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

FORM S-8

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

IONIS PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State of Incorporation)

33-0336973
(I.R.S. Employer Identification No.)

2855 Gazelle Court
Carlsbad, CA 92010
(Address of principal executive offices, including zip code)

Amended and Restated Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan
(Full title of the plan)

Brett Monia
Chief Executive Officer
IONIS PHARMACEUTICALS, INC.
2855 Gazelle Court
Carlsbad, California 92010
(760) 931-9200

(Name, address, and telephone number, including area code, of agent for service)

Copies to:
Patrick R. O'Neil, Esq.
Executive Vice President, Legal, General Counsel and Corporate Secretary
IONIS PHARMACEUTICALS, INC.
2855 Gazelle Court
Carlsbad, California 92010
(760) 931-9200

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

CALCULATION OF REGISTRATION FEE

Title of Securities to be Registered	Amount to be Registered (1)(2)	Proposed Maximum Offering Price per Share (3)	Proposed Maximum Aggregate Offering Price (3)	Amount of Registration Fee
Common Stock, par value \$.001 per share	6,700,000 shares	\$ 37.19	\$ 249,173,000	\$ 27,184.77

- (1) In accordance with Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), this Registration Statement on Form S-8 (this "Registration Statement") shall be deemed to cover any additional securities that may from time to time be offered or issued by Ionis Pharmaceuticals, Inc. ("Ionis," the "Registrant," "we," "our" and "us") to prevent dilution resulting from stock splits, stock dividends or similar transactions.
 - (2) Includes 6,700,000 shares issuable pursuant to the Registrant's Amended and Restated 2011 Equity Incentive Plan.
 - (3) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(c) and Rule 457(h) of the Securities Act. The price per share and the aggregate offering price are calculated on the basis of \$37.19, the average of the high and low sales prices of Registrant's Common Stock on July 30, 2021, as reported on the Nasdaq Global Market.
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PART I

INFORMATION REQUIRED IN THE SECTION 10(A) PROSPECTUS

The information called for by Part I of Form S-8 is omitted from this Registration Statement in accordance with Rule 428 of the Securities Act and the instructions to Form S-8. In accordance with the rules and regulations of the Securities and Exchange Commission (the "Commission") and the instructions to Form S-8, such documents are not being filed with the Commission either as part of this Registration Statement or as prospectuses or prospectus supplements pursuant to Rule 424.

Part II

INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

Item 3. Incorporation of Documents by Reference.

The following documents filed with the Commission by the Registrant are hereby incorporated by reference into this Registration Statement:

- (a) the Registrant's Annual Report on Form 10-K for the year ended December 31, 2020, as filed with the Commission on [February 24, 2021](#), and the information specifically incorporated by reference into the Registrant's Annual Report on Form 10-K for the year ended December 31, 2020, from the Registrant's Definitive Proxy Statement on Schedule 14A, as filed with the Commission on [April 23, 2021](#);
- (b) the Registrant's Quarterly Report on Form 10-Q for the quarterly period ended March 31, 2021, as filed with the Commission on [May 5, 2021](#) and Quarterly Report on Form 10-Q for the quarterly period ended June 30, 2021, as filed with the Commission on [August 4, 2021](#);
- (c) the Registrant's Current Reports on Form 8-K filed with the Commission on [March 23, 2021](#), [March 29, 2021](#), [April 6, 2021](#), [April 13, 2021](#), and [June 4, 2021](#); and
- (d) the description of the Registrant's Common Stock contained in the Registrant's registration statement on Form 8-A filed with the SEC on April 12, 1991, as updated by its Certificate of Amendment of its Restated Certificate of Incorporation filed with its Definitive Proxy Statement on Schedule 14A filed on [April 25, 2014](#), and its Certificate of Amendment of its Restated Certificate of Incorporation filed with its current report on Form 8-K filed on [December 18, 2015](#).

All documents filed by the Registrant with the Commission pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), after the date hereof and prior to the filing of a post-effective amendment which indicates that all securities offered pursuant to this Registration Statement have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference herein and to be a part hereof from the date of filing of such documents; provided, however, that documents, reports and definitive proxy or information statements, or portions thereof, which are furnished and not filed in accordance with the rules of the SEC shall not be deemed incorporated by reference into this registration statement. Any statement contained in a document incorporated by reference herein shall be deemed to be modified or superseded for purposes of this registration statement to the extent that a statement contained herein or in any other subsequently filed document which also is or is deemed to be incorporated by reference herein modifies or supersedes such statement. Any statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this registration statement..

Item 5. Interests of Named Experts and Counsel.

The validity of the issuance of the common stock offered in this Registration Statement will be passed upon for the Registrant by Patrick R. O'Neil, Executive Vice President, Legal, General Counsel and Corporate Secretary of Ionis.

Mr. O'Neil holds or has the right to acquire shares of Ionis' Common Stock in an aggregate amount that is less than 1% of Ionis' outstanding Common Stock.

