

UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549  
SCHEDULE 13G

Under the Securities Exchange Act of 1934

(Amendment No. 1)

IONIS PHARMACEUTICALS INC  
(Name of Issuer)

COMMON STOCK  
(Title of Class of Securities)

462222100  
(CUSIP NUMBER)

December 31, 2021  
(Date of Event which Requires Filing of 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)

1. Name of Reporting Person  
T. ROWE PRICE ASSOCIATES, INC.  
52-0556948

2. Check the Appropriate Box if a Member of a Group  
NOT APPLICABLE

3. SEC Use Only

4. Citizenship or Place of Organization  
Maryland

Number of Shares Beneficially Owned by Each Reporting Person With

5. Sole Voting Power\* 4,094,894

6. Shared Voting Power\* 0

7. Sole Dispositive Power\* 12,490,280

8. Shared Dispositive Power 0

9. Aggregate Amount Beneficially Owned by Each Reporting Person  
12,490,280

10. Check Box if the Aggregate Amount in Row (9) Excludes Certain Shares  
NOT APPLICABLE

11. Percent of Class Represented by Amount in Row 9  
8.8%

12. Type of Reporting Person  
IA

\*Any shares reported in Items 5 and 6 are also reported in Item 7.

Item 1(a) Name of Issuer:  
IONIS PHARMACEUTICALS INC

Item 1(b) Address of Issuer's Principal Executive Offices:  
2855 GAZELLE COURT, CARLSBAD, CALIFORNIA 92010

Item 2(a) Name of Person(s) Filing:  
(1) T. ROWE PRICE ASSOCIATES, INC. ("Price Associates")

Item 2(b) Address of Principal Business Office:  
100 E. Pratt Street, Baltimore, MD 21202

Item 2(c) Citizenship or Place of Organization:  
(1) Maryland

Item 2(d) Title of Class of Securities: COMMON STOCK

Item 2(e) Cusip Number: 462222100

Item 3: The person filing this Schedule 13G is an:

X Investment Adviser registered under Section 203 of the Investment Advisers Act of 1940

Item 4: Reference is made to Items 5-11 on the preceding pages of this Schedule 13G.

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

(1) Price Associates does not serve as custodian of the assets of any of its clients; accordingly, in each instance only the client or the client's custodian or trustee bank has the right to receive dividends paid with respect to, and proceeds from the sale of, such securities.

The ultimate power to direct the receipt of dividends paid with respect to, and the proceeds from the sale of, such securities, is vested in the individual and institutional clients which Price Associates serves as investment adviser. Any and all discretionary authority which has been delegated to Price Associates may be revoked in whole or in part at any time.

Except as may be indicated if this is a joint filing with one of the registered investment companies sponsored by Price Associates which it also serves as investment adviser ("T. Rowe Price Funds"), not more than 5% of the class of such securities is owned by any one client subject to the investment advice of Price Associates.

(2) With respect to securities owned by any one of the T. Rowe Price Funds, only the custodian for each of such Funds, has the right to receive dividends paid with respect to, and proceeds from the sale of, such securities. No other person is known to have such right, except that the shareholders of each such Fund participate proportionately in any dividends and distributions so paid.

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 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. T. Rowe Price Associates, Inc. hereby declares and affirms that the filing of Schedule 13G shall not be construed as an admission that Price Associates is the beneficial owner of the securities referred to, which beneficial ownership is expressly denied.

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.

T. ROWE PRICE ASSOCIATES, INC.

Date: February 14, 2022

Signature: /s/ David Oestreicher

Name & Title: David Oestreicher, Executive Vice President

12/31/2021