Instruction 1(b).

FORM 4

## UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See

## STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

**OMB APPROVAL** 3235-0287 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*  KLEIN JOSEPH III						2. Issuer Name and Ticker or Trading Symbol  IONIS PHARMACEUTICALS INC [ IONS ]										ionship of Reportin all applicable) Director Officer (give title		g Person(s) to Iss 10% Ow Other (s		vner
(Last) (First) (Middle) 2855 GAZELLE COURT					3. Date of Earliest Transaction (Month/Day/Year) 09/26/2023											below			below)	Speemy
(Street) CARLSBAD CA 920				0	4. If	4. If Amendment, Date of Original Filed (Month/Day/Year)										vidual or Joint/Group Filing (Check Applicable  Form filed by One Reporting Person  Form filed by More than One Reporting  Person				on
(City) (State) (Zip)					Rule 10b5-1(c) Transaction Indication  Check this box to indicate that a transaction was made pursuant to a contract, satisfy the affirmative defense conditions of Rule 10b5-1(c). See Instruction 10										act, instr		ten pl	lan that is inte	ended to	
Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned																				
1. Title of Security (Instr. 3)				2. Transaction Date (Month/Day/Ye	ear) it	2A. Deem Execution if any (Month/D		Ti C	3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and				5)	5. Amount of Securities Beneficially Owned Following		6. Ownership Form: Direct (D) or Indirect (I)		7. Nature of Indirect Beneficial Ownership
								С	ode	v	Amoun		(A) or (D)	Price			orted (In saction(s) cr. 3 and 4)		nstr. 4)	(Instr. 4)
Common Stock				09/26/2023					S		2,000	(1)	D	\$45.126	38 <sup>(2)</sup>	1	18,346		D	
Common													100			I	by Son(3)			
Common Stock																	6,000		I	by Trust
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)	e Conversion Date Ex or Exercise (Month/Day/Year) if a		Exe if a	ny Coonth/Day/Year) 8)		action (Instr.	5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)		Exp (Mo	piration onth/Da	y/Year)  Expiration		Amo Secu Unde Deriv Secu 3 and	Amount or Number of	8. Price of Derivative Security (Instr. 5)		9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4)		10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)

## **Explanation of Responses:**

- $1.\ Shares\ sold\ pursuant\ to\ a\ Rule\ 10b5-1\ Trading\ Plan\ adopted\ by\ the\ reporting\ person\ on\ November\ 17,2022$
- 2. The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$45.05 to \$45.25, inclusive. The reporting person undertakes to provide to Ionis Pharmaceuticals, Inc., any security holder of Ionis Pharmaceuticals, Inc. 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 footnote (2) on this Form 4
- 3. The reporting person disclaims beneficial ownership of all securities held by his son, 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.

By: Patrick R. O'Neil, attorney-in-fact For: Joseph

09/28/2023

Klein III

\*\* 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.