Item 6. Indemnification of Directors and Officers.

Under Section 145 of the Delaware General Corporation Law (the “DGCL”), we have broad powers to indemnify our directors and officers against liabilities they may incur in such capacities, including liabilities under the Securities Act.

Our certificate of incorporation and bylaws include provisions to (i) eliminate the personal liability of its directors for monetary damages resulting from breaches of their fiduciary duty to the extent permitted by Section 102(b)(7) of the DGCL and (ii) require us to indemnify our directors and officers to the fullest extent permitted by Section 145 of the DGCL, including circumstances in which indemnification is otherwise discretionary. Pursuant to Section 145 of the DGCL, a corporation generally has the power to indemnify its present and former directors, officers, employees and agents against expenses incurred by them in connection with any suit to which they are, or are threatened to be made, a party by reason of their serving in such positions so long as they acted in good faith and in a manner they reasonably believed to be in, or not opposed to, the best interest of the corporation, and with respect to any criminal action, they had no reasonable cause to believe their conduct was unlawful. We believe that these provisions are necessary to attract and retain qualified persons as directors and officers. These provisions do not eliminate the directors’ duty of care, and, in appropriate circumstances, equitable remedies such as injunctive or other forms of non-monetary relief will remain available under Delaware law. In addition, each director will continue to be subject to liability for breach of the director’s duty of loyalty to us, for acts or omissions not in good faith or involving intentional misconduct, for knowing violations of law, for acts or omissions that the director believes to be contrary to the best interests of Ionis or our stockholders, for any transaction from which the director derived an improper personal benefit, for acts or omissions involving a reckless disregard for the director’s duty to Ionis or our stockholders when the director was aware or should have been aware of a risk of serious injury to Ionis or our stockholders, for acts or omissions that constitute an unexcused pattern of inattention that amounts to an abdication of the director’s duty to Ionis or our stockholders, for improper transactions between the director and us and for improper distributions to stockholders and loans to directors and officers. The provision also does not affect a director’s responsibilities under any other law, such as the federal securities law or state or federal environmental laws.

We have entered into indemnity agreements with each of our directors and executive officers that require us to indemnify such persons against expenses, judgments, fines, settlements and other amounts incurred (including expenses of a derivative action) in connection with any proceeding, whether actual or threatened, to which any such person may be made a party by reason of the fact that such person is or was a director or an executive officer of Ionis or any of our affiliated enterprises, provided such person acted in good faith and in a manner such persons reasonably believed to be in, or not opposed to, the best interests of Ionis and, with respect to any criminal proceeding, has no reasonable cause to believe his conduct was unlawful. The indemnification agreements also set forth procedures that will apply in the event of a claim for indemnification thereunder.

We have an insurance policy covering our officers and directors with respect to certain liabilities, including liabilities arising under the Securities Act or otherwise.

Item 8. Exhibits.

Exhibit Number	Description
5.1	Opinion of Patrick R. O’Neil.
23.1	Consent of Independent Registered Public Accounting Firm.
23.2	Consent of Patrick R. O’Neil. Reference is made to Exhibit 5.1.
24.1	Power of Attorney is contained on the signature pages.
99.1	Amended and Restated Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan (1).
99.2	Form of Option Agreement for Options granted under the Amended and Restated Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan (2).
99.3	Form of Time-Vested Restricted Stock Unit Agreement for Restricted Stock Units granted under the Amended and Restated Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan (3).

- (1) Filed as an appendix to the Registrant’s Notice of 2021 Annual Meeting of Stockholders and Proxy Statement filed with the SEC on [April 23, 2021](#), and incorporated herein by reference.
- (2) Filed as an exhibit to the Registrant’s Quarterly Report on Form 10-Q for the quarter ended September 30, 2015, filed with the SEC on [November 9, 2015](#), and incorporated herein by reference.
- (3) Filed as an exhibit to the Registrant’s Registration Statement on Form S-8 filed with the SEC on [August 8, 2011](#), and incorporated herein by reference.

Item 9. Undertakings.

(a) The undersigned Registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this Registration Statement:

(i) To include any prospectus required by section 10(a)(3) of the Securities Act;

(ii) To reflect in the prospectus any facts or events arising after the effective date of the Registration Statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the Registration Statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20% change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective Registration Statement; and

(iii) To include any material information with respect to the plan of distribution not previously disclosed in the Registration Statement or any material change to such information in the Registration Statement;

Provided, however, that paragraphs (a)(1)(i) and (a)(1)(ii) of this section do not apply if the information required to be included in a post-effective amendment by those paragraphs is contained in reports filed with or furnished to the Commission by the Registrant pursuant to section 13 or section 15(d) of the Exchange Act that are incorporated by reference in the Registration Statement.

