

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))

Item 5.02. Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

In January 2007, Isis Pharmaceuticals, Inc. ("Isis") recruited Jeff Jonas, MD as Executive Vice President responsible for development, to whom Dr. Mark K. Wedel reports. To incentivize Dr. Wedel to continue to contribute to Isis through the first half of 2008 and to assure effective integration of Dr. Jonas, Isis entered an employee retention agreement with Dr. Wedel, a copy of which is attached to this Report as Exhibit 10.1 (the "Retention Agreement").

Although Isis does not generally enter formal employment agreements with its employees, Isis designed the Retention Agreement to present Dr. Wedel with an opportunity to contribute as an Isis employee through the first half of 2008 and in recognition of the significant change represented by the recruitment of Dr. Jonas. As such, if Dr. Wedel's employment is terminated due to involuntary dismissal, other than for cause, he will be eligible to receive 18 months of continued salary and benefits from the termination date (the "Separation Payment"). In addition, if Dr. Wedel remains an active employee of Isis through June 30, 2008, he will receive an incentive payment equal to \$50,000 (the "Incentive Payment").

Under the Retention Agreement, Dr. Wedel will cease being an active employee of Isis on June 30, 2008. However, if Dr. Wedel voluntarily terminates his employment at any time before June 30, 2008, he will not be eligible for the Separation Payment or the Incentive Payment. If he voluntarily terminates his employment before December 31, 2007, he will not be eligible for a 2007 Bonus. In addition, the Separation Payment will cease if at any time during the 18-month period Dr. Wedel becomes otherwise employed, part-time or full time, as an employee or consultant, except Dr. Wedel may sit on one board of directors so long as that company is not involved in any way in RNA targeted drug discovery or development.

Finally, if ISIS 301012 is licensed to a third party before Dr. Wedel's active employment terminates, vesting of Dr. Wedel's stock options will continue through the period of the Separation Payment.

The description of the Retention Agreement set forth above is qualified in its entirety by reference to the full and complete terms set forth in such agreement filed as an exhibit to this Report and incorporated by reference herein.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

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 26, 2007

By: /s/ B. Lynne Parshall**B. LYNNE PARSHALL**

Executive Vice President,

Chief Financial Officer and Director

INDEX TO EXHIBITS

10.1 Retention Agreement dated September 21, 2007 between Isis and Mark K. Wedel.

RETENTION AGREEMENT

This **RETENTION AGREEMENT** ("Agreement") is made and entered into by and between Mark K. Wedel ("Dr. Wedel") and Isis Pharmaceuticals, Inc. ("Isis") as of the Execution Date of this Agreement, September 21, 2007, and will be effective as of the Effective Date defined in Section 9 below.

WHEREAS, Isis wishes to provide Dr. Wedel with certain benefits in consideration of Dr. Wedel's service to Isis and the promises and covenants of Dr. Wedel 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. TERMINATION; SEPARATION PAYMENTS.

- a. Dr. Wedel will cease to be an "active employee" of Isis on June 30, 2008 unless his employment is terminated earlier in accordance with the terms of this Agreement, the actual date of termination of active employment being his "Separation Date".
- b. If Dr. Wedel's employment at Isis has not terminated for any reason before June 30, 2008, he will then become "an inactive employee" and will receive a Separation Payment in the form of 18 months (the "Separation Period") of salary and employee benefits continuance. Salary will be paid on regularly scheduled Isis paydays and will be subject to normal withholdings including deductions for employee benefits.
- c. If Dr. Wedel's employment at Isis has not terminated for any reason before June 30, 2008 he will also receive an Incentive Payment in the amount of \$50,000 payable on that date.
- d. If Dr. Wedel's employment at Isis is terminated at any time before June 30, 2008, due to involuntary dismissal (other than for cause), he will receive the Separation Payment described in 1.b. above beginning on the day after his last day of employment or the last day of employment prior to the change of control.
- e. If Dr. Wedel's employment at Isis is terminated at any time, for any reason, before June 30, 2008, he will not receive the Incentive Payment described in 1.c above.
- f. If Dr. Wedel's employment at Isis is not terminated before December 31, 2007, he will be eligible for a 2007 Bonus, payable in January, 2008, as determined by the Board of Directors.
- g. Dr. Wedel will not be eligible for salary increases or additional stock option grants at any time for the remainder of his employment from and after the Effective Date.
- h. At all times during Dr. Wedel's active employment at Isis and during the Separation Period his employee benefits, specifically including life insurance and disability benefits, will continue. If his employment at Isis ends before June 30, 2008 due to death, or Dr. Wedel dies during the Separation Period, Separation Payments will no longer be paid and employee benefits will cease.
- i. If Dr. Wedel voluntarily terminates his employment at any time before June 30, 2008 he will not be eligible for the Separation Payment or the Incentive Payment. If he

