

SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

SCHEDULE 13D

Under the Securities Exchange Act of 1934

Regulus Therapeutics Inc

(Name of Issuer)

Common Stock

(Title of Class of Securities)

75915K 101

(CUSIP Number)

**B. Lynne Parshall
Isis Pharmaceuticals, Inc.
2855 Gazelle Court
Carlsbad, CA 92010
(760) 931-9200**

(Name, Address and Telephone Number of Person
Authorized to Receive Notices and Communications)

October 10, 2012

(Date of Event Which Requires Filing of this Statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of §§240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box.

Note: Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See Rule 13d-7 for other parties to whom copies are to be sent.

* The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

CUSIP No. 75915K 101

13D

1. Name of Reporting Persons
Isis Pharmaceuticals, Inc. ("Isis")

2. Check the Appropriate Box if a Member of a Group (See Instructions)

(a)

(b)

3. SEC Use Only

4. Source of Funds (See Instructions)
WC

5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)

6. Citizenship or Place of Organization

7. Sole Voting Power
7,049,500

Number of
Shares
Beneficially
Owned by
Each
Reporting
Person With

8. Shared Voting Power
0

9. Sole Dispositive Power
7,049,500

10. Shared Dispositive Power
0

11. Aggregate Amount Beneficially Owned by Each Reporting Person
7,049,500

12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)

13. Percent of Class Represented by Amount in Row 11
20.7%

14. Type of Reporting Person (See Instructions)
CO

1. Name of Reporting Persons
Stanley T. Crooke ("Crooke")

2. Check the Appropriate Box if a Member of a Group (See Instructions)

(a)

(b)

3. SEC Use Only

4. Source of Funds (See Instructions)
N/A

5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)

6. Citizenship or Place of Organization
United States

Number of
Shares
Beneficially
Owned by
Each
Reporting
Person With

7. Sole Voting Power
0

8. Shared Voting Power
7,049,500 shares held by Isis. Crooke, an executive officer and director of Isis, may be deemed to have shared voting power over these shares.

9. Sole Dispositive Power
0

10. Shared Dispositive Power
7,049,500 shares held by Isis. Crooke, an executive officer and director of Isis, may be deemed to have shared dispositive power over these shares.

11. Aggregate Amount Beneficially Owned by Each Reporting Person
7,049,500

12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)

13. Percent of Class Represented by Amount in Row 11
20.7%

14. Type of Reporting Person (See Instructions)
IN

1. Name of Reporting Persons
B. Lynne Parshall ("Parshall")

2. Check the Appropriate Box if a Member of a Group (See Instructions)

(a)

(b)

3. SEC Use Only

4. Source of Funds (See Instructions)
N/A

5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)

6. Citizenship or Place of Organization
United States

7. Sole Voting Power
0

Number of
Shares
Beneficially
Owned by
Each
Reporting
Person With

8. Shared Voting Power
7,049,500 shares held by Isis. Parshall, an executive officer and director of Isis, may be deemed to have shared voting power over these shares.

9. Sole Dispositive Power
0

10. Shared Dispositive Power
7,049,500 shares held by Isis. Parshall, an executive officer and director of Isis, may be deemed to have shared dispositive power over these shares.

11. Aggregate Amount Beneficially Owned by Each Reporting Person
7,049,500

12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)

13. Percent of Class Represented by Amount in Row 11
20.7%

14. Type of Reporting Person (See Instructions)
IN

Item 1. Security and Issuer.

This Schedule 13D relates to shares of the Common Stock, \$0.001 par value per share ("Common Stock") of Regulus Therapeutics Inc., a Delaware corporation (the "Issuer"). The principal executive offices of the Issuer are located at 3545 Johns Hopkins Court, Suite 210, San Diego, CA 92121.

Item 2. Identity and Background.

(a) This Schedule 13D is being filed by Isis Pharmaceuticals, Inc., a Delaware corporation ("Isis"), Stanley T. Crooke ("Crooke") and B. Lynne Parshall ("Parshall") (collectively, the "Reporting Persons").

Crooke and Parshall are executive officers and directors of Isis and may be deemed to beneficially own shares of the Issuer owned by Isis. Crooke and Parshall hereby disclaim beneficial ownership of these shares except to the extent of their pecuniary interest therein.

(b) The business address for the Reporting Persons is c/o Isis Pharmaceuticals, Inc. 2855 Gazelle Court, Carlsbad, CA 92010.

- (c) Isis is engaged in the business of biopharmaceuticals.

Set forth on Schedule A to this Schedule 13D are the present principal occupation or employment and name, principal business and address of any corporation or other organization in which such employment is conducted for Crooke and Parshall and for directors and executive officers of Isis required to be listed on Schedule A.

- (d) During the past five years, neither the Reporting Persons nor, to the best knowledge of the Reporting Persons, any of the directors and executive officers identified on Schedule A to this Schedule 13D, have been convicted in any criminal proceeding (excluding traffic violations and similar misdemeanors).
- (e) During the past five years, neither the Reporting Persons nor, to the best knowledge of the Reporting Persons, any of the directors and executive officers identified on Schedule A to this Schedule 13D, have been a party to any civil proceeding of a judicial or administrative body of competent jurisdiction which resulted in any judgment, decree or final order enjoining future violations of, or prohibiting or mandating activities subject to, federal or state securities laws or finding any violations with respect to such laws.
- (f) Reference is made to Rows 1 and 6 of the cover pages for the names and citizenship or place of organization, respectively of the Reporting Persons. All of the directors and executive officers of Isis required to be listed on Schedule A are United States citizens.

Item 3. Source and Amount of Funds or Other Consideration.

On October 10, 2012, the Reporting Persons acquired 750,000 shares of Common Stock sold in the Issuer's initial public offering of shares of its Common Stock at a purchase price of \$4.00 per share. The funds used by the Reporting Persons to acquire the shares described herein were from the Reporting Persons' working capital. As of the date hereof, the total number of shares of Common Stock of the Issuer held by the Reporting Persons is 7,049,500 shares.

Item 4. Purpose of Transaction.

The Reporting Persons purchased the Issuer's Common Stock for investment purposes. Neither the Reporting Persons, nor any of the directors and executive officers identified on Schedule A to this Schedule 13D, have any plans or proposals that relate to or would result in any of the matters listed in Items 4(a) to 4(j) of Schedule 13D. The Reporting Persons reserve the right to acquire additional securities of the Issuer, to dispose of such securities at any time, or to formulate other purposes, plans or proposals regarding the Issuer or any of its securities.

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Item 5. Interest in Securities of the Issuer.

The following information with respect to the ownership of the Common Stock of the Issuer by the Reporting Persons filing this Schedule 13D is provided as of October 10, 2012:

- (a) The Reporting Persons beneficially own 7,049,500 shares of the Common Stock of the Issuer, or approximately 20.7% of the Issuer's outstanding Common Stock.
- (b) Isis has sole power to vote and dispose of the securities of the Issuer held by it. Crooke and Parshall may be deemed to beneficially own the securities of the Issuer held by Isis and have shared voting and dispositive powers over the securities. Crooke and Parshall disclaim beneficial ownership of the securities except to the extent of their pecuniary interest therein.
- (c) The Reporting Persons have not effected any other transactions in the Issuer's Common Stock within the past sixty days, except as provided herein.
- (d) Not applicable.
- (e) Not applicable.

Item 6. Contracts, Arrangements, Understandings or Relationships with Respect to Securities of the Issuer.

None.

Item 7. Material to Be Filed as Exhibits.

None.

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SIGNATURE

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Date: October 19, 2012

ISIS PHARMACEUTICALS, INC.

By: /s/ B. Lynne Parshall
B. Lynne Parshall
Chief Operating Officer and

The original statement shall be signed by each person on whose behalf the statement is filed or his authorized representative. If the statement is signed on behalf of a person by his authorized representative (other than an executive officer or general partner of the filing person), evidence of the representative's authority to sign on behalf of such person shall be filed with the statement: provided, however, that a power of attorney for this purpose which is already on file with the Commission may be incorporated by reference. The name and any title of each person who signs the statement shall be typed or printed beneath his signature.

Attention: Intentional misstatements or omissions of fact constitute Federal criminal violations (See 18 U.S.C. 1001)

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**SCHEDULE A
DIRECTORS AND EXECUTIVE OFFICERS OF ISIS**

The following table sets forth the name, business address, present principal occupation or employment and material occupations, positions, offices or employment of each of the directors and executive officers of Isis. All directors and executive officers listed below are citizens of the United States unless otherwise noted herein.

Name	Position	Present Principal Occupation or Employment and Business Address
Stanley T. Crooke, M.D., Ph.D.	Director, Chief Executive Officer	2855 Gazelle Court Carlsbad, CA 92010
B. Lynne Parshall, Esq.	Director, Chief Operating Officer and Chief Financial Officer	2855 Gazelle Court Carlsbad, CA 92010
C Frank Bennett	Senior Vice President, Research	2855 Gazelle Court Carlsbad, CA 92010
Richard S. Geary, Ph.D.	Senior Vice President, Development	2855 Gazelle Court Carlsbad, CA 92010
Brett P. Monia, Ph.D.	Senior Vice President, Antisense Drug Discovery	2855 Gazelle Court Carlsbad, CA 92010
Spencer R. Berthelsen, M.D.	Director	2855 Gazelle Court Carlsbad, CA 92010
Joseph Klein, III	Director	2855 Gazelle Court Carlsbad, CA 92010
Frederick T. Muto, Esq.	Director	2855 Gazelle Court Carlsbad, CA 92010
John C. Reed, M.D., Ph.D.	Director	2855 Gazelle Court Carlsbad, CA 92010
Joseph H. Wender	Director	2855 Gazelle Court Carlsbad, CA 92010

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