

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
PURSUANT TO SECTION 13 OR 15(d) OF THE
SECURITIES EXCHANGE ACT OF 1934

Date of report (Date of earliest event reported): March 22, 2019

IONIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware

(State or Other Jurisdiction of Incorporation)

000-19125

(Commission File No.)

33-0336973

(IRS Employer Identification No.)

2855 Gazelle Court
Carlsbad, CA 92010

(Address of Principal Executive Offices and Zip Code)

Registrant's telephone number, including area code: **(760) 931-9200**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (Section 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (Section 240.12b-2 of this chapter).

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 13(a) of the Exchange Act.

Item 5.02 Departure of Directors or Certain Officers; Election of Directors; Appointment of Certain Officers; Compensatory Arrangements of Certain Officers.

(d) Appointment of Dr. Brett Monia to Board of Directors

On March 22, 2019, the Board of Directors (the “**Board**”) of Ionis Pharmaceuticals, Inc. (the “**Company**”) increased the size of the Board from ten directors to eleven directors and appointed Brett Monia, Ph.D, the Company’s Chief Operating Officer, to the Board to fill the resulting vacancy. Dr. Monia will serve on the Board’s Agenda Committee, effective immediately.

Since the beginning of the Company’s last fiscal year through the present, there have been no related person transactions between Dr. Monia and the Company, and there are currently no proposed related person transactions between Dr. Monia and the Company, within the meaning of Item 404(a) of Regulation S-K. There are no arrangements or understandings between Dr. Monia and any other persons pursuant to which Dr. Monia was appointed as a director of the Company.

A copy of the press release announcing the appointment of Dr. Monia is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

(e) Amended and Restated Advisory Services Agreement between the Company and B. Lynne Parshall

As the Company previously reported on its Current Report on Form 8-K filed on January 16, 2018, B. Lynne Parshall, who was with the Company for 27 years and was the Company’s former Chief Operating Officer, became a Senior Strategic Advisor to the Company effective January 2018. The Company and Ms. Parshall entered into a Strategic Advisory Services Agreement on January 15, 2018 to reflect her new role (the “**Advisory Services Agreement**”). In 2018, Ms. Parshall performed significantly more services than originally expected. The Company thus agreed, with the approval of the Compensation Committee, to increase the amount of fees to be paid to Ms. Parshall commensurate with the amount of additional work performed and agreed that Ms. Parshall would be eligible for a bonus with a target of 30% of her fees with a personal performance factor and final bonus amount to be approved by the Compensation Committee.

On March 22, 2019, the Company and Ms. Parshall entered into an amendment and restatement of the Advisory Services Agreement (the “**Amended and Restated Advisory Services Agreement**”). Pursuant to the Amended and Restated Advisory Services Agreement, Ms. Parshall will receive compensation of \$500,000 for services we expect Ms. Parshall to provide in the fiscal year ending December 31, 2019, which amount may be increased (but will not exceed \$750,000 for the year) if Ms. Parshall renders more services than currently expected. In addition, at the conclusion of each fiscal year, Ms. Parshall will be eligible for a bonus with a target of 35% of her fees with a personal performance factor to be approved by the Compensation Committee. Payment for services after 2019 will be set by mutual written agreement between the Company and Ms. Parshall.

Ms. Parshall will continue to serve on the board of directors of the Company and Akcea Therapeutics, Inc. (“*Akcea*”). Ms. Parshall will receive for her board service the same compensation as the Company and Akcea provide their other nonemployee directors. If in the future Ms. Parshall ends her board of director service for the Company, for 18 months following such date, the Company will pay Ms. Parshall’s COBRA premium payments, or if COBRA is not available, an amount equal to the cost of comparable health insurance coverage. The Amended and Restated Advisory Services Agreement will continue until terminated by the Company or Ms. Parshall upon 120 days’ advance written notice.

The foregoing summary of the Amended and Restated Advisory Services Agreement does not purport to be complete and is qualified in its entirety by reference to the Amended and Restated Advisory Services Agreement, a copy of which is attached hereto as Exhibit 10.1 to this Current Report on Form 8-K and incorporated herein by reference.

(e) Amendment and Restatement of Employee Stock Purchase Plan

On March 22, 2019, the Board adopted and approved an amendment and restatement of the Company’s 2000 Employee Stock Purchase Plan (the “*ESPP*”) to extend the ESPP so that it will terminate on March 21, 2029. No additional shares were added to the ESPP.

The foregoing description of the amended and restated ESPP does not purport to be complete and is qualified in its entirety by reference to the amended and restated ESPP, a copy of which is attached hereto as Exhibit 10.2 to this Current Report on Form 8-K and incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

- [10.1](#) Amended and Restated Advisory Services Agreement dated March 22, 2019
 - [10.2](#) Ionis Pharmaceuticals, Inc. Amended and Restated 2000 Employee Stock Purchase Plan
 - [99.1](#) Press Release dated March 25, 2019
-

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

IONIS PHARMACEUTICALS, INC

Dated: March 26, 2019

By: /s/ Patrick R. O'Neil

PATRICK R. O'NEIL

Senior Vice President, Legal, General
Counsel and Chief Compliance Officer



**AMENDED AND RESTATED IONIS PHARMACEUTICALS, INC.
STRATEGIC ADVISORY SERVICES AGREEMENT
("SUMMARY PAGE")**

This Amended and Restated Strategic Advisory Services Agreement is entered into and made effective as of March 22, 2019, and amends and restates the Strategic Advisory Service Agreement dated January 15, 2018, by and between B. Lynne Parshall and Ionis Pharmaceuticals, Inc. ("**Ionis**")

Date of Strategic Advisory Services Agreement: (" Agreement ")	January 15, 2018 (" Effective Date "). Effective Date of Amendment and Restatement March 22, 2019.
Name of Strategic Advisor:	B. Lynne Parshall (hereinafter " Strategic Advisor ").
Scope of Strategic Advisory Services:	As set forth on Schedule A attached hereto.
Duration of Strategic Advisory Services (the " Strategic Advisory Period "):	Until termination by Ionis or Strategic Advisor in accordance with Section 8 of Exhibit A below.
Consideration for Strategic Advisory Services:	As set forth on Schedule B attached hereto.
Time Provided by Strategic Advisor:	As set forth on Schedule A attached hereto.

In addition to such compensation, Ionis will reimburse Strategic Advisor for Ionis approved travel and other out-of-pocket costs reasonably incurred in the course of performing Strategic Advisory Services under this Agreement as further described on Schedule B attached hereto.

Strategic Advisor agrees to provide Ionis with Strategic Advisory Services on the terms described above and according to the additional terms attached hereto as Exhibit A. In this Agreement references to Ionis, including but not limited to Sections 3-6 of Exhibit A, will include Ionis' affiliate companies where applicable.

