
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): December 20, 2016

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))
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Item 2.03. Creation of a Direct Financial Obligation or an Obligation under an Off-Balance Sheet Arrangement of a Registrant.

The information set forth in Item 8.01 of this Current Report on Form 8-K is incorporated herein by reference.

Item 3.02. Unregistered Sales of Equity Securities.

The information set forth in Item 8.01 of this Current Report on Form 8-K is incorporated herein by reference.

Item 8.01. Other Events.

On December 20, 2016, Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) (the “Company”) entered into separate privately negotiated exchange agreements with certain holders of its 2.75% Convertible Senior Notes due 2019 (the “2019 Notes”) to exchange in a private placement in reliance on Section 4(a)(2) and Regulation D of the Securities Act of 1933, as amended (the “Securities Act”), \$60.8 million in aggregate principal amount of 2019 Notes (the “Exchange Transactions”) for an estimated \$182.7 million in aggregate principal amount (based on today’s closing price of the Company’s common stock of \$51.92) of the Company’s 1.00% Convertible Senior Notes due 2021 (the “2021 Notes”), subject to the final exchange ratio (which is calculated by reference to the volume-weighted average closing price of the Company’s common stock over a five trading day period ending on December 28, 2016 (the “valuation period”).

The Company anticipates that the closings of the Exchange Transactions will occur on or about December 30, 2016. The Company expects that the exchange holders will purchase shares of the Company’s common stock during the valuation period, which could increase (or reduce the size of any decrease in) the market price of the Company’s common stock.

Following the closings of the Exchange Transactions, \$0.4 million in principal amount of the 2019 Notes will remain outstanding.

The new issuance of 2021 Notes will occur under the existing indenture related to the 2021 Notes, dated as of November 17, 2014, between the Company and Wells Fargo Bank, National Association, as trustee (the “Indenture”), and the terms of the new 2021 Notes will be the same as the existing 2021 Notes.

The description of the 2021 Notes and the Indenture is incorporated by reference to the Company’s Current Report on Form 8-K filed on November 21, 2014 and qualified in its entirety by reference to the text of the Indenture, a copy of which was attached as Exhibit 4.1 to such Current Report on Form 8-K. The description of the exchange agreements, including the formula for determining the exchange ratio of 2021 Notes for 2019 Notes in the Exchange Transactions, is qualified in its entirety by reference to the form of exchange agreement, a copy of which is attached as Exhibit 99.1 to this Current Report on Form 8-K.

This Current Report on Form 8-K does not constitute an offer to sell or the solicitation of an offer to buy any securities, nor shall it constitute an offer to sell, solicitation or sale in any jurisdiction in which such offer, solicitation or sale would be unlawful. These securities have not been registered under the Securities Act or any state securities laws and, unless so registered, may not be offered or sold in the United States or to U.S. persons except pursuant to an exemption from, or in a transaction not subject to, the registration requirements of the Securities Act and applicable state laws.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits.

99.1 Form of Exchange Agreement

Forward-Looking Statements

This Current Report on Form 8-K includes forward-looking statements regarding the expected closing and the terms of the Exchange Transactions. Such statements are subject to certain risks and uncertainties, including the ability to satisfy closing conditions specified in the exchange agreements. The Company's forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although the Company's forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by the Company. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning the Company are described in additional detail in the Company's Annual Report on Form 10-K for the year ended December 31, 2015, and its most recent Quarterly Report on Form 10-Q, which are on file with the SEC. Copies of these and other documents are available from the Company.

Ionis PharmaceuticalsTM is a trademark of Ionis Pharmaceuticals, Inc.

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: December 20, 2016

By: /s/ B. Lynne Parshall

B. LYNNE PARSHALL
Chief Operating Officer
and Director

[99.1](#) Form of Exchange Agreement.

