

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 1, 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))

Item 1.01. Entry into a Material Definitive Agreement.

On February 1, 2007, Jeffrey M. Jonas started his employment with Isis Pharmaceuticals, Inc. (the "Company") as the Company's Executive Vice President.

As part of his employment, Dr. Jonas is eligible to receive:

- a one-time signing bonus of \$75,000;
- a base salary of \$485,000 per year;
- an at-risk opportunity to earn a year-end management by objective bonus (MBO);
- an option to purchase 130,000 shares of the Company's common stock at an exercise price of \$10.77 per share;
- senior level relocation benefits; and
- healthcare and retirement benefits offered to all the Company's employees.

In addition, the Company entered into a severance benefit agreement with Dr. Jonas (the "Severance Agreement").

The Severance Agreement provides Dr. Jonas severance benefits as follows:

- In the event his employment is terminated without cause by the Company on or before February 1, 2008, he will be eligible to receive salary continuation equal to his then current base salary, less payroll deductions and withholdings until the sooner to occur of the date he secures new employment or the twelve-month anniversary of the date of his termination; and
- If within the first twelve months of a specified change in control, his employment is terminated without cause by the Company or the acquirer, or he elects to terminate his employment because in his sole judgment his job responsibilities are significantly reduced, he will receive a severance payment equal to a total of 24 months of his then current base salary, less payroll deductions and withholdings.

The description of the Severance Agreement set forth above is qualified in its entirety by reference to the full and complete terms set forth in such agreement, a copy of which is filed as an exhibit to this Current Report on Form 8-K and incorporated by reference herein.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

10.1 Severance Agreement dated February 1, 2007 between the Company and Jeffrey M. Jonas.

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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: February 1, 2007

By: /s/ B. Lynne Parshall

B. LNNE PARSHALL

Executive Vice President,

Chief Financial Officer and Director

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February 1, 2007

VIA HAND DELIVERY

Jeffrey M. Jonas, M.D.
 Executive Vice President
 Isis Pharmaceuticals, Inc.
 1896 Rutherford Road
 Carlsbad, CA 92008

Dear Jeff:

Isis Pharmaceuticals, Inc. ("Isis") is pleased to offer you certain severance benefits in light of your future contribution to Isis. As Isis has no policy or procedure requiring such benefits, we request that you keep the terms and conditions of this letter agreement confidential.

In the event that your employment is terminated without "cause" (as defined herein) by Isis on or before February 1, 2008 (the "Severance Period"), you will be eligible to receive salary continuation equal to your then current base salary, less payroll deductions and withholdings until the sooner to occur of (a) the date you secure new employment (including part-time employment and consulting) or (b) the twelve-month anniversary of the date of your termination. For purposes of this letter agreement, "cause" will be defined as follows: (i) engaging or in any manner participating in any activity which is competitive with or intentionally injurious to Isis or which violates any provision of the Proprietary Information and Inventions Agreement; (ii) commission of any fraud against Isis or use or appropriation for personal use or benefit of any funds or properties of Isis not authorized by the Company to be so used or appropriated; (iii) conviction of a crime involving dishonesty or moral turpitude; (iv) conduct by you which in the good faith and reasonable determination of the Company demonstrates gross unfitness to serve in your then current capacity at Isis. In order to be eligible to receive the severance payments described herein, you will be required to execute an Employee Separation Agreement substantially in the form attached hereto as Exhibit A.

If within the first twelve months of a Change in Control (as defined herein), your employment is terminated without "cause" (as defined above) by Isis or the acquirer, or you elect to terminate your employment because in your sole judgment your job responsibilities are significantly reduced, you will receive a severance payment equal to a total of 24 months of your then current base salary, less payroll deductions and withholdings. For purposes of this letter agreement, Change in Control will be defined as follows: (i) a sale of all or substantially all of the assets of Isis; (ii) a merger or consolidation in which Isis is not the surviving corporation and in which beneficial

ownership of securities of Isis 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 Isis 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 Isis 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 Isis or subsidiary of Isis or other entity controlled by Isis) of the beneficial ownership (within the meaning of Rule 13d-3 promulgated under the Exchange Act, or comparable successor rule) of securities of Isis representing at least fifty percent (50%) of the combined voting power entitled to vote in the election of Directors.

