

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**SCHEDULE TO
TENDER OFFER STATEMENT UNDER SECTION 14(D)(1) OR 13(E)(1)
OF THE SECURITIES EXCHANGE ACT OF 1934
(Amendment No. 4)**

AKCEA THERAPEUTICS, INC.

(Name of Subject Company (Issuer))

AVALANCHE MERGER SUB, INC.
a wholly owned subsidiary of

IONIS PHARMACEUTICALS, INC.
(Names of Filing Persons (Offeror))

Common Stock, Par Value \$0.001 Per Share
(Title of Class of Securities)

00972L 107
(Cusip Number of Class of Securities)

Brett Monia
Chief Executive Officer
Ionis Pharmaceuticals, Inc.
2855 Gazelle Court
Carlsbad, CA 92010
(760) 931-9200

(Name, Address and Telephone Number of Person Authorized to Receive Notices and Communications on Behalf of Filing Persons)

Copies to:

Graham Robinson
Laura Knoll
Skadden, Arps, Slate, Meagher & Flom LLP
500 Boylston Street
Boston, MA 02116
(617) 573-4850

CALCULATION OF FILING FEE

Transaction Valuation*	Amount of Filing Fee**
\$ 535,900,072	\$69,559.83

* Estimated for purposes of calculating the filing fee only. The transaction valuation was calculated as the sum of (i) 24,665,090 outstanding shares, which is the difference between 101,759,772, the number of shares of common stock of Akcea Therapeutics, Inc., par value \$0.001 per share ("Shares"), outstanding as of September 8, 2020, and 77,094,682, the number of Shares beneficially owned by Ionis Pharmaceuticals, Inc. or its affiliates, multiplied by \$18.15, (ii) 5,881,651 Shares issuable pursuant to outstanding options with an exercise price less than \$18.15 per Share, multiplied by \$4.52 (which is the offer price of \$18.15 minus the weighted average exercise price for such options of \$13.63 per share), (iii) 1,521,514 Shares subject to issuance pursuant to outstanding Akcea restricted stock units multiplied by \$18.15, and (iv) 1,874,829 Shares reserved for issuance pursuant to Akcea's employee stock purchase plan multiplied by the offer price of \$18.15. The calculation of the filing fee is based on information provided by Akcea as of September 8, 2020.

** The filing fee was calculated in accordance with Rule 0-11 under the Securities Exchange Act of 1934, as amended, and Fee Rate Advisory No. 1 for Fiscal Year 2020, by multiplying the transaction value by 0.0001298.

Check box if any part of the fee is offset as provided by Rule 0-11(a)(2) and identify the filing with which the offsetting fee was previously paid. Identify the previous filing by registration statement number, or the Form or Schedule and the date of its filing.

Amount Previously Paid: \$69,559.83 Filing Party: Avalanche Merger Sub, Inc. and Ionis Pharmaceuticals, Inc.
Form or Registration No.: Schedule TO Date Filed: September 14, 2020

Check the box if the filing relates solely to preliminary communications made before the commencement of a tender offer.

Check the appropriate boxes below to designate any transactions to which the statement relates:

- third-party tender offer subject to Rule 14d-1.
- issuer tender offer subject to Rule 13e-4.
- going-private transaction subject to Rule 13e-3.
- amendment to Schedule 13D under Rule 13d-2.

Check the following box if the filing is a final amendment reporting the results of the tender offer.

This Amendment No. 4 amends and supplements the Tender Offer Statement on Schedule TO, filed by Avalanche Merger Sub, Inc., a Delaware corporation (“Purchaser”), and Ionis Pharmaceuticals, Inc., a Delaware corporation (“Parent”), with the U.S. Securities and Exchange Commission on September 14, 2020 (together with any subsequent amendments and supplements thereto, the “Schedule TO”). The Schedule TO relates to the offer by Purchaser to purchase all outstanding shares of common stock, \$0.001 par value per share (“Shares”), of Akcea Therapeutics, Inc., a Delaware corporation (“Akcea”), not owned by Parent at a price of \$18.15 per Share, net to the seller in cash, without interest and subject to any withholding of taxes, upon the terms and subject to the conditions described in the Offer to Purchase dated September 14, 2020 (together with any amendments or supplements thereto, the “Offer to Purchase”) and in the accompanying Letter of Transmittal (together with any amendments or supplements thereto and with the Offer to Purchase, the “Offer”), copies of which are incorporated by reference to Exhibits (a)(1)(i) and (a)(1)(ii) of the Schedule TO respectively.