Form of Exchange Agreement

December 20, 2016

Ionis Pharmaceuticals, Inc.
2855 Gazelle Court
Carlsbad, CA 92010
Attention: Chief Operating Officer

Re: Exchange for Ionis Pharmaceuticals, Inc. 1.00% Convertible Senior Notes due 2021

Ladies and Gentlemen:

Ionis Pharmaceuticals, Inc. (f/k/a Isis Pharmaceuticals, Inc.), a Delaware corporation (the “**Company**”), is offering a new issuance of its outstanding 1.00% Convertible Senior Notes due 2021 (CUSIP 464337 AJ3 and ISIN US464337AJ35) (the “**New Notes**”) in exchange (the “**Exchange**”) for its outstanding 2.75% Convertible Senior Notes due 2019 (CUSIP 464337 AG9 and ISIN US464337AG95) (the “**Old Notes**”) as set forth on Annex A hereto. The undersigned is a beneficial owner (the “**Investor**”) of Old Notes issued by the Company and shall participate in the Exchange subject to the terms and conditions set forth in this agreement (the “**Exchange Agreement**”).

The undersigned Investor understands that the Exchange is being made without registration under the Securities Act of 1933, as amended (the “**Securities Act**”), or any securities laws of any state of the United States or of any other jurisdiction, and that the Exchange is only being made to Investors who are both “accredited investors” (as defined in Rule 501 of Regulation D under the Securities Act) and “qualified institutional buyers” (as defined in Rule 144A under the Securities Act) in reliance upon a private placement exemption from registration under the Securities Act. The New Notes will be issued pursuant to the Indenture (as defined herein).

1. The Exchange. Subject to the terms and conditions of this Exchange Agreement, the undersigned Investor hereby agrees to (a) exchange the aggregate principal amount of Old Notes (such principal amount of Old Notes, the “**Exchanged Old Notes**”) set forth on Annex A hereto for New Notes having an aggregate principal amount equal to the product of the Exchange Ratio set forth on Annex A hereto and the Exchanged Old Notes, rounded to the nearest integral multiple of \$1,000 in principal amount, if applicable (such aggregate principal amount of New Notes, as so rounded, if applicable, the “**Exchanged New Notes**”), and the Company hereby agrees to issue such Exchanged New Notes to the Investor in exchange for such Exchanged Old Notes.

2. The Closing. The closing of the Exchange (the “**Closing**”) shall take place at the offices of Davis Polk & Wardwell LLP, 1600 El Camino Real, Menlo Park, California 94025 at 10:00 a.m., New York City time, on December 30, 2016, or at such other time and place as the Company may designate by notice to the undersigned (the “**Closing Date**”).

3. The Terms of the Exchange; Closing Mechanics.

Subject to the terms and conditions of this Exchange Agreement, the undersigned Investor hereby (a) waives any and all other rights with respect to such Exchanged Old Notes and (b) releases and discharges the Company from any and all claims the undersigned may now have, or may have in the future, arising out of, or related to, such Exchanged Old Notes.

(a) The Depository Trust Company (“**DTC**”) will act as securities depository for the New Notes. At or prior to the times set forth in the Exchange Procedures set forth in Annex B hereto (the “**Exchange Procedures**”), the Investor shall cause the Exchanged Old Notes to be delivered, by book entry transfer through the facilities of DTC, to Wells Fargo Bank, National Association, in its capacity as trustee of the Old Notes (in such capacity, the “**Old Notes Trustee**”), for the account/benefit of the Company for cancellation as instructed in the Exchange Procedures; and

(b) On the Closing Date, subject to satisfaction of the conditions precedent specified in Section 6 hereof, and the prior receipt by the Old Notes Trustee from the undersigned Investor of the Exchanged Old Notes, the Company shall execute, cause Wells Fargo Bank, National Association, in its capacity as trustee of the New Notes (in such capacity, the “**New Notes Trustee**”) to authenticate and cause to be delivered to the DTC account specified by the undersigned Investor on the signature page hereto, the Exchanged New Notes.

All questions as to the form of all documents and the validity and acceptance of the Old Notes and the New Notes will be determined by the Company, in its sole discretion, which determination shall be final and binding.

4. Representations and Warranties of the Company. The Company represents and warrants to the Investor that:

(a) *Organization.* The Company is duly organized and is validly existing under the laws of the State of Delaware.

(b) *Due Authorization.* This Exchange Agreement has been duly authorized, executed and delivered by the Company.

(c) *New Notes.