

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

**SCHEDULE 13G**

Under the Securities Exchange Act of 1934  
(Amendment No. 02)\*

**ISIS PHARMACEUTICALS INC**

(Name of Issuer)

**Common Stock**

(Title of Class of Securities)

**464330109**

(CUSIP Number)

**December 31, 2013**

(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

<b>1</b>	NAMES OF REPORTING PERSONS I.R.S. IDENTIFICATION NOS. OF ABOVE PERSONS (ENTITIES ONLY) Clearbridge Investments, LLC 01-0846058	
<b>2</b>	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (SEE INSTRUCTIONS)  (a) <input type="radio"/> (b) <input type="radio"/>	
<b>3</b>	SEC USE ONLY	
<b>4</b>	CITIZENSHIP OR PLACE OF ORGANIZATION  Delaware Limited Liability Corporation	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:	<b>5</b>	SOLE VOTING POWER 7,005,575
	<b>6</b>	SHARED VOTING POWER 0
	<b>7</b>	SOLE DISPOSITIVE POWER 7,197,661
	<b>8</b>	SHARED DISPOSITIVE POWER 0
<b>9</b>	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 7,197,661	
<b>10</b>	CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (SEE INSTRUCTIONS)  <input type="radio"/>	
<b>11</b>	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)  6.20%	
<b>12</b>	TYPE OF REPORTING PERSON (SEE INSTRUCTIONS)  IA	

FOOTNOTES

**Item 1.**

- (a) Name of Issuer  
Isis Pharmaceuticals Inc
- (b) Address of Issuer's Principal Executive Offices  
2855 Gazelle Court  
Carlsbad, CA 92010

**Item 2.**

- (a) Name of Person Filing  
ClearBridge Investments, LLC
- (b) Address of Principal Business Office or, if none, Residence  
620 8th Avenue  
New York, NY 10018
- (c) Citizenship  
Delaware Limited Liability Corporation
- (d) Title of Class of Securities  
Common Stock
- (e) CUSIP Number  
464330109

**Item 3. If this statement is filed pursuant to §§240.13d-1(b) or 240.13d-2(b) or (c), check whether the person filing is a:**

- (a)  Broker or dealer registered under section 15 of the Act (15 U.S.C. 78o).
  - (b)  Bank as defined in section 3(a)(6) of the Act (15 U.S.C. 78c).
  - (c)  Insurance company as defined in section 3(a)(19) of the Act (15 U.S.C. 78c).
  - (d)  Investment company registered under section 8 of the Investment Company Act of 1940 (15 U.S.C 80a-8).
  - (e)  An investment adviser in accordance with §240.13d-1(b)(1)(ii)(E);
  - (f)  An employee benefit plan or endowment fund in accordance with §240.13d-1(b)(1)(ii)(F);
  - (g)  A parent holding company or control person in accordance with § 240.13d-1(b)(1)(ii)(G);
  - (h)  A savings associations as defined in Section 3(b) of the Federal Deposit Insurance Act (12 U.S.C. 1813);
  - (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 (15 U.S.C. 80a-3);
  - (j)  A non-U.S. institution in accordance with § 240.13d-1(b)(1)(ii)(J).
  - (k)  A group, in accordance with § 240.13d-1(b)(1)(ii)(K). If filing as a non-U.S. institution in accordance with § 240.13d-1(b)(1)(ii)(J), please specify the type of institution:
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**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.

- (a) Amount beneficially owned: 7,197,661
- (b) Percent of class: 6.20
- (c) Number of shares as to which the person has:
  - (i) Sole power to vote or to direct the vote: 7,005,575
  - (ii) Shared power to vote or to direct the vote: 0
  - (iii) Sole power to dispose or to direct the disposition of: 7,197,661
  - (iv) Shared power to dispose or to direct the disposition of: 0

**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 o .

N/A

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

N/A

**Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company**

N/A

**Item 8. Identification and Classification of Members of the Group**

N/A

**Item 9. Notice of Dissolution of Group**

N/A

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**Item Certification**  
**10.**

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.

**ClearBridge Investments, LLC**

Date: February 14, 2014

By: /s/ Barbara Brooke Manning  
Name: Barbara Brooke Manning  
Title: General Counsel & Chief Compliance Officer

**Footnotes:**

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

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