

Schedule 13G

Under the Securities Exchange Act of 1934  
(New)

ISIS PHARMACEUTICAL  
(Name of Issuer)

Common Stock  
(Title of Class of Securities)

464330109  
(CUSIP Number)

December 31, 2008  
(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)

\*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 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).

BARCLAYS GLOBAL INVESTORS, NA., 943112180  
-----

(2) Check the appropriate box if a member of a Group\*

(a) / /  
(b) /X/

-----  
(3) SEC Use Only

-----  
(4) Citizenship or Place of Organization  
U.S.A.

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

(5) Sole Voting Power  
1883024

-----  
(6) Shared Voting Power  
-

-----  
(7) Sole Dispositive Power  
2,165,831

-----  
(8) Shared Dispositive Power  
-

-----  
(9) Aggregate Amount Beneficially Owned by Each Reporting Person  
2,165,831

-----  
(10) Check Box if the Aggregate Amount in Row (9) Excludes Certain Shares\*

-----  
(11) Percent of Class Represented by Amount in Row (9)  
2.23%

-----  
(12) Type of Reporting Person\*  
BK

CUSIP No. 464330109  
-----

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

BARCLAYS GLOBAL FUND ADVISORS

(2) Check the appropriate box if a member of a Group\*

(a) / /

(b) /X/

(3) SEC Use Only

(4) Citizenship or Place of Organization  
U.S.A.

Number of Shares  
Beneficially Owned  
by Each Reporting  
Person With

(5) Sole Voting Power  
3053861

(6) Shared Voting Power  
-

(7) Sole Dispositive Power  
3,053,861

(8) Shared Dispositive Power  
-

(9) Aggregate Amount Beneficially Owned by Each Reporting Person  
3,053,861

(10) Check Box if the Aggregate Amount in Row (9) Excludes Certain Shares\*

(11) Percent of Class Represented by Amount in Row (9)  
3.15%

(12) Type of Reporting Person\*  
IA

CUSIP No. 464330109  
-----

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

BARCLAYS GLOBAL INVESTORS, LTD

(2) Check the appropriate box if a member of a Group\*

(a) / /

(b) /X/

(3) SEC Use Only

(4) Citizenship or Place of Organization  
England

Number of Shares  
Beneficially Owned  
by Each Reporting  
Person With

(5) Sole Voting Power

(6) Shared Voting Power  
-

(7) Sole Dispositive Power  
-

(8) Shared Dispositive Power  
-

(9) Aggregate  
-

(10) Check Box if the Aggregate Amount in Row (9) Excludes Certain Shares\*

(11) Percent of Class Represented by Amount in Row (9)  
0.00%

(12) Type of Reporting Person\*  
FI

CUSIP No. 464330109  
-----

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

BARCLAYS GLOBAL INVESTORS JAPAN LIMITED

(2) Check the appropriate box if a member of a Group\*

(a) / /  
(b) /X/

(3) SEC Use Only

(4) Citizenship or Place of Organization  
Japan

Number of Shares  
Beneficially Owned  
by Each Reporting  
Person With

(5) Sole Voting Power

(6) Shared Voting Power  
-

(7) Sole Dispositive Power  
-

(8) Shared Dispositive Power  
-

(9) Aggregate  
-

(10) Check Box if the Aggregate Amount in Row (9) Excludes Certain Shares\*

(11) Percent of Class Represented by Amount in Row (9)  
0.00%

(12) Type of Reporting Person\*  
FI

CUSIP No. 464330109  
-----

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

BARCLAYS GLOBAL INVESTORS CANADA LIMITED

(2) Check the appropriate box if a member of a Group\*

(a) / /  
(b) /X/

(3) SEC Use Only

(4) Citizenship or Place of Organization  
Canada

-----  
Number of Shares (5) Sole Voting Power  
Beneficially Owned -----  
by Each Reporting (6) Shared Voting Power  
Person With -----  
-----  
(7) Sole Dispositive Power  
-----  
(8) Shared Dispositive Power  
-----

-----  
(9) Aggregate  
-----

-----  
(10) Check Box if the Aggregate Amount in Row (9) Excludes Certain Shares\*  
-----

-----  
(11) Percent of Class Represented by Amount in Row (9)  
0.00%  
-----

-----  
(12) Type of Reporting Person\*  
FI  
-----

CUSIP No. 464330109  
-----

-----  
(1) Names of Reporting Persons.  
I.R.S. Identification Nos. of above persons (entities only).  
  
