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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): **April 15, 2009**

## 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**

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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 8.01. Other Events.**

The Board of Directors of Isis Pharmaceuticals, Inc. ("Isis") recently approved an amendment to Isis' 1989 Stock Option Plan (the "Plan") such that the only circumstances where Isis could accelerate the vesting of options issued under the Plan are in connection with a change in control of Isis or an option holder's death or permanent disability. A copy of the Plan, as amended is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

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

(d) Exhibits.

99.1 1989 Stock Option Plan, as amended.

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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: April 10, 2009

By: /s/ B. Lynne Parshall

**B. LYNNE PARSHALL**

Executive Vice President,

INDEX TO EXHIBITS

99.1 1989 Stock Option Plan, as amended.

**ISIS PHARMACEUTICALS, INC.**  
**1989 STOCK OPTION PLAN**

As Amended September 5, 1991  
As Amended September 4, 1992  
As Amended January 4, 1993  
As Amended December 2, 1993 and January 20, 1994  
As Amended December 7, 1994  
As Amended February 27, 1995 and December 14, 1995  
As Amended September 6, 1996  
As Amended February 27, 1998  
As Amended March 29, 2004  
As Amended June 5, 2008  
As Amended February 27, 2009

1. PURPOSE.

(a) The purpose of the Plan is to provide a means by which selected employees and directors (if declared eligible under paragraph 4) of and consultants to Isis Pharmaceuticals, Inc., a Delaware corporation (the "Company"), and its Affiliates, as defined in subparagraph 1(b), may be given an opportunity to benefit from increases in value of the stock of the Company through the granting of (i) incentive stock options and (ii) supplemental stock options, all as defined below.

(b) The word "Affiliate" as used in the Plan means any parent corporation or subsidiary corporation of the Company, as those terms are defined in Sections 424(e) and (f), respectively, of the Internal Revenue Code of 1986, as amended (the "Code").

(c) The Company, by means of the Plan, seeks to retain the services of persons now employed by or serving as consultants or directors to the Company, to secure and retain the services of new employees/persons capable of filling such positions, and to provide incentives for such persons to exert maximum efforts for the success of the Company.

(d) The Company intends that the rights issued under the Plan will, in the discretion of the Compensation Committee of the Board of Directors of the Company (the "Committee"), be stock options granted pursuant to paragraph 5 hereof, including incentive stock options as that term is used in Section 422 of the Code ("Incentive Stock Options"), or options which do not qualify as Incentive Stock Options ("Supplemental Stock Options") (together hereinafter referred to as "Options"). All Options will be separately designated Incentive Stock Options or Supplemental Stock Options at the time of grant, and in such form as issued pursuant to paragraph 5, and a separate certificate or certificates will be issued for shares purchased on exercise of each type of Option. An Option designated as a Supplemental Stock Option will not be treated as an Incentive Stock Option.

2. ADMINISTRATION.

(a) The Plan will be administered by the Committee.

(b) The Committee will have the power, subject to, and within the limitations of, the express provisions of the Plan:

(1) To determine from time to time which of the persons eligible under the Plan will be granted Options; when and how Options will be granted; whether an Option will be an Incentive Stock Option or a Supplemental Stock Option; the provisions of Option granted (which need not be identical), including the time or times when a person will be permitted to purchase or receive stock pursuant to an Option; and the number of shares with respect to which Options will be granted to each such person.

(2) To construe and interpret the Plan and Options granted under it, and to establish, amend and revoke rules and regulations for its administration. The Committee, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan or in any Option, in a manner and to the extent it will deem necessary or expedient to make the Plan fully effective.

(3) To amend the Plan as provided in paragraph 11.

(4) Generally, to exercise such powers and to perform such acts as the Committee deems necessary or expedient to promote the best interests of the Company.

(c) The Committee may delegate to a single member of the Board of Directors the authority to grant one or more Options, without further approval of the Committee, to any person eligible pursuant to Section 4 (other than a person who, at the time of such grant, is an executive officer or member of the Board of Directors); provided, however, that each such Option will be subject to the terms and conditions of the appropriate standard form of Option Agreement approved by the Committee and will conform to the provisions of the Plan and such other guidelines as the Committee may establish from time to time.

