FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

| Washington, | D.C. 20549 | |
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STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

| OMB APPROVAL | | | | | | | | | |
|--------------------------|-----------|--|--|--|--|--|--|--|--|
| OMB Number: | 3235-0287 | | | | | | | | |
| Estimated average burden | | | | | | | | | |
| hours por rosponso: | 0.5 | | | | | | | | |

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* Baroldi Joseph (Last) (First) (Middle) 2855 GAZELLE COURT | | | | | | Issuer Name and Ticker or Trading Symbol IONIS PHARMACEUTICALS INC [IONS] Date of Earliest Transaction (Month/Day/Year) 01/15/2023 | | | | | | | 5. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director 10% Owner X Officer (give title Other (specify below) EVP, Chief Business Officer | | | | | |
|-------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------|--------------------------------------------|--------------|-----------------------|--------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------|-----|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|------------------------------------------------------------|-----------------|----------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------|----------------------------------------|--------------------------------------------------------------------------|------------------------------------------------------------------|--|
| (Street) CARLSBA | AD CA | te) (Z | 2010 Zip) | - | If Amendment, Date of Original Filed (Month/Day/Year) Ative Securities Acquired, Disposed of, or Benefi | | | | | | | Line | X Form filed by One Reporting Person Form filed by More than One Reporting Person | | | | | |
| 1. Title of Security (Instr. 3) 2. Transa Date | | | | | | | | 3. Transac Code (Ir 8) | tion | 4. Securities Acquired (A) Disposed Of (D) (Instr. 3, 4 | | | 5. Amount of | | Form: Direct | | 7. Nature of ndirect Beneficial Ownership (Instr. 4) | |
| 1. Title of Derivative Security (Instr. 3) | 2. Conversion or Exercise Price of Derivative Security | 3. Transaction Date (Month/Day/Year) | | puts, 4. Transa | tuts, calls, warrants, 4. Transaction of Operivative | | | uired, Disposed of, or Benefic, options, convertible securitie 6. Date Exercisable and Expiration Date (Month/Day/Year) 7. Title and A of Securities Underlying Derivative Se (Instr. 3 and 4 | | | | Amount es | 8. Price of Derivative Security (Instr. 5) | 9. Number derivative Securities Beneficiall Owned Following Reported Transactio (Instr. 4) | Owr Forr Dire or Ir (I) (I | 10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | Beneficial Ownership (Instr. 4) | |
| | | | | Code | v | (A) | (D) | Date Exercisab | | Expiration Date | Title | Amount or Number of Shares | | | | | | |
| Performance Restricted Stock Units ⁽¹⁾ | \$0.0 | 01/15/2023 | | A | | 12,290 | | (2) | | (2) | Common Stock | 12,290 | \$0.0 | 12,290 | | D | | |
| Restricted Stock Unit ⁽³⁾ | \$0.0 ⁽⁴⁾ | 01/15/2023 | | A | | 14,749 | | (5) | | (5) | Common Stock | 14,749 | \$0.0 | 58,099 | | D | | |
| Restricted Stock Unit ⁽⁶⁾ | \$0.0 ⁽⁴⁾ | 01/15/2023 | | A | | 1,800 | | (5) | | (5) | Common Stock | 1,800 | \$0.0 | 4,866 | | I | by Spouse | |

Explanation of Responses:

- 1. Grant to reporting person of Performance Restricted Stock Units under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan.
- 2. Represents an award of performance based restricted stock units ("PRSUs"). The PRSUs may vest at the end of the three-year performance period 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 200% 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 the performance period may be anywhere from zero to the amount stated.
- 3. Grant to reporting person of Restricted Stock Units under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan.
- 4. Each Restricted Stock Unit represents a contingent right to receive one share of Ionis common stock, or its equivalent cash value.
- 5. 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.
- 6. Grant to reporting person's spouse of Restricted Stock Units under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan.

<u>By: Patrick R. O'Neil, attorney-in-fact For: Joseph T. Baroldi</u>

** 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.