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

SCHEDULE 13G

Under the Securities Exchange Act of 1934

(Amendment No. 1)*

ISIS PHARMACEUTICALS, INC.

(Name of Issuer)

Common Stock, Par Value \$.001 per share

(Title of Class of Securities)

464330109

(CUSIP Number)

December 31, 1999

(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).

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(1) NAME OF REPORTING PERSON
Reliance Financial Services Corporation

S.S. or I.R.S. IDENTIFICATION NO. OF ABOVE PERSON
I.R.S. Employer Identification No.: 51-0113548

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

(a) | |

(b) | |

(3) SEC USE ONLY

(4) CITIZENSHIP OR PLACE OF ORGANIZATION
Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	(5)	SOLE VOTING POWER	
		800,000	(See Note 1)
	(6)	SHARED VOTING POWER	
	(7)	SOLE DISPOSITIVE POWER	
		800,000	(See Note 1)
	(8)	SHARED DISPOSITIVE POWER	

(9) AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON
800,000 (See Note 1)

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

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(11) PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9
2.6% (See Note 1)

(12) TYPE OF REPORTING PERSON*
HC

*SEE INSTRUCTION BEFORE FILLING OUT!

- Item 1. (a) Name of Issuer:
Isis Pharmaceuticals, Inc.
- (b) Address of Issuer's Principal Executive Offices:
2292 Faraday Avenue, Carlsbad, California 92008
- Item 2. (a) Name of Person Filing:
Reliance Financial Services Corporation
- (b) Address of Principal Business Office or, if none, Residence:
Park Avenue Plaza, 55 East 52nd Street, New York, NY 10055
- (c) Citizenship:
Delaware
- (d) Title of Class of Securities:
Common Stock, Par Value \$.001
- (e) CUSIP Number:
464330109
- Item 3. (g) Parent Holding Company, in accordance with Section
240.13d-1(b)(1)(ii)(G)
- Item 4. Ownership.
- (a) Amount Beneficially Owned As of December 31, 1999:
800,000 (See Note 1)
- (b) Percent of Class:
2.6% (See Note 1)
- (c) Number of shares as to which such person has:
- (i) sole power to vote or to direct the vote:
800,000 (See Note 1)
- (ii) shared power to vote or to direct the vote:
-0- (See Note 1)
- (iii) sole power to dispose or to direct the disposition of:
800,000 (See Note 1)
- (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 /X/

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.
Reliance Insurance Company

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 11, 2000 as of December 31, 1999

RELIANCE FINANCIAL SERVICES CORPORATION

By: /s/ James E. Yacobucci

James E. Yacobucci
Senior Vice President-Investments

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Note 1. At December 31, 1999, Reliance Insurance Company ("RIC") beneficially owned Common Stock Purchase Warrants entitling RIC to purchase 800,000 shares of Common Stock at a price of \$25.00 per share. The Securities beneficially owned by RIC (assuming exercise of the Warrants) total 800,000 shares of Common Stock and represent 2.6% of the Securities outstanding.