FORM 4

## UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

| OMB APPROVAL           |           |  |  |  |  |  |  |  |  |
|------------------------|-----------|--|--|--|--|--|--|--|--|
| OMB Number:            | 3235-0287 |  |  |  |  |  |  |  |  |
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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

| Name and Address of Reporting Person*  |   |                  |            |                |                                       |  |              |                                     |                        |         |   |                  | 5. Relationship of Reporting Person(s) to Issuer (Check all applicable) |   |  |                                 |  |   |              |            |
|--|---|------------------|------------|----------------|---------------------------------------|--|--------------|-------------------------------------|------------------------|---------|---|------------------|---|---|--|---------------------------------|--|---|--------------|------------|
| HERMAN JOAN E  |   |                  |            | l <del>i</del> | 1                                     |  |              |                                     |                        |         |   |                  | X Director  |   |  | 10% Ov                          | vner   |   |              |            |
| (Last)   | (Fi   | rst)             | Middle)    |                | Ľ                                     | 1  |              |                                     |                        |         |   |                  |   |   | Officer (give title below)   |                                 |  | specify   |              |            |
| C/O ION  | IS PHARN  | ,<br>IACEUTICALS | . INC.     |                |                                       | 3. Date of Earliest Transaction (Month/Day/Year)         |              |                                     |                        |         |   |                  |   |   |  |                                 |  |   |              |            |
| 2855 GAZELLE COURT   |   |                  |            | 06/            | 06/10/2020                            |  |              |                                     |                        |         |   |                  |   |   |  |                                 |  |   |              |            |
| 2033 GAZELLE COURT   |   |                  |            |                | 4. If                                 | 4. If Amendment, Date of Original Filed (Month/Day/Year) |              |                                     |                        |         |   |                  |   | 6. Ir   | 6. Individual or Joint/Group Filing (Check Applicable  |                                 |  |   |              |            |
| (Street)   |   |                  |            |                |                                       |  |              |                                     |                        |         |   |                  |   |   | Line   | ,                               |  |   |              |            |
| CARLSI   | BAD C   | A                | 92010      |                |                                       |  |              |                                     |                        |         |   |                  |   |   | -  | -                               | ,  | •   | orting Perso |            |
| ,  |   |                  |            |                |                                       |  |              |                                     |                        |         |   |                  |   | Form f<br>Persor                                    | filed by More than One Reporting<br>on   |                                 |  | rting   |              |            |
| (City)   | (S  | tate)            | (Zip)      |                |                                       |  |              |                                     |                        |         |   |                  |   |   |  |                                 |  |   |              |            |
|  |   | Tab              | le I - Non | -Deriv         | ative                                 | Sec  | uriti        | ies Ac                              | quir                   | ed, [   | Dis   | osed c           | of, oı  | r Ben   | eficial  | ly Owne                         | d  |   |              |            |
| 1. Title of Security (Instr. 3)  2. Transac Date (Month/Date)  |   |                  |            |                | Execution Date,                       |  |              | , Tr                                | Code (Instr. 5)        |         |   |                  |   | Benefici<br>Owned                                   | es For<br>ally (D)<br>Following (I) (  |                                 | n: Direct<br>or Indirect<br>ostr. 4)                                     | 7. Nature<br>of Indirect<br>Beneficial<br>Ownership |              |            |
|  |   |                  |            |                |                                       |  |              |                                     | C                      | ode     | v   | Amount           |   | (A) or<br>(D)                                       | Price  | Reporte<br>Transac<br>(Instr. 3 | tion(s)  |   |              | (Instr. 4) |
| Common Stock 06/10   |   |                  | 06/10      | )/2020         |                                       | N  | <b>1</b> (1) |                                     | 3,556 <sup>(1)</sup> A |         | \$0   | 3,               | 3,556   |   | D  |                                 |  |   |              |            |
|  | Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned |                  |            |                |                                       |  |              |                                     |                        |         |   |                  |   |   |  |                                 |  |   |              |            |
|  |   |                  | (          | e.g., p        | uts,                                  | calls  | , wa         | rrants                              | s, op                  | tions   | s, c  | onverti          | ble s   | secur   | ities)   |                                 |  |   |              |            |
| 1. Title of Derivative Security (Instr. 3)  2. Conversion or Exercise Price of Derivative Security  (Instr. 3)  3. Transaction Date (Month/Day/Year)  (Month/Day/Year)  3A. Deemed Execution Date, if any (Month/Day/Year) |   |                  | Date,      |                | ransaction of Code (Instr. Derivative |  | Expir        | Expiration Date<br>(Month/Day/Year) |                        |         | 7. Title and<br>Amount of<br>Securities<br>Underlying<br>Derivative Securit<br>(Instr. 3 and 4) |                  | 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)<br>(Instr. 4) |                                 | 10.<br>Ownership<br>Form:<br>Direct (D)<br>or Indirect<br>(I) (Instr. 4) | Beneficial<br>Ownership<br>(Instr. 4)               |              |            |
|  |   |                  |            |                | Code                                  | v  | (A)          | (D)                                 | Date<br>Exerc          | cisable |   | xpiration<br>ate | Title   | N<br>O  | Amount<br>or<br>Number<br>of<br>Shares   |                                 |  |   |              |            |
| Restricted<br>Stock Unit   | (2)   | 06/10/2020       | 06/10/20   | )20            | M                                     |  |              | 3,556                               | (                      | (3)     |   | (3)              | Com   |   | 3,556  | \$0                             | 10,665   | 5   | D            |            |

## **Explanation of Responses:**

- 1. Acquired pursuant to vesting and release of shares pursuant to a Restricted Stock Unit Award
- 2. Each Restricted Stock Unit represents a contingent right to receive one share of Ionis common stock, or its equivalent cash value.
- 3. Restricted Stock Units vest in four equal annual installments. Upon vesting, the Restricted Stock Units will be paid in whole shares of Ionis common stock or cash as may be determined by the Company.

## Remarks:

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

06/17/2020

\*\* Signature of Reporting Person

Date

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

- $^{\star}$  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.

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