

SCHEDULE 13G

(Rule 13d-102)

Information to be Included in Statements Filed Pursuant to Rule 13d-1(b), (c) and (d) and Amendments Thereto Filed Pursuant to Rule 13d-2.

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

Under the Securities Exchange Act of 1934
(Amendment No. 2)*

Isis Pharmaceuticals Inc

(Name of Issuer)

Common Stock

(Title of Class of Securities)

464330109

(CUSIP Number)

March 12, 2014

(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).

1 NAME OF REPORTING PERSONArtisan Partners Limited Partnership
-----2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(see Instructions)(a)
(b) Not Applicable
-----3 SEC USE ONLY

4 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

5 SOLE VOTING POWER

None
-----NUMBER OF
SHARES
BENEFICIALLY
OWNED BY

6 SHARED VOTING POWER

9,010,897
-----EACH
REPORTING
PERSON
WITH

7 SOLE DISPOSITIVE POWER

None

8 SHARED DISPOSITIVE POWER

9,778,160

9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

9,778,160
-----10 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES
(see Instructions)Not Applicable

11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

8.3%
-----12 TYPE OF REPORTING PERSON
(see Instructions)IA

1 NAME OF REPORTING PERSONArtisan Investments GP LLC
-----2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(see Instructions)(a)
(b) Not Applicable
-----3 SEC USE ONLY

4 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

5 SOLE VOTING POWER

None
-----NUMBER OF
SHARES
BENEFICIALLY
OWNED BY
EACH
REPORTING
PERSON
WITH

6 SHARED VOTING POWER

9,010,897

7 SOLE DISPOSITIVE POWER

None

8 SHARED DISPOSITIVE POWER

9,778,160

9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

9,778,160
-----10 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES
(see Instructions)Not Applicable

11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

8.3%
-----12 TYPE OF REPORTING PERSON
(see Instructions)HC

1 NAME OF REPORTING PERSON

Artisan Partners Holdings LP

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(see Instructions)

(a)
(b)

Not Applicable

3 SEC USE ONLY

4 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

5 SOLE VOTING POWER

None

NUMBER OF
SHARES
BENEFICIALLY
OWNED BY
EACH
REPORTING
PERSON
WITH

6 SHARED VOTING POWER

9,010,897

7 SOLE DISPOSITIVE POWER

None

8 SHARED DISPOSITIVE POWER

9,778,160

9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

9,778,160

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

Not Applicable

11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

8.3%

12 TYPE OF REPORTING PERSON
(see Instructions)

HC

1 NAME OF REPORTING PERSONArtisan Partners Asset Management Inc.
-----2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(see Instructions)(a)
(b) Not Applicable
-----3 SEC USE ONLY

4 CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

5 SOLE VOTING POWER

None
-----NUMBER OF
SHARES
BENEFICIALLY
OWNED BY
EACH
REPORTING
PERSON
WITH

6 SHARED VOTING POWER

9,010,897

7 SOLE DISPOSITIVE POWER

None

8 SHARED DISPOSITIVE POWER

9,778,160

9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

9,778,160
-----10 CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES
(see Instructions)Not Applicable

11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

8.3%
-----12 TYPE OF REPORTING PERSON
(see Instructions)HC

1 NAME OF REPORTING PERSON

Artisan Partners Funds, Inc.

2 CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP
(see Instructions)

(a)
(b)

Not Applicable

3 SEC USE ONLY

4 CITIZENSHIP OR PLACE OF ORGANIZATION

Wisconsin

5 SOLE VOTING POWER

None

NUMBER OF
SHARES
BENEFICIALLY
OWNED BY
EACH
REPORTING
PERSON
WITH

6 SHARED VOTING POWER

5,597,870

7 SOLE DISPOSITIVE POWER

None

8 SHARED DISPOSITIVE POWER

5,597,870

9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

5,597,870

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

Not Applicable

11 PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

4.8%

12 TYPE OF REPORTING PERSON
(see Instructions)

IC

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:/1/

Artisan Partners Limited Partnership ("APLP")
Artisan Investments GP LLC ("Artisan Investments")
Artisan Partners Holdings LP ("Artisan Holdings")
Artisan Partners Asset Management Inc. ("APAM")
Artisan Partners Funds, Inc. ("Artisan Funds")

