

| OMB APPROVAL                                 |           |
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**STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP**

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*<br><u>IONIS PHARMACEUTICALS INC</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>AKCEA THERAPEUTICS, INC. [ AKCA ]</u> | 5. Relationship of Reporting Person(s) to Issuer (Check all applicable)<br><br>Director <input checked="" type="checkbox"/> 10% Owner<br><br>Officer (give title below) Other (specify below) |
|  | 3. Date of Earliest Transaction (Month/Day/Year)<br><u>12/17/2019</u>                   |   |
| 4. If Amendment, Date of Original Filed (Month/Day/Year)   |   |   |

**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 |   |  |   |
| Common Stock                    | 12/17/2019                           |  | j <sup>(1)</sup>               |   | 6,873,344   | A          | (1)   | 77,094,682  | 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) | 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) |
|--|--|--------------------------------------|--|--------------------------------|--|--|-----------------|---|--|--|---|--|
|  |  |                                      |  |                                |  | Date Exercisable   | Expiration Date |   |  |  |   |  |

**Explanation of Responses:**

1. Shares issued in satisfaction of the Issuer's obligations to the Reporting Person pursuant to that certain Development, Commercialization and License Agreement, dated December 18, 2015, between the Issuer and the Reporting Person.

**Remarks:**

/s/ By Elizabeth L. Hougen, Sr.  
Vice President, Finance and  
Chief Financial Officer of Ionis 12/19/2019  
Pharmaceuticals, Inc.

\*\* 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.