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 | STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP |
|---------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------|
| Instruction 1(b). | Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 |
| | |

| | OMB APPROVAL | | | | | | | | | | |
|---|--------------------------|-----------|--|--|--|--|--|--|--|--|--|
| | OMB Number: | 3235-0287 | | | | | | | | | |
| | Estimated average burden | | | | | | | | | | |
| - | hours nor resnance. | 0.5 | | | | | | | | | |

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* Geary Richard S (Last) (First) (Middle) C/O IONIS PHARMACEUTICALS, INC. 2855 GAZELLE COURT | | | | | 3. D 07/ | Issuer Name and Ticker or Trading Symbol IONIS PHARMACEUTICALS INC IONS IONS | | | | | | | | | Relationship of Reporting Person(s) to Issuer Check all applicable) Director 10% Owner X Officer (give title other (specify below) SVP, Development | | | Owner r (specify r) | |
|----------------------------------------------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|--|---------------------|--------------------------------------|----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|------|---------------------------------------------------------------------------------------------|------|--------|-----------------------------------------------------------------------------------------------------------------|---|--------------------------|---------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------|-------------------------------------------------------------------|--------------------------------------------------------------------|------------|
| (Street) CARLSBAD CA 92010 (City) (State) (Zip) | | | | | | 4. If Amendment, Date of Original Filed (Month/Day/Year) | | | | | | | | | Individual or Joint/Group Filing (Check Applicable Line) X Form filed by One Reporting Person Form filed by More than One Reporting Person | | | | |
| | Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned | | | | | | | | | | | | | | | | | | |
| 1. Title of Security (Instr. 3) 2. Transact Date (Month/Date) | | | | | | Execution Date, | | | | | ies Acquired (A) o Of (D) (Instr. 3, 4 | | | and 5) Secu Bene | | cially d Following | 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) | | | (111501.4) |
| Common Stock 07/01/2 | | | | | 2016 07/01/201 | | 2016 | J ⁽¹⁾ | V | 163(1) | | A | \$20.757 | | 8,517 | | 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) | Derivative Conversion Date Execution E Security or Exercise (Month/Day/Year) if any | | n Date, ay/Year) | 4. Transaction Code (Instr. 8) | | of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) | | 6. Date Exercisable and Expiration Date (Month/Day/Year) Date Exercisable Expiration Date | | | 7. Title and Amount of Securities Underlying Derivative Security (Instr. and 4) Amoun or Numbe of Title Shares | | nstr. 3 nount mber | t r | | 9. Number of derivative Securities Beneficially Owned Following Reported Transaction (Instr. 4) | Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 11. Nature of Indirect Beneficial Ownership (Instr. 4) | |

Explanation of Responses:

1. Reporting 163 shares acquired under the Ionis Pharmaceuticals, Inc. Amended and Restated 2000 Employee Stock Purchase Plan on July 1, 2016. These 163 shares may not be sold until January 2, 2017.

Remarks:

/s/B. Lynne Parshall, attorney-07/01/2016 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.