Please keep in mind that this letter agreement is not intended to change your status as an at-will employee with Isis. As with all employees at Isis, you or Isis may terminate your employment at any time, for any reason whatsoever, with or without cause or advance notice subject to the provisions set forth herein.

Very truly yours,

/s/ Stanley T. Crooke
 Isis Pharmaceuticals, Inc.

Stanley T. Crooke, M.D., Ph.D.
 Chairman and CEO

EXHIBIT A

FORM OF SEPARATION AGREEMENT

This **SEPARATION AGREEMENT** ("Agreement") is made and entered into by and between _____ ("Employee") and _____ ("the Company") as of the Effective Date of this Agreement, as defined in paragraph 10 below.

WHEREAS, the Company wishes to provide Employee with certain benefits in consideration of Employee's service to the Company and the promises and covenants of Employee as contained herein;

NOW, THEREFORE, in consideration of the mutual promises and covenants contained herein, it is hereby agreed by and between the parties hereto as follows:

1. **SEVERANCE PAYMENTS.** On (“Separation Date”), Employee shall cease to be an employee or officer of the Company for all purposes. In return for executing this Agreement, Employee will receive the payments described in the severance benefits letter attached hereto as Schedule 1.
 2. **ACCRUED SALARY AND PAID TIME OFF.** On or about the Separation Date, the Company will pay Employee all accrued salary, and all accrued and unused vacation, subject to standard payroll deductions and withholdings. Employee is entitled to these payments regardless of whether or not Employee signs this Agreement.
 3. **HEALTH INSURANCE.** To the extent permitted by law and by the Company’s current group health insurance policies, after the Separation Date, Employee will be eligible to continue receiving health insurance benefits under the federal or state COBRA law at Employee’s own expense and later to convert to an individual policy if desired. Employee will be provided with a separate notice regarding COBRA benefits. If Employee elects continued coverage under COBRA, the Company will reimburse Employee’s COBRA premiums for one (1) month as part of this Agreement. In addition, to the extent permitted by law and by the Company’s current vision and dental insurance policies, after the Separation Date, the Company will reimburse Employee’s vision and dental benefit premiums for one (1) month.
 4. **STOCK OPTIONS.** Pursuant to the Company’s equity incentive plans), vesting of Employee’s stock options will cease on the Separation Date. Employee’s rights to exercise Employee’s option as to any vested shares will be as set forth in the Plan and Employee’s Stock Option Agreement.
 5. **OTHER BENEFITS.** Except as expressly provided herein, Employee acknowledges that Employee will not receive (nor is entitled to receive) any additional compensation or benefits.
 6. **RETURN OF COMPANY PROPERTY.** By three (3) days after the Separation Date, Employee will return to the Company all Company documents (and all copies thereof) and other Company property and materials in Employee’s possession, or control, including, but not limited to, Company files, notes, memoranda, correspondence, lists, drawings, records, plans and forecasts, financial information, personnel information, customer and customer prospect information, sales and marketing information, product development and pricing information, specifications, computer-recorded information, tangible property, equipment, credit cards, entry cards, identification badges and keys; and any materials of any kind which contain or embody any proprietary or confidential information of the Company (and all reproductions thereof).
 7. **PROPRIETARY INFORMATION OBLIGATIONS.** Employee acknowledges that nothing herein shall impair the covenants and obligations set forth in Employee’s Proprietary Information and Inventions Agreement.
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8. **EMPLOYEE’S RELEASE OF CLAIMS.** Except as otherwise set forth in this Agreement, in exchange for consideration under this Agreement to which Employee would not otherwise be entitled, Employee hereby releases, acquits and forever discharges the Company, its parents and subsidiaries, and their officers, directors, agents, servants, employees, attorneys, shareholders, successors, assigns and affiliates, of and from any and all claims, liabilities, demands, causes of action, costs, expenses, attorneys fees, damages, indemnities and obligations of every kind and nature, in law, equity, or otherwise, known and unknown, suspected and unsuspected, disclosed and undisclosed, arising out of or in any way related to agreements, events, acts or conduct at any time prior to and including the execution date of this Agreement, including but not limited to: all such claims and demands directly or indirectly arising out of or in any way connected with Employee’s employment with the Company or the termination of that employment; claims or demands related to salary, bonuses, commissions, stock, stock options, or any other ownership interests in the Company, vacation pay, fringe benefits, expense reimbursements, severance pay, or any other form of compensation; claims pursuant to any federal, state or local law, statute, or cause of action including, but not limited to, the federal Civil Rights Act of 1964, as amended; the federal Americans with Disabilities Act of 1990; the federal Age Discrimination in Employment Act of 1967, as amended (“ADEA”); the California Fair Employment and Housing Act, as amended; tort law; contract law; wrongful discharge; discrimination; harassment; fraud; defamation; emotional distress; and breach of the implied covenant of good faith and fair dealing.

