

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

Check this box if no longer subject to  
Section 16. Form 4 or Form 5  
obligations may continue. See  
Instruction 1(b).

Check this box to indicate that a  
transaction was made pursuant to a  
contract, instruction or written plan for  
the purchase or sale of equity  
securities of the issuer that is  
intended to satisfy the affirmative  
defense conditions of Rule 10b5-1(c).  
See Instruction 10.

|                                                                                                                                                                                                       |                                                                                                                                                                                                                                       |                                                                                                                                                                                                                                                                                                                                                                                       |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| 1. Name and Address of Reporting Person*<br><u>Reikes Peter N</u><br><br>(Last) (First) (Middle)<br><u>2855 GAZELLE COURT</u><br><br>(Street)<br><u>CARLSBAD CA 92010</u><br><br>(City) (State) (Zip) | 2. Issuer Name and Ticker or Trading Symbol<br><u>IONIS PHARMACEUTICALS INC [ IONS ]</u><br><br>3. Date of Earliest Transaction (Month/Day/Year)<br><u>07/15/2026</u><br><br>4. If Amendment, Date of Original Filed (Month/Day/Year) | 5. Relationship of Reporting Person(s) to Issuer<br>(Check all applicable)<br><input checked="" type="checkbox"/> Director 10% Owner<br>Officer (give title below) Other (specify below)<br><br>6. Individual or Joint/Group Filing (Check Applicable Line)<br><input checked="" type="checkbox"/> Form filed by One Reporting Person<br>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. Transaction Date (Month/Day/Year) | 2A. Deemed Execution Date, if any (Month/Day/Year) | 3. Transaction Code (Instr. 8) |   | 4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5) |            |       | 5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4) | 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 |                                                                                               |                                                          |                                                       |

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) | 2. Conversion or Exercise Price of Derivative Security | 3. Transaction Date (Month/Day/Year) | 3A. Deemed Execution Date, if any (Month/Day/Year) | 4. Transaction Code (Instr. 8) | 5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) |       | 6. Date Exercisable and Expiration Date (Month/Day/Year) |                 | 7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4) |                            | 8. Price of Derivative Security (Instr. 5) | 9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4) | 10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 11. Nature of Indirect Beneficial Ownership (Instr. 4) |
|--------------------------------------------|--------------------------------------------------------|--------------------------------------|----------------------------------------------------|--------------------------------|----------------------------------------------------------------------------------------|-------|----------------------------------------------------------|-----------------|-----------------------------------------------------------------------------------|----------------------------|--------------------------------------------|----------------------------------------------------------------------------------------------------|-----------------------------------------------------------|--------------------------------------------------------|
|                                            |                                                        |                                      |                                                    |                                | Code                                                                                   | V     | Date Exercisable                                         | Expiration Date | Title                                                                             | Amount or Number of Shares |                                            |                                                                                                    |                                                           |                                                        |
| Restricted Stock Unit                      | \$0.0 <sup>(1)</sup>                                   | 07/15/2026                           |                                                    | A                              |                                                                                        | 3,399 | (2)                                                      | (2)             | Common Stock                                                                      | 3,399                      | \$0.0                                      | 3,399                                                                                              | D                                                         |                                                        |

Explanation of Responses:

1. Each Restricted Stock Unit represents a contingent right to receive one share of Ionis common stock, or its equivalent cash value.
2. Grant on July 15, 2026 to reporting person of Restricted Stock Unit Award under the Ionis Pharmaceuticals, Inc. Amended and Restated 2002 Non-Employee Directors' Stock Option Plan. Restricted Stock Units vest in three equal annual installments, the first installment vesting on July 15, 2027. Upon vesting, the restricted stock units will be paid out in whole shares of Ionis common stock or cash as may be determined by the Company. The RSU shall be fully vested on July 15, 2029. The RSU is vested as to 0 shares on July 15, 2026.

By: Patrick R. O'Neil, attorney-  
in-fact For: Peter N. Reikes 07/17/2026

\*\* 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.