

| 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>PARSHALL B LYNNE</u> (Last) (First) (Middle) <u>C/O IONIS PHARMACEUTICALS, INC.</u> <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>01/15/2021</u> | |
| 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 Indirect Beneficial Ownership (Instr. 4) |
|---------------------------------|--------------------------------------|--|--------------------------------|---|---|------------|---------|---|--|---|
| | | | Code | V | Amount | (A) or (D) | Price | | | |
| Common Stock | 01/15/2021 | 01/15/2021 | M ⁽¹⁾ | | 10,655 ⁽¹⁾ | A | \$0 | 68,119 | D | |
| Common Stock | 01/15/2021 | 01/15/2021 | F ⁽²⁾ | | 2,741 ⁽²⁾ | D | \$61.28 | 65,378 | 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 |
| Restricted Stock Units | (3) | 01/15/2021 | 01/15/2021 | M | | | 10,655 | (4) | (4) | Common Stock | 10,655 | \$0 | 5,754 | D | |

Explanation of Responses:

- Acquired pursuant to vesting and release of shares in accordance with Restricted Stock Unit awards.
- Shares withheld to cover the required tax withholding obligations pursuant to 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 monthly 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.

Remarks:

/s/Patrick R. O'Neil, attorney- 01/20/2021
in-fact

** 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.