

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, 2010

(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. BlackRock, Inc.

(2) Check the appropriate box if a member of a group
(a)
(b)

(3) SEC use only

(4) Citizenship or place of organization

Delaware

Number of shares beneficially owned by each reporting person with:

(5) Sole voting power

5649805

(6) Shared voting power

None

(7) Sole dispositive power

5649805

(8) Shared dispositive power

None

(9) Aggregate amount beneficially owned by each reporting person

5649805

(10) Check if the aggregate amount in Row (9) excludes certain shares

(11) Percent of class represented by amount in Row 9

5.69%

(12) Type of reporting person

HC

Item 1.

Item 1(a) Name of issuer:

ISIS PHARMACEUTICALS INC

Item 1(b) Address of issuer's principal executive offices:

1896 Rutherford Road
Carlsbad CA 92008

Item 2.

2(a) Name of person filing:

BlackRock, Inc.

2(b) Address or principal business office or, if none, residence:

BlackRock Inc.
40 East 52nd Street
New York, NY 10022

2(c) Citizenship:

See Item 4 of Cover Page

2(d) Title of class of securities:

Common Stock

2(e) CUSIP No.:

See 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:

- Broker or dealer registered under Section 15 of the Act;
- Bank as defined in Section 3(a)(6) of the Act;
- Insurance company as defined in Section 3(a)(19) of the Act;
- Investment company registered under Section 8 of the Investment Company Act of 1940;
- An investment adviser in accordance with Rule 13d-1(b)(1)(ii)(E);
- An employee benefit plan or endowment fund in accordance with

Rule 13d-1(b)(1)(ii)(F);

A parent holding company or control person in accordance with

Rule 13d-1(b)(1)(ii)(G);

A savings associations as defined in Section 3(b) of the Federal Deposit Insurance Act (12 U.S.C. 1813);

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;

A non-U.S. institution in accordance with

Rule 240.13d-1(b)(1)(ii)(J);

Group, in accordance with Rule 240.13d-1(b)(1)(ii)(K). If filing as a non-U.S. institution in accordance with Rule 240.13d-1(b)(1)(ii)(J), please specify the type of institution:

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.

Amount beneficially owned:

5649805

Percent of class

5.69%

Number of shares as to which such person has:

Sole power to vote or to direct the vote

5649805

Shared power to vote or to direct the vote

None

Sole power to dispose or to direct the disposition of

5649805

Shared power to dispose or to direct the disposition of

None

Item 5.

Ownership of 5 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 5 percent of the class of securities, check the following [].

Item 6. Ownership of More than 5 Percent on Behalf of Another Person

If any other person is known to have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, such securities, a statement to that effect should be included in response to this item and, if such interest relates to more than 5 percent of the class, such person should be identified. A listing of the shareholders of an investment company registered under the Investment Company Act of 1940 or the beneficiaries of employee benefit plan, pension fund or endowment fund is not required.

Various persons have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of the common stock of

ISIS PHARMACEUTICALS INC.

No one person's interest in the common stock of

ISIS PHARMACEUTICALS INC

is more than five percent of the total outstanding common shares.

Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on by the Parent Holding Company or Control Person.

See Exhibit A

Item 8. Identification and Classification of Members of the Group

If a group has filed this schedule pursuant to Rule 13d-1(b)(ii)(J), so indicate under Item 3(j) and attach an exhibit stating the identity and Item 3 classification of each member of the group. If a group has filed this schedule pursuant to Rule 13d-1(c) or Rule 13d-1(d), attach an exhibit stating the identity of each member of the group.

Item 9. Notice of Dissolution of Group

Notice of dissolution of a group may be furnished as an exhibit stating the date of the dissolution and that all further filings with respect to transactions in the security reported on will be filed, if required, by members of the group, in their individual capacity.

See Item 5.

Item 10. Certifications

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 21, 2011
BlackRock, Inc.

Signature: Matthew J. Fitzgerald

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Name/Title Attorney-In-Fact

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.

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

Exhibit A

Subsidiary

BlackRock Japan Co. Ltd.
BlackRock Institutional Trust Company, N.A.
BlackRock Fund Advisors
BlackRock Asset Management Australia Limited
BlackRock Advisors, LLC
BlackRock Investment Management, LLC
BlackRock International Limited

*Entity beneficially owns 5% or greater of the outstanding shares of the security class being reported on this Schedule 13G.
Exhibit B

POWER OF ATTORNEY

The undersigned, BLACKROCK, INC., a corporation duly organized under the laws of the State of Delaware, United States (the "Company"), does hereby make, constitute and appoint each of Robert Connolly, Howard Surloff, Edward Baer, Bartholomew Battista, Daniel Waltcher, Karen Clark, John Stelley, Denis Molleur, Daniel Ronnen, Brian Kindelan, Nicholas Hall, Con Tzatzakis, John Blevins, Rick F. Froio and Matthew Fitzgerald acting severally, as its true and lawful attorneys-in-fact, for the purpose of, from time to time, executing in its name and on its behalf, whether the Company is acting individually or as representative of others, any and all documents, certificates, instruments, statements, other filings and amendments to the foregoing (collectively, "documents") determined by such person to be necessary or appropriate to comply with ownership or control-person reporting requirements imposed by any United States or non-United States governmental or regulatory authority, including without limitation Forms 3, 4, 5, 13D, 13F and 13G and any amendments to any of the foregoing as may be required to be filed with the Securities and Exchange Commission, and delivering, furnishing or filing any such documents with the appropriate governmental, regulatory authority or other person, and giving and granting to each such attorney-in-fact power and authority to act in the premises as fully and to all intents and purposes as the Company might or could do if personally present by one of its authorized signatories, hereby ratifying and confirming all that said attorney-in-fact shall lawfully do or cause to be done by virtue hereof. Any such determination by an attorney-in-fact named herein shall be conclusively evidenced by such person's execution, delivery, furnishing or filing of the applicable document.

This power of attorney shall expressly revoke the power of attorney dated January 11, 2008 in respect of the subject matter hereof, shall be valid from the date hereof and shall remain in full force and effect until either revoked in writing by the Company, or, in respect of any attorney-in-fact named herein, until such person ceases to be an employee of the Company or one of its affiliates.

IN WITNESS WHEREOF, the undersigned has caused this power of attorney to be executed as of this 14th day of December, 2009.

BLACKROCK, INC.

By: /s/ Robert W. Doll, Jr.
Name: Robert W. Doll, Jr.
Title: Vice Chairman