FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

| OMB APPROVAL | | | | | | | | | |
|--------------------------|-----|--|--|--|--|--|--|--|--|
| OMB Number: 3235-0287 | | | | | | | | | |
| Estimated average burden | | | | | | | | | |
| hours per response. | 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* <u>Diaz Allene M.</u> | | | | | 2. Issuer Name and Ticker or Trading Symbol IONIS PHARMACEUTICALS INC [IONS] | | | | |] (Che | Relationship of Reporting Person(s) to Issuer (Check all applicable) X Director 10% Owner | | | | | |
|--|--|------------|---|---|---|--|--------|---|---------------------------|---|---|---|---|--------------------------------------|-----------------|--|
| (Last) | ` | First) | (Middle) | | 3. Date of Earliest Transaction (Month/Day/Year) 07/03/2023 | | | | | | Officer (below) | give title | | ner (sp ow) | ecify | |
| 2855 GAZELLE COURT | | | | 4. | 4. If Amendment, Date of Original Filed (Month/Day/Year) | | | | | 6. Individual or Joint/Group Filing (Check Applicable Line) | | | | | | |
| (Street) CARLSI | BAD C | Ž A | 92010 | | | | | | | | X | | , | Reporting P than One F | | ng |
| (City) (State) (Zip) | | | | | Rule 10b5-1(c) Transaction Indication | | | | | | | | | | | |
| Check this box to indicate that a transaction was made pursuant to a contract, instruction or written plan that is intended to satis the affirmative defense conditions of Rule 10b5-1(c). See Instruction 10. | | | | | | | | | satisfy | | | | | | | |
| | Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned | | | | | | | | | | | | | | | |
| Date | | | action 2A. Deemed Execution Date if any (Month/Day/Yea | | Code (Instr. 5) | | | 5. Amoun Securities Beneficia Owned Fo Reported | s lly ollowing | 6. Ownershi Form: Direc (D) or Indire (I) (Instr. 4) | t Inct B | 7. Nature of Indirect Beneficial Ownership | | | | |
| | | | | | | Code V | Amount | (A) or (D) | Price | Transacti (Instr. 3 a | on(s) | | (1) | (Instr. 4) | | |
| 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 | | 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 Exerci Expiration Dat (Month/Day/Ye | te | Amount of | | 8. Price of Derivative Security (Instr. 5) | 9. Number derivative Securities Beneficial Owned Following Reported Transactio | ly Owner Form Direct or Inc. (I) (In | t (D) lirect | 11. Nature of Indirect Beneficial Ownership (Instr. 4) |
| | | | | Code | v | (A) | (D) | Date Exercisable | Expiration Date | Title | Amount or Number of Shares | | (Instr. 4) | ,,,,, | | |
| Non- Qualified Stock Option (right to buy) | \$41.08 | 07/03/2023 | | A | | 10,321 ⁽¹⁾ | | 07/03/2024 ⁽²⁾ | 07/02/2033 ⁽²⁾ | Common Stock | 10,321 | \$0.0 | 10,321 | |) | |
| Restricted Stock Unit | \$0.0 ⁽³⁾ | 07/03/2023 | | A | | 4,677 ⁽¹⁾ | | (4) | (4) | Common Stock | 4,677 | \$0.0 | 10,010 |)] |) | |

Explanation of Responses:

- 1. Pursuant to the Company's Non-Employee Director Compensation Policy, these grants were adjusted downward such that the non-employee Director's annual equity compensation in 2023 totals no more than \$450,000 based on the aggregate grant date fair value as determined in accordance with FASB Topic ASC 718.
- 2. Grant on July 3, 2023 to reporting person of stock options under the Amended and Restated Ionis Pharmaceuticals, Inc. 2002 Non-Employee Directors' Stock Option Plan. 100% of the shares subject to the option vest and become exercisable on either the first anniversary of the date of grant or the next regularly scheduled annual meeting of stockholders of the Company, whichever occurs earlier. The option is exercisable to 0 shares on July 3, 2023.
- 3. Each Restricted Stock Unit represents a contingent right to receive one share of Ionis common stock, or its equivalent cash value.
- 4. Grant on July 3, 2023 to reporting person of Restricted Stock Unit award under the Amended and Restated Ionis Pharmaceuticals, Inc. 2002 Non-Employee Directors' Stock Option Plan. These Restricted Stock Units vest 100% on either the first anniversary of the date of grant or the next regularly scheduled annual meeting of stockholders of the Company, whichever occurs earlier, and will be delivered to the reporting person on the July 15th following the vesting date. The Restricted Stock Unit is vested as to 0 shares on July 3, 2023.

By: Patrick R. O'Neil, attorney-07/05/2023 in-fact For: Allene M. Diaz

** 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.