BARCLAYS GLOBAL INVESTORS AUSTRALIA LIMITED  
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-----  
(2) Check the appropriate box if a member of a Group\*  
(a) / /  
(b) /X/  
-----

-----  
(3) SEC Use Only  
-----

-----  
(4) Citizenship or Place of Organization  
Australia  
-----

Number of Shares (5) Sole Voting Power  
Beneficially Owned -----  
by Each Reporting (6) Shared Voting Power  
Person With -----  
-----  
(7) Sole Dispositive Power  
-----  
(8) Shared Dispositive Power  
-----

-----  
(9) Aggregate  
-----

-----  
(10) Check Box if the Aggregate Amount in Row (9) Excludes Certain Shares\*  
-----

-----  
(11) Percent of Class Represented by Amount in Row (9)  
0.00%  
-----

-----  
(12) Type of Reporting Person\*  
FI  
-----

CUSIP No. 464330109  
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-----  
(1) Names of Reporting Persons.  
I.R.S. Identification Nos. of above persons (entities only).  
-----

(2) Check the appropriate box if a member of a Group\*

- (a) / /
- (b) /X/

(3) SEC Use Only

(4) Citizenship or Place of Organization  
Germany

Number of Shares  
Beneficially Owned  
by Each Reporting  
Person With

(5) Sole Voting Power

(6) Shared Voting Power

(7) Sole Dispositive Power

(8) Shared Dispositive Power

(9) Aggregate

(10) Check Box if the Aggregate Amount in Row (9) Excludes Certain Shares\*

(11) Percent of Class Represented by Amount in Row (9)  
0.00%

(12) Type of Reporting Person\*  
FI

ITEM 1(A). NAME OF ISSUER  
ISIS PHARMACEUTICAL

ITEM 1(B). ADDRESS OF ISSUER'S PRINCIPAL EXECUTIVE OFFICES  
1896 Rutherford Road

ITEM 2(A). NAME OF PERSON(S) FILING  
BARCLAYS GLOBAL INVESTORS, NA

ITEM 2(B). ADDRESS OF PRINCIPAL BUSINESS OFFICE OR, IF NONE, RESIDENCE  
400 Howard Street  
San Francisco, CA 94105

ITEM 2(C). CITIZENSHIP  
U.S.A

ITEM 2(D). TITLE OF CLASS OF SECURITIES  
Common Stock

ITEM 2(E). CUSIP NUMBER  
464330109

ITEM 3. IF THIS STATEMENT IS FILED PURSUANT TO RULES 13D-1(B),  
OR 13D-2(B), CHECK WHETHER THE PERSON FILING IS A

- (a) // Broker or Dealer registered under Section 15 of the Act (15 U.S.C. 78o).
- (b) /X/ 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(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) // A savings association 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 (15U.S.C. 80a-3).
- (j) // Non-U.S.institution, in accordance with section 240.13d-1(b)(1)(ii)(J)

(k) // Group, in accordance with section 240.13d-1(b)(1)(ii)(K)

ITEM 1(A). NAME OF ISSUER  
ISIS PHARMACEUTICAL

ITEM 1(B). ADDRESS OF ISSUER'S PRINCIPAL EXECUTIVE OFFICES  
1896 Rutherford Road

ITEM 2(A). NAME OF PERSON(S) FILING  
BARCLAYS GLOBAL FUND ADVISORS

ITEM 2(B). ADDRESS OF PRINCIPAL BUSINESS OFFICE OR, IF NONE, RESIDENCE  
400 Howard Street  
San Francisco, CA 94105

ITEM 2(C). CITIZENSHIP  
U.S.A

ITEM 2(D). TITLE OF CLASS OF SECURITIES  
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- (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 (15U.S.C. 80a-3).
- (j) // Non-U.S. institution, in accordance with section 240.13d-1(b)(1)(ii)(J)
- (k) // Group, in accordance with section 240.13d-1(b)(1)(ii)(K)

ITEM 1(A). NAME OF ISSUER  
ISIS PHARMACEUTICAL

ITEM 1(B). ADDRESS OF ISSUER'S PRINCIPAL EXECUTIVE OFFICES  
1896 Rutherford Road

ITEM 2(A). NAME OF PERSON(S) FILING  
BARCLAYS GLOBAL INVESTORS, LTD

ITEM 2(B). ADDRESS OF PRINCIPAL BUSINESS OFFICE OR, IF NONE, RESIDENCE  
Murray House  
1 Royal Mint Court  
LONDON, EC3N 4HH

ITEM 2(C). CITIZENSHIP  
England

ITEM 2(D). TITLE OF CLASS OF SECURITIES  
Common Stock

ITEM 2(E). CUSIP NUMBER  
464330109

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OR 13D-2(B), CHECK WHETHER THE PERSON FILING IS A

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  - (k) // Group, in accordance with section 240.13d-1(b)(1)(ii)(K)

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ISIS PHARMACEUTICAL

ITEM 1(B). ADDRESS OF ISSUER'S PRINCIPAL EXECUTIVE OFFICES  
1896 Rutherford Road

ITEM 2(A). NAME OF PERSON(S) FILING

BARCLAYS GLOBAL INVESTORS JAPAN LIMITED

ITEM 2(B). ADDRESS OF PRINCIPAL BUSINESS OFFICE OR, IF NONE, RESIDENCE  
Ebisu Prime Square Tower 8th Floor  
1-1-39 Hiroo Shibuya-Ku  
Tokyo 150-8402 Japan

ITEM 2(C). CITIZENSHIP  
Japan

ITEM 2(D). TITLE OF CLASS OF SECURITIES  
Common Stock

ITEM 2(E). CUSIP NUMBER  
464330109

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ITEM 1(A). NAME OF ISSUER  
ISIS PHARMACEUTICAL

ITEM 1(B). ADDRESS OF ISSUER'S PRINCIPAL EXECUTIVE OFFICES  
1896 Rutherford Road

ITEM 2(A). NAME OF PERSON(S) FILING

BARCLAYS GLOBAL INVESTORS CANADA LIMITED

ITEM 2(B). ADDRESS OF PRINCIPAL BUSINESS OFFICE OR, IF NONE, RESIDENCE  
Brookfield Place 161 Bay Street  
Suite 2500, PO Box 614  
Toronto, Canada  
Ontario M5J 2S1

ITEM 2(C). CITIZENSHIP  
Canada

ITEM 2(D). TITLE OF CLASS OF SECURITIES  
Common Stock

ITEM 2(E). CUSIP NUMBER  
464330109

ITEM 3. IF THIS STATEMENT IS FILED PURSUANT TO RULES 13D-1(B),  
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- (k) // Group, in accordance with section 240.13d-1(b)(1)(ii)(K)

ITEM 1(A). NAME OF ISSUER  
ISIS PHARMACEUTICAL

ITEM 1(B). ADDRESS OF ISSUER'S PRINCIPAL EXECUTIVE OFFICES  
1896 Rutherford Road

ITEM 2(A). NAME OF PERSON(S) FILING  
BARCLAYS GLOBAL INVESTORS AUSTRALIA LIMITED

ITEM 2(B). ADDRESS OF PRINCIPAL BUSINESS OFFICE OR, IF NONE, RESIDENCE  
Level 43, Grosvenor Place, 225 George Street  
PO Box N43  
Sydney, Australia NSW 1220

ITEM 2(C). CITIZENSHIP  
Australia

ITEM 2(D). TITLE OF CLASS OF SECURITIES  
Common Stock

ITEM 2(E). CUSIP NUMBER  
464330109

ITEM 3. IF THIS STATEMENT IS FILED PURSUANT TO RULES 13D-1(B),  
OR 13D-2(B), CHECK WHETHER THE PERSON FILING IS A

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- (k) // Group, in accordance with section 240.13d-1(b)(1)(ii)(K)

ITEM 1(A). NAME OF ISSUER  
ISIS PHARMACEUTICAL

ITEM 1(B). ADDRESS OF ISSUER'S PRINCIPAL EXECUTIVE OFFICES  
1896 Rutherford Road



-----  
ITEM 2(A). NAME OF PERSON(S) FILING

BARCLAYS GLOBAL INVESTORS (DEUTSCHLAND) AG  
-----

ITEM 2(B). ADDRESS OF PRINCIPAL BUSINESS OFFICE OR, IF NONE, RESIDENCE

Apianstrasse 6  
D-85774  
Unterfohring, Germany  
-----

ITEM 2(C). CITIZENSHIP

Germany  
-----

ITEM 2(D). TITLE OF CLASS OF SECURITIES

Common Stock  
-----

ITEM 2(E). CUSIP NUMBER

464330109  
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ITEM 3. IF THIS STATEMENT IS FILED PURSUANT TO RULES 13D-1(B),  
OR 13D-2(B), CHECK WHETHER THE PERSON FILING IS A

- (a) // Broker or Dealer registered under Section 15 of the Act  
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(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  
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(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(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) // A savings association 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  
(15U.S.C. 80a-3).  
(j) /X/ Non-U.S. institution, in accordance with section 240.13d-1(b)(1)(ii)(J)  
(k) // Group, in accordance with section 240.13d-1(b)(1)(ii)(K)

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) Amount Beneficially Owned:  
5219692  
-----

(b) Percent of Class:  
5.38%  
-----

(c) Number of shares as to which such person has:

(i) sole power to vote or to direct the vote  
4936885  
-----

(ii) shared power to vote or to direct the vote  
-  
-----

(iii) sole power to dispose or to direct the disposition of  
5219692  
-----

(iv) shared power to dispose or to direct the disposition of  
-  
-----

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

The shares reported are held by the company in trust accounts for the  
economic benefit of the beneficiaries of those accounts. See also  
Items 2(a) above.

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

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.

By signing below, I further certify that, to the best of my knowledge and belief, the foreign regulatory scheme applicable to each of: Barclays Global Investors Australia Limited, Barclays Global Investors Canada Limited, Barclays Global Investors (Deutschland) AG, Barclays Global Investors Japan Limited and Barclays Global Investors Limited, is substantially comparable to the regulatory scheme applicable to the functionally equivalent U.S. institutions. I also undertake to furnish to the Commission staff, upon request, information that would otherwise be disclosed in a Schedule 13D by such entities.

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.

February 6, 2009

-----  
Date

-----  
Signature

John McGahan  
Principal

-----  
Name/Title