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FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

| Check this box if no longer subject to |
|--|
| Section 16. Form 4 or Form 5 |
| obligations may continue. See |
| Instruction 1(b). |

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

OMB APPROVAL OMB Number: 3235-0287 Estimated average burden

| Estimated average burden | 0.5 |
|--------------------------|-----|
| hours per response: | 0.5 |

| 1. Name and Address of Reporting Person [*] PARSHALL B LYNNE | | | 2. Issuer Name and Ticker or Trading Symbol IONIS PHARMACEUTICALS INC [IONS | 5. Relationship of Reporting Person(s) to Issuer (Check all applicable) | | | | | |
|--|---------|----------|---|--|---|-----------------------|--|--|--|
| PARSHALL | | | 1 | X | Director | 10% Owner | | | |
| (Last) | (First) | (Middle) | [| | Officer (give title below) | Other (specify below) | | | |
| C/O IONIS PH | () | | 3. Date of Earliest Transaction (Month/Day/Year) 03/12/2019 | | , |) | | | |
| 2855 GAZELL | E COURT | | | | | | | | |
| (Street) CARLSBAD CA 92010 | | 92010 | 4. If Amendment, Date of Original Filed (Month/Day/Year) | 6. Indi Line) X | lividual or Joint/Group Filing (Check Applicable Form filed by One Reporting Person Form filed by More than One Reporting | | | | |
| (City) | (State) | (Zip) | — | | Person | an one reporting | | | |

Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned

| Table 1 Non Derivative occurrice, Disposed of, of Derivitiany office | | | | | | | | | | | | |
|--|---|--|--|---|---|---|--|---|--|--|--|--|
| 2. Transaction Date (Month/Day/Year) | 2A. Deemed Execution Date, if any (Month/Day/Year) | Transaction Code (Instr. | | Disposed Of | | | | 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 | Transaction(s) (Instr. 3 and 4) | | (1150.4) | | | |
| 03/12/2019 | 03/12/2019 | M ⁽¹⁾ | | 8,334(1) | Α | \$39.87 | 61,011 | D | | | | |
| 03/12/2019 | 03/12/2019 | S ⁽¹⁾ | | 8,334(1) | D | \$75 | 52,677 | D | | | | |
| - | 2. Transaction Date (Month/Day/Year) 03/12/2019 | 2. Transaction Date (Month/Day/Year) 2A. Deemed Execution Date, if any (Month/Day/Year) 03/12/2019 03/12/2019 | 2. Transaction Date (Month/Day/Year) 2A. Deemed Execution Date, if any (Month/Day/Year) 3. Transa Code (8) 03/12/2019 03/12/2019 M ⁽¹⁾ | 2. Transaction Date (Month/Day/Year) 2A. Deemed Execution Date, if any (Month/Day/Year) 3. Transaction Code (Instr. 8) 03/12/2019 03/12/2019 M ⁽¹⁾ | 2. Transaction Date (Month/Day/Year) 2A. Deemed Execution Date, if any (Month/Day/Year) 3. Transaction Code (Instr. 8) 4. Securities / Disposed Of (5) 03/12/2019 03/12/2019 M ⁽¹⁾ 8,334 ⁽¹⁾ | $ \begin{array}{c} 2. \mbox{ Transaction Date (Month/Day/Year)} \\ \hline 24. \mbox{ Deemed Execution Date, if any (Month/Day/Year)} \\ \hline & & & & & \\ \hline & & & & \\ \hline & & & & \\ \hline & & & &$ | 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) 0.3/12/2019 0.3/12/2019 M ⁽¹⁾ 8,334 ⁽¹⁾ A \$39.87 | 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) 03/12/2019 03/12/2019 M ⁽¹⁾ 8,334 ⁽¹⁾ A \$39.87 61,011 | 2. Transaction Date (Month/Day/Year) 2A. Deemed Execution Date, if any (Month/Day/Year) 3. Transaction Code [Instr. 4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5) 5. Amount of Securities Beneficially Owned Following (D) 6. Ownership Form: Direct (D) or Indirect (D) or Indirect (D) or Indirect (D) (Instr. 4) 03/12/2019 03/12/2019 M ⁽¹⁾ 8,334 ⁽¹⁾ A \$39.87 61,011 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. Transa Code (8) | | of | | 6. Date Exerc Expiration Da (Month/Day/Y | ate | 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 | Amount or Number of Shares | | | | |
| Employee Stock Option (right to buy) | \$39.87 | 03/12/2019 | 03/12/2019 | М | | 8,334 | | 01/02/2018 | 01/01/2021 | Common Stock | 8,334 | \$0 | 57,500 | D | |

Explanation of Responses:

1. Acquired as a result of exercising a stock option pursuant to Rule 10b5-1 Trading Plan. The purchase and sale reported on this Form 4 was effective pursuant to Rule 10b5-1 Trading Plan adopted by the reporting person on 8/8/2017.

Remarks:

/s/Patrick R. O'Neil, attorney-

in-fact

03/14/2019

** 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.