FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

| Washington, | D.C. | 20549 |
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| l | OMB APPRO | VAL |
|---|------------------------|-----------|
| | OMB Number: | 3235-0287 |
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| l | hours per response: | 0.5 |

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

| | | | | | | | . , | | | | | | | | | | | | | |
|-----------------------------------------------------------|-----------------------------------------------------------------------|--------------------------------------------|----------------------------------------------|---------|--------------------------------------------------|-------------------------------------------------------------------------------|-------------------------------------------------------------|-------------------------|---------------------------------------|--------------------------------------|-------------------|----------------------------|--------------------------------|------------------------------------|--------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------|---------------|--------------------------------------------------------------------------|--------------------------------------------------------------------|--|
| 1. Name and Address of Reporting Person* PARSHALL B LYNNE | | | | | | 2. Issuer Name and Ticker or Trading Symbol IONIS PHARMACEUTICALS INC [IONS | | | | | | | | | Relationship of Reporting Person(s) to Issuer (Check all applicable) X Director 10% Owner | | | | | |
| (Last) | ` | , | (Middle) | | 3. Date of Earliest Transaction (Month/Day/Year) | | | | | | | | | | | r (give title | | Other (s below) | | |
| C/O IONIS PHARMACEUTICALS, INC. 2855 GAZELLE COURT | | | | | | /27/2 | | Doto | of Original | Filod | (Month/D | ov/Voor) | | 6 Ind | ividual or | loint/Croun | Filing | y (Chook An | plianbla | |
| (Street) | BAD C. | A | 92010 | | - 4. | 4. If Amendment, Date of Original Filed (Month/Day/Year) | | | | | | | | | ividual or Joint/Group Filing (Check Appli Form filed by One Reporting Person Form filed by More than One Reportir | | | | n | |
| (City) | (S | tate) | (Zip) | | | | | | | | | | | | Perso | า | | | | |
| | | Tab | le I - No | n-Deriv | /ative | Se | curitie | s Ac | quired, | Dis | posed c | of, or B | enefic | cially | Owned | i | | | | |
| Date | | | | | action Day/Yea | ar) E | 2A. Deemed Execution Date, if any (Month/Day/Year) | | Code (| Transaction Disposed Code (Instr. 5) | | ties Acqui I Of (D) (Ir | | 4 and Securiti Benefic Owned | | es ally Following | Form (D) o | n: Direct r Indirect istr. 4) | 7. Nature of Indirect Beneficial Ownership | |
| | | | | | | | | | Code | v | Amount | (A) or (D) Pr | | ice | Reported Transaction(s) (Instr. 3 and 4) | | | | (Instr. 4) | |
| Common Stock 02/27 | | | | | 7/2019 | 2019 02/27/2019 | | M ⁽¹⁾ | | 8,3330 | (1) A | . \$ | \$39.87 | | 1,010 | | D | | | |
| Common | Common Stock 02/27/ | | | | 7/2019 | 9 | 02/27/2019 | | S ⁽¹⁾ | | 8,333(| (1) D | | \$70 | 52 | ,677 | D | | | |
| | | 7 | able II - | | | | | | uired, C s, optior | | | | | | Owned | | | | | |
| 1. Title of Derivative Security (Instr. 3) | 2. Conversion or Exercise Price of Derivative Security | 3. Transaction Date (Month/Day/Year) | 3A. Deem Execution if any (Month/Da | Date, | 4. Transa Code (8) | | n of | | 6. Date Ex Expiration (Month/Da | Date | Amount of | | of s ng re Secu | S (1 | 8. Price of Derivative Security (Instr. 5) | 9. Number derivative Securities Beneficial Owned Following Reported Transactio (Instr. 4) | ly | 10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 11. Nature of Indirect Beneficial Ownership (Instr. 4) | |
| | | | | | Code | v | (A) | (D) | Date Exercisab | | xpiration late | Title | Amo or Num of Shar | ber | | | | | | |
| Employee Stock Option (right to buy) | \$39.87 | 02/27/2019 | 02/27/2 | 2019 | 9 M | | 8,333 | | 01/02/201 | .8 0 | 1/01/2021 | Commor Stock | 8,3 | 33 | \$0 | 65,834 | ı | 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-

03/01/2019

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.