

OMB APPROVAL	
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**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>  (Last) (First) (Middle) 2855 GAZELLE COURT  (Street) CARLSBAD CA 92010  (City) (State) (Zip)	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 Corp Dev and Cml Offc</u>
	3. Date of Earliest Transaction (Month/Day/Year) 01/15/2022	
4. If Amendment, Date of Original Filed (Month/Day/Year)		

**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			

**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
Performance Restricted Stock Units <sup>(1)</sup>	\$0.0	01/15/2022	01/15/2022	A		12,419 <sup>(2)</sup>		(2)	(2)	Common Stock	12,419	\$0.0	12,419	D	
Restricted Stock Unit <sup>(3)</sup>	\$0.0 <sup>(4)</sup>	01/15/2022	01/15/2022	A		16,559		(5)	(5)	Common Stock	16,559	\$0.0	57,787	D	

**Explanation of Responses:**

- Grant to reporting person of Performance Restricted Stock Units under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan.
- Represents an award of performance based restricted stock units ("PRSUs"). One-third of the PRSUs may vest at the end of three separate performance periods spread over the three years following the date of grant based on the Issuer's relative total shareholder return as compared to a peer group of companies. The number of PRSUs reported represents the maximum that may be earned, which is 150% of the target number. No number of PRSUs is guaranteed to vest and the actual number of PRSUs that will vest at the end of each performance period may be anywhere from zero to the amount stated.
- Grant to reporting person of Restricted Stock Units under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan.
- 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 Ionis.

By: Patrick R. O'Neil, attorney-in-fact For: Onaiza Cadoret-Manier 01/19/2022

\*\* 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.