

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

SCHEDULE 13G

Under the Securities Exchange Act of 1934
(Amendment No. 10)*

Ionis Pharmaceuticals, Inc.
(Name of Issuer)

Common Stock, \$.001 Par Value

(Title of Class of Securities)

462222100
(CUSIP Number)

December 31, 2020
(Date of Event Which Requires Filing of this Statement)

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)

*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 the disclosures provided in a prior cover page.

The information required in 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).

1. NAMES OF REPORTING PERSONS.

ClearBridge Investments, LLC

2. CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP

- (a)
(b) X

3. SEC USE ONLY

4. CITIZENSHIP OR PLACE OF ORGANIZATION

Delaware

NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH:

5. SOLE VOTING POWER

(See Item 4)

6. SHARED VOTING POWER

(See Item 4)

7. SOLE DISPOSITIVE POWER

(See Item 4)

8. SHARED DISPOSITIVE POWER

(See Item 4)

9. AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON

6,915,147

10. CHECK IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES []

11. PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (9)

4.95%

12. TYPE OF REPORTING PERSON

IA, 00 (See Item 4)

Item 1.

- (a) Name of Issuer
Ionis Pharmaceuticals, Inc.
- (b) Address of Issuer's Principal Executive Offices
2855 Gazelle Court,
Carlsbad, California 92010

Item 2.

- (a) Name of Person Filing
ClearBridge Investments, LLC
 - (b) Address of Principal Business Office or, if none, Residence
620 8th Ave.
New York, NY 10018
 - (c) Citizenship
Delaware
 - (d) Title of Class of Securities
Common Stock, \$.001 Par Value
 - (e) CUSIP Number
462222100
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- Item 3. If this statement is filed pursuant to §§240.13d-1(b) or 240.13d-2(b) or (c), check whether the person filing is a:
- (a) Broker or dealer registered under section 15 of the Act (15 U.S.C. 80).
 - (b) Bank as defined in section 3(a)(6) of the Act (15 U.S.C. 78c).
 - (c) Insurance company as defined in section 3(a)(19) of the Act (15 U.S.C. 78c).
 - (d) Investment company registered under section 8 of the Investment Company Act of 1940 (15 U.S.C 80a -8).
 - (e) An investment adviser in accordance with §240.13d-1(b)(1)(ii)(E);
 - (f) An employee benefit plan or endowment fund in accordance with §240.13d-1(b)(1)(ii)(F);
 - (g) A parent holding company or control person in accordance with §240.13d-1(b)(1)(ii)(G);
 - (h) A savings associations as defined in Section 3(b) of the Federal Deposit Insurance Act (12 U.S.C. 1813);
 - (i) A church plan that is excluded from the definition of an investment company under section 3(c)(14) of the Investment Company Act of 1940 (15 U.S.C. 80a-3);
 - (j) A non-U.S. institution in accordance with §240.13d-1(b)(ii)(J);
 - (k) Group, in accordance with §240.13d-1(b)(1)(ii)(K).

If filing as a non-U.S. institution in accordance with §240.13d-1(b)(1)(ii)(J), please specify the type of institution

Item 4. Ownership

The securities reported herein are beneficially owned by one or more open-end investment companies or other managed accounts that are investment management clients of ClearBridge Investments, LLC ("CIL"), an indirect wholly owned subsidiary of Franklin Resources, Inc. ("FRI"). When an investment management contract (including a sub-advisory agreement) delegates to CIL investment discretion or voting power over the securities held in the investment advisory accounts that are subject to that agreement, FRI treats CIL as having sole investment discretion or voting authority, as the case may be, unless the agreement specifies otherwise. Accordingly, CIL reports on Schedule 13G that it has sole investment discretion and voting authority over the securities covered by any such investment management agreement, unless otherwise noted in this Item 4. As a result, for purposes of Rule 13d-3 under the Act, CIL may be deemed to be the beneficial owner of the securities reported in this Schedule 13G.

Beneficial ownership by investment management subsidiaries and other affiliates of FRI is being reported in conformity with the guidelines articulated by the SEC staff in Release No. 34-39538 (January 12, 1998) relating to organizations, such as FRI, where related entities exercise voting and investment powers over the securities being reported independently from each other. The voting and investment powers held by CIL are exercised independently from FRI (CIL's parent holding company) and from all other investment management subsidiaries of FRI (FRI, its affiliates and investment management subsidiaries other than CIL are, collectively, "FRI affiliates"). Furthermore, internal policies and procedures of CIL and FRI affiliates establish informational barriers that prevent the flow between CIL and the FRI affiliates of information that relates to the voting and investment powers over the securities owned by their respective investment management clients. Consequently, CIL and the FRI affiliates report the securities over which they hold investment and voting power separately from each other for purposes of Section 13 of the Act.

Charles B. Johnson and Rupert H. Johnson, Jr. (the "Principal Shareholders") each own in excess of 10% of the outstanding common stock of FRI and are the principal stockholders of FRI. However, because CIL exercises voting and investment powers on behalf of its investment management clients independently of FRI affiliates, beneficial ownership of the securities reported by CIL is not attributed to the Principal Shareholders. CIL disclaims any pecuniary interest in any of the securities reported in this Schedule 13G. In addition, the filing of this Schedule 13G on behalf of CIL should not be construed as an admission that it is, and it disclaims that it is, the beneficial owner, as defined in Rule 13d-3, of any of such securities.

Furthermore, CIL believes that it is not a "group" with FRI affiliates, the Principal Shareholders, or their respective affiliates within the meaning of Rule 13d-5 under the Act and that none of them is otherwise required to attribute to any other the beneficial ownership of the securities held by such person or by any persons or entities for whom or for which CIL or the FRI affiliates provide investment management services.

(a) Amount beneficially owned:

6,915,147

(b) Percent of class:

4.95%

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

(i) Sole power to vote or to direct the vote

ClearBridge Investments, LLC: 6,725,514

(ii) Shared power to vote or to direct the vote

0

(iii) Sole power to dispose or to direct the disposition of

ClearBridge Investments, LLC: 6,915,147

(iv) Shared power to dispose or to direct the disposition of

0

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

If this statement is being filed to report the fact that as of the date hereof the reporting person has ceased to be the beneficial owner of more than five percent of the class of securities, check the following [X].

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

The clients of ClearBridge Investments, LLC, including investment companies registered under the Investment Company Act of 1940 and other managed accounts, have the right to receive or power to direct the receipt of dividends from, and the proceeds from the sale of, the securities reported herein.

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

Not Applicable

Item 8. Identification and Classification of Members of the Group

Not Applicable

Item 9. Notice of Dissolution of Group

Not Applicable

Item 10. Certification

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, other than activities solely in connection with a nomination under § 240.14a-11

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.

Dated: February 5, 2021

ClearBridge Investments, LLC

By: /s/BARBARA MANNING

Barbara Manning
General Counsel & Chief Compliance Officer of ClearBridge Investments, LLC