
- (i) Sole power to vote or to direct the vote -0-
 - (ii) Shared power to vote or to direct the vote 9,980,130
 - (iii) Sole power to dispose or to direct the disposition of -0-
 - (iv) Shared power to dispose or to direct the disposition of 9,980,130

D. Rhodora J. Donahue

- (a) Amount beneficially owned: 9,980,130
- (b) Percent of class: 13.60%
- (c) Number of shares as to which the person has:
- (i) Sole power to vote or to direct the vote -0-
 - (ii) Shared power to vote or to direct the vote 9,980,130
 - (iii) Sole power to dispose or to direct the disposition of -0-
 - (iv) Shared power to dispose or to direct the disposition of 9,980,130

E. J. Christopher Donahue

- (a) Amount beneficially owned: 9,980,130
- (b) Percent of class: 13.60%
- (c) Number of shares as to which the person has:
- (i) Sole power to vote or to direct the vote -0-
 - (ii) Shared power to vote or to direct the vote 9,980,130
 - (iii) Sole power to dispose or to direct the disposition of -0-
 - (iv) Shared power to dispose or to direct the disposition of 9,980,130

Instruction. For computations regarding securities which represent a right to acquire an underlying security see ss.240.13d-3(d)(1).

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 ____.

Instruction: Dissolution of a group requires a response to this item.

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 See Exhibit "1" Attached

Item 8. Identification and Classification of Members of the Group NOT APPLICABLE

Item 9. Notice of Dissolution of Group NOT APPLICABLE

Item 10. Certification

(a) The following certification shall be included if the statement is filed pursuant to ss.240.13d-1(b):

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.

(b) The following certification shall be included if the statement is filed pursuant to ss.240.13d-1(c):

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.

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.

Date: February 13, 2006
By: /s/J. Christopher Donahue
Name/Title: J. Christopher Donahue, as President of Federated Investors, Inc.

Date: February 13, 2006
By: /s/John F. Donahue, individually and as Trustee of Voting Shares Irrevocable Trust, by
J. Christopher Donahue, as attorney-in-fact

Date: February 13, 2006
By: /s/Rhodora J. Donahue, individually and as Trustee of Voting Shares Irrevocable Trust, by
J. Christopher Donahue, as attorney-in-fact

Date: February 13, 2006
By: /s/J. Christopher Donahue
Name/Title: J. Christopher Donahue, individually and as Trustee of Voting Shares Irrevocable Trust

The original statement shall be signed by each person on whose behalf the statement is filed or his authorized representative. If the statement is signed on behalf of a person by his authorized representative other than an executive officer or general partner of the filing person, evidence of the representative's authority to sign on behalf of such person shall be filed with the statement, provided, however, that a power of attorney for this purpose which is already on file with the Commission may be incorporated by reference. The name and any title of each person who signs the statement shall be typed or printed beneath his signature.

NOTE: Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See ss.240.13d-7 for other parties for whom copies are to be sent.

Attention: Intentional misstatements or omissions of fact constitute Federal criminal violations (See 18 U.S.C. 1001)

EXHIBIT "1"

ITEM 3 CLASSIFICATION OF
REPORTING PERSONS
Identity and Classification of Each Reporting Person

IDENTITY	CLASSIFICATION UNDER ITEM 3
Federated Equity Funds	(d) Investment company registered under section 8 of the Investment Company Act of 1940 (15 U.S.C. 80a-8).
Federated Index Trust	(d) Investment company registered under section 8 of the Investment Company Act of 1940 (15 U.S.C. 80a-8).
Federated Insurance Series	(d) Investment company registered under section 8 of the Investment Company Act of 1940 (15 U.S.C. 80a-8).
Federated Equity Management Company of Pennsylvania	(e) Investment Adviser registered under section 203 of the Investment Advisers Act of 1940
Federated Global Investment Management Corp.	(e) Investment Adviser registered under section 203 of the Investment Advisers Act of 1940
Federated Investors, Inc.	(g) Parent Holding Company, in accordance with Section 240.13d-1(b)(ii)(G)
FII Holdings, Inc.	(g) Parent Holding Company, in accordance with Section 240.13d-1(b)(ii)(G)
Voting Shares Irrevocable Trust	(g) Parent Holding Company, in accordance with Section 240.13d-1(b)(ii)(G)
John F. Donahue	(g) Parent Holding Company, in accordance with Section 240.13d-1(b)(ii)(G)
Rhodora J. Donahue	(g) Parent Holding Company, in accordance with Section 240.13d-1(b)(ii)(G)
J. Christopher Donahue	(g) Parent Holding Company, in accordance with Section 240.13d-1(b)(ii)(G)

