
United States
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

SCHEDULE 13G

Under the Securities Exchange Act of 1934
(Amendment No. 12)*

IONIS PHARMACEUTICALS, INC.

(Name of Issuer)

Common Stock
(Title of Class of Securities)

462222100
(CUSIP Number)

December 31, 2022
(Date of Event Which Requires Filing 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 BB Biotech AG	
2.	Check the Appropriate Box if a Member of a Group (See Instructions) (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
3.	SEC Use Only	
4.	Citizenship or Place of Organization Switzerland	
Number of Shares Beneficially Owned by Each Reporting Person with:	5.	Sole Voting Power 0
	6.	Shared Voting Power 9,635,000
	7.	Sole Dispositive Power 0
	8.	Shared Dispositive Power 9,635,000
9.	Aggregate Amount Beneficially Owned by Each Reporting Person 9,635,000	
10.	Check if the Aggregate Amount in Row (9) Excludes Certain Shares <input type="checkbox"/>	
11.	Percent of Class Represented by amount in Row (9) 6.8%	
12.	Type of Reporting Person (See Instructions) HC,CO	

1.	Names of Reporting Persons Biotech Invest N.V.	
2.	Check the Appropriate Box if a Member of a Group (See Instructions) (a) <input checked="" type="checkbox"/> (b) <input type="checkbox"/>	
3.	SEC Use Only	
4.	Citizenship or Place of Organization Curacao	
Number of Shares Beneficially Owned by Each Reporting Person with:	5.	Sole Voting Power 0
	6.	Shared Voting Power 9,635,000
	7.	Sole Dispositive Power 0
	8.	Shared Dispositive Power 9,635,000
9.	Aggregate Amount Beneficially Owned by Each Reporting Person 9,635,000	
10.	Check if the Aggregate Amount in Row (9) Excludes Certain Shares <input type="checkbox"/>	
11.	Percent of Class Represented by amount in Row (9) 6.8%	
12.	Type of Reporting Person (See Instructions) CO	

Item 1

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

Item 2

- 2(a) Name of Person Filing: BB Biotech AG ("BB Biotech") on behalf of its wholly-owned subsidiary, Biotech Invest N.V. ("Biotech Invest")
2(b) Address of Principal Business Office or, if none, Residence:
BB Biotech AG: Schwertstrasse 6, CH-8200 Schaffhausen, Switzerland
Biotech Invest N.V.: Ara Hill Top Building, Unit A-5, Pletterijweg Oost 1, Curaçao
2(c) Citizenship: BB Biotech AG: Switzerland
Biotech Invest N.V.: Curacao
2(d) Title of Class of Securities Common Stock, \$0.001 Par Value
2(e) CUSIP Number 462222100

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: 9,635,000
(b) Percent of class: 6.8%
(c) Number of shares as to which the person has:
(i) Sole power to vote or to direct the vote 0
(ii) Shared power to vote or to direct the vote 9,635,000
(iii) Sole power to dispose or to direct the disposition of 0
(iv) Shared power to dispose or to direct the disposition of 9,635,000

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

This statement is filed jointly by BB Biotech and Biotech Invest. Biotech Invest is a wholly-owned subsidiary of BB Biotech.

Item 10. Certification

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above 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.

SIGNATURES

After reasonable inquiry and the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

BB Biotech AG

Date: **February 10, 2023**

By: /s/ Daniel Koller

Signatory Authority

Name: **Daniel Koller**

Title: **Signatory Authority**

Date: **February 10, 2023**

By: /s/ Ivo Betschart

Signatory Authority

Name: Ivo Betschart

Title: Signatory Authority

Biotech Invest N.V.

Date: **February 10, 2023**

By: /s/ Jan Bootsma

Signatory Authority

Name: **Jan Bootsma**

Title: **Signatory Authority**

Date: **February 10, 2023**

By: /s/ Nathalie M.A. Isidora-Kwidama

Signatory Authority

Name: **Hugo van Neutegem**

Title: **Signatory Authority**

Exhibit Index

Exhibit A: Agreement by and between BB Biotech AG and Biotech Invest N.V. with respect to the filing of this disclosure statement.*

Exhibit B: Power of Attorney

* Previously filed as an exhibit to BB Biotech AG and Biotech Invest N.V.'s Schedule 13G filed with the Securities and Exchange Commission on February 13, 2020.

Exhibit B

POWER OF ATTORNEY

The Undersigned,

Hugo van Neutegem

herewith gives Power of Attorney to **Mrs. Nathalie M.A. Isidora-Kwidama**, born in Curacao on, holder of a passport issued by the Kingdom of the Netherlands, with number, to represent the Company in the broadest sense of the word and in the best interest of the Company and further to do if were the Undersigned personally present.

This Power of Attorney is valid for the period February 6, 2023 up and to including February 28, 2023.

Willemstad, Curaçao, February 3, 2023.

Mrs. Nathalie M.A. Isidora-Kwidama will sign as follows:

/s/ Nathalie M.A. Isidora-Kwidama

Mrs. Nathalie M.A. Isidora-Kwidama

/s/ Hugo van Neutegem

Mr. Hugo van Neutegem