

SECURITIES AND EXCHANGE COMMISSION  
Washington, DC 20549

SCHEDULE 13D

Under the Securities Exchange Act of 1934  
(Amendment No. 4)\*

**Akcea Therapeutics, Inc.**

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(Name of Issuer)

**Common Stock**

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(Title of Class of Securities)

**00972L 107**

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(CUSIP Number)

**Elizabeth L. Hougen**  
**Ionis Pharmaceuticals, Inc.**  
**2855 Gazelle Court**  
**Carlsbad, CA 92010**  
**(760) 931-9200**

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(Name, Address and Telephone Number of Person  
Authorized to Receive Notices and Communications)

**March 29, 2019**

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(Date of Event Which Requires Filing of this Statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of §§240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box.

**Note:** Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See Rule 13d-7 for other parties to whom copies are to be sent.

\* The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

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1. Name of Reporting Persons  
Ionis Pharmaceuticals, Inc. ("Ionis")

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2. Check the Appropriate Box if a Member of a Group (See Instructions)

(a)

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(b)

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3. SEC Use Only

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4. Source of Funds (See Instructions)  
WC

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5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)

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6. Citizenship or Place of Organization  
Delaware

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7. Sole Voting Power  
70,221,338

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8. Shared Voting Power

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9. Sole Dispositive Power  
70,221,338

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10. Shared Dispositive Power

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11. Aggregate Amount Beneficially Owned by Each Reporting Person  
70,221,338

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12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)

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13. Percent of Class Represented by Amount in Row 11  
75.8%

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14. Type of Reporting Person (See Instructions)

Number of  
Shares  
Beneficially  
Owned by  
Each  
Reporting  
Person With



**Item 1. Security and Issuer.**

This Amendment No. 4 to Schedule 13D is being filed as an amendment to the initial statement on Schedule 13D relating to the Common Stock, \$0.001 par value per share (“Common Stock”) of Akcea Therapeutics, Inc., a Delaware corporation (the “Issuer”) as filed with the Securities and Exchange Commission (the “SEC”) on July 27, 2017 (the “Original Schedule 13D”) as amended by Amendment No. 1 filed April 26, 2018, Amendment No. 2 filed August 7, 2018 and Amendment No. 3 filed October 22, 2018. The principal executive offices of the Issuer are located at 22 Boston Wharf Road, 9<sup>th</sup> Floor, Boston, Massachusetts 02210. This Amendment is being filed to report the acquisition of an aggregate of 2,837,373 shares of the Issuer’s Common Stock by Ionis Pharmaceuticals, Inc., a Delaware corporation (“Ionis” or the “Reporting Person”), on March 29, 2019.

Items 2(c), 4 and 5 of the Original Schedule 13D are hereby amended and supplemented to the extent hereinafter expressly set forth and, except as amended and supplemented hereby, the Original Schedule 13D remains in full force and effect. All capitalized terms used in this Amendment No. 4 but not defined herein shall have the meanings ascribed thereto in the Original Schedule 13D.

**Item 2. Identity and Background.**

*Schedule A to Item 2(c) is hereby amended.*

**Item 4. Purpose of Transaction.**

*Item 4 of the Original Schedule 13D is hereby amended and supplemented by adding the following paragraph at the end of Item 4:*

On March 29, 2019, the Reporting Person received 2,837,373 shares of the Issuer’s Common Stock 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.

**Item 5. Interest in Securities of the Issuer.**

*Item 5 of the Original Schedule 13D is hereby amended and restated in its entirety as follows:*

The following information with respect to the ownership of the Common Stock of the Issuer by the Reporting Person filing this Schedule 13D is provided as of March 29, 2019:

- (a) The Reporting Person beneficially owns 70,221,338 shares of the Common Stock of the Issuer, or approximately 75.8% of the Issuer’s outstanding Common Stock.
- (b) Ionis has sole power to vote and dispose of the securities of the Issuer held by it.
- (c) The Reporting Person has not effected any other transactions in the Issuer’s Common Stock within the past sixty days, except as provided herein.
- (d) Not applicable.
- (e) Not applicable.

**Item 6. Contracts, Arrangements, Understandings or Relationships with Respect to Securities of the Issuer.**

None.

**Item 7. Material to be Filed as Exhibits.**

None.

**SIGNATURE**

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Date: April 2, 2019

**IONIS PHARMACEUTICALS, INC.**

By: /s/ Elizabeth L. Hougen  
Elizabeth L. Hougen  
Sr. Vice President, Finance and  
Chief Financial Officer

The original statement shall be signed by each person on whose behalf the statement is filed or his authorized representative. If the statement is signed on behalf of a person by his authorized representative (other than an executive officer or general partner of the filing person), evidence of the representative's authority to sign on behalf of such person shall be filed with the statement: provided, however, that a power of attorney for this purpose which is already on file with the Commission may be incorporated by reference. The name and any title of each person who signs the statement shall be typed or printed beneath his signature.

**Attention: Intentional misstatements or omissions of fact  
constitute Federal criminal violations (See 18 U.S.C. 1001)**

**SCHEDULE A**  
**DIRECTORS AND EXECUTIVE OFFICERS OF IONIS**

The following table sets forth the name, business address, present principal occupation or employment and material occupations, positions, offices or employment of each of the directors and executive officers of Ionis. All directors and executive officers listed below are citizens of the United States unless otherwise noted herein.

**DIRECTORS**

Name	Current Principal Affiliation	Business Address
Stanley T. Crooke, M.D., Ph.D.	Chairman of the Board and Chief Executive Officer, Ionis Pharmaceuticals, Inc.	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
B. Lynne Parshall, Esq.	Senior Strategic Advisor to Ionis Pharmaceuticals, Inc.	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Spencer R. Berthelsen, M.D.	Chairman and Managing Director, Kelsey-Seybold Clinic	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Breaux Castleman	President and Chief Executive Officer, Syntiro Healthcare Services, Inc.	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Joseph Klein, III	Managing Director, Gauss Capital Advisors, LLC	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Joseph Loscalzo, M.D., Ph.D.	Head of Department of Medicine and Physician-in-Chief, Brigham & Woman's Hospital, Harvard Medical School	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Brett P. Monia, Ph.D.	Chief Operating Officer and Senior Vice President, Translational Medicine, Ionis Pharmaceuticals, Inc.	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Frederick T. Muto, Esq.	Partner, Cooley LLP	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Joseph H. Wender	Senior Consultant, Goldman Sachs & Co.	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Michael Hayden	Killam Professor at the University of British Columbia and the Director of the Translational Laboratory in Genetic Medicine	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Peter N. Reikes	Vice Chairman, Investment Banking Division, Stifel, Nicolaus & Company, Inc.	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010

**OFFICERS**

Name	Position	Business Address
Stanley T. Crooke, M.D., Ph.D.	Chief Executive Officer	c/o Ionis Pharmaceuticals, Inc.

Brett P. Monia, Ph.D.	Chief Operating Officer and Senior Vice President, Translational Medicine	2855 Gazelle Court Carlsbad, CA 92010 c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Elizabeth Hougen	Senior Vice President, Finance and Chief Financial Officer	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
C Frank Bennett	Senior Vice President, Research	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Richard S. Geary, Ph.D.	Senior Vice President, Development	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Patrick R. O'Neil, Esq.	Senior Vice President, Legal and General Counsel	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010
Damien McDevitt, Ph.D.	Chief Business Officer	c/o Ionis Pharmaceuticals, Inc. 2855 Gazelle Court Carlsbad, CA 92010