
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

SCHEDULE 13D

UNDER THE SECURITIES EXCHANGE ACT OF 1934
(Amendment No. 1)

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)

November 3, 2014
(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*).

1.	Name of Reporting Persons Isis Pharmaceuticals, Inc. ("Isis")	
2.	Check the Appropriate Box if a Member of a Group (see instructions) (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
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) <input type="checkbox"/>	
6.	Citizenship or Place of Organization California	
Number of Shares Beneficially Owned by Each Reporting Person With	7.	Sole Voting Power 5,516,305
	8.	Shared Voting Power 25,000 (1)
	9.	Sole Dispositive Power 5,516,305
	10.	Shared Dispositive Power 25,000 (1)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 5,541,305 (1)	
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (see instructions) <input type="checkbox"/>	
13.	Percent of Class Represented by Amount in Row 11 11.4% (2)	
14.	Type of Reporting Person (see instructions) CO	

- (1) Includes 25,000 shares that Stanley T. Croke, an executive officer and director of Isis, has the right to acquire from the Issuer pursuant to the exercise of stock options.
- (2) This percentage is calculated based upon 48,590,499 shares of the Issuer's Common Stock reported to be outstanding as of November 3, 2014.

1.	Name of Reporting Persons Stanley T. Crooke ("Crooke")
2.	Check the Appropriate Box if a Member of a Group (see instructions) (a) <input type="checkbox"/> (b) <input type="checkbox"/>
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) <input type="checkbox"/>
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 5,541,305 shares held by Isis. Crooke, an executive officer and director of Isis, may be deemed to have shared voting power over these shares. (1)
	9. Sole Dispositive Power 0
	10. Shared Dispositive Power 5,541,305 shares held by Isis. Crooke, an executive officer and director of Isis, may be deemed to have shared dispositive power over these shares. (1)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 5,541,305 (1)
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (see instructions) <input type="checkbox"/>
13.	Percent of Class Represented by Amount in Row 11 11.4% (2)
14.	Type of Reporting Person (see instructions) IN

(1) Includes 25,000 shares that Stanley T. Crooke, an executive officer and director of Isis, has the right to acquire from the Issuer pursuant to the exercise of stock options.

(2) This percentage is calculated based upon 48,590,499 shares of the Issuer's Common Stock reported to be outstanding as of November 3, 2014.

1.	Name of Reporting Persons B. Lynne Parshall ("Parshall")
2.	Check the Appropriate Box if a Member of a Group (see instructions) (a) <input type="checkbox"/> (b) <input type="checkbox"/>
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) <input type="checkbox"/>
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 5,541,305 shares held by Isis. Parshall, an executive officer and director of Isis, may be deemed to have shared voting power over these shares. (1)
	9. Sole Dispositive Power 0
	10. Shared Dispositive Power 5,541,305 shares held by Isis. Parshall, an executive officer and director of Isis, may be deemed to have shared dispositive power over these shares. (1)
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 5,541,305 (1)
12.	Check if the Aggregate Amount in Row (11) Excludes Certain Shares (see instructions) <input type="checkbox"/>
13.	Percent of Class Represented by Amount in Row 11 11.4% (2)
14.	Type of Reporting Person (see instructions) IN

(1) Includes 25,000 shares that Stanley T. Crooke, an executive officer and director of Isis, has the right to acquire from the Issuer pursuant to the exercise of stock options.

(2) This percentage is calculated based upon 48,590,499 shares of the Issuer's Common Stock reported to be outstanding as of November 3, 2014.

Item 1. Security and Issuer.

This Amendment No. 1 to Schedule 13D (the "**Amendment**") is being filed as an amendment to the original statement on Schedule 13D relating to the Common Stock, \$0.001 par value per share ("**Common Stock**") of Regulus Therapeutics Inc., a Delaware corporation (the "**Issuer**") as filed with the Securities and Exchange Commission (the "**SEC**") on October 19, 2012 (the "**Original Schedule 13D**"). This Amendment is being filed by the Reporting Persons to report (i) the sale between June 25, 2014 and October 24, 2014 of an aggregate of 253,784 shares of the Issuer's Common stock by Isis pursuant to a Rule 10b5-1 trading plan adopted on May 22, 2014 and (ii) the sale on November 3, 2014 of 1,279,411 shares of the Issuer's Common Stock by Isis to the underwriters in connection with a registered public offering pursuant to the Issuer's Registration Statement on Form S-3 (No. 333-194293).

Items 4, 5 and 7 and Schedule A of the Original Schedule 13D are hereby amended and supplemented to the extent hereinafter expressly set forth and, except as amended and supplemented hereby, the Original Schedule 13D remains in full force and effect. All capitalized terms used in this Amendment but not defined herein shall have the meanings ascribed thereto in the Original Schedule 13D.

Item 4. Purpose of Transaction.

Item 4 of the Original Schedule 13D is hereby amended and supplemented by adding the following paragraph at the end of Item 4:

Between June 25, 2014 and October 24, 2014, Isis sold an aggregate of 253,784 shares of the Issuer's Common Stock pursuant to a Rule 10b5-1 trading plan adopted on May 22, 2014. On November 3, 2014, Isis sold 1,279,411 shares of the Issuer's Common Stock in connection with a registered public offering pursuant to the Issuer's Registration Statement on Form S-3 (No. 333-194293).

Item 5. Interest in Securities of the Issuer.

Item 5 of the Original Schedule 13D is hereby amended and restated in its entirety as follows:

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 November 3, 2014:

- (a) The Reporting Persons beneficially own 5,541,305 shares of the Common Stock of the Issuer, or approximately 11.4% 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 7. Material to Be Filed as Exhibits.

- A. Agreement regarding joint filing of Amendment No. 1 to Schedule 13D.

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: November 5, 2014

ISIS PHARMACEUTICALS, INC.

By: /s/ B. Lynne Parshall

B. Lynne Parshall
Chief Operating Officer

/s/ B. Lynne Parshall

B. LYNNE PARSHALL

/s/ Stanley T. Crooke

STANLEY T. CROOKE

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)**

Schedule A of the Original Schedule 13D is hereby amended and restated in its entirety as follows:

**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	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
Elizabeth L. Housen	Senior Vice President of Finance and Chief Financial Officer	2855 Gazelle Court Carlsbad, CA 92010
Patrick R. O'Neil, Esq.	Senior Vice President of Legal and General Counsel	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
Joseph H. Wender	Director	2855 Gazelle Court Carlsbad, CA 92010
Breaux Castleman	Director	2855 Gazelle Court Carlsbad, CA 92010
Joseph Loscalzo, M.D., Ph.D.	Director	2855 Gazelle Court Carlsbad, CA 92010

EXHIBIT A

JOINT FILING AGREEMENT

In accordance with Rule 13d-1(k) under the Securities Exchange Act of 1934, as amended, the undersigned agree to the joint filing on behalf of each of them of a statement on Schedule 13D (including amendments thereto) with respect to the Common Stock of Regulus Therapeutics Inc. and further agree that this agreement be included as an exhibit to such filing. Each party to the agreement expressly authorizes each other party to file on its behalf any and all amendments to such statement. Each party to this agreement agrees that this joint filing agreement may be signed in counterparts.

In evidence whereof, the undersigned have caused this Agreement to be executed on their behalf this 5th day of November, 2014.

ISIS PHARMACEUTICALS, INC.

By: /s/ B. Lynne Parshall

Name: B. Lynne Parshall

Title: *Chief Operating Officer*

 /s/ B. Lynne Parshall

B. LYNNE PARSHALL

 /s/ Stanley T. Crooke

STANLEY T. CROOKE