

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. )\*

Isis Pharmaceuticals Inc

-----  
(Name of Issuer)

Common Stock

-----  
(Title of Class of Securities)

464330109

-----  
(CUSIP Number)

December 31, 2012

-----  
(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 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

5,532,400  
-----

## 7 SOLE DISPOSITIVE POWER

None  
-----

## 8 SHARED DISPOSITIVE POWER

5,862,500  
-----

## 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

5,862,500  
-----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)

5.8%  
-----12 TYPE OF REPORTING PERSON  
(see Instructions)HC  
-----

-----  
1 NAME OF REPORTING PERSONArtisan Investment Corporation  
-----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

5,532,400  
-----

## 7 SOLE DISPOSITIVE POWER

None  
-----

## 8 SHARED DISPOSITIVE POWER

5,862,500  
-----

## 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

5,862,500  
-----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)

5.8%  
-----12 TYPE OF REPORTING PERSON  
(see Instructions)HC  
-----

-----  
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

5,532,400  
-----EACH  
REPORTING  
PERSON  
WITH

## 7 SOLE DISPOSITIVE POWER

None  
-----

## 8 SHARED DISPOSITIVE POWER

5,862,500  
-----

## 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

5,862,500  
-----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)

5.8%  
-----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

5,532,400  
-----

## 7 SOLE DISPOSITIVE POWER

None  
-----

## 8 SHARED DISPOSITIVE POWER

5,862,500  
-----

## 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

5,862,500  
-----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)

5.8%  
-----12 TYPE OF REPORTING PERSON  
(see Instructions)HC  
-----

-----  
1 NAME OF REPORTING PERSONZFIC, 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

5,532,400  
-----

## 7 SOLE DISPOSITIVE POWER

None  
-----

## 8 SHARED DISPOSITIVE POWER

5,862,500  
-----

## 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

5,862,500  
-----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)

5.8%  
-----12 TYPE OF REPORTING PERSON  
(see Instructions)HC  
-----

-----  
1 NAME OF REPORTING PERSONAndrew A. Ziegler  
-----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

U.S.A.  
-----

## 5 SOLE VOTING POWER

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

## 6 SHARED VOTING POWER

5,532,400  
-----

## 7 SOLE DISPOSITIVE POWER

None  
-----

## 8 SHARED DISPOSITIVE POWER

5,862,500  
-----

## 9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

5,862,500  
-----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)

5.8%  
-----12 TYPE OF REPORTING PERSON  
(see Instructions)IN  
-----

1 NAME OF REPORTING PERSON

Carlene M. Ziegler

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

U.S.A.

5 SOLE VOTING POWER

None

NUMBER OF  
SHARES  
BENEFICIALLY  
OWNED BY  
EACH  
REPORTING  
PERSON  
WITH

6 SHARED VOTING POWER

5,532,400

7 SOLE DISPOSITIVE POWER

None

8 SHARED DISPOSITIVE POWER

5,862,500

9 AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

5,862,500

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)

5.8%

12 TYPE OF REPORTING PERSON  
(see Instructions)

IN



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:

Artisan Partners Holdings LP ("Artisan Holdings")  
Artisan Investment Corporation, the general partner of  
Artisan Holdings ("Artisan Corp.")  
Artisan Partners Limited Partnership ("Artisan Partners")  
Artisan Investments GP LLC, the general partner of  
Artisan Partners ("Artisan Investments")  
ZFIC, Inc., the sole stockholder of Artisan Corp. ("ZFIC")  
Andrew A. Ziegler  
Carlene M. Ziegler

Item 2(b) Address of Principal Business Office:

Artisan Holdings, Artisan Corp., Artisan Partners, Artisan  
Investments, ZFIC,  
Mr. Ziegler and Ms. Ziegler are all located at:

875 East Wisconsin Avenue, Suite 800  
Milwaukee, WI 53202

Item 2(c) Citizenship:

Artisan Holdings is a Delaware limited partnership  
Artisan Corp. is a Wisconsin corporation  
Artisan Partners is a Delaware limited partnership  
Artisan Investments is a Delaware limited liability company  
ZFIC is a Wisconsin corporation  
Mr. Ziegler and Ms. Ziegler are U.S. citizens

Item 2(d) Title of Class of Securities:

Common Stock

Item 2(e) CUSIP Number:

464330109

Item 3 Type of Person:

(e) Artisan Partners is an investment adviser registered under section 203 of the Investment Advisers Act of 1940; Artisan Holdings is the sole limited partner of Artisan Partners; Artisan Investments is the general partner of Artisan Partners; Artisan Corp is the general partner of Artisan Holdings; ZFIC is the sole stockholder of Artisan Corp.; Mr. Ziegler and Ms. Ziegler are the principal stockholders of ZFIC.

