FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

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

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

OMB APPROVAL OMB Number: Estimated average burden hours per response: 0.5

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* BERTHELSEN SPENCER R							2. Issuer Name and Ticker or Trading Symbol IONIS PHARMACEUTICALS INC IONS								cable) or	•		Ssuer Owner (specify	
(Last) (First) (Middle) C/O IONIS PHARMACEUTICALS, INC. 2855 GAZELLE COURT						3. Date of Earliest Transaction (Month/Day/Year) 02/24/2017 4. If Amendment, Date of Original Filled (Month/Day/Year)								below) below) 6. Individual or Joint/Group Filing (Check Applicable					
(Street) CARLSBAD CA 92010 (City) (State) (Zip)					- 4.1	4. If Amendment, Date of Original Filed (Month/Day/Year)								X Form filed by One Reporting Person Form filed by More than One Reporting Person					
		Tab	le I - N	on-Deri	vativ	e Se	curit	ties Ac	quired	l, Di	sposed o	f, or Be	neficia	ally Owne	t				
1. Title of Security (Instr. 3) 2. Transacti Date (Month/Day)					Exe r) if a	Deemed ecution Date, any onth/Day/Year)		3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 a 5)					6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)		7. Nature of Indirect Beneficial Ownership (Instr. 4)		
									Code	v	Amount	(A) or (D)	Price	Transacti (Instr. 3 a				(
Common Stock 02/24/20					/2017	017 02/24/2017			M ⁽¹⁾		12,500 ⁽¹⁾) A	\$9.7	7 88,9	58 D)		
Common Stock														70	70(2)			By Daughter ⁽²⁾	
Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)																			
1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	Execution Date, if any (Month/Day/Year)		4. Transa Code (8)		of Deri Sec Acq (A) o Disp of (I	ivative urities uired or oosed D) (Instr. and 5)	6. Date Exercisable and Expiration Date (Month/Day/Year)			7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)		Derivative Security	9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4)		10. Ownersl Form: Direct (E or Indire (I) (Instr.	Beneficial Ownership ct (Instr. 4)	
					Code	le V (A)		(D)	Date Exercis	able	Expiration Date	Title	Amour or Number of Shares	r					
Director Stock Option (right to	\$9.77	02/24/2017	02/24/2017		M			12,500	07/02/2	2011	07/01/2017	Common Stock	12,50	0 \$0		0	D		

Explanation of Responses:

- 1. Acquired as a result of exercising a stock option that was scheduled to expire on 7/1/2017.
- 2. The reporting person disclaims beneficial ownership of all securities held by his daughter, and this report should not be deemed an admission that the reporting person is the beneficial owner of such securities for purposes of Section 16 or for any other purpose.

Remarks:

/s/B. Lynne Parshall, attorney-

02/27/2017

in-fact

** 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.