| SEC | Form | 4 |
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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
hours per response: 0.5

| 1. Walle and Address of Reporting Ferson |         |          | 2. Issuer Name and Ticker or Trading Symbol<br>IONIS PHARMACEUTICALS INC [ IONS ] | 5. Relationship of Reporting Person(s) to Issuer<br>(Check all applicable) |                                  |                       |  |  |  |
|--|---------|----------|---|--|----------------------------------|-----------------------|--|--|--|
| PARSHALL B LYNNE                         |         |          |   | X  | Director                         | 10% Owner             |  |  |  |
| (Last)                                   | (First) | (Middle) | 3. Date of Earliest Transaction (Month/Day/Year)                                  | X  | Officer (give title below)       | Other (specify below) |  |  |  |
| C/O IONIS PHARMACEUTICALS, INC.          |         |          | 01/01/2018  | COO  |                                  |                       |  |  |  |
| 2855 GAZELLI                             | E COURT |          |   |  |                                  |                       |  |  |  |
| (Street)                                 |         |          | 4. If Amendment, Date of Original Filed (Month/Day/Year)                          | 6. Indiv<br>Line)  | vidual or Joint/Group Filir      | ng (Check Applicable  |  |  |  |
| CARLSBAD                                 | CA      | 92010    |   | X  | Form filed by One Re             | porting Person        |  |  |  |
|  | -       |          |   |  | Form filed by More the<br>Person | an One Reporting      |  |  |  |
| (City)                                   | (State) | (Zip)    |   | 1  |                                  |                       |  |  |  |

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

| 1. Title of Security (Instr. 3) | 2. Transaction<br>Date<br>(Month/Day/Year) | 2A. Deemed<br>Execution Date,<br>if any<br>(Month/Day/Year) |                  |   | 4. Securities Acquired (A) or<br>Disposed Of (D) (Instr. 3, 4 and 5) |               |          | 5. Amount of<br>Securities<br>Beneficially<br>Owned Following<br>Reported | Form: Direct | 7. Nature of<br>Indirect<br>Beneficial<br>Ownership |
|---------------------------------|--|---|------------------|---|--|---------------|----------|---|--------------|---|
|                                 |  |   | Code             | v | Amount   | (A) or<br>(D) |          | Transaction(s)<br>(Instr. 3 and 4)  |              | (Instr. 4)  |
| Common Stock                    | 01/01/2018                                 | 01/01/2018  | J <sup>(1)</sup> | v | 86(1)  | A             | \$42.755 | 25,827  | D            |   |

# Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

| 1. Title of<br>Derivative<br>Security<br>(Instr. 3) | 2.<br>Conversion<br>or Exercise<br>Price of<br>Derivative<br>Security | 3. Transaction<br>Date<br>(Month/Day/Year) | 3A. Deemed<br>Execution Date,<br>if any<br>(Month/Day/Year) | 4.<br>Transa<br>Code (<br>8) |   | Derivative |     | 6. Date Exercisable and<br>Expiration Date<br>(Month/Day/Year) |                    | 7. Title and Amount<br>of Securities<br>Underlying<br>Derivative Security<br>(Instr. 3 and 4) |                                     | 8. Price of<br>Derivative<br>Security<br>(Instr. 5) | 9. Number of<br>derivative<br>Securities<br>Beneficially<br>Owned<br>Following<br>Reported<br>Transaction(s) | 10.<br>Ownership<br>Form:<br>Direct (D)<br>or Indirect<br>(I) (Instr. 4) | 11. Nature<br>of Indirect<br>Beneficial<br>Ownership<br>(Instr. 4) |
|---|---|--|---|------------------------------|---|------------|-----|--|--------------------|---|-------------------------------------|---|--|--|--|
|   |   |  |   | Code                         | v | (A)        | (D) | Date<br>Exercisable  | Expiration<br>Date | Title   | Amount<br>or<br>Number<br>of Shares |   | (Instr. 4)   |  |  |
| Employee<br>Stock<br>Option<br>(right to<br>buy)    | \$49.25   | 01/02/2018                                 | 01/02/2018  | A                            |   | 103,575    |     | 01/02/2019 <sup>(2)</sup>                                      | 01/01/2025         | Common<br>Stock   | 103,575                             | \$0   | 103,575  | D  |  |

#### Explanation of Responses:

1. Reporting 86 shares acquired under the Ionis Pharmaceuticals, Inc. Amended and Restated 2000 Employee Stock Purchase Plan on January 1, 2018. These 86 shares may not be sold until July 2, 2018. 2. Grant of 1/2/2018 to reporting person of stock options under the Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan. 25% of the shares subject to the option vest and become exercisable on 1/2/2019.

Thereafter, the remaining shares subject to the option vest and become exercisable in 36 equal monthly installments, at the rate of 25,894 shares per year. Following this transaction, the option was exercisable as to 0 on 1/2/2018.

### **Remarks:**

/s/B. Lynne Parshall, attorney-

<u>in-fact</u>

01/02/2018

\*\* 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.