

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Schedule 13G

Under the Securities Exchange Act of 1934
(Amendment No.: 1)*

Name of issuer: Isis Pharmaceuticals Inc

Title of Class of Securities: Common Stock

CUSIP Number: 464330109

Date of Event Which Requires Filing of this Statement: **December 31, 2013**

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).

(Continued on the following page(s))

CUSIP No.: 464330109

1. NAME OF REPORTING PERSON
S.S. OR I.R.S. IDENTIFICATION NO. OF ABOVE PERSON

The Vanguard Group - 23-1945930

2. CHECK THE APPROPRIATE [LINE] IF A MEMBER OF A GROUP

A.

B. X

3. SEC USE ONLY

4. CITIZENSHIP OF PLACE OF ORGANIZATION

Pennsylvania

(For questions 5-8, report the number of shares beneficially owned by each reporting person with:)

5. SOLE VOTING POWER

159,970

6. SHARED VOTING POWER

7. SOLE DISPOSITIVE POWER

7,529,476

8. SHARED DISPOSITIVE POWER

152,470

9. AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

7,681,946

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

N/A

11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9

6.61%

12. TYPE OF REPORTING PERSON

IA

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

SCHEDULE 13G
Under the Securities Act of 1934

Check the following [line] if a fee is being paid with this statement N/A

Item 1(a) - Name of Issuer:

Isis Pharmaceuticals Inc

Item 1(b) - Address of Issuer's Principal Executive Offices:

2855 Gazelle Court
Carlsbad, Ca 92010

Item 2(a) - Name of Person Filing:

The Vanguard Group - 23-1945930

Item 2(b) - Address of Principal Business Office or, if none, residence:

100 Vanguard Blvd.
Malvern, PA 19355

Item 2(c) - Citizenship:

Pennsylvania

Item 2(d) - Title of Class of Securities:

Common Stock

Item 2(e) - CUSIP Number

464330109

Item 3 - Type of Filing:

This statement is being filed pursuant to Rule 13d-1. An investment adviser in accordance with §240.13d-1(b)(1)(ii)(E).

Item 4 - Ownership:

(a) Amount Beneficially Owned:

7,681,946

(b) Percent of Class:

6.61%

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

(i) sole power to vote or direct to vote: 159,970

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

(iii) sole power to dispose of or to direct the disposition of: 7,529,476

(iv) shared power to dispose or to direct the disposition of: 152,470

Comments:

Item 5 - Ownership of Five Percent or Less of a Class:

Not Applicable

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 Attached Appendix A

Item 8 - Identification and Classification of Members of 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 in the ordinary course of business and were not acquired for the purpose of and do not have the effect of changing or influencing the control of the issuer of such securities and were not acquired in connection with or as a participant in any transaction having such 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: 2/6/14

By /s/ F. William McNabb III*

F. William McNabb III

President and Chief Executive Officer

*By: /s/ Glenn Booraem

Glenn Booraem, pursuant to a Power of Attorney filed September 9, 2013, see File Number 005-56905, Incorporated by Reference

Appendix A

Vanguard Fiduciary Trust Company ("VFTC"), a wholly-owned subsidiary of The Vanguard Group, Inc., is the beneficial owner of 152,470 shares or .13% of the Common Stock outstanding of the Company as a result of its serving as investment manager of collective trust accounts.

Vanguard Investments Australia, Ltd. ("VIA"), a wholly-owned subsidiary of The Vanguard Group, Inc., is the beneficial owner of 7,500 shares or .00% of the Common Stock outstanding of the Company as a result of its serving as investment manager of Australian investment offerings.

By /s/ F. William McNabb III*

F. William McNabb III

President and Chief Executive Officer

*By: /s/ Glenn Booraem

Glenn Booraem, pursuant to a Power of Attorney filed September 9, 2013, see File Number 005-56905, Incorporated by Reference