- Item 4 Ownership (at December 31, 2012):
- (a) Amount owned "beneficially" within the meaning of rule 13d-3:  
5,862,500
  - (b) Percent of class:  
5.8% (based on 101,210,828 shares outstanding as of November 1, 2012)
  - (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:  
5,532,400
    - (iii) sole power to dispose or to direct the disposition of:  
None
    - (iv) shared power to dispose or to direct the disposition of:  
5,862,500

- 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 Artisan Partners. Persons other than Artisan Partners are entitled to receive all dividends from, and proceeds from the sale of, those shares. None of those persons, to the knowledge of Artisan Partners, Artisan Holdings, Artisan Investments, Artisan Corp., ZFIC, Mr. Ziegler or Ms. Ziegler, has an economic interest in more than 5% of the class.

- 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: February 6, 2013

ARTISAN INVESTMENT CORPORATION,  
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\*  
-----

ZFIC, INC.

By: Gregory K. Ramirez\*  
-----

ANDREW A. ZIEGLER

Andrew A. Ziegler\*  
-----

CARLENE M. ZIEGLER

Carlene M. Ziegler\*  
-----

\*By: /s/ Gregory K. Ramirez  
-----

Gregory K. Ramirez  
Senior Vice President - Chief  
Accounting Officer & Assistant  
Treasurer of Artisan Investment  
Corporation  
Vice President of Artisan  
Investments GP LLC  
Attorney-in-Fact for ZFIC, Inc.  
Attorney-in-Fact for Andrew A.  
Ziegler  
Attorney-in-Fact for Carlene M.  
Ziegler

Exhibit Index

- Exhibit 1 Joint Filing Agreement dated February 6, 2013 by and among Artisan Partners Holdings LP, Artisan Investment Corporation, Artisan Partners Limited Partnership, Artisan Investments GP LLC, ZFIC, Inc., Andrew A. Ziegler and Carlene M. Ziegler
- Exhibit 2 Power of Attorney of ZFIC, Inc., dated August 31, 2012
- Exhibit 3 Power of Attorney of Andrew A. Ziegler dated August 31, 2012
- Exhibit 4 Power of Attorney of Carlene M. Ziegler dated August 31, 2012

JOINT FILING AGREEMENT

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

Dated: February 6, 2013

ARTISAN INVESTMENT CORPORATION,  
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\*  
-----

ZFIC, INC.

By: Gregory K. Ramirez\*  
-----

ANDREW A. ZIEGLER

Andrew A. Ziegler\*  
-----

CARLENE M. ZIEGLER

Carlene M. Ziegler\*  
-----

\*By: /s/ Gregory K. Ramirez  
-----

Gregory K. Ramirez  
Senior Vice President - Chief  
Accounting Officer & Assistant  
Treasurer of Artisan Investment  
Corporation  
Vice President of Artisan  
Investments GP LLC  
Attorney-in-Fact for ZFIC, Inc.  
Attorney-in-Fact for Andrew A.  
Ziegler  
Attorney-in-Fact for Carlene M.  
Ziegler

POWER OF ATTORNEY

The undersigned, ZFIC, Inc., hereby appoints Charles J. Daley, Jr., Sarah A. Johnson, Gregory K. Ramirez and Rebecca Himmelspach, and each of them individually, its true and lawful attorney-in-fact and agent, with full power to execute and file with the United States Securities and Exchange Commission and any stock exchange or similar authority, for and on its behalf in any and all capacities, any and all reports required to be filed pursuant to Section 13 of the Securities Exchange Act of 1934 and the rules thereunder, including but not limited to reports on Schedule 13D or 13G, any and all amendments to such reports, with all exhibits, and any other forms or documents as may be necessary in connection with the filing of such reports with the United States Securities and Exchange Commission and any stock exchange or similar authority, granting unto said attorney full power and authority to do and perform any and all acts for and on behalf of the undersigned which may be necessary or desirable to complete, as fully as the undersigned might or could do in person.

This Power of Attorney shall remain in full force and effect until revoked by the undersigned in a signed writing delivered to the foregoing attorneys-in-fact and agents.

IN WITNESS WHEREOF the undersigned has caused this Power of Attorney to be executed this 31st day of August, 2012.