	Strategic Advisor	Ionis Pharmaceuticals, Inc.
By (Signature):	<u>/s/ B. Lynne Parshall</u>	<u>/s/ Stanley T. Crooke</u>
Date:		<u>3/21/19</u>
Printed Name:	<u>B. Lynne Parshall</u>	<u>Stanley T. Crooke</u>
Title:	<u>Individual</u>	
Address:	<u>Provided Separately</u>	<u>2855 Gazelle Court,</u>
Telephone:	<u>Provided Separately</u>	<u>Carlsbad, CA 92010</u>
Fax:	<u>Provided Separately</u>	<u>760-931-9200</u>
e-mail:	<u>Provided Separately</u>	<u>760-603-3820</u>

Social Security or Employer Tax ID Number to be provided separately via W-9 form or foreign equivalent.

TERMS OF STRATEGIC ADVISORY AGREEMENT

1. **Engagement of Services**

Strategic Advisor is retained to perform certain services, as needed and requested by Ionis, which services are specifically described on Schedule A attached hereto ("**Strategic Advisory Services**"). Strategic Advisor will perform such Strategic Advisory Services to the best of Strategic Advisor's talent and ability.

2. **Compensation**

As full and complete compensation for Strategic Advisory Services and for the discharge of all of Strategic Advisor's obligations hereunder, Ionis will pay Strategic Advisor at the rate set forth on Schedule B attached hereto. Strategic Advisor will invoice Ionis on a quarterly basis for Strategic Advisor fees and reimbursable expenses, and Ionis, upon its approval, will pay all undisputed fees and expenses within 30 days after Ionis' receipt of the invoice.

3. **Independent Contractor**

Strategic Advisor is an independent contractor and not an employee of Ionis. Strategic Advisor has no authority to obligate Ionis by contract or otherwise. Strategic Advisor will not be eligible for any employee benefits. Taxes will be the sole responsibility of Strategic Advisor.

4. **Additional Activities**

- (a) Strategic Advisor agrees that during the Strategic Advisory Period and for one year thereafter, Strategic Advisor will not attempt to induce any employee or employees of Ionis to terminate their employment with, or otherwise cease their relationship with Ionis.
- (b) Strategic Advisor acknowledges that Ionis has developed, through an extensive acquisition process, valuable information regarding actual or prospective partners, licensors, licensees, clients, customers and accounts of Ionis ("**Trade Secret Information**"). Strategic Advisor acknowledges that Strategic Advisor's use of such Trade Secret Information after the termination of the Strategic Advisory Period would cause Ionis irreparable harm. Therefore, Strategic Advisor also agrees that Strategic Advisor will not utilize any Trade Secret Information to solicit the business relationship or patronage of any of the actual or prospective partners, licensors, licensees, clients, customers or accounts of Ionis.
- (c) The restrictions set forth in this Section 4 are considered by the parties to be reasonable for the purposes of protecting Ionis' business. However, if any such restriction is found by a court of competent jurisdiction to be unenforceable because it extends for too long a period of time or over too great a range of activities or in too broad a geographic area, it will be interpreted to extend only over the maximum period of time, range of activities or geographic areas as to which it may be enforceable.

5. **Confidential Information**

- (a) Ionis possesses confidential information that has been created, discovered, developed by, or otherwise become known to Ionis (including, without limitation, information created, discovered, developed or made known by Strategic Advisor arising from the Strategic Advisory Services).
- (i) All such information is hereinafter referred to as “**Confidential Information.**” By way of illustration, but not limitation, Confidential Information includes: (A) inventions, developments, designs, improvements, trade secrets, ideas, formulas, source and object codes, programs, other works of authorship, organisms, plasmids, expression vectors, know-how, processes, cell lines, discoveries, techniques, data and documentation systems (hereinafter collectively referred to as “**Inventions**”); and (B) information regarding plans for research, development, new products, clinical data, pre-clinical product data, clinical trial patient data, marketing and selling, business plans, budgets and unpublished financial statements, licenses, prices and costs, as well as information regarding the skills and compensation of employees of Ionis.
- (ii) All Confidential Information will be the sole property of Ionis and its assigns, and Ionis and its assigns will be the sole owner of all patents, copyrights and other rights in connection with such Confidential Information. At all times, both during the term of this Agreement and for five years after its termination, Strategic Advisor will keep in confidence and trust all Confidential Information and will not use, disclose, lecture upon or publish any Confidential Information or anything related to such information without Ionis’ prior written consent. Any permitted disclosures will be made in strict compliance with the Ionis publication and presentation clearance policy.
- (b) Strategic Advisor also understands that Ionis has received and in the future, will receive valuable information from third parties that is confidential or proprietary (“**Third-Party Information**”) subject to a duty on the part of Ionis to maintain the confidentiality of such information and to use it only for certain limited purposes. During the term of this Agreement and for five years thereafter, Strategic Advisor will hold Third-Party Information in the strictest confidence and will not disclose or use Third-Party Information except as permitted by the agreement between Ionis and such third party, unless expressly authorized to act otherwise by an officer of Ionis in writing. Any permitted disclosures will be made in strict compliance with Ionis publication and presentation clearance policy.
- (c) The obligations of Section 5 will not apply to information that Strategic Advisor can establish by written records: (i) was known by Strategic Advisor prior to the receipt of Confidential Information; (ii) was disclosed to Strategic Advisor by a third party having the right to do so; (iii) was, or subsequently became, in the public domain through no fault of Strategic Advisor, its officers, directors, affiliates employees or agents; (iv) was independently developed by Strategic Advisor without use of Confidential Information; or (v) was disclosed by Strategic Advisor pursuant to any judicial, governmental or stock exchange request, requirement or order, so long as Strategic Advisor provided Ionis with sufficient prior notice in order to allow Ionis to contest such request, requirement or order.

6. **Inventions**

In the course of performing Strategic Advisory Services for Ionis, Strategic Advisor may develop new ideas or Inventions or make other contributions of value to Ionis.