Federated Investors, Inc. (the "Parent") is filing this Schedule 13G because it is the parent holding company of Federated Equity Management Company of Pennsylvania and Federated Global Investment Management Corp. (the "Investment Advisers"), which act as investment advisers to registered investment companies and separate accounts that own shares of common stock in ISIS PHARMACEUTICALS, INC. (the "Reported Securities"). The Investment Advisers are wholly owned subsidiaries of FII Holdings, Inc., which is wholly owned subsidiary of Federated Investors, Inc., the Parent. All of the Parent's outstanding voting stock is held in the Voting Shares Irrevocable Trust (the "Trust") for which John F. Donahue, Rhodora J. Donahue and J. Christopher Donahue act as trustees (collectively, the "Trustees"). The Trustees have joined in filing this Schedule 13G because of the collective voting control that they exercise over the Parent. In accordance with Rule 13d-4 under the Securities Act of 1934, as amended, the Parent, the Trust, and each of the Trustees declare that this statement should

not be construed as an admission that they are the beneficial owners of the Reported Securities, and the Parent, the Trust, and each of the Trustees expressly disclaim beneficial ownership of the Reported Securities

EXHIBIT "2"

AGREEMENT FOR JOINT FILING OF
SCHEDULE 13G

The following parties hereby agree to file jointly the statement on Schedule 13G to which this Agreement is attached and any amendments thereto which may be deemed necessary pursuant to Regulation 13D-G under the Securities Exchange Act of 1934:

1. Federated Investors, Inc. as parent holding company of the investment advisers to registered investment companies that beneficially own the securities.

Voting Shares Irrevocable Trust, as holder of all the voting shares of Federated Investors, Inc.

John F. Donahue, individually and as Trustee

Rhodora J. Donahue, individually and as Trustee

J. Christopher Donahue, individually and as Trustee

It is understood and agreed that each of the parties hereto is responsible for the timely filing of such statement and any amendments thereto, and for the completeness and accuracy of the information concerning such party contained therein, but such party is not responsible for the completeness or accuracy of information concerning the other parties unless such party knows or has reason to believe that such information is incomplete or inaccurate.

It is understood and agreed that the joint filing of Schedule 13G shall not be construed as an admission that the reporting persons named herein constitute a group for purposes of Regulation 13D-G of the Securities Exchange Act of 1934, nor is a joint venture for purposes of the Investment Company Act of 1940.

Date: February 13, 2006

By: /s/J. Christopher Donahue
Name/Title: J. Christopher Donahue, as President of Federated Investors, Inc.

By: /s/ John F. Donahue
Name/Title: John F. Donahue, individually and as Trustee of Voting Shares Irrevocable Trust, by J. Christopher Donahue, as attorney-in-fact.

By: /s/ Rhodora J. Donahue
Name/Title: Rhodora J. Donahue, individually and as Trustee as Voting Shares Irrevocable Trust, by J. Christopher Donahue, as attorney-in-fact.

By: /s/ J. Christopher Donahue
Name/Title: J. Christopher Donahue, individually and as Trustee of Voting Shares Irrevocable Trust

1. The number of shares indicated represent shares beneficially owned by registered investment companies and separate accounts advised by subsidiaries of Federated Investors, Inc. that have been delegated the power to direct investments and power to vote the securities by the registered investment companies' board of trustees or directors and by the separate accounts' principals. All of the voting securities of Federated Investors, Inc. are held in the Voting Shares Irrevocable Trust ("Trust"), the trustees of which are John F. Donahue, Rhodora J. Donahue, and J. Christopher Donahue ("Trustees"). In accordance with Rule 13d-4 under the 1934 Act, the Trust, Trustees, and parent holding company declare that the filing of this statement should not be construed as an admission that any of the investment advisers, parent holding company, Trust, and Trustees are beneficial owners (for the purposes of Sections 13(d) and/or 13(g) of the Act) of any securities covered by this statement, and such advisers, parent holding company, Trust, and Trustees expressly disclaim that they are the beneficial owners such securities.

EXHIBIT 3

POWER OF ATTORNEY

Each person whose signature appears below hereby constitutes and appoints J. Christopher Donahue their true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution for them and in their names, place and stead, in any and all capacities, to sign any and all Schedule 13Ds and/or Schedule 13Gs, and any amendments thereto, to be filed with the Securities and Exchange Commission pursuant to Regulation 13D-G of the Securities Exchange Act of 1934, as amended, by means of the Securities and Exchange Commission's electronic disclosure system known as EDGAR; and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorney-in-fact and agent, full power and authority to sign and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as each of them might or could do in person, hereby ratifying and confirming all that said attorney-in-fact and agent, or their or his substitute or substitutes, may lawfully do or cause to be done by virtue thereof.

SIGNATURES

TITLE OR CAPACITY

/s/John F. Donahue
John F. Donahue

Individually and as Trustee of
the Voting Shares Irrevocable Trust

/s/Rhodora J. Donahue
Rhodora J. Donahue

Individually and as Trustee of
the Voting Shares Irrevocable Trust

Sworn to and subscribed before me this 23rd day of September, 2004.

/s/Madaline P. Kelly
Notary Public

My Commission Expires: February 22, 2008