

SCHEDULE 13G

Amendment No.16
IONIS PHARMACEUTICALS INC
COMMON STOCK
Cusip #462222100

Check the appropriate box to designate the rule pursuant to which this
Schedule is filed:

- Rule 13d-1(b)
 Rule 13d-1(c)
 Rule 13d-1(d)

Cusip #462222100
Item 1: Reporting Person - FMR LLC
Item 2: (a)
(b)
Item 4: Delaware
Item 5: 21,305,988
Item 6: 0
Item 7: 21,307,519
Item 8: 0
Item 9: 21,307,519
Item 11: 14.999%
Item 12: HC

Cusip #462222100
Item 1: Reporting Person - Abigail P. Johnson
Item 2: (a)
(b)
Item 4: United States of America
Item 5: 0
Item 6: 0
Item 7: 21,307,519
Item 8: 0
Item 9: 21,307,519
Item 11: 14.999%
Item 12: IN

Item 1(a). Name of Issuer:

IONIS PHARMACEUTICALS INC

Item 1(b). Address of Issuer's Principal Executive Offices:

2855 GAZELLE COURT
Carlsbad, CA 92010
USA

Item 2(a). Name of Person Filing:

FMR LLC

Item 2(b). Address or Principal Business Office or, if None, Residence:

245 Summer Street, Boston, Massachusetts 02210

Item 2(c). Citizenship:

Not applicable

Item 2(d). Title of Class of Securities:

COMMON STOCK

Item 2(e). CUSIP Number:

462222100

Item 3. This statement is filed pursuant to Rule 13d-1(b) or 13d-2(b) or (c)
and the person filing, FMR LLC, is a parent holding company in accordance with
Section 240.13d-1(b) (1) (ii) (G). (Note: See Exhibit A).

Item 4. Ownership

(a) Amount Beneficially Owned: 21,307,519

(b) Percent of Class: 14.999%

(c) Number of shares as to which such person has:

(i) sole power to vote or to direct the vote: Please see the responses to Items 5 and 6 on the cover page

(ii) shared power to vote or to direct the vote: 0

(iii) sole power to dispose or to direct the disposition of: 21,307,519

(iv) shared power to dispose or to direct the disposition of: 0

Item 5. Ownership of Five Percent or Less of a Class.

Not applicable.

Item 6. Ownership of More than Five Percent on Behalf of Another Person.

One or more other persons are known to have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the COMMON STOCK of IONIS PHARMACEUTICALS INC.

The interest of Fidelity Growth Company Commingled Pool, in the COMMON STOCK of IONIS PHARMACEUTICALS INC, amounted to 9,164,615 shares or 6.451% of the total outstanding COMMON STOCK at December 30, 2022.

Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company.

See attached Exhibit A.

Item 8. Identification and Classification of Members of the Group.

Not applicable.

Item 9. Notice of Dissolution of Group.

Not applicable.

Item 10. Certifications.

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired and are held in the ordinary course of business and were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect.

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.

February 9, 2023

Date

/s/ Stephanie J. Brown

Signature

Stephanie J. Brown

Duly authorized under Power of Attorney effective as of January 3, 2023, by and on behalf of FMR LLC and its direct and indirect subsidiaries*

* This power of attorney is incorporated herein by reference to Exhibit 24 to the Schedule 13G filed by FMR LLC on January 10, 2023, accession number: 0000315066-23-000003.

Exhibit A

Pursuant to the instructions in Item 7 of Schedule 13G, the following table lists the identity and Item 3 classification, if applicable, of each relevant entity that beneficially owns shares of the security class being reported on this Schedule 13G.

Entity ITEM 3 Classification

Fidelity Management & Research Company LLC * IA

Fidelity Management Trust Company * BK

* Entity beneficially owns 5% or greater of the outstanding shares of the security class being reported on this Schedule 13G.

Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC.

Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC.

This filing reflects the securities beneficially owned, or that may be deemed to be beneficially owned, by FMR LLC, certain of its subsidiaries and affiliates, and other companies (collectively, the "FMR Reporters"). This filing does not reflect securities, if any, beneficially owned by certain other companies whose beneficial ownership of securities is disaggregated from that of the FMR Reporters in accordance with Securities and Exchange Commission Release No. 34-39538 (January 12, 1998).

RULE 13d-1(k) (1) AGREEMENT

The undersigned persons, on February 9, 2023, agree and consent to the joint filing on their behalf of this Schedule 13G in connection with their beneficial ownership of the COMMON STOCK of IONIS PHARMACEUTICALS INC at December 30, 2022.

FMR LLC

By /s/ Stephanie J. Brown
Stephanie J. Brown

Duly authorized under Power of Attorney effective as of January 3, 2023, by and on behalf of FMR LLC and its direct and indirect subsidiaries*

Abigail P. Johnson

By /s/ Stephanie J. Brown
Stephanie J. Brown

Duly authorized under Power of Attorney effective as of January, 26, 2023, by and on behalf of Abigail P. Johnson**

* This power of attorney is incorporated herein by reference to Exhibit 24 to the Schedule 13G filed by FMR LLC on January 10, 2023, accession number: 0000315066-23-000003.

** This power of attorney is incorporated herein by reference to Exhibit 24 to the Schedule 13G filed by FMR LLC on January 31, 2023, accession number: 0000315066-23-000038.