
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): **September 27, 2007**

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.)

1896 Rutherford Road

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)
 - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
 - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
 - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
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Item 2.01. Completion of Acquisition or Disposition of Assets.

On September 27, 2007 Isis Pharmaceuticals, Inc. completed its purchase of all of the equity of Symphony GenIsis at the pre-negotiated price of \$120 million.

On September 27, 2007 Isis filed a press release describing this transaction. A copy of this press release is attached as Exhibit 99.1 to this Current Report and incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Press Release dated September 27, 2007.

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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: September 27, 2007

By: /s/ B. Lynne Parshall
B. LYNNE PARSHALL
Executive Vice President,

INDEX TO EXHIBITS

99.1 Press Release dated September 27, 2007.

Isis Acquires Symphony GenIsis

ISIS 301012 now under Isis' ownership in preparation for partnering

CARLSBAD, Calif., Sept 27, 2007 /PRNewswire-FirstCall via COMTEX News Network/ — Isis Pharmaceuticals, Inc. (Nasdaq: ISIS), today announced its purchase of all of the equity of Symphony GenIsis at the pre-negotiated price of \$120 million. Prompting this transaction, on September 13, 2007, Isis announced its metabolic disease-focused collaboration with Ortho-McNeil, Inc., a Johnson & Johnson company, to discover, develop and commercialize up to four antisense drugs. The collaboration includes licensing of two of the drugs previously held by Symphony GenIsis, ISIS 325568 and ISIS 377131, which target glucagon receptor and glucocorticoid receptor. In addition, Isis has required full ownership of ISIS 301012, its cholesterol-lowering drug targeting apolipoprotein B-100.

Symphony GenIsis was the entity formed in April 2006 by Symphony Capital Partners, L.P., and capitalized with \$75 million, to fund development of three of Isis' drugs. As part of that transaction, Isis licensed to Symphony GenIsis its ISIS 301012 program, and two diabetes programs for the development of ISIS 325568 and ISIS 377131. Isis has been conducting the development of ISIS 301012, ISIS 325568, and ISIS 377131 with funding from Symphony GenIsis.

As part of the \$120 million Symphony GenIsis purchase price, Isis paid Symphony Capital \$80.4 million in cash and approximately 3.4 million shares of Isis stock, for an aggregate value of \$39.6 million based on a 60-day average closing price prior to the date Isis exercised the repurchase.

B. Lynne Parshall, Executive Vice President and CFO of Isis Pharmaceuticals, commented, "We have been very satisfied with our Symphony GenIsis financing. It provided us with the capital to advance the two diabetes programs, and with the Symphony funding we have been able to assemble a full Phase 2 and supportive toxicology profile for ISIS 301012, upon which we are now basing our licensing discussions for that drug. Because all three of the programs appreciated in value so rapidly, we were able to purchase the Symphony GenIsis equity early in the four-year collaboration term, saving ourselves \$75 million in additional capital."

Mark Kessel, Managing Director of Symphony Capital, added, "We are pleased that Isis was able to use the capital we provided so effectively and that our clinical involvement with these programs benefited Isis."

ABOUT ISIS PHARMACEUTICALS, INC.

Isis is exploiting its expertise in RNA to discover and develop novel drugs for its product pipeline and for its partners. The Company has successfully commercialized the world's first antisense drug and has 17 drugs in development. Isis' drug development programs are focused on treating cardiovascular and metabolic diseases. Isis' partners are developing drugs for a wide variety of diseases. Ibis Biosciences, Inc., Isis' wholly owned subsidiary, is developing and commercializing the Ibis T5000(TM) Biosensor System, a revolutionary system to identify infectious organisms. As an innovator in RNA-based drug discovery and development, Isis is the owner or exclusive licensee of over 1,500 issued patents worldwide. Additional information about Isis is available at <http://www.isispharm.com>.

This press release includes forward-looking statements regarding Isis' collaboration with Symphony GenIsis, its collaboration with Ortho-McNeil, Inc., and its financial and business development activities. Any statement describing Isis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement, including those statements that are described as Isis' goals. Such statements are subject to certain risks and uncertainties, particularly those inherent in the process of discovering, developing and commercializing drugs that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such products. Isis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Isis'

forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Isis. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Isis' programs are described in additional detail in Isis' annual report on Form 10-K for the year ended December 31, 2006, and its quarterly report on Form 10-Q for the quarter ended June 30, 2007, which are on file with the SEC. Copies of these and other documents are available from the Company.

In this press release, unless the context requires otherwise, "Isis," "Company," "we," "our," and "us" means Isis Pharmaceuticals and its subsidiaries.

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