- (a) Strategic Advisor hereby assigns to Ionis Strategic Advisor's entire right, title and interest in and to any and all Inventions (and all patent rights, copyrights, and all other rights in connection therewith, hereinafter referred to as "**Proprietary Rights**") whether or not patentable or registrable under patent, copyright or similar statutes, made or conceived of or reduced to practice or learned by Strategic Advisor, either alone or jointly with others, as a result of performing Strategic Advisory Services hereunder. All Inventions assigned to Ionis pursuant to this section will be known as "**Company Inventions**". Strategic Advisor agrees that all Proprietary Rights and Company Inventions are Ionis' sole property. Strategic Advisor agrees, upon request, to execute, verify and deliver assignments of such Proprietary Rights to Ionis or its designee. Strategic Advisor understands that, to the extent this Agreement will be construed in accordance with the laws of any state which precludes a requirement in an agreement to assign certain classes of inventions made by an individual acting as a Strategic Advisor, this section will be interpreted not to apply to any inventions that a court rules and/or Ionis agrees falls within such classes.
- (b) Strategic Advisor further agrees to assist Ionis in every proper way to obtain, from time to time, and to enforce United States and foreign Proprietary Rights relating to Company Inventions in any and all countries. To that end Strategic Advisor will execute, verify and deliver such documents and perform such other acts (including appearances as a witness) as Ionis may reasonably request for use in applying for, obtaining, sustaining and enforcing such Proprietary Rights relating to Company Inventions. Strategic Advisor's obligation to assist Ionis in obtaining and enforcing Proprietary Rights relating to Company Inventions in any and all countries will continue beyond the termination of this Agreement, but Ionis will compensate Strategic Advisor at a reasonable rate after such termination for the time actually spent by Strategic Advisor at Ionis' request in connection with such assistance. If Ionis is unable, after reasonable effort, to secure Strategic Advisor's signature on any document needed to apply for or prosecute any Proprietary Rights relating to a Company Invention, Strategic Advisor hereby irrevocably designates and appoints Ionis and its duly authorized officers and agents as her agent and attorney in fact, to act for and on Strategic Advisor's behalf to execute, verify and file any such applications and to do all other lawfully permitted acts to further the prosecution and issuance of any such Proprietary Rights with the same legal force and effect as if executed by Strategic Advisor.

(d) During the term of this Agreement, Strategic Advisor will promptly disclose to Ionis, or any persons designated by it, fully and in writing and will hold in trust for the sole right and benefit of Ionis any and all Company Inventions, whether or not patentable or protectable by copyright. At the time of each such disclosure, Strategic Advisor will advise Ionis in writing of any Inventions that Strategic Advisor believes are not subject to the assignment provisions of Section 6(a) above, and Strategic Advisor will at that time provide to Ionis in writing all evidence necessary to substantiate that belief. Strategic Advisor will not be obligated to disclose information received by Strategic Advisor from others under a contract of confidentiality. In addition, after termination of this Agreement, Strategic Advisor will disclose to Ionis all patent applications filed by Strategic Advisor relating to any Company Inventions or relating to any work performed by Strategic Advisor on behalf of Ionis.

7. **Previous Strategic Advisory Relationships**

Strategic Advisor represents that Strategic Advisor's performance of Strategic Advisory Services, as well as Strategic Advisor's performance of the rest of Strategic Advisor's obligations under the terms of this Agreement, will not breach any agreement to keep in confidence any proprietary information acquired by Strategic Advisor in confidence or in trust from another entity prior to the date of this Agreement. Strategic Advisor agrees not to bring to Ionis or to use in the performance of Strategic Advisory Services for Ionis any materials or documents of a present or former employer or client of Strategic Advisor, or any materials or documents obtained by Strategic Advisor under a confidentiality agreement imposed by reason of another of Strategic Advisor's Strategic Advisory relationships, unless such materials or documents are generally available to the public or Strategic Advisor has authorization from such present or former employer or client for the possession and unrestricted use of such materials.

8. **Termination; Survival**

(a) The term of this Agreement will begin on January 15, 2018 and will end when terminated by either Ionis or Strategic Advisor. Ionis may terminate this Agreement at any time for any reason by providing Strategic Advisor at least 120 days advance written notice. Strategic Advisor may terminate this Agreement at any time for any reason by providing Ionis at least 120 days advance written notice; *provided*, once Strategic Advisor delivers such a termination notice, Ionis may elect to accelerate the effective date of such termination. Upon any termination, Ionis will pay Strategic Advisor for any Strategic Advisory Services appropriately rendered and for any out of pocket expenses reasonably incurred on behalf of Ionis, up to and including the termination date.

(b) Sections 9 and 10, the last sentence of the second paragraph of Schedule B and the last paragraph of Schedule B will survive termination of this Agreement. In addition, upon expiration or termination of this Agreement, each party will be released from all obligations and liabilities to the other occurring or arising after the date of such expiration or termination, except that any termination or expiration of this Agreement will not relieve Strategic Advisor of Strategic Advisor's obligations under Sections 4, 5, 6, 7, 9, 10 and 11 hereof, nor will any such expiration or termination relieve Strategic Advisor or Ionis from any liability arising from any breach of this Agreement. Upon expiration or termination of this Agreement for any reason whatsoever, Strategic Advisor will promptly surrender and deliver to Ionis any and all notes, business records, memoranda, specifications, devices, formulas, molecules, cells, storage media, including calculations, sequences, data and other materials of any nature pertaining to Strategic Advisory Services for Ionis, as well as any documents or data of any description (or any reproduction of any documents or data) containing or pertaining to any Trade Secret Information, Ionis' Confidential Information or Third Party Information.

9. **Arbitration**

- (a) Ionis and Strategic Advisor agree to resolve by arbitration all disputes, claims or controversies (“**Claims**”), past, present or future, whether or not arising out of this Agreement or its termination, that Ionis may have against Strategic Advisor or that Strategic Advisor may have against any of the following (i) Ionis; (ii) Ionis officers, directors; employees or agents; (iii) Ionis’ subsidiary or affiliated entities, joint ventures, or joint employers; (iv) Ionis’ benefit plans or the plans’ sponsors, fiduciaries, administrators, affiliates and agents; and/or (v) all successors and assigns of any of the foregoing. The Claims covered by this Agreement include all disputes that Ionis or Strategic Advisor could otherwise pursue in state or federal court including, but not limited to, Claims based on any state, federal, or local statute, regulation or ordinance (including Claims for discrimination, retaliation, harassment, unpaid wages or violation of state or federal wage and hour laws), as well as common law Claims (including Claims for breach of contract, breach of the implied covenant of good faith and fair dealing, wrongful discharge, defamation, misrepresentation, fraud, or infliction of emotional distress). Ionis and Strategic Advisor anticipates that this Section 9 provides the benefits of a speedy, less formal, impartial, final and binding dispute resolution procedure.
- (b) To the maximum extent permitted by law, Strategic Advisor hereby waives any right to bring on behalf of persons other than Strategic Advisor, or to otherwise participate with other persons in, any class, collective or representative action (i.e. a type of lawsuit in which one or several persons sue on behalf of a larger group of persons).
- (c) The arbitration will be conducted by a single neutral arbitrator in accordance with the then-current Commercial Arbitration and Mediation Procedures of the American Arbitration Association (“**AAA**”). The arbitration will take place in San Diego, California. Ionis will pay the arbitrator’s fee and will bear all administrative charges by AAA. All parties will be entitled to engage in reasonable pre-hearing discovery to obtain information to prosecute or defend the asserted claims. Any disputes between the parties regarding the nature or scope of discovery will be decided by the arbitrator. The arbitrator will hear and issue a written ruling upon any dispositive motions brought by either party, including but not limited to, motions for summary judgment or summary adjudication of issues. After the hearing, the arbitrator will issue a written decision setting forth the award, if any, and explaining the basis therefore. The arbitrator will have the power to award any type of relief that would be available in court. The arbitrator’s award will be final and binding upon the parties and may be entered as a judgment in any court of competent jurisdiction. If there is conflict in the arbitration procedures set forth in this Agreement and the AAA rules specified above, the AAA rules will control. Notwithstanding the foregoing, and regardless of what is provided by the AAA rules, the arbitrator will not have authority or jurisdiction to consolidate claims of different individuals or entities into one proceeding, nor will the arbitrator have authority or jurisdiction to hear the arbitration as a class action. As noted above, Strategic Advisor has agreed to waive any right to bring any class, collective or representative action. To the extent that the class, collective or representative action waiver described above is not enforceable, the issue of whether to certify any alleged or putative class for a class action proceeding must be decided by a court of competent jurisdiction. The arbitrator will not have authority or jurisdiction to decide class certification, collective or representative action issues. Until any class certification, collective, or representative action issues are decided by the court, all arbitration proceedings will be stayed, and the arbitrator will take no action with respect to the matter. However, once any issues regarding class certification, collective, or representative action have been decided by the court, the arbitrator will have authority to decide the substantive claims.