Item 2(b) Address of Principal Business Office:

APLP, Artisan Investments, Artisan Holdings,
APAM, and Artisan Funds are all located at:

875 East Wisconsin Avenue, Suite 800
Milwaukee, WI 53202

Item 2(c) Citizenship:

APLP is a Delaware limited partnership
Artisan Investments is a Delaware limited liability company
Artisan Holdings is a Delaware limited partnership
APAM is a Delaware corporation
Artisan Funds is a Wisconsin corporation

Item 2(d) Title of Class of Securities:

Common Stock

Item 2(e) CUSIP Number:

464330109

Item 3 Type of Person:

(d) Artisan Funds is an Investment Company under section 8 of the Investment Company Act.

(e) APLP is an investment adviser registered under section 203 of the Investment Advisers Act of 1940.

(g) Artisan Holdings is the sole limited partner of APLP and the sole member of Artisan Investments; Artisan Investments is the general partner of APLP; APAM is the general partner of Artisan Holdings.

/1/ This amendment to the Schedule 13G is being filed solely as a result of the change in control of Artisan Partners Limited Partnership. As of March 12, 2014, Artisan Investment Corporation, ZFIC, Inc., Andrew A. Ziegler and Carlene M. Ziegler are no longer deemed to be controlling persons of Artisan Partners Limited Partnership and are no longer joint filers with the other reporting persons.

Item 4 Ownership (at March 12, 2014):

(a) Amount owned "beneficially" within the meaning of rule 13d-3:

9,778,160

(b) Percent of class:

8.3% (based on 117,270,225 shares outstanding as of February 21, 2014)

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

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

None

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

9,010,897

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

None

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

9,778,160

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:

The shares reported herein have been acquired on behalf of discretionary clients of APLP; as reported herein, APLP holds 9,778,160 shares, including 5,597,870 shares on behalf of Artisan Funds. Persons other than APLP are entitled to receive all dividends from, and proceeds from the sale of, those shares.

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

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.

Date: March 24, 2014

ARTISAN PARTNERS ASSET MANAGEMENT INC,
for itself and as the general partner of
ARTISAN PARTNERS HOLDINGS LP

By: Gregory K. Ramirez*

ARTISAN INVESTMENTS GP LLC,
for itself and as the general partner of
ARTISAN PARTNERS LIMITED PARTNERSHIP

By: Gregory K. Ramirez *

ARTISAN PARTNERS FUNDS, INC.

By: Gregory K. Ramirez *

*By: /s/ Gregory K. Ramirez

Gregory K. Ramirez
Senior Vice President of Artisan
Partners Asset Management Inc.
Vice President of Artisan
Investments GP LLC
Chief Financial Officer, Vice
President and Treasurer of
Artisan Partners Funds, Inc.

Exhibit Index

Exhibit 1 Joint Filing Agreement dated March 24, 2014 by and among Artisan Partners Limited Partnership, Artisan Investments GP LLC, Artisan Partners Holdings LP, Artisan Partners Asset Management Inc., and Artisan Partners Funds, Inc.

JOINT FILING AGREEMENT

The undersigned hereby agree to the joint filing of the Schedule 13G to which this Agreement is attached.

Dated: March 24, 2014

ARTISAN PARTNERS ASSET MANAGEMENT INC,
for itself and as the general partner of
ARTISAN PARTNERS HOLDINGS LP

By: Gregory K. Ramirez*

ARTISAN INVESTMENTS GP LLC,
for itself and as the general partner of
ARTISAN PARTNERS LIMITED PARTNERSHIP

By: Gregory K. Ramirez *

ARTISAN PARTNERS FUNDS, INC.

By: Gregory K. Ramirez *

*By: /s/ Gregory K. Ramirez

Gregory K. Ramirez
Senior Vice President of Artisan
Partners Asset Management Inc.
Vice President of Artisan
Investments GP LLC
Chief Financial Officer, Vice
President and Treasurer of
Artisan Partners Funds, Inc.