

SECURITIES AND EXCHANGE COMMISSION  
Washington, D.C. 20549

SCHEDULE 13G

Under the Securities Exchange Act of 1934

Ionis Pharmaceuticals, Inc.  
(Amendment No. 4)

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(Name of Issuer)

Common Stock

-----  
(Title of Class of Securities)

462222100

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(CUSIP Number)

31st December 2018

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(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 persons 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).

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB control number.

SEC 1745 (3-06)

CUSIP No. 462222100

1. Names of Reporting Persons.  
I.R.S. Identification Nos. of above persons (entities only).

Baillie Gifford & Co (Scottish partnership)

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

3. SEC Use Only

4. Citizenship or Place of Organization

SCOTLAND UK

Number of Shares Beneficially Owned by Each Reporting	5. Sole Voting Power	4,010,945
	6. Shared Voting Power	0
	7. Sole Dispositive Power	8,750,014

Person With:

8. Shared Dispositive Power 0

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9. Aggregate Amount Beneficially Owned by Each Reporting Person  
8,750,014

10. Check if the Aggregate Amount in Row (9) Excludes Certain Shares  
(See Instructions)

11. Percent of Class Represented by Amount in Row (9) 6.36%

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12. Type of Reporting Person (See Instructions) IA

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Item 1.

(a) Name of Issuer Ionis Pharmaceuticals, Inc.

(b) Address of Issuers Principal Executive Offices  
2855 Gazelle Court,  
Carlsbad  
CA 92010

Item 2.

(a) Name of Person Filing Baillie Gifford & Co

(b) Address of Principal Business Office or, if none, Residence  
Calton Square  
1 Greenside Row  
Edinburgh EH1 3AN  
Scotland  
UK

(c) Citizenship Scotland UK

(d) Title of Class of Securities Common stock

(e) CUSIP Number 462222100

Item 3. If this statement is filed pursuant to rule 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. 78o).
- (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 rule 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 rule 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) Group in accordance with rule 240.13d-1(b)(1)(ii)(J).

Item 4. Ownership.

Provide the following information regarding the aggregate number and Percentage of the class of securities of the issuer identified in Item 1.

(a) Amount beneficially owned: see row (9) on page 2.

(b) Percent of Class: see row (11) on page 2.

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

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

See row (5) on page 2.

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

See row (6) on page 2

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

See row (7) on page 2

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

See row (8) on page 2

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.

[ ]

Not applicable.

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

Securities reported on this Schedule 13G as being beneficially owned by Baillie Gifford & Co. are held by Baillie Gifford & Co. and/or one or more of its investment adviser subsidiaries, which may include Baillie Gifford Overseas Limited, on behalf of investment advisory clients, which may include investment companies registered under the Investment Company Act, employee benefit plans, pension funds or other institutional clients.

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.

- the foreign regulatory scheme applicable to investment advisers is substantially comparable to the functionally equivalent U.S. institution(s).

I also undertake to furnish the Commission staff, upon request, information that would otherwise be disclosed in a Schedule 13D.

SIGNATURE

After reasonable enquiry and to the best of my knowledge and belief, I

certify that the information set forth in this statement is true,  
complete and correct

11 January 2019

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Date

Lindsay Gold

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Signature

Lindsay Gold  
Compliance Director - Baillie Gifford & Co

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Name/Title

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 representatives 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.

NOTE: Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See rule 240.13d-7 for other parties for whom copies are to be sent.

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