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# 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): **February 27, 2006**

### **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 Agreement.**

On February 27, 2006, Isis Pharmaceuticals, Inc. (the "Company") extended Stanley T. Crooke and B. Lynne Parshall's severance benefit agreements dated April 8, 2003. Copies of the letters effecting the extension are attached to this report as Exhibits 99.1 and 99.2 and are incorporated herein by reference.

#### **Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits.

- 99.1 Letter dated February 27, 2005 extending Dr. Crooke's severance benefit agreement.
- 99.2 Letter dated February 27, 2005 extending Ms. Parhsall's severance benefit agreement.

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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: March 1, 2006

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

**INDEX TO EXHIBITS**

- 99.1 Letter dated February 27, 2005 extending Dr. Crooke's severance benefit agreement.
- 99.2 Letter dated February 27, 2005 extending Ms. Parhsall's severance benefit agreement.

**ISIS PHARMACEUTICALS, INC.**  
**1896 Rutherford Road**  
**Carlsbad, CA 92008**

**MEMORANDUM**



**Date:** February 27, 2006  
**To:** STANLEY T. CROOKE  
**From:** Joseph H. Wender  
**Subject:** **SEVERANCE BENEFIT AMENDMENT**

Dear Stan:

By letter dated April 8, 2003 the Company offered you a 36 month lump sum severance payment to be made in the event that your employment was terminated as a result of a Change of Control. The Company now extends the Severance Period for so long as you are employed by the Company.

Yours truly,

/s/ Joseph H. Wender

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Joseph H. Wender  
Chairman, Compensation Committee

Telephone 760-603-3848

**ISIS PHARMACEUTICALS, INC.**  
**1896 Rutherford Road**  
**Carlsbad, CA 92008**

**MEMORANDUM**



**Date:** February 27, 2006  
**To:** B. LYNNE PARSHALL  
**From:** Joseph H. Wender  
**Subject:** **SEVERANCE BENEFIT AMENDMENT**

Dear Lynne:

By letter dated April 8, 2003 the Company offered you severance payments in the event that your employment was terminated without cause or as a result of a Change of Control. The Company now extends the Severance Period for so long as you are employed by the Company. Your severance benefits will be 18 months in the event that your employment is terminated without cause and 30 months in the event that your employment is terminated as a result of a Change in Control.

Yours truly,

/s/ Joseph H. Wender

Joseph H. Wender  
Chairman, Compensation Committee

Telephone 760-603-3848