voluntarily terminates his employment before December 31, 2007, he will not be eligible for the 2007 Bonus.

- j. Separation Payments will cease if at any time during the Separation Period Dr. Wedel becomes otherwise employed, part-time or full time, as an employee or consultant. Provided, however, that Dr. Wedel may sit on one Board of Directors so long as that company is not involved in any way in RNA targeted drug discovery or development.

2. **ACCRUED VACATION.** If Dr. Wedel receives Separation Payments he will use all previously accrued vacation during the Separation Period. Vacation will not accrue during the Separation Period. If Dr. Wedel's active employment terminates at any time without Separation Payments, accrued vacation will be paid subject to standard payroll deductions and withholdings, on his Separation Date.

3. **HEALTH INSURANCE.** To the extent permitted by law and by Isis's current group health insurance policies, after the Separation Period, Dr. Wedel will be eligible to continue receiving health insurance benefits under the federal or state COBRA law at Dr. Wedel's own expense and later to convert to an individual policy if desired. Dr. Wedel will be provided with a separate notice regarding COBRA benefits.

4. **STOCK OPTIONS.** Pursuant to Isis' equity incentive plans, vesting of Dr. Wedel's stock options will cease on the Separation Date. Dr. Wedel's rights to exercise his stock options as to any vested shares will expire in accordance with the terms of the applicable Isis option plan. Dr. Wedel's rights to exercise vested options expire 90 days after the Separation Date. Provided, however, if ISIS 301012 is licensed to a third party before Dr. Wedel's active employment terminates, vesting of Dr. Wedel's stock options will continue through the Separation Period, if applicable, and his rights to exercise vested options will continue until 90 days after the end of the Separation Period, in accordance with the terms of the applicable Isis option plan.

5. **RETURN OF COMPANY PROPERTY.** On the Separation Date, Dr. Wedel will return to Isis all Isis documents (and all copies thereof) and other Isis property and materials in Dr. Wedel's possession, or control, including, but not limited to, Isis 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 Isis (and all reproductions thereof).

6. **PROPRIETARY INFORMATION OBLIGATIONS.** Dr. Wedel acknowledges that nothing herein will impair the covenants and obligations set forth in Dr. Wedel's Proprietary Information and Inventions Agreement. Any breach of Dr. Wedel's Proprietary Information and Inventions Agreement will be a breach of this Agreement.

7. **NO STATEMENTS/HIRING RESTRICTIONS.**

- a. From the Effective Date and continuing for a period of 5 years following the Separation Date, Dr. Wedel will not (i) make or cause to be made any negative, disparaging or defamatory statements and/or comments related to Isis, or its employees, technology, products or patents, (ii) participate in or supply information to any investors, analysts, electronic user groups, chat rooms or bulletin boards or news or trade interviews or

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publications related to Isis (whether positive or negative), or (iii) take any actions whatsoever to cause, or assist in, the prosecution of any and all claims, legal or otherwise, which allegedly existed or could have existed at anytime prior to, during and/or subsequent to the parties' business relationship, including, but not limited to acting as an advisor or expert witness for third parties against Isis.

- b. From the Effective Date and continuing for a period of 2 years following the last payment made under Section 2 above, Dr. Wedel will not (i) attempt to induce any employee or employees of Isis to terminate their employment with, or otherwise cease their relationship with Isis or (ii) induce any company to hire any employee or employees of Isis.
- c. From the Effective Date and continuing for a period of 5 years following the Separation Date, Isis, its officers and directors will not make or cause to be made any negative, disparaging or defamatory statements and/or comments related to Dr. Wedel.
- d. The restrictions set forth in this Section 7 are considered by the parties to be reasonable for the purpose of protecting the business of Isis. However, if any such restriction is found by a court of competent jurisdiction to be unenforceable because it extends for too long a period of time or over too great a range of activities or in too broad a geographic area, it will be interpreted to extend only over the maximum period of time, range of activities or geographic areas as to which it may be enforceable.

8. **RELEASE OF CLAIMS.**

- a. Except as otherwise set forth in this Agreement, in exchange for consideration under this Agreement to which Dr. Wedel would not otherwise be entitled, Dr. Wedel hereby releases, acquits and forever discharges Isis, its parents and subsidiaries, and their officers, directors, agents, servants, employees, attorneys, shareholders, employee benefit plans, 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 Dr. Wedel's employment with Isis or the termination of that employment; claims or demands related to salary, bonuses, commissions, stock, stock options, or any other ownership interests in Isis, 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.
- b. Except as otherwise set forth in this Agreement, in exchange for consideration under this Agreement to which Isis would not otherwise be entitled, Isis hereby releases, acquits and forever discharges Dr. Wedel, of and from any and all claims, liabilities, demands, causes of action, costs, expenses, attorneys fees, damages, indemnities and obligations of every

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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 Dr. Wedel's employment with Isis or the termination of that employment; claims or demands related to salary, bonuses, commissions, stock, stock options, or any other ownership interests in Isis, 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, tort law, contract law, fraud, defamation; and breach of the implied covenant of good faith and fair dealing.

9. **ADEA WAIVER.** Dr. Wedel acknowledges that he knowingly and voluntarily waives and releases any rights he may have under the ADEA, as amended. Dr. Wedel 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 Dr. Wedel was already entitled. Dr. Wedel further acknowledges that he has been advised by this writing, as required by the ADEA, that: (a) Dr. Wedel's waiver and release do not apply to any rights or claims that may arise after the execution date of this Agreement; (b) Dr. Wedel has the right to consult with an attorney prior to executing this Agreement; (c) Dr. Wedel has forty-five (45) days to consider this Agreement (although Dr. Wedel may choose to voluntarily execute this Agreement earlier); (d) Dr. Wedel has seven (7) days following the execution of this Agreement by the parties to revoke the Agreement; and (e) this Agreement will not be effective until the date upon which the revocation period has expired, which will be the eighth day after this Agreement is executed by Dr. Wedel ("*Effective Date*").

10. **SECTION 1542 WAIVER.** Each of Dr. Wedel and Isis 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.

Each of Dr. Wedel and Isis 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.

11. **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 Dr. Wedel'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. The Arbitrator in such arbitration shall have the power but not the obligation to award the prevailing party some or all of its attorney's fees and costs including arbitrator fees or administrative costs. 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.
12. **ENTIRE AGREEMENT.** This Agreement and the Employee Confidential Information and Inventions Agreement signed by Dr. Wedel, constitute the complete, final and exclusive embodiment of the entire agreement between Dr. Wedel and Isis with regard to the subject matter

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hereof. Together they supersede any and all agreements entered into by and between Dr. Wedel and Isis 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 Dr. Wedel and a duly authorized officer of Isis. 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.

13. **MISCELLANEOUS.** This Agreement will 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 will be deemed to have been entered into and will 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 hereof will be unimpaired, the invalid or unenforceable term or provision will 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 will be deemed an original, all of which together will constitute one and the same instrument.

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

/s/ Mark K. Wedel

Mark K. Wedel

/s/ Jeffrey M. Jonas

ISIS PHARMACEUTICALS, INC.
Jeffrey M. Jonas
Executive Vice President

Date: September 21, 2007

Date: September 21, 2007

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