3. SHARES SUBJECT TO THE PLAN.

(a) Subject to the provisions of paragraph 10 relating to adjustments upon changes in stock, the stock that may be issued pursuant to Options granted under the Plan will not exceed in the aggregate 16,700,000 shares of the Company's common stock. If any Option granted under the Plan will for any reason expire or otherwise terminate without having been exercised in full, the stock not purchased under such Option will again become available for the Plan.

(b) The stock subject to the Plan may be unissued shares or reacquired shares, bought on the market or otherwise.

(c) An Incentive Stock Option may be granted to an eligible person under the Plan only if the aggregate fair market value (determined at the time the Option is granted) of the stock with respect to which incentive stock options (as defined in the Code) granted after 1986 are exercisable for the first time by such optionee during any calendar year under all Incentive Stock Option plans of the Company and its Affiliates does not exceed \$100,000. If it is determined that an entire Option or any portion thereof does not qualify for treatment as an Incentive Stock Option by reason of exceeding such maximum, such Option or the applicable portion will be considered a Supplemental Stock Option.

#### 4. ELIGIBILITY.

(a) Incentive Stock Options may be granted only to employees (including officers) of the Company or its Affiliates. A director of the Company will not be eligible to receive Incentive Stock Options unless such director is also an employee (including an officer) of the Company or any Affiliate. Options other than Incentive Stock Options may be granted only to employees (including officers) of, directors of or consultants to the Company or its Affiliates.

(b) No person will be eligible for the grant of an Incentive Stock Option under the Plan if, at the time of grant, such person owns (or is deemed to own pursuant to Section 424(d) of the Code) stock possessing more than 10% of the total combined voting power of all classes of stock of the Company or of any of its Affiliates unless the exercise price of such Option is at least 110% of the fair market value of such stock at the date of grant and the term of the Option does not exceed 5 years from the date of grant.

(c) No person will be eligible to be granted Options covering more than 294,873 shares of the Company's common stock in any 12 month period.

#### 5. OPTION PROVISIONS.

Each Option will be in such form and will contain such terms and conditions as the Committee will deem appropriate. The provisions of separate Options need not be identical, but each Option will include (through incorporation of provisions hereof by reference in the Option or otherwise) the substance of each of the following provisions:

(a) No Option will be exercisable after the expiration of 7 years from the date it was granted.

(b) The exercise price of each Option (whether an Incentive Stock Option or Supplemental Stock Option) will be not less than 100% of the fair market value of the stock subject to the Option on the date the Option is granted. Notwithstanding the foregoing, an Option (whether an Incentive Stock Option or Supplemental Stock Option) may be granted with an exercise price lower than set forth in the preceding sentences if such Option is granted pursuant to an assumption or substitution for another option in a manner satisfying the provisions of Section 424(a) of the Code.

(c) The purchase price of stock acquired pursuant to an Option will be paid in cash at the time the Option is exercised.

(d) An Incentive Option will not be transferable except by will or by the laws of descent and distribution, and will be exercisable during the lifetime of the person to whom the Option is granted only by such person. A Supplemental Stock Option may be transferable at the discretion of the Committee.

(e) The total number of shares of stock subject to an Option may, but need not, be allotted in periodic installments (which may, but need not, be equal). From time to time during each of such installment periods, the Option may become exercisable ("vest") with respect to some or all of the shares allotted to that period, and may be exercised with respect to some or all of the shares allotted to such period and/or any prior period as to which the Option was not fully exercised; *provided, however*, that no Option granted to an employee or member of the Company's Board of Director will become 100% vested in a period of less than 2 years after the grant of such Option (except as provided in Section 10(b)). During the remainder of the term of the Option (if its term extends beyond the end of the installment periods), the Option may be exercised from time to time with respect to any shares then remaining subject to the Option. The provisions of this subparagraph 5(e) are subject to any Option provisions governing the minimum number of shares as to which an Option may be exercised.

(f) The Company may require any optionee, or any person to whom an Option is transferred under subparagraph 5(d), as a condition of exercising any such Option, (1) to give written assurances satisfactory to the Company as to the optionee's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters, and that he or she is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Option; and (2) to give written assurances satisfactory to the Company stating that such person is acquiring the stock subject to the Option for such person's own account and not with any present intention of selling or otherwise distributing the stock. These requirements, and any assurances given pursuant to such requirements, will be inoperative as to any particular requirement, if a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws.