9. **ADEA WAIVER.** Employee acknowledges that Employee knowingly and voluntarily waives and releases any rights Employee may have under the ADEA, as amended. Employee also acknowledges that the consideration given for the waiver and release in the preceding paragraph hereof is in addition to anything of value to which Employee was already entitled. Employee further acknowledges that Employee has been advised by this writing, as required by the ADEA, that: (a) Employee’s waiver and release do not apply to any rights or claims that may arise after the execution date of this Agreement; (b) Employee has the right to consult with an attorney prior to executing this Agreement; (c) Employee has forty-five (45) days to consider this Agreement (although Employee may choose to voluntarily execute this Agreement earlier); (d) Employee has seven (7) days following the execution of this Agreement by the parties to revoke the Agreement; and (e) this Agreement shall not be effective until the date upon which the revocation period has expired, which shall be the eighth day after this Agreement is executed by Employee, provided that the Company has also executed this Agreement by that date (“Effective Date”).

10. **SECTION 1542 WAIVER.** Employee acknowledges reading and understanding Section 1542 of the Civil Code of the State of California:

A general release does not extend to claims which the creditor does not know or suspect to exist in his favor at the time of executing the release, which if known by him must have materially affected his settlement with the debtor.

Employee hereby expressly waives and relinquishes all rights and benefits under that section and any law or legal principle of similar effect in any jurisdiction with respect to the release of unknown and unsuspected claims granted in this Agreement.

12. **ARBITRATION.** To ensure rapid and economical resolution of any and all disputes that may arise in connection with the Agreement, the parties agree that any and all disputes, claims, causes of action, in law or equity, arising from or relating to this Agreement or its enforcement, performance, breach, or interpretation, with the sole exception of those disputes that may arise from Employee’s Proprietary Information and Inventions Agreement, will be resolved by final and binding confidential arbitration held in San Diego, California and conducted by the American Arbitration Association (“AAA”) under its then-existing Rules and Procedures. Nothing in this paragraph is intended to prevent either party from obtaining injunctive relief in court to prevent irreparable harm pending the conclusion of any such arbitration.

13. **ENTIRE AGREEMENT.** This Agreement, including all exhibits, constitutes the complete, final and exclusive embodiment of the entire agreement between Employee and the Company with regard to the subject matter hereof. It supersedes any and all agreements entered into by and between Employee and the

Company where such other agreement may conflict with this agreement. It is entered into without reliance on any promise or representation, written or oral, other than those expressly contained herein. It may not be modified except in a writing signed by Employee and a duly authorized officer of the Company. The parties have carefully read this Agreement, have been afforded the opportunity to be advised of its meaning and consequences by their respective attorneys, and signed the same of their own free will.

14. **MISCELLANEOUS.** This Agreement shall bind the heirs, personal representatives, successors, assigns, executors and administrators of each party, and inure to the benefit of each party, its heirs, successors and assigns. This Agreement shall be deemed to have been entered into and shall be construed and enforced in accordance with the laws of the State of California as applied to contracts made and to be performed entirely within California. If an arbitrator or court of competent jurisdiction determines that any term or provision of this Agreement is invalid or unenforceable, in whole or in part, then the remaining terms and provisions hereof shall be unimpaired, the invalid or unenforceable term or provision shall be modified or replaced so as to render it valid and enforceable in a manner which represents the parties' intention with respect to the invalid or unenforceable term or provision insofar as possible. This Agreement may be executed in two counterparts, each of which shall be deemed an original, all of which together shall constitute one and the same instrument.

IN WITNESS WHEREOF, the parties have duly authorized and caused this Agreement to be executed as follows:

EMPLOYEE

By:
