FORM 4

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

| OMB APPROVAL | | | | | | | | | | | | |
|--------------|----------|--|--|--|--|--|--|--|--|--|--|--|
| OMB Number: | 3235-028 | | | | | | | | | | | |
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0.5

hours per response:

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP Estimated average burden

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* BENNETT C FRANK (Last) (First) (Middle) C/O IONIS PHARMACEUTICALS, INC. 2855 GAZELLE COURT | | | | | 3. E 11/ | 2. Issuer Name and Ticker or Trading Symbol IONIS PHARMACEUTICALS INC [IONS] 3. Date of Earliest Transaction (Month/Day/Year) 11/07/2016 4. If Amendment, Date of Original Filed (Month/Day/Year) | | | | | | | | S. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director | | | | | | |
|---|--|--------------------------------------|---|----------|-------------|---|-------|------------------|-------------------|--|--------------------|---|--------------------------------|--|--|--|--------------------------------------|--|--|--|
| (Street) CARLSE (City) | | | 92010 (Zip) | | - | | | | | | | | | | 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. Transac Date (Month/Date) | | | | | ar) E | 2A. Deemed Execution Date, if any (Month/Day/Year) | | Code (Instr. | | 4. Securities Acquired (A) Disposed Of (D) (Instr. 3, 4 | | | 4 and Securiti Benefici | | es ally Following | Form (D) or | : Direct Indirect str. 4) | 7. Nature of Indirect Beneficial Ownership (Instr. 4) | | |
| | | | | | | | | | | v | Amount (A) or (D) | | or Pri | ice | Transaction(s) (Instr. 3 and 4) | | | | msu. 4) | |
| Common Stock 11/07/2 | | | | | | 2016 11/07/2016 | | | M ⁽¹⁾ | | 5,000 | (1) A | \$1 | 11.27 | 15,803 | | D | | | |
| Common Stock 11/07/2 | | | | | 7/2016 | 2016 11/07/2016 | | S ⁽¹⁾ | | 5,000 | (1) D \$ | | \$34 | 10,803 | | D | | | | |
| | | | | (e.g., p | outs, | | s, wa | rrants | s, optio | ns, c | onverti | ble sec | uritie | s) ¯ | | | | | | |
| 1. Title of Derivative Security (Instr. 3) | 2. Conversion or Exercise Price of Derivative Security | 3. Transaction Date (Month/Day/Year) | 3A. Deeme Execution if any (Month/Da | Date, | | ransaction Code (Instr. | | n of | | 6. Date Exercisa Expiration Date (Month/Day/Yea | | 7. Title and Amount of Securities Underlying Derivative Securit (Instr. 3 and 4) | | | 8. Price of Derivative Security (Instr. 5) | 9. Number derivative Securities Beneficiall Owned Following Reported Transactio (Instr. 4) | Own For Dire or I (I) (I | 10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 11. Nature of Indirect Beneficial Ownership (Instr. 4) | |
| | | | | | Code | v | (A) | (D) | Date Exercisal | | expiration Pate | Title | Amo or Num of Shar | ber | | | | | | |
| Employee Stock Option (right to buy) | \$11.27 | 11/07/2016 | 11/07/2 | 2016 | М | | | 5,000 | 01/04/20 | 14 0 | 1/03/2017 | Commor Stock | 5,00 | 00 | \$0 | 22,805 | | D | | |

Explanation of Responses:

1. Acquired as a result of exercising a stock option that was scheduled to expire on 1/3/17. The purchase and sale reported on this Form 4 was effective pursuant to a Rule 10b5-1 Trading Plan adopted by the reporting person on 9/16/17.

Remarks:

11/07/2016 /s/C. Frank Bennett

** Signature of Reporting Person Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

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.

^{*} 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).