
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): **May 16, 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 1.01. Entry into a Material Definitive Agreement.

On May 16, 2007, the Compensation Committee of the Board of Directors of Isis Pharmaceuticals, Inc. (the "Company") approved amending the stock option agreements of Dr. Stanley Crooke, B. Lynne Parshall and Dr. Jeffrey Jonas, the Company's Chief Executive Officer and Executive Vice Presidents, respectively, such that in the event of a Change in Control the vesting and exercisability of their stock options will be accelerated in full.

For purposes of these amendments, Change in Control means: (i) a sale of all or substantially all of the assets of the Company; (ii) a merger or consolidation in which the Company is not the surviving corporation and in which beneficial ownership of securities of the Company representing at least fifty percent (50%) of the combined voting power entitled to vote in the election of Directors has changed; (iii) a reverse merger in which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger are converted by virtue of the merger into other property, whether in the form of securities, cash or otherwise, and in which beneficial ownership of securities of the Company representing at least fifty percent (50%) of the combined voting power entitled to vote in the election of Directors has changed; or (iv) an acquisition by any person, entity or group within the meaning of Section 13(d) or 14(d) of the Exchange Act, or any comparable successor provisions (excluding any employee benefit plan, or related trust, sponsored or maintained by the Company or subsidiary of the Company or other entity controlled by the Company) of the beneficial ownership (within the meaning of Rule 13d-3 promulgated under the Exchange Act, or comparable successor rule) of securities of the Company representing at least fifty percent (50%) of the combined voting power entitled to vote in the election of Directors.

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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: May 17, 2007

By: /s/ B. LYNNE PARSHALL
B. LYNNE PARSHALL
Executive Vice President,
Chief Financial Officer and Director