

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

**STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP**

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

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

1. Name and Address of Reporting Person* <u>Cadoret-Manier Onaiza</u>			2. Issuer Name and Ticker or Trading Symbol <u>IONIS PHARMACEUTICALS INC [ IONS ]</u>			5. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director 10% Owner <input checked="" type="checkbox"/> Officer (give title below) Other (specify below) <u>EVP, Chf GL Pdt Str &amp; Oper Ofc</u>		
(Last)	(First)	(Middle)	3. Date of Earliest Transaction (Month/Day/Year) <u>04/17/2023</u>			6. Individual or Joint/Group Filing (Check Applicable Line) <input checked="" type="checkbox"/> Form filed by One Reporting Person Form filed by More than One Reporting Person		
<u>2855 GAZELLE COURT</u>			4. If Amendment, Date of Original Filed (Month/Day/Year)					
(Street)	<u>CARLSBAD</u>	<u>CA</u>	<u>92010</u>			Rule 10b5-1(c) Transaction Indication <input type="checkbox"/> Check this box to indicate that a transaction was made pursuant to a contract, instruction or written plan that is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c). See Instruction 10.		
(City)	(State)	(Zip)						

**Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned**

1. Title of Security (Instr. 3)	2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any (Month/Day/Year)	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 Reported Transaction(s) (Instr. 3 and 4)	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Beneficial Ownership (Instr. 4)
			Code	V	Amount	(A) or (D)	Price			
<u>Common Stock</u>	<u>04/17/2023</u>		<u>M<sup>(1)</sup></u>		<u>5,667<sup>(1)</sup></u>	<u>A</u>	<u>\$0.0</u>	<u>26,894</u>	<u>D</u>	
<u>Common Stock</u>	<u>04/18/2023</u>		<u>s<sup>(2)</sup></u>		<u>2,582<sup>(2)</sup></u>	<u>D</u>	<u>\$36.5026<sup>(3)</sup></u>	<u>24,312</u>	<u>D</u>	

**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)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transaction Code (Instr. 8)		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)	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)	
				Code	V	(A)	(D)	Date Exercisable	Expiration Date						Title
<u>Restricted Stock Unit</u>	<u>\$0.0<sup>(4)</sup></u>	<u>04/17/2023</u>		<u>M</u>			<u>5,667</u>	<u>(5)</u>	<u>(5)</u>	<u>Common Stock</u>	<u>5,667</u>	<u>\$0.0</u>	<u>49,659</u>	<u>D</u>	

**Explanation of Responses:**

- Acquired pursuant to vesting and release of shares in accordance with a Restricted Stock Unit award.
- The sale was made pursuant to an automatic sale to cover the required tax withholding obligations pursuant to the 2011 Equity Incentive Plan Restricted Stock Unit Agreement and Grant Notice.
- The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$36.19 to \$36.50953 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 (3) on this Form 4.
- Each Restricted Stock Unit represents a contingent right to receive one share of Ionis common stock, or its equivalent cash value.
- Restricted Stock Units vest in four equal annual installments. Upon vesting, the restricted stock units will be paid out in whole shares of Ionis common stock or cash as may be determined by the Company.

By: Patrick R. O'Neil, attorney-in-fact For: Onaiza Cadoret-Manier 04/19/2023

\*\* 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.