

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

SCHEDULE 13G

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

Isis Pharmaceuticals

(Name of Issuer)

Class A Common

(Title of Class of Securities)

464330109

(CUSIP Number)

December 31, 2004

(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 on 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).

SCHEDULE 13G
CUSIP No. 464330109

1. Names of Reporting Persons.
MAZAMA CAPITAL MANAGEMENT, INC.
I.R.S. Identification Nos. of above persons (entities only).
93-1290809
2. Check the Appropriate Box if a Member of a Group (See Instructions)
(a) (b)
3. SEC USE ONLY
4. Citizenship or Place of Organization
OREGON

Number of
Shares
Beneficially
Owned by
Each Reporting
Person With:

5. Sole Voting Power
2,466,150 See Item 4
6. Shared Voting Power
0
7. Sole Dispositive Power
4,372,702 See Item 4

8. Shared Dispositive Power
0

9. Aggregate Amount Beneficially Owned by Each Reporting Person
4,372,702

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares (See Instructions) []

11. Percent of Class Represented by Amount in Row (9)
7.63%

12. Type of Reporting Person
IA

2

Item 1.

(a) Name of Issuer

Isis Pharmaceuticals

(b) Address of Issuer's Principal Executive Offices

2292 Faraday Avenue
Carlsbad, CA 92008

Item 2.

(a) Name of Person Filing

Mazama Capital Management, Inc.

(b) Address of Principal Business Office or, if none, Residence

One S.W. Columbia, Suite 1500, Portland, Oregon 97258

(c) Citizenship

State of Oregon

(d) Title of Class of Securities

Class A Common

(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) [X] 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) [] Group, in accordance with §240.13d-1(b)(1)(ii)(J).

Item 4. Ownership.

(a) Amount beneficially owned:

4,372,702

(b) Percent of class:

7.63%

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

(i) Sole power to vote or to direct the vote

2,466,150

(ii) Shared power to vote or to direct the vote

0

(iii) Sole power to dispose or to direct the disposition of

4,372,702

(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 [].

Instruction: Dissolution of a group requires a response to this item.

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

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 10, 2005

Mazama Capital Management, Inc.

By: /s/ Brian P. Alfrey

Brian P. Alfrey

Title: Executive Vice President and Chief Operating Officer