SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

CURRENT REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

Date of report (Date of earliest event reported): June 23, 2005

ISIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware

(State or Other Jurisdiction of Incorporation)

000-19125

(Commission File No.)

33-0336973

(IRS Employer Identification No.)

2292 Faraday Avenue Carlsbad, CA 92008

(Address of Principal Executive Offices and Zip Code)

Registrant's telephone number, including area code: (760) 931-9200

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 1.01 Entry into a Material Agreement.

On June 23, 2005, Isis Pharmaceuticals, Inc. (the "Company") sold its real property located at 2292 Faraday Avenue, Carlsbad, California to Shenco LLC. The real property included an approximately 18,848 square foot building which the Company primarily used for office space. After repaying approximately \$1.6 million of debt which was secured by the property and after deducting commissions, taxes, and other expenses, the Company received net proceeds of approximately \$950,000 for the sale of the property.

Item 2.05. Costs Associated With Exit or Disposal Activities.

Reference is made to Item 1.01 above. The Company sold the property as part of its ongoing restructuring efforts. The Company estimates the restructuring charges associated with the sale of the property to be approximately \$330,000.

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SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

ISIS PHARMACEUTICALS, INC.

Dated: June 23, 2005 By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL Executive Vice President,

Chief Financial Officer and Director