The information set forth in the Offer to Purchase, including all schedules thereto, is hereby expressly incorporated by reference in response to all of the items of the Schedule TO, including, without limitation, all of the information required by Schedule 13E-3 that is not included in or covered by the items in Schedule TO, and is supplemented by the information specifically provided herein, except as otherwise set forth below. Capitalized terms used but not defined herein have the applicable meanings ascribed to them in the Schedule TO or the Offer to Purchase.

Item 1 through 9, Item 11 and Item 13.

Items 1 through 9, Item 11 and Item 13 of the Schedule TO, to the extent such Items incorporate by reference the information contained in the Offer to Purchase, are hereby amended and supplemented as follows:

1. The information set forth in the section entitled “24. Certain Legal Matters; Regulatory Approvals—Legal Proceedings Relating to the Tender Offer” on page 80 of the Offer to Purchase is amended and supplemented by adding the following paragraphs:

“On October 2, 2020, a purported stockholder of Akcea named Scott Crum filed a lawsuit against Akcea and members of the Akcea Board in the United States District Court for the Eastern District of New York, captioned *Crum v. Akcea Therapeutics, Inc., et al.*, Case No. 20-cv-04692 (the “Crum Complaint”). The Crum Complaint alleges that Akcea and the members of the Akcea Board violated Sections 14(e) and 14(d) of the Exchange Act, as well as Rule 14d-9 thereunder, by failing to disclose certain supposedly material information in the Schedule 14D-9 in connection with the Transactions, which they allege rendered the Schedule 14D-9 false and misleading. In addition, the Crum Complaint alleges that members of the Akcea Board acted as controlling persons of Akcea within the meaning and in violation of Section 20(a) of the Exchange Act to influence and control the dissemination of the allegedly defective Solicitation/Recommendation Statement. The Crum Complaint seeks, among other things, an order enjoining consummation of the Transactions; rescission of the Transactions if they have already been consummated and rescissory damages; a declaration that the defendants violated Sections 14(e), 14(d)(4) and 20(a) of the Exchange Act, and Rule 14d-9; and an award of plaintiff’s costs, including reasonable allowance for attorneys’ and experts’ fees and expenses.

The outcome of this lawsuit cannot be predicted with certainty. If a preliminary injunction were to be granted it could delay or jeopardize the completion of the Transactions, and an adverse judgment granting permanent injunctive relief could indefinitely enjoin the completion of such Transactions. Parent and Purchaser believe the claims asserted in the Crum Complaint are without merit. If additional similar complaints are filed, absent new or different allegations that are material, Akcea will not necessarily announce such additional filings.

The foregoing description does not purport to be complete and is qualified in its entirety by reference to the Crum Complaint, a copy of which is attached as Exhibit (a)(5)(H) to the Schedule 14D-9 and is incorporated by reference herein.”

Item 12. Exhibits.

Item 12 of the Schedule TO is hereby amended and supplemented by adding the following exhibits:

Exhibit No.	
(a)(2)(vi)	Solicitation/Recommendation Statement (Amendment No. 5) on Schedule 14D-9 (incorporated by reference to the Solicitation/Recommendation Statement on Schedule 14D-9 filed by Akcea with the Securities and Exchange Commission on October 2, 2020).
(a)(5)(ix)	Complaint, dated October 2, 2020 (Crum v. Akcea Therapeutics, Inc., et al.) (incorporated by reference to Exhibit (a)(5)(H) to the Solicitation/Recommendation Statement (Amendment No. 5) on Schedule 14D-9 filed by Akcea with the Securities and Exchange Commission on October 2, 2020).

SIGNATURE

After due 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.

Dated: October 2, 2020

By: /s/ Brett Monia

Name: Brett Monia, Ph.D.

Title: *Chief Executive Officer of Ionis
Pharmaceuticals, Inc.*

By: /s/ Brett Monia

Name: Brett Monia, Ph.D.

Title: *President of Avalanche Merger Sub., Inc.*