

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

SCHEDULE 13G

Under the Securities Exchange Act of 1934

(Amendment No. )\*

ISIS PHARMACEUTICALS, INC.

-----  
(Name of Issuer)

Common Stock, Par Value \$.001 per share

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

464330109

-----  
(CUSIP Number)

May 5, 1998

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(Date of Event Which Requires Filing of This Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

/X/ 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  
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G Page 2 of 6 Pages  
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1. NAME OF REPORTING PERSON

S.S. or I.R.S. IDENTIFICATION NO. OF ABOVE PERSON

Reliance Financial Services Corporation  
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

5. SOLE VOTING POWER

1,607,500 (See Note 1)

NUMBER OF SHARES

6. SHARED VOTING POWER

BENEFICIALLY OWNED

BY EACH REPORTING

7. SOLE DISPOSITIVE POWER

PERSON WITH

1,607,500 (See Note 1)

8. SHARED DISPOSITIVE POWER

9. AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

1,607,500 (See Note 1 )

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

11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9

5.8% (See Note 1 )

12. TYPE OF REPORTING PERSON\*

HC

\*SEE INSTRUCTION BEFORE FILLING OUT!

Item 1(a) Name of Issuer:

ISIS Pharmaceuticals, Inc.

Item 1(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

Item 2(b) Address of Principal Business Office or, if none, Residence:

Park Avenue Plaza, 55 East 52nd Street, New York, NY 10055

Item 2(c) Citizenship:

Delaware

.....  
Item 2(d) Title of Class of Securities:  
Common Stock, Par Value \$.001

.....  
Item 2(e) CUSIP Number:  
464330109

.....  
Item 3 (g) [X ] Parent Holding Company, in accordance with  
ss.240.13d-1(b) (1) (ii) (G)

Item 4. Ownership.  
(a) Amount Beneficially Owned As of December 31, 1998  
1,607,500 (See Note 1)

.....  
(b) Percent of Class:  
5.8% (See Note 1)

.....  
(c) Number of shares as to which such person has:  
(i) sole power to vote or to direct the vote  
1,607,500 (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  
1,607,500 (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.  
Not Applicable

.....  
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 such securities and were not acquired and are not held in connection with or as a participant in any transaction having such purposes or effect.

SIGNATURE

February 11, 1999 as of December 31, 1998

.....  
Date

RELIANCE FINANCIAL SERVICES CORPORATION

By:/s/ James E. Yacobucci

James E. Yacobucci  
Senior Vice President-Investments

Note 1. At December 31, 1998, Reliance Insurance Company ("RIC") beneficially owned 807,500 shares of Common Stock and 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 1,607,500 shares of Common Stock and represent 5.8% of the Securities outstanding.