(g) An Option will terminate 3 months after termination of the optionee's employment or relationship as a consultant or director with the Company or an Affiliate, unless (i) such termination is due to such person's permanent and total disability, within the meaning of Section 422(c)(6) of the Code, in which case the Option may, but need not, provide that it may be exercised at any time within 1 year following such termination of employment or relationship as a consultant or director; or (ii) the optionee dies while in the employ of or while serving as a consultant or director to the Company or an Affiliate, or within not more than 3 months after termination of such relationship, in which case the Option may, but need not, provide that it may be exercised at any time within 18 months following the death of the optionee by the person or persons to whom the optionee's rights under such Option pass by will or by the laws of descent and distribution; or (iii) the Option by its terms specifies either (a) that it will terminate sooner than 3 months after termination of the optionee's employment or relationship as a consultant or director or (b) that it may be exercised more than 3 months after termination of the relationship with the Company or an Affiliate. This subparagraph 5(g) will not be construed to extend the term of any Option or to permit anyone to exercise

the Option after expiration of its term, nor will it be construed to increase the number of shares as to which any Option is exercisable from the amount exercisable on the date of termination of the optionee's employment or relationship as a consultant or director.

(h) To the extent provided by the terms of an Option, the optionee may satisfy any federal, state or local tax withholding obligation relating to the exercise of such Option by any of the following means or by a combination of such means: (1) tendering a cash payment; (2) authorizing the Company to withhold from the shares of the common stock otherwise issuable to the participant as a result of the exercise of the Option a number of shares having a fair market value less than or equal to the amount of the withholding tax obligation; or (3) delivering to the Company owned and unencumbered shares of the common stock having a fair market value less than or equal to the amount of the withholding tax obligation.

6. COVENANTS OF THE COMPANY.

(a) During the terms of the Options granted under the Plan, the Company will keep available at all times the number of shares of stock required to satisfy such Options.

(b) The Company will seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to issue and sell shares of stock under the Options granted under the Plan; provided, however, that this undertaking will not require the Company to register under the Securities Act either the Plan, any Option granted under the Plan or any stock issued or issuable pursuant to any such Option. If, after reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority which counsel for the Company deems necessary for the lawful issuance and sale of stock under the Plan, the Company will be relieved from any liability for failure to issue and sell stock upon exercise of such Options unless and until such authority is obtained.

7. USE OF PROCEEDS FROM STOCK.

Proceeds from the sale of stock pursuant to Options granted under the Plan will constitute general funds of the Company.

8. MISCELLANEOUS.

(a) Subject to the limitation set forth in Section 5(e), and *solely* in connection with (i) an optionee's death, permanent and total disability within the meaning of Section 422(c)(6) of the Code or retirement from the Company; or (ii) a Change in Control, the Committee will have the power to accelerate the time during which an Option may be exercised or the time during which an Option or any part thereof will vest, notwithstanding the provisions in the Option stating the time during which it may be exercised or the time during which it will vest. For purposes of this Section 8(a), 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 the Company's Board 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 the Company's Board of Directors."

(b) Neither an optionee nor any person to whom an Option is transferred under subparagraph 5(d) will be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares subject to such Option unless and until such person has satisfied all requirements for exercise of the Option pursuant to its terms.

(c) Throughout the term of any Option granted pursuant to the Plan, the Company will make available to the holder of such Option, not later than 120 days after the close of each of the Company's fiscal years during the Option term, upon request, such financial and other information regarding the Company as comprises the annual report to the stockholders of the Company provided for in the bylaws of the Company.

(d) Nothing in the Plan or any instrument executed or Option granted pursuant thereto will confer upon any eligible employee, consultant, director or holder of Options under the Plan any right to continue in the employ of the Company or any Affiliate (or to continue acting as a consultant or director) or will affect the right of the Company or any Affiliate to terminate the employment or consulting relationship or directorship of any eligible employee, consultant, director or holder of Options under the Plan with or without cause. In the event that a holder of Options is permitted or otherwise entitled to take a leave of absence, the Company will have the unilateral right to (i) determine whether such leave of absence will be treated as a termination of employment or relationship as consultant or director for purposes of paragraph 5(g) hereof and corresponding provisions of any outstanding Options, and (ii) suspend or otherwise delay the time or times at which exercisability or vesting would otherwise occur with respect to any outstanding Options under the Plan.