(2) That, for the purpose of determining any liability under the Securities Act, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered herein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

(4) That, for the purpose of determining liability of the Registrant under the Securities Act to any purchaser in the initial distribution of the securities: The undersigned Registrant undertakes that in a primary offering of securities of the undersigned Registrant pursuant to this Registration Statement, regardless of the underwriting method used to sell the securities to the purchaser, if the securities are offered or sold to such purchaser by means of any of the following communications, the undersigned Registrant will be a seller to the purchaser and will be considered to offer or sell such securities to such purchaser:

(i) Any preliminary prospectus or prospectus of the undersigned Registrant relating to the offering required to be filed pursuant to Rule 424 (§ 230.424);

(ii) Any free writing prospectus relating to the offering prepared by or on behalf of the undersigned Registrant or used or referred to by the undersigned Registrant;

(iii) The portion of any other free writing prospectus relating to the offering containing material information about the undersigned Registrant or its securities provided by or on behalf of the undersigned Registrant; and

(iv) Any other communication that is an offer in the offering made by the undersigned Registrant to the purchaser.

(b) The undersigned Registrant hereby undertakes that, for purposes of determining any liability under the Securities Act, each filing of the Registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Exchange Act) that is incorporated by reference in the Registration Statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial *bona fide* offering thereof.

(c) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the foregoing provisions, or otherwise, the Registrant has been advised that in the opinion of the Securities and Exchange Commission (the "Commission") such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the Registrant of expenses incurred or paid by a director, officer or controlling person of the Registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the Registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Carlsbad, State of California, on August 5, 2021.

IONIS PHARMACEUTICALS, INC.

By: /s/ Brett Monia
Brett Monia
Chief Executive Officer

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes Brett Monia and Elizabeth Hougen, and each or any one of them, as his or her true and lawful attorney-in-fact and agent, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, and to file the same, with all exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in connection therewith, as fully to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them, or their or his or her substitutes or substitute, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated.

Signature	Title	Date
<u>/s/ Brett Monia</u> Brett Monia	Chief Executive Officer (Principal Executive Officer)	August 5, 2021
<u>/s/ Elizabeth Hougen</u> Elizabeth Hougen	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	August 5, 2021
<u>/s/ Joseph Loscalzo</u> Joseph Loscalzo	Chairman of the Board	August 5, 2021
<u>/s/ Spencer R. Berthelsen</u> Spencer R. Berthelsen	Director	August 5, 2021
<u>/s/ Allene Diaz</u> Allene Diaz	Director	August 5, 2021
<u>/s/ Michael Hayden</u> Michael Hayden	Director	August 5, 2021
<u>/s/ Joan Herman</u> Joan Herman	Director	August 5, 2021
<u>/s/ Joseph Klein, III</u> Joseph Klein, III	Director	August 5, 2021
<u>/s/ Frederick Muto</u> Frederick Muto	Director	August 5, 2021
<u>/s/ B. Lynne Parshall</u> B. Lynne Parshall	Director	August 5, 2021
<u>/s/ Peter Reikes</u> Peter Reikes	Director	August 5, 2021
<u>/s/ Joseph Wender</u> Joseph Wender	Director	August 5, 2021

August 5, 2021

Ionis Pharmaceuticals, Inc.
2855 Gazelle Court
Carlsbad, CA 92010

Ladies and Gentlemen:

You have requested my opinion with respect to certain matters in connection with the filing by Ionis Pharmaceuticals, Inc. (the "Company") of a Registration Statement on Form S-8 (the "Registration Statement") with the Securities and Exchange Commission, covering the offering of an additional 6,700,000 shares of the Company's Common Stock, \$.001 par value (the "Shares"), of which, 6,700,000 Shares are issuable pursuant to its Amended and Restated 2011 Equity Incentive Plan (the "2011 Plan") as described in the Registration Statement.

In connection with this opinion, I have examined and relied upon the Registration Statement, the Company's Restated Certificate of Incorporation, as amended, and Bylaws and the originals or copies certified to my satisfaction, of such records, documents, certificates, memoranda and other instruments as in my judgment are necessary or appropriate to enable me to render the opinion expressed below.

On the basis of the foregoing, and in reliance thereon, I am of the opinion that the Shares, when issued and sold in accordance with the 2011 Plan and related prospectuses, will be validly issued, fully paid and nonassessable.

I consent to the reference to myself under the caption "Interests of Named Experts and Counsel" in the Registration Statement and to the filing of this opinion as an exhibit to the Registration Statement.

Very truly yours,

/s/ Patrick R. O'Neil

Patrick R. O'Neil
Executive Vice President, Legal, General Counsel and
Corporate Secretary

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8) pertaining to the Amended and Restated 2011 Equity Incentive Plan of Ionis Pharmaceuticals, Inc. of our reports dated February 24, 2021, with respect to the consolidated financial statements of Ionis Pharmaceuticals, Inc. and the effectiveness of internal control over financial reporting of Ionis Pharmaceuticals, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2020, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

San Diego, California
August 5, 2021
