

| 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>BERTHELSEN SPENCER R</u> (Last) (First) (Middle) <u>2855 GAZELLE COURT</u> (Street) <u>CARLSBAD CA 92010</u> (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) <input checked="" type="checkbox"/> Director 10% Owner Officer (give title below) Other (specify below) | |
| | 3. Date of Earliest Transaction (Month/Day/Year) <u>07/01/2024</u> | | |
| | 4. If Amendment, Date of Original Filed (Month/Day/Year) | 6. Individual or Joint/Group Filing (Check Applicable Line) <input checked="" type="checkbox"/> Form filed by One Reporting Person <input type="checkbox"/> Form filed by More than One Reporting Person | |
| | 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. | | |

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 Indirect 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 |
| Non-Qualified Stock Option (right to buy) | \$47.11 | 07/01/2024 | | A | | 10,111 ⁽¹⁾ | | 07/01/2025 ⁽²⁾ | 06/30/2034 ⁽²⁾ | Common Stock | 10,111 | \$0.0 | 10,111 | D | |
| Restricted Stock Unit | \$0.0 ⁽³⁾ | 07/01/2024 | | A | | 4,079 ⁽¹⁾ | | (4) | (4) | Common Stock | 4,079 | \$0.0 | 8,756 | D | |

Explanation of Responses:

- 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 2024 totals no more than \$450,000 based on the aggregate grant date fair value as determined in accordance with FASB Topic ASC 718.
- Grant on July 1, 2024 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 1, 2024.
- Each Restricted Stock Unit represents a contingent right to receive one share of Ionis common stock, or its equivalent cash value.
- Grant on July 1, 2024 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 1, 2024.

By: Patrick R. O'Neil, attorney-in-fact For: Spencer R. Berthelsen 07/02/2024

** 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.