9. OPTION REPRICING PROHIBITED.

The Board will not have the authority, at any time, without obtaining the approval of a majority of the shares present or represented and entitled to vote at a duly convened meeting of stockholders, to (1) reduce the exercise price of any Options under the Plan that are currently outstanding; or (2) cancel any outstanding Options under the Plan and grant in substitution therefore new Options under the Plan at a lower exercise price (including entering into any "6 month and 1 day" cancellation and re-grant scheme), regardless of whether or not the cancelled Options revert to and again become available for issuance under the Plan. This Section 10 may not be amended without the affirmative vote of the holders of a majority of the shares present or represented

and entitled to vote at a duly convened meeting of the stockholders of the Company. Notwithstanding the foregoing, this paragraph will not be construed to apply to "issuing or assuming a stock option in a transaction to which section 424(a) applies," within the meaning of Section 424 of the Code.

10. ADJUSTMENTS UPON CHANGES IN STOCK.

(a) If any change is made in the stock subject to the Plan, or subject to any Option granted under the Plan (through merger, consolidation, reorganization, recapitalization, stock dividend, dividend in property other than cash, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or otherwise), the Plan and outstanding Options will be appropriately adjusted in the class(es) and maximum number of shares subject to the Plan or an Option under paragraph 4(c) and the class(es) and number of shares and price per share of stock subject to outstanding Options.

(b) In the event of: (1) a dissolution or liquidation of the Company; (2) a merger or consolidation in which the Company is not the surviving corporation; or (3) a reverse merger in which the Company is the surviving corporation but the shares of the Company's 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 then to the extent permitted by applicable law: (i) any surviving corporation will assume any Options outstanding under the Plan or will substitute similar Options for those outstanding under the Plan, or (ii) such Options will continue in full force and effect. In the event any surviving corporation refuses to assume or continue such Options, or to substitute similar Options for those outstanding under the Plan, then, with respect to Options held by persons then performing services as employees or as consultants or directors for the Company, as the case may be, the time during which such Options become vested or may be exercised will be accelerated and the Options terminated if not exercised prior to such event.

11. AMENDMENT OF THE PLAN.

(a) The Committee at any time, and from time to time, may amend the Plan. However, except as provided in paragraph 10 relating to adjustments upon changes in stock, no amendment will be effective unless approved by the stockholders of the Company within 12 months before or after the adoption of the amendment, where such amendment (i) increases the maximum aggregate number of shares of the Company's common stock that may be issued pursuant to Options granted under the Plan, (ii) requires stockholder approval in order for the Plan to satisfy the requirements of Section 422 of the Code, Rule 16(b)(3) promulgated under the Securities Exchange Act of 1934, as amended or (iii) requires stockholder approval in order for the Plan to satisfy any applicable Nasdaq or securities exchange requirements.

(b) It is expressly contemplated that the Committee may amend the Plan in any respect the Committee deems necessary or advisable to provide optionees with the maximum benefits provided or to be provided under the provisions of the Code and the regulations promulgated thereunder relating to employee Incentive Stock Options and/or to bring the Plan and/or Incentive Stock Options granted under it into compliance therewith.

(c) Rights and obligations under any Option granted before amendment of the Plan will not be altered or impaired by any amendment of the Plan unless (i) the Company requests the consent of the person to whom the Option was granted and (ii) such person consents in writing.

12. TERMINATION OR SUSPENSION OF THE PLAN.

(a) The Committee may suspend or terminate the Plan at any time. Unless sooner terminated, the Plan will terminate on January 31, 2014. No Options may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) Rights and obligations under any Option granted while the Plan is in effect will not be altered or impaired by suspension or termination of the Plan, except with the consent of the person to whom the Option was granted.

13. EFFECTIVE DATE OF PLAN.

The Plan is effective April 19, 1991.