ZFIC, INC.

By: /s/ Andrew A. Ziegler  
-----  
Andrew A. Ziegler  
Vice President

STATE OF WISCONSIN )  
                          ) SS.  
COUNTY OF MILWAUKEE)

I, Lisa Moran, a Notary Public in and for the County of Milwaukee, State of Wisconsin, DO HEREBY CERTIFY that Andrew A. Ziegler, who is personally known to me to be the same person whose name is subscribed to the foregoing instrument, appeared before me this day in person and acknowledged that he signed and delivered the said instrument as his own free and voluntary act, for the uses and purposes therein set forth.

Given under my hand and notarial seal, this 31st day of August, 2012.

/s/ Lisa Moran  
-----  
Notary Public

POWER OF ATTORNEY

The undersigned, Andrew A. Ziegler, hereby appoints Charles J. Daley, Jr., Sarah A. Johnson, Gregory K. Ramirez and Rebecca Himmelspach, and each of them individually, his true and lawful attorney-in-fact and agent, with full power to execute and file with the United States Securities and Exchange Commission and any stock exchange or similar authority, for and on his behalf in any and all capacities, any and all reports required to be filed pursuant to Section 13 of the Securities Exchange Act of 1934 and the rules thereunder, including but not limited to reports on Schedule 13D or 13G, any and all amendments to such reports, with all exhibits, and any other forms or documents as may be necessary in connection with the filing of such reports with the United States Securities and Exchange Commission and any stock exchange or similar authority, granting unto said attorney full power and authority to do and perform any and all acts for and on behalf of the undersigned which may be necessary or desirable to complete, as fully as the undersigned might or could do in person.

This Power of Attorney shall remain in full force and effect until revoked by the undersigned in a signed writing delivered to the foregoing attorneys-in-fact and agents.

IN WITNESS WHEREOF the undersigned has caused this Power of Attorney to be executed this 31st day of August, 2012.

/s/ Andrew A. Ziegler  
-----  
Andrew A. Ziegler

STATE OF WISCONSIN )  
                          ) SS.  
COUNTY OF MILWAUKEE)

I, Lisa Moran, a Notary Public in and for the County of Milwaukee, State of Wisconsin, DO HEREBY CERTIFY that Andrew A. Ziegler, who is personally known to me to be the same person whose name is subscribed to the foregoing instrument, appeared before me this day in person and acknowledged that he signed and delivered the said instrument as his own free and voluntary act, for the uses and purposes therein set forth.

Given under my hand and notarial seal, this 31st day of August, 2012.

/s/ Lisa Moran  
-----  
Notary Public

POWER OF ATTORNEY

The undersigned, Carlene M. Ziegler, hereby appoints Charles J. Daley, Jr., Sarah A. Johnson, Gregory K. Ramirez and Rebecca Himmelspach, and each of them individually, her true and lawful attorney-in-fact and agent, with full power to execute and file with the United States Securities and Exchange Commission and any stock exchange or similar authority, for and on her behalf in any and all capacities, any and all reports required to be filed pursuant to Section 13 of the Securities Exchange Act of 1934 and the rules thereunder, including but not limited to reports on Schedule 13D or 13G, any and all amendments to such reports, with all exhibits, and any other forms or documents as may be necessary in connection with the filing of such reports with the United States Securities and Exchange Commission and any stock exchange or similar authority, granting unto said attorney full power and authority to do and perform any and all acts for and on behalf of the undersigned which may be necessary or desirable to complete, as fully as the undersigned might or could do in person.

This Power of Attorney shall remain in full force and effect until revoked by the undersigned in a signed writing delivered to the foregoing attorneys-in-fact and agents.

IN WITNESS WHEREOF the undersigned has caused this Power of Attorney to be executed this 31st day of August, 2012.

/s/ Carlene M. Ziegler  
-----  
Carlene M. Ziegler

STATE OF WISCONSIN )  
                          ) SS.  
COUNTY OF MILWAUKEE)

I, Lisa Moran, a Notary Public in and for the County of Milwaukee, State of Wisconsin, DO HEREBY CERTIFY that Carlene M. Ziegler, who is personally known to me to be the same person whose name is subscribed to the foregoing instrument, appeared before me this day in person and acknowledged that she signed and delivered the said instrument as her own free and voluntary act, for the uses and purposes therein set forth.

Given under my hand and notarial seal, this 31st day of August, 2012.

/s/ Lisa Moran  
-----  
Notary Public