10. **Indemnification**

- (a) Ionis will indemnify, defend and hold Strategic Advisor harmless against any and all losses, costs, expenses and damages (including reasonable attorney's fees) ("Loss(es)") incurred as a result of any third party claims, suits, actions, demands or proceedings resulting or arising from the performance of Strategic Advisory Services as specifically directed by Ionis in accordance with the Agreement to the extent such Loss(es) are not the result of Strategic Advisor's gross negligence, intentional misconduct or material breach of this Agreement.
- (b) Ionis' agreement to indemnify, defend and hold Strategic Advisor harmless is conditioned upon the Strategic Advisor (i) providing written notice to Ionis of any claim, demand or action arising out of the indemnified activities within thirty (30) days after Strategic Advisor has knowledge of such claim, demand or action, *provided* that the failure to so notify Ionis shall not relieve Ionis of its obligations hereunder except to the extent such failure shall have actually materially prejudiced Ionis; (ii) permitting Ionis to assume full responsibility to investigate, prepare for and defend against any such claim or demand; (iii) assisting Ionis, at Ionis' reasonable expense, in the investigation of, preparation of and defense of any such claim or demand; (iv) undertaking reasonable steps to mitigate any loss, damage or expense with respect to the applicable claim or demand; and (v) not settling such claim or demand without Ionis' prior written consent.
- (c) Ionis will endeavor to include Strategic Advisor as a covered attorney on its insurance policy for attorneys who advise Ionis.

11. **Miscellaneous**

- (a) The rights and liabilities of the parties hereto will bind and inure to the benefit of their respective successors, heirs, executors and administrators, as the case may be; *provided that*, as Ionis has specifically contracted for Strategic Advisor's services, Strategic Advisor may not assign or delegate Strategic Advisor's obligations under this Agreement either in whole or in part without Ionis' prior written consent.
- (b) Because Strategic Advisor's services are personal and unique and because Strategic Advisor has access to and become acquainted with Ionis' Confidential Information, the parties agree that in the event of a threatened or actual material breach of this Agreement by Strategic Advisor injunctive relief would be appropriate. As such, Ionis has the right to enforce this Agreement and any of its provisions by injunction, specific performance or other equitable relief without prejudice to any other rights and remedies that Ionis may have for a breach of this Agreement.
- (c) This Agreement will be governed by and construed according to the laws of the State of California as such laws are applied to contracts entered into and performed entirely within such State. If any provision of this Agreement is held to be or becomes invalid, illegal or unenforceable, such provision will be validly reformed to approximate as nearly as possible the intent of the parties and the remainder of this Agreement will not be affected thereby and will remain valid and enforceable to the greatest extent permitted by law.
- (d) This Agreement, and all other documents mentioned herein, constitute the final, exclusive and complete understanding and agreement of the parties hereto and supersedes all prior understandings and agreements. Any waiver, modification or amendment of any provision of this Agreement will be effective only if in writing and signed by the parties hereto.
- (e) Any notices required or permitted hereunder will be given to the appropriate party at the address specified on the Summary Page or at such other address as the party will specify in writing. Such notice will be deemed given upon personal delivery to the appropriate address, or by facsimile transmission (receipt verified and with confirmation copy followed by another permitted method), sent by express courier service, or, if sent by certified or registered mail, three (3) days after the date of mailing.

[END OF EXHIBIT A]

SCHEDULE A

Strategic Advisory Services

Ionis Board of Directors

You will serve on the Ionis board of directors as a nonemployee director until your resignation or removal in accordance with Ionis' corporate charter. Ionis will recommend that you serve on the Agenda committee of the Board, and periodically evaluate your ability to serve on other Board committees to the extent permitted by applicable SEC and Nasdaq rules. You will participate in other Board Committee meetings as requested as a non-member.

Akcea Board of Directors

Ionis will recommend that you serve on the Akcea board of directors as a nonemployee director until your resignation or removal in accordance with Akcea's corporate charter. You will serve on the Audit Committee during Akcea's first year as a public company and as permitted by applicable SEC and Nasdaq rules, and participate in other committees as a member or non-member as requested.

Strategic Neurology/Rare Disease Subsidiary Board of Directors

When Ionis forms a strategic neurological/rare disease focused subsidiary, you will serve on the board of directors of such subsidiary as a non employee director on the same terms as other non employee directors until your resignation or removal in accordance with the subsidiary's corporate charter.

Additional Strategic Advisory Services

You will provide Ionis strategic advice regarding Ionis' business, including but not limited to the following:

Through July 1, 2018, you will provide approximately forty hours per week of strategic advice. After July 1, 2018 and continuing through the end of 2018 it is anticipated you will provide approximately five business days of strategic advice each month. For each year following 2018, you and Ionis will mutually agree on the approximate number of business days each month you will provide strategic advice during such year. You will make yourself generally available for conference calls and in person meetings Ionis invites you to attend. You will travel to locations as reasonably requested by Ionis, including to Ionis, Akcea, Ionis' partners, or other locations where Ionis is conducting corporate development activities (e.g. JP Morgan conference or strategic off-site meetings). You and Ionis expect that, you will participate in Ionis' development management committee (DMC) meetings, Ionis' affiliate's and Biogen joint steering committee meetings, and through July 1, 2018 and thereafter when requested, Ionis' strategic management meetings (e.g. G8 meetings). As requested by Ionis, you will facilitate Ionis' strategic partnerships and help develop Ionis' subsidiaries' and affiliates' senior management teams. You will help Ionis' new CBO be trained and assimilated into Ionis' business team. You will help Ionis' new COO as requested be trained and assimilated into Ionis' business team. You will work with the CEO, COO and others on strategic planning and direction for the Company. You will participate in major corporate communication initiatives, including business/financial messaging and rebranding project. You will participate in structuring and negotiating as requested new strategic alliances. Your advisory services may include providing Ionis legal advice.

You and Ionis will reasonably coordinate to have you present on site for board of directors meetings, and a few days before and/or after such meetings to perform strategic advisory services. The time you spend preparing for or attending board of directors or board committee meetings for Ionis, Akcea or any subsidiary will not count towards your commitment to perform additional strategic advisory services outlined above, except if you attend Akcea Board committee meetings as an observer on Ionis' behalf (and Akcea does not compensate you for such attendance), such attendance will count as strategic advisory services.

While you are providing such services, Ionis will make an appropriate level of administrative and technical personnel available to facilitate your performance of Advisory Services at no cost to you, including, without limitation IT support and access to Ionis' electronic calendar and IT systems that are necessary to perform your duties.

SCHEDULE B

Compensation for Strategic Advisory Services

Ionis Board of Directors

For your service on the Ionis board of directors, starting with the first quarter of 2018, you will receive the same compensation as Ionis provides its other nonemployee directors. You will not receive an initial nonemployee director award. Starting in 2018, you will receive the same annual equity awards as Ionis' other nonemployee directors. You will also be eligible for any benefits (including any applicable health benefits) Ionis provides to its nonemployee directors.

Akcea Board of Directors

For your service on the Akcea board of directors, you will receive the same compensation as Akcea provides its other nonemployee directors. On January 15, 2018, you will receive an initial nonemployee director stock option award of 52,837 shares with an option exercise price equal to the fair market value of Akcea's stock on that day. Thereafter, you will receive the same annual equity awards as Akcea's other nonemployee /outside directors.

Strategic Neurology/Rare Disease Subsidiary Board of Directors

For your service on the board of directors of Ionis' strategic neurological/rare disease subsidiary (if formed), you will receive the same compensation (including equity awards) as such subsidiary provides its other nonemployee /outside directors.

Additional Strategic Advisory Services

For your other strategic advisory services, starting in the fiscal year ending in 2018, Ionis will pay you as follows:

- \$375,000 for services rendered through June 30, 2018 to be paid in two installments.
- \$125,000 for services rendered July 1, 2018 through December 31, 2018 paid in quarterly installments; *provided, however*, that if you provide more than thirty-seven full days during the aforementioned period, then payment for additional days will be made on a pro-rata basis, such compensation to be confirmed by the Ionis Compensation Committee and not to exceed \$750,000 for any year.
- Upon the conclusion of each fiscal year, you will be eligible to receive a bonus at the 35% bonus level of Ionis' MBO Plan with the personal performance factor recommended by the Ionis CEO and approved by the Ionis Compensation Committee and the corporate performance factor determined and approved by the Ionis Board of Directors pro-rated by the total number of full days of service you provided in the applicable fiscal year. For purposes of the Ionis MBO Plan 220 days constitutes full-time employment.

Since you are transitioning seamlessly from an Ionis employee to a nonemployee director, the stock options and RSUs you received for your previous service as an Ionis employee will continue to vest so long as your Continuous Service (as defined in the applicable equity plan) continues. Once you are no longer serving on the Ionis board and no longer providing strategic advisory services, to the extent permitted by the terms of the applicable stock option agreement, your vested stock options will not terminate until the earlier of 18 months following your retirement or the expiration of the original term of such stock option.

For Ionis-directed travel and lodging Ionis will reimburse you for such travel, lodging and related expenses or reasonable rate equivalents for lodging, car and meals you provide. All such reimbursements will be in accordance with Ionis' travel policy and you will provide Ionis reasonably acceptable supporting documentation.

For the 18 months following the end of your Ionis board of directors services, if you are eligible for continued health coverage under COBRA, Ionis will pay your COBRA premium payments sufficient to continue your coverage at your then current level, or if COBRA is not available, Ionis will pay you an amount equal to the cost of comparable replacement coverage.

IONIS PHARMACEUTICALS, INC.

2000 EMPLOYEE STOCK PURCHASE PLAN

Approved by the Board of Directors on January 6, 2000

Approved by Stockholders on June 8, 2000

Amended on September 23, 2003

Amended and Restated by the Board of Directors on February 27, 2009

Amended and Restated by the Stockholders on June 2, 2009

Amended and Restated by the Board of Directors on March 22, 2019

1. PURPOSE.

(a) The purpose of this Amended and Restated 2000 Employee Stock Purchase Plan (the "Plan") is to provide a means by which employees of Ionis Pharmaceuticals, Inc. (the "Company") and its Affiliates, as defined in Subsection 1(b), which are designated as provided in Subsection 2(b), may be given an opportunity to purchase common stock of the Company (the "Common Stock"). Effective March 22, 2019 (the "A&R Effective Date") this Plan supersedes and replaces the 2000 Employee Stock Purchase Plan adopted by the Company's stockholders on June 2, 2009, as amended.

(b) The word "Affiliate" as used in the Plan means any parent corporation or subsidiary corporation of the Company, as those terms are defined in Sections 424(e) and (f), respectively, of the Internal Revenue Code of 1986, as amended (the "Code").

(c) The Company, by means of the Plan, seeks to retain the services of its employees, to secure and retain the services of new employees, and to provide incentives for such persons to exert maximum efforts for the success of the Company.

(d) The Company intends that the rights to purchase stock of the Company granted under the Plan be considered options issued under an "employee stock purchase plan" as that term is defined in Section 423(b) of the Code.

2. ADMINISTRATION.

(a) The Plan shall be administered by the Board of Directors (the "Board") of the Company unless and until the Board delegates administration to a Committee, as provided in Subsection 2(c). Whether or not the Board has delegated administration, the Board shall have the final power to determine all questions of policy and expediency that may arise in the administration of the Plan.

(b) The Board shall have the power, subject to, and within the limitations of, the express provisions of the Plan:

(i) To determine when and how rights to purchase stock of the Company shall be granted and the provisions of each offering of such rights (which need not be identical).

(ii) To designate from time to time which Affiliates of the Company shall be eligible to participate in the Plan.

(iii) To construe and interpret the Plan and rights granted under it, and to establish, amend and revoke rules and regulations for its administration. The Board, in the exercise of this power, may correct any defect, omission or inconsistency in the Plan, in a manner and to the extent it shall deem necessary or expedient to make the Plan fully effective.

(iv) To amend the Plan as provided in Section 13.

(v) To terminate or suspend the Plan as provided in Section 15.

(vi) Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company and its Affiliates and to carry out the intent that the Plan be treated as an "employee stock purchase plan" within the meaning of Section 423 of the Code.

(c) The Board may delegate administration of the Plan to a Committee composed of not fewer than two (2) members of the Board (the "Committee"). If administration is delegated to a Committee, the Committee shall have, in connection with the administration of the Plan, the powers theretofore possessed by the Board, subject, however, to such resolutions, not inconsistent with the provisions of the Plan, as may be adopted from time to time by the Board. The Board may abolish the Committee at any time and revert in the Board the administration of the Plan.

3. SHARES SUBJECT TO THE PLAN.

(a) The Company's board of directors and stockholders have previously approved reserving a number of shares for purchase under this plan (the "Reserved Shares"). As of the A&R Effective Date, and subject to the provisions of Section 12 relating to the adjustments upon changes in stock, there were 749,699 shares available for future sale under the Plan. If any right granted under the Plan shall for any reason terminate without having been exercised, the Common Stock not purchased under such right shall again become available for the Plan.

(b) The stock subject to the Plan may be unissued shares or reacquired shares, bought on the market or otherwise.

4. GRANT OF RIGHTS; OFFERING.

The Board or the Committee may from time to time grant or provide for the grant of rights to purchase Common Stock of the Company under the Plan to eligible employees (an "Offering") on a date or dates (the "Offering Date(s)") selected by the Board or the Committee. Each Offering shall be in such form and shall contain such terms and conditions as the Board or the Committee shall deem appropriate, which shall comply with the requirements of Section 423(b)(5) of the Code that all employees granted rights to purchase stock under the Plan shall have the same rights and privileges.

The terms and conditions of an Offering shall be incorporated by reference into the Plan and treated as part of the Plan. The provisions of separate Offerings need not be identical, but each Offering shall include (through incorporation of the provisions of this Plan by reference in the document comprising the Offering or otherwise) the period during which the Offering shall be effective, which period shall not exceed six (6) months beginning with the Offering Date (except the first offering following the A&R Effective Date may be nine (9) months, and the substance of the provisions contained in Sections 5 through 8, inclusive).

5. ELIGIBILITY.

(a) Rights may be granted only to employees of the Company or, as the Board or the Committee may designate as provided in Subsection 2(c), to employees of any Affiliate of the Company. Except as provided in Subsection 5(b), an employee of the Company or any Affiliate shall not be eligible to be granted rights under the Plan unless, on the Offering Date, such employee has been in the employ of the Company or any Affiliate for such continuous period preceding such grant as the Board or the Committee may require, but in no event shall the required period of continuous employment be greater than two (2) years. In addition, unless otherwise determined by the Board or the Committee and set forth in the terms of the applicable Offering, no employee of the Company or any Affiliate shall be eligible to be granted rights under the Plan, unless, on the Offering Date, such employee's customary employment with the Company or such Affiliate is for at least twenty (20) hours per week and at least five (5) months per calendar year. The Company, in its sole discretion, may exclude from participation in the Plan employees of the Company or any Affiliate of the Company who reside and/or perform services in certain specific jurisdictions if the laws of those jurisdictions make participation in the Plan impractical.

(b) The Board or the Committee may provide that each person who, during the course of an Offering, first becomes an eligible employee of the Company or designated Affiliate will, on a date or dates specified in the Offering which coincides with the day on which such person becomes an eligible employee or occurs thereafter, receive a right under that Offering, which right shall thereafter be deemed to be a part of that Offering. Such right shall have the same characteristics as any rights originally granted under that Offering, as described herein, except that:

(i) the date on which such right is granted shall be the "Offering Date" of such right for all purposes, including determination of the exercise price of such right;

(ii) the period of the Offering with respect to such right shall begin on its Offering Date and end coincident with the end of such Offering; and

(iii) the Board or the Committee may provide that if such person first becomes an eligible employee within a specified period of time before the end of the Offering, he or she will not receive any right under that Offering.

(c) No employee shall be eligible for the grant of any rights under the Plan if, immediately after any such rights are granted, such employee owns stock possessing five percent (5%) or more of the total combined voting power or value of all classes of stock of the Company or of any Affiliate. For purposes of this Subsection 5(c), the rules of Section 424(d) of the Code shall apply in determining the stock ownership of any employee, and stock which such employee may purchase under all outstanding rights and options shall be treated as stock owned by such employee.

(d) An eligible employee may be granted rights under the Plan only if such rights, together with any other rights granted under "employee stock purchase plans" of the Company and any Affiliates, as specified by Section 423(b)(8) of the Code, do not permit such employee's rights to purchase stock of the Company or any Affiliate to accrue at a rate which exceeds twenty-five thousand dollars (\$25,000) of fair market value of such stock (determined at the time such rights are granted) for each calendar year in which such rights are outstanding at any time.

(e) Officers of the Company and any designated Affiliate shall be eligible to participate in Offerings under the Plan; *provided, however*, that the Board may provide in an Offering that certain employees who are highly compensated employees within the meaning of Section 423(b)(4)(D) of the Code shall not be eligible to participate.

6. RIGHTS; PURCHASE PRICE.

(a) On each Offering Date, each eligible employee, pursuant to an Offering made under the Plan, shall be granted the right to purchase up to the number of shares of Common Stock of the Company purchasable with a percentage designated by the Board or the Committee not exceeding ten percent (10%) of such employee's Earnings (as defined in Subsection 7(a)) during the period which begins on the Offering Date (or such later date as the Board or the Committee determines for a particular Offering) and ends on the date stated in the Offering, which date shall be no later than the end of the Offering. In addition, the Board or the Committee may specify a maximum dollar amount that each employee may use to purchase shares during any Offering made under the Plan. The Board or the Committee shall establish one or more dates during an Offering (the "Exercise Date(s)") on which rights granted under the Plan shall be exercised and purchases of Common Stock carried out in accordance with such Offering.

(b) In connection with each Offering made under the Plan, the Board or the Committee may specify a maximum number of shares that may be purchased by any employee as well as a maximum aggregate number of shares that may be purchased by all eligible employees pursuant to such Offering. In addition, in connection with each Offering that contains more than one Exercise Date, the Board or the Committee may specify a maximum aggregate number of shares which may be purchased by all eligible employees on any given Exercise Date under the Offering. If the aggregate purchase of shares upon exercise of rights granted under the Offering would exceed any such maximum aggregate number, the Board or the Committee shall make a pro rata allocation of the shares available in as nearly a uniform manner as shall be practicable and as it shall deem to be equitable.

(c) The purchase price of stock acquired pursuant to rights granted under the Plan shall be not less than the lesser of:

- (i) an amount equal to eighty-five percent (85%) of the fair market value of the stock on the Offering Date; or
- (ii) an amount equal to eighty-five percent (85%) of the fair market value of the stock on the Exercise Date.

7. PARTICIPATION; WITHDRAWAL; TERMINATION.

(a) An eligible employee may become a participant in the Plan pursuant to an Offering by delivering a participation agreement to the Company within the time specified in the Offering, in such form as the Company provides. Each such agreement shall authorize payroll deductions of up to the maximum percentage specified by the Board or the Committee of such employee's Earnings during the Offering. "Earnings" is defined as the total compensation paid to an employee including all salary, wages (including amounts thereof elected to be deferred by the employee, that would otherwise have been paid, under any arrangement established by the Company that is intended to comply with Section 125, Section 401(k), Section 402(h) or Section 403(b) of the Code or that provides non-qualified deferred compensation), which shall include overtime pay, commissions, bonuses and other remuneration paid directly to the employee, but shall exclude profit sharing, the cost of employee benefits paid for by the Company or an Affiliate, education or tuition reimbursements, imputed income arising under any group insurance or benefit program, traveling expenses, business and moving expense reimbursements, income received in connection with stock awards, contributions made by the Company or an Affiliate under any employee benefit plan, and similar items of compensation, as determined by the Board or the Committee. The payroll deductions made for each participant shall be credited to an account for such participant under the Plan and shall be deposited with the general funds of the Company. A participant may reduce (including to zero) or increase such payroll deductions, and an eligible employee may begin such payroll deductions, after the beginning of any Offering only as provided for in the Offering. A participant may make additional payments into his or her account only if specifically provided for in the Offering and only if the participant has not had the maximum permitted amount withheld during the Offering.

(b) At any time during an Offering, a participant may terminate his or her payroll deductions under the Plan and withdraw from the Offering by delivering to the Company a notice of withdrawal in such form as the Company provides. Such withdrawal may be elected at any time prior to the end of the Offering except as provided by the Board or the Committee in the Offering. Upon such withdrawal from the Offering by a participant, the Company shall distribute to such participant all of his or her accumulated payroll deductions (reduced to the extent, if any, such deductions have been used to acquire stock for the participant) under the Offering, without interest, and such participant's interest in that Offering shall be automatically terminated. A participant's withdrawal from an Offering will have no effect upon such participant's eligibility to re-enroll in the Offering or to participate in any other Offerings under the Plan but such participant will be required to deliver a new participation agreement in order to participate in subsequent Offerings under the Plan.

(c) Rights granted pursuant to any Offering under the Plan shall terminate immediately upon cessation of any participating employee's employment with the Company and any designated Affiliate, for any reason, and the Company shall distribute to such terminated employee all of his or her accumulated payroll deductions (reduced to the extent, if any, such deductions have been used to acquire stock for the terminated employee), under the Offering, without interest.

(d) Rights granted under the Plan shall not be transferable by a participant otherwise than by will or the laws of descent and distribution, or by a beneficiary designation as provided in Section 14 and, otherwise during his or her lifetime, shall be exercisable only by the person to whom such rights are granted.

8. EXERCISE; MINIMUM HOLDING PERIOD.

(a) On each Exercise Date specified therefor in the relevant Offering, each participant's accumulated payroll deductions and other additional payments specifically provided for in the Offering (without any increase for interest) will be applied to the purchase of whole shares of stock of the Company, up to the maximum number of shares permitted pursuant to the terms of the Plan and the applicable Offering, at the purchase price specified in the Offering. No fractional shares shall be issued upon the exercise of rights granted under the Plan. The amount, if any, of accumulated payroll deductions remaining in each participant's account after the purchase of shares which is less than the amount required to purchase one share of stock on the final Exercise Date of an Offering shall be held in each such participant's account for the purchase of shares under the next Offering under the Plan, unless such participant withdraws from such next Offering, as provided in Subsection 7(b), or is no longer eligible to be granted rights under the Plan, as provided in Section 5, in which case such amount shall be distributed to the participant after such final Exercise Date, without interest. The amount, if any, of accumulated payroll deductions remaining in any participant's account after the purchase of shares which is equal to the amount required to purchase whole shares of stock on the final Exercise Date of an Offering shall be distributed in full to the participant after such Exercise Date, without interest.

(b) No rights granted under the Plan may be exercised to any extent unless the shares to be issued upon such exercise under the Plan (including rights granted thereunder) are covered by an effective registration statement pursuant to the Securities Act of 1933, as amended (the "Securities Act") and the Plan is in material compliance with all applicable state, foreign and other securities and other laws applicable to the Plan. If on an Exercise Date in any Offering hereunder the Plan is not so registered or in such compliance, no rights granted under the Plan or any Offering shall be exercised and all payroll deductions accumulated during the Offering (reduced to the extent, if any, such deductions have been used to acquire stock) shall be distributed to the participants, without interest.

(c) With respect to any Common Stock of the Company purchased under any Offering initiated after the Effective Date, as a condition to participating in, and purchasing shares of Common Stock under this Plan, each participant irrevocably agrees that, without the prior written consent of the Company, such participant will not, directly or indirectly, (1) offer for sale, sell, pledge, or otherwise dispose of (or enter into any transaction or device that is designed to, or could be expected to, result in the disposition by any person at any time in the future of) any shares of Common Stock of the Company (the "Held Shares") purchased by such participant in an Offering that was initiated after the Effective Date, or (2) enter into any swap or other derivatives transaction that transfers to another, in whole or in part, any of the economic benefits or risks of ownership of the Held Shares, in each case before the passage of the six-month anniversary of the date the participant purchased the applicable Held Shares (the "Holding Period"). The Company may impose stop-transfer instructions with respect to the shares of Common Stock subject to the foregoing restriction until the end of the applicable Holding Period.

(d) Each participant understands and agrees that on any certificates evidencing the shares of Common Stock purchased under the Plan, the Company may place a legend, substantially in the form of the following:

THE SHARES EVIDENCED BY THIS CERTIFICATE CANNOT BE SOLD UNTIL [INSERT DATE THAT IS 6 MONTHS FROM DATE OF PURCHASE].

9. COVENANTS OF THE COMPANY.

(a) During the terms of the rights granted under the Plan, the Company shall keep available at all times the number of shares of stock required to satisfy such rights.

(b) The Company shall seek to obtain from each federal, state, foreign or other regulatory commission or agency having jurisdiction over the Plan such authority as may be required to issue and sell shares of stock upon exercise of the rights granted under the Plan. If, after reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority which counsel for the Company deems necessary for the lawful issuance and sale of stock under the Plan, the Company shall be relieved from any liability for failure to issue and sell stock upon exercise of such rights unless and until such authority is obtained.

10. USE OF PROCEEDS FROM STOCK.

Proceeds from the sale of stock pursuant to rights granted under the Plan shall constitute general funds of the Company.

11. RIGHTS AS A STOCKHOLDER.

A participant shall not be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares subject to rights granted under the Plan unless and until the participant's shareholdings acquired upon exercise of rights under the Plan are recorded in the books of the Company.

12. ADJUSTMENTS UPON CHANGES IN STOCK.

(a) If any change is made in the stock subject to the Plan, or subject to any rights granted under the Plan, due to a change in corporate capitalization and without the receipt of consideration by the Company (through reincorporation, stock dividend, stock split, reverse stock split, combination or reclassification of shares), the Plan will be appropriately adjusted in the class(es) and maximum number of securities subject to the Plan pursuant to subsection 3(a), and the outstanding rights will be appropriately adjusted in the class(es) and number of securities and price per share of stock subject to such outstanding rights. Such adjustments shall be made by the Board, the determination of which shall be final, binding and conclusive.

(b) In the event of: (1) a dissolution, liquidation or sale of all or substantially all of the assets of the Company, (2) a merger or consolidation in which the Company is not the surviving corporation, or (3) a reverse merger in which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger are converted by virtue of the merger into other property, whether in the form of securities, cash or otherwise or (4) any other capital reorganization in which more than fifty percent (50%) of the securities of the Company entitled to vote are sold or otherwise exchanged, then any surviving corporation may assume outstanding rights or substitute similar rights for those under the Plan. In the event that no surviving corporation assumes such outstanding rights or substitutes similar rights therefor, participants' accumulated payroll deductions will be used to purchase Common Stock immediately prior to the transaction described above and the participants' rights under the ongoing Offering terminated immediately following such purchase.

13. AMENDMENT OF THE PLAN.

(a) The Board at any time, and from time to time, may amend the Plan. However, except as provided in Section 12 relating to adjustments upon changes in stock, no amendment shall be effective unless approved by the stockholders of the Company within twelve (12) months before or after the adoption of the amendment, where the amendment will:

(i) Increase the number of shares reserved for rights under the Plan;

(ii) Modify the provisions as to eligibility for participation in the Plan (to the extent such modification requires stockholder approval in order for the Plan to obtain employee stock purchase plan treatment under Section 423 of the Code or to comply with the requirements of Rule 16b-3 promulgated under the Securities Exchange Act of 1934, as amended ("Rule 16b-3")); or

(iii) Modify the Plan in any other way if such modification requires stockholder approval in order for the Plan to obtain employee stock purchase plan treatment under Section 423 of the Code or to comply with the requirements of Rule 16b-3.

It is expressly contemplated that the Board may amend the Plan in any respect the Board deems necessary or advisable to provide eligible employees with the maximum benefits provided or to be provided under the provisions of the Code and the regulations promulgated thereunder relating to employee stock purchase plans and/or to bring the Plan and/or rights granted under it into compliance therewith.

(b) Rights and obligations under any rights granted before amendment of the Plan shall not be impaired by any amendment of the Plan, except with the consent of the person to whom such rights were granted, or except as necessary to comply with any laws or governmental regulations, or except as necessary to ensure that the Plan and/or rights granted under the Plan comply with the requirements of Section 423 of the Code.

14. DESIGNATION OF BENEFICIARY.

(a) A participant may file a written designation of a beneficiary who is to receive any shares and cash, if any, from the participant's account under the Plan in the event of such participant's death subsequent to the end of an Offering but prior to delivery to the participant of such shares and cash. In addition, a participant may file a written designation of a beneficiary who is to receive any cash from the participant's account under the Plan in the event of such participant's death during an Offering.

(b) Such designation of beneficiary may be changed by the participant at any time by written notice. In the event of the death of a participant and in the absence of a beneficiary validly designated under the Plan who is living at the time of such participant's death, the Company shall deliver such shares and/or cash to the executor or administrator of the estate of the participant, or if no such executor or administrator has been appointed (to the knowledge of the Company), the Company, in its sole discretion, may deliver such shares and/or cash to the spouse or to any one or more dependents or relatives of the participant, or if no spouse, dependent or relative is known to the Company, then to such other person as the Company may designate.

15. TERMINATION OR SUSPENSION OF THE PLAN.

(a) The Board in its discretion may suspend or terminate the Plan at any time. No rights may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) Rights and obligations under any rights granted while the Plan is in effect shall not be altered or impaired by suspension or termination of the Plan, except as expressly provided in the Plan or with the consent of the person to whom such rights were granted, or except as necessary to comply with any laws or governmental regulation, or except as necessary to ensure that the Plan and/or rights granted under the Plan comply with the requirements of Section 423 of the Code.

(c) Notwithstanding the foregoing, the Plan shall terminate on March 21, 2029 and no rights may be granted under the Plan after such termination.

16. EFFECTIVE DATE OF PLAN.

The Plan shall become effective on the date on which it is first approved by the stockholders of the Company (the "Effective Date").



Ionis announces appointment of Brett P. Monia Ph.D. to its board of directors

CARLSBAD, Calif., March 25, 2019 – Ionis Pharmaceuticals, Inc. (NASDAQ: IONS), the leader in RNA-targeted therapeutics, today announced that Brett P. Monia, Ph.D., has been appointed to the company’s board of directors. Dr. Monia currently serves as Ionis’ chief operating officer and, as was previously announced, will be appointed chief executive officer of the company in January 2020, succeeding current CEO Stanley T. Crooke, M.D., Ph.D., who will become executive chairman of the Ionis board of directors. With the addition of Dr. Monia, the Ionis board now has a total of 11 members.

“I am pleased to welcome Brett to the board. His business leadership, expertise in developing antisense medicines for nearly 30 years, commitment to the Ionis business model and culture and bringing transformational therapies to patients make him an ideal addition to our board,” said Dr. Crooke.

Dr. Monia is a founding member of Ionis and has been an executive officer of the company since 2012. Prior to becoming COO in 2018, he was senior vice president of translational medicine and the franchise leader for programs in oncology and rare diseases. Dr. Monia has also served as Ionis’ head of drug discovery where he supervised the discovery of more than 40 antisense-based medicines reaching clinical development, resulting in several market approvals, including TEGSEDI™.

Dr. Monia has published more than 200 primary research manuscripts, reviews and book chapters, and he is an inventor on more than 100 issued patents. He is a senior editor for the journal *Nucleic Acid Therapeutics*, a member of the Board of Directors of Dynacure Therapeutics and a past president of the Oligonucleotide Therapeutics Society. Dr. Monia is also an adjunct professor of biology at San Diego State University where he lectures at the graduate level on pharmacology.

About Ionis Pharmaceuticals

As the leader in RNA-targeted drug discovery and development, Ionis has created an efficient, broadly applicable, drug discovery platform called antisense technology that can treat diseases where no other therapeutic approaches have proven effective. Our drug discovery platform has served as a springboard for actionable promise and realized hope for patients with unmet needs. We created the first and only approved treatment for children and adults with spinal muscular atrophy as well as the world’s first RNA-targeted therapeutic approved for the treatment of polyneuropathy in adults with hereditary transthyretin amyloidosis. Our sights are set on all the patients we have yet to reach with a pipeline of more than 40 novel medicines designed to treat a broad range of diseases including cardiovascular diseases, neurological diseases, infectious diseases, pulmonary diseases and cancer.

To learn more about Ionis follow us on twitter [@ionispharma](https://twitter.com/ionispharma) or visit www.ionispharma.com.

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