

Deutsche Bank AG
Taunusanlage 12, D-60325
Frankfurt am Main
Federal Republic of Germany

Jeffrey A. Ruiz
Vice President
Telephone: (212) 250-3667

February 13, 2004

Securities and Exchange Commission
SEC Document Control
450 Fifth Street, N.W.
Washington, DC 20549
Attn: Filing Desk

Dear Sir or Madame:

Re: Filing of Schedule 13G - Isis Pharmaceuticals Incorporated

Pursuant to Rule 13d-1 of the Securities Exchange Act of 1934, attached is one copy of Schedule 13G with respect to the common stock of the above referenced corporation.

Please acknowledge your receipt of the Schedule 13G by return e-mail confirmation.

Sincerely,

Jeffrey A. Ruiz

Enclosures

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

SCHEDULE 13G
(Amendment No. 1)

Under the Securities Exchange Act of 1934

Isis Pharmaceuticals Incorporated

NAME OF ISSUER:

Common Stock (\$0.001 Par Value)

TITLE OF CLASS OF SECURITIES

464330109

CUSIP NUMBER

December 31, 2003

(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)

1. NAME OF REPORTING PERSONS

S.S. OR I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS

Deutsche Bank AG*

2. CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP

(A) (B)

3. SEC USE ONLY

4. CITIZENSHIP OR PLACE OF ORGANIZATION

Federal Republic of Germany

NUMBER OF	5.	SOLE VOTING POWER
SHARES		981,820
BENEFICIALLY	6.	SHARED VOTING POWER
OWNED BY		0
EACH	7.	SOLE DISPOSITIVE POWER
REPORTING		985,820
PERSON WITH	8.	SHARED DISPOSITIVE POWER

9. AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

985,820

10. CHECK BOX IF THE AGGREGATE AMOUNT IN ROW 9 EXCLUDES CERTAIN SHARES

11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9

1.77%

12. TYPE OF REPORTING PERSON

HC, CO, BK

* In accordance with Securities Exchange Act Release No. 39538 (January 12, 1998), this filing reflects the securities beneficially owned by the Private Clients and Asset Management business group ("PCAM") of Deutsche Bank AG and its subsidiaries and affiliates (collectively, "DBAG"). This filing does not reflect securities, if any, beneficially owned by any other business group of DBAG. Consistent with Rule 13d-4 under the Securities Exchange Act of 1934 ("Act"), this filing shall not be construed as an admission that PCAM is, for purposes of Section 13(d) under the Act, the beneficial owner of any securities covered by the filing.

- Item 1(a). Name of Issuer:
Isis Pharmaceuticals, Inc. ("the Issuer")
- Item 1(b). Address of Issuer's Principal Executive Offices:
The address of the Issuer's principal executive offices is:
2292 Faraday Avenue Carlsbad, CA 92008
- Item 2(a). Name of Person Filing:
This statement is filed on behalf of Deutsche Bank AG,
("Reporting Person").
- Item 2(b). Address of Principal Business Office or, if none, Residence:
The principal place of business of the Reporting Person is:
Taunusanlage 12, D-60325
Frankfurt am Main
Federal Republic of Germany
- Item 2(c). Citizenship:
The citizenship of the Reporting Person is set forth on the
cover page.
- Item 2(d). Title of Class of Securities:
The title of the securities is common stock, \$0.001 par value
("Common Stock").
- Item 2(e). CUSIP Number:
The CUSIP number of the Common Stock is set forth on the cover
page.
- Item 3. If this statement is filed pursuant to Rules 13d-1(b),
or 13d-2(b) or (c), check whether the person filing is a:
- (a) Broker or dealer registered under section 15 of the
Act;
 - (b) Bank as defined in section 3(a)(6) of the Act;
 - (c) Insurance Company as defined in section 3(a)(19) of
the Act;
 - (d) Investment Company registered under section 8 of the
Investment Company Act of 1940;
 - (e) An investment adviser in accordance with Rule
13d-1(b)(1)(ii)(E);
 - (f) An employee benefit plan, or endowment fund in
accordance with Rule 13d-1 (b)(1)(ii)(F);
 - (g) Parent holding company or control person in accordance
with Rule 13d-1 (b)(1)(ii)(G);
 - (h) A savings association as defined in section 3(b) of the
Federal Deposit Insurance Act;
 - (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;
 - (j) Group, in accordance with Rule 13d-1 (b)(1)(ii)(J).
- Item 4. Ownership.
- (a) Amount beneficially owned:
The Reporting Person owns the amount of the Common Stock as

set forth on the cover page.

(b) Percent of class:

The Reporting Person owns the percentage of the Common Stock as set forth on the cover page.

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

(i) sole power to vote or to direct the vote:

The Reporting Person has the sole power to vote or direct the vote of the Common Stock as set forth on the cover page.

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

The Reporting Person has the shared power to vote or direct the vote of the Common Stock as set forth on the cover page.

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

The Reporting Person has the sole power to dispose or direct the disposition of the Common Stock as set forth on the cover page.

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

The Reporting Person has the shared power to dispose or direct the disposition of the Common Stock as set forth on the cover page.

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 [X].

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.

Not applicable.

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: 2/13/04

DEUTSCHE BANK AG

By: /s/ Jeffrey A. Ruiz
Name: Jeffrey A. Ruiz
Title: Vice President

By: /s/ Pasquale Antolino
Name: Pasquale Antolino
Title: Associate