FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL

OMB Number: 3235-0287 Estimated average burden 0.5 hours per response:

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b)

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

1. Name and Address of Reporting Person* <u>ISIS PHARMACEUTICALS INC</u>						2. Issuer Name and Ticker or Trading Symbol Regulus Therapeutics Inc. [RGLS]								Relationship of Reporting Person(s) to Issuer (Check all applicable) X Director X 10% Owner				
(Last) 2855 GA	(Fi ZELLE CC	irst) (Middle)				3. Date of Earliest Transaction (Month/Day/Year) 10/22/2014									Offic belov	er (give title v)	Other below	(specify)
(Street) CARLSBAD CA 92010 (City) (State) (Zip)					4. If Amendment, Date of Original Filed (Month/Day/Year) 10/24/2014								6. Indiv Line) X	vidual or Joint/Group Filing (Check Applicable Form filed by One Reporting Person Form filed by More than One Reporting Person				
		Tab	le I - No	n-Deriva	tive	Secu	ırities	s Ac	quire	ed, C	Disposed o	of, or E	3enefic	cially (Owne	ed		
			Da	2. Transaction Date (Month/Day/Year		2A. Deemed Execution Date, if any (Month/Day/Year)		e,	3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and		d (A) or r. 3, 4 and	5)	5. Amount of Securities Beneficially Owned Following Reported		6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial Ownership
									Code V		Amount	(A) or (D)	(A) or (D) Price		Transaction(s) (Instr. 3 and 4)			(Instr. 4)
Common Stock				10/22/201	4				S ⁽¹⁾		9,283	D	\$12.1	792 ⁽²⁾	6,	899,517	D ⁽³⁾	
Common Stock				10/22/2014					S ⁽¹⁾		15,791	D	\$12.8	2.8309(4)		883,726	D ⁽³⁾	
Common Stock				0/22/2014					S ⁽¹⁾		57,753	D	\$13.9	.9112 ⁽⁵⁾		825,973	D (3)	
Common Stock				10/22/201	22/2014				S ⁽¹⁾		15,156	D	\$14.6	.6707 ⁽⁶⁾ 6,		810,817	D (3)	
Common Stock				10/22/2014					S ⁽¹⁾		11,376	D	\$16.5	6.5881 ⁽⁷⁾ 6,799		799,441	D (3)	
Common Stock				10/22/2014					S ⁽¹⁾		175	D	\$17.	\$17.11(8)		799,266	D ⁽³⁾	
Common Stock				10/23/2014					S ⁽¹⁾		1,200	D	\$13.9	\$13.939 ⁽⁹⁾		798,066	D ⁽³⁾	
Common Stock				10/23/2014					S ⁽¹⁾		450	D	\$14.8956(10)		6,	797,616	D (3)	
Common Stock				10/23/2014					S ⁽¹⁾		50	D	\$15.4	\$15.45(11)		797,566	D (3)	
Common Stock				10/24/2014					S ⁽¹⁾		1,054	D	\$14.62	\$14.6277(12)		796,512	D (3)	
Common Stock 10				10/24/2014					S ⁽¹⁾		350	D	\$15.50	15.5014(13)		796,162	D (3)	
Common Stock 10/24/201				4				S ⁽¹⁾		446	D	\$16.29	922(14)	6,795,716		D (3)		
Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)																		
Derivative Conversion Date Executity Or Exercise (Month/Day/Year) if an		3A. Deem Execution if any	Deemed 4. ution Date, Tran				nber tive ities red sed 3, 4	6. Date Ex Expiration (Month/Da		ercisable and Date			8. Pri Deriv Secu (Insti	ative Irity	9. Number of derivative Securities Beneficially Owned Following Reported Transaction((Instr. 4)	Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)	
	planation of Bosponsos:			c	Code V		(A)	(D)	Date Exerc	cisable	Expiration e Date	Title	Amount or Number of Shares	r				

- 1. The sales reported in the Form 4 were effected pursuant to a Rule 10b5-1 trading plan adopted by the reporting person on May 22, 2014.
- 2. This Form 4 is being amended to itemize the sales prices which were not available at the time the Form 4 was originally filed. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$11.47 to \$12.47 inclusive. The reporting person undertakes to provide to RGLS, any security holder of RGLS, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth in this footnote to this Form 4.
- 3. The shares are held directly by Isis Pharmaceuticals, Inc. Ms. Parshall is an officer and director of Isis and therefore may be deemed to have voting or investment power over the shares beneficially owned by Isis. Ms. Parshall disclaims beneficial ownership over the shares beneficially owned by Isis, except to the extent of her proportionate pecuniary interest therein as a stockholder of Isis.
- 4. This Form 4 is being amended to itemize the sales prices which were not available at the time the Form 4 was originally filed. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$12.48 to \$13.44 inclusive. The reporting person undertakes to provide to RGLS, any security holder of RGLS, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth in this footnote to this Form 4.
- 5. This Form 4 is being amended to itemize the sales prices which were not available at the time the Form 4 was originally filed. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$13.47 to \$14.47 inclusive. The reporting person undertakes to provide to RGLS, any security holder of RGLS, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth in this footnote to this Form 4.
- 6. This Form 4 is being amended to itemize the sales prices which were not available at the time the Form 4 was originally filed. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$14.48 to \$15.27 inclusive. The reporting person undertakes to provide to RGLS, any security holder of RGLS, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth in this footnote to this Form 4.
- 7. This Form 4 is being amended to itemize the sales prices which were not available at the time the Form 4 was originally filed. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$16.00 to \$17.00 inclusive. The reporting person undertakes to provide to RGLS, any security holder of RGLS, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth in this footnote to this Form 4.
- 8. This Form 4 is being amended to itemize the sales prices which were not available at the time the Form 4 was originally filed.

- 9. This Form 4 is being amended to itemize the sales prices which were not available at the time the Form 4 was originally filed. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$13.30 to \$14.27 inclusive. The reporting person undertakes to provide to RGLS, any security holder of RGLS, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth in this footnote to this Form 4.
- 10. This Form 4 is being amended to itemize the sales prices which were not available at the time the Form 4 was originally filed. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$14.42 to \$15.30 inclusive. The reporting person undertakes to provide to RGLS, any security holder of RGLS, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth in this footnote to this Form 4.
- 11. This Form 4 is being amended to itemize the sales prices which were not available at the time the Form 4 was originally filed.
- 12. This Form 4 is being amended to itemize the sales prices which were not available at the time the Form 4 was originally filed. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$14.12 to \$15.02 inclusive. The reporting person undertakes to provide to RGLS, any security holder of RGLS, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth in this footnote to this Form 4.
- 13. This Form 4 is being amended to itemize the sales prices which were not available at the time the Form 4 was originally filed. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$15.23 to \$15.71 inclusive. The reporting person undertakes to provide to RGLS, any security holder of RGLS, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth in this footnote to this Form 4.
- 14. This Form 4 is being amended to itemize the sales prices which were not available at the time the Form 4 was originally filed. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$16.29 to \$16.31 inclusive. The reporting person undertakes to provide to RGLS, any security holder of RGLS, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the ranges set forth in this footnote to this Form 4.

Remarks:

<u>/s/ Christopher Aker, Attorney-in-Fact for All Reporting 10/28/2014</u>
Persons

** Signature of Reporting Person Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.