
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

SCHEDULE 13D

(Amendment No. 2)
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)

July 22, 2015
(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 2,843,172
	8.	Shared Voting Power
	9.	Sole Dispositive Power 2,843,172
	10.	Shared Dispositive Power
11.	Aggregate Amount Beneficially Owned by Each Reporting Person 2,843,172	
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 5.57% (1)	
14.	Type of Reporting Person (see instructions) CO	

- (1) This percentage is calculated based upon 51,017,405 shares of the Issuer's Common Stock reported to be outstanding as of April 24, 2015, as disclosed in the Issuer's Form 10-Q, filed with the Securities and Exchange Commission on May 8, 2015.

Item 1. Security and Issuer.

This Amendment No. 2 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 Person to report the sales between July 15, 2015 and July 22, 2015 of an aggregate of 2,673,133 shares of the Issuer's Common Stock.

Items 4 and 5 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 July 15, 2015 and July 22, 2015, the Reporting Person sold an aggregate of 2,673,133 shares of the Issuer's Common Stock.

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 Person filing this Schedule 13D is provided as of July 22, 2015:

- (a) The Reporting Person beneficially owns 2,843,172 shares of the Common Stock of the Issuer, or approximately 5.57% of the Issuer's outstanding Common Stock.
- (b) The Reporting Person has sole power to vote and dispose of the securities of the Issuer held by it.
- (c) The Reporting Person has 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.

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: July 31, 2015

ISIS PHARMACEUTICALS, INC.

By: */s/ Patrick R. O'Neil*

Patrick R. O'Neil

SVP Legal & General Counsel

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.

<u>Name</u>	<u>Position</u>	<u>Present Principal Occupation or Employment and Business Address</u>
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
Sarah Boyce	Chief Business Officer	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. Hougen	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