

FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

| OMB APPROVAL | |
|--|-----------|
| OMB Number: | 3235-0287 |
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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

Check this box to indicate that a transaction was made pursuant to a contract, instruction or written plan for the purchase or sale of equity securities of the issuer that is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c). See Instruction 10.

| | | | | | | | | | |
|---|-----------|--------------|--|--|--|---|--|--|--|
| 1. Name and Address of Reporting Person* <u>Birchler Brian</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, Corp and Development Ops</u> | | | |
| (Last) | (First) | (Middle) | 3. Date of Earliest Transaction (Month/Day/Year) <u>01/15/2026</u> | | | | | | |
| <u>2855 GAZELLE COURT</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 | | | |
| (Street) | (City) | (State) | (Zip) | | | | | | |
| <u>CARLSBAD</u> | <u>CA</u> | <u>92010</u> | | | | | | | |
| (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 Indirect Beneficial Ownership (Instr. 4) |
|---------------------------------|--------------------------------------|--|--------------------------------|---|---|------------|------------------------|---|--|---|
| | | | Code | V | Amount | (A) or (D) | Price | | | |
| Common Stock | 01/15/2026 | | M ⁽¹⁾ | | 20,089 ⁽¹⁾ | A | \$0.0 | 68,915 | D | |
| Common Stock | 01/16/2026 | | S ⁽²⁾ | | 8,480 ⁽²⁾ | D | \$75.11 ⁽³⁾ | 60,435 | D | |

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 ⁽⁴⁾ | \$0.0 | 01/15/2026 | | A | | 25,800 | | 01/15/2029 ⁽⁵⁾ | (5) | Common Stock | 25,800 | \$0.0 | 79,138 | D | |
| Restricted Stock Unit | \$0.0 ⁽⁶⁾ | 01/15/2026 | | M | | 20,089 | | 01/15/2026 ⁽⁷⁾ | (7) | Common Stock | 20,089 | \$0.0 | 41,126 | D | |
| Restricted Stock Unit ⁽⁸⁾ | \$0.0 ⁽⁶⁾ | 01/15/2026 | | A | | 9,675 | | 01/15/2027 ⁽⁷⁾ | (7) | Common Stock | 9,675 | \$0.0 | 50,801 | D | |

Explanation of Responses:

- Acquired pursuant to vesting and release of shares in accordance with Restricted Stock Unit awards.
- 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 \$75.07 to \$75.14 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.
- Grant to reporting person of Performance Restricted Stock Units (RSUs) under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan.
- The RSUs 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 RSUs reported represents the maximum that may be earned, which is 200% of the target number. No number of RSUs is guaranteed to vest and the actual number of RSUs that will vest at the end of the performance period may be anywhere from zero to the amount stated.
- 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.
- Grant to reporting person of Restricted Stock Units under the Ionis Pharmaceuticals, Inc. Amended and Restated 2011 Equity Incentive Plan.

By: Patrick R. O'Neil, attorney-in-fact For: Brian Birchler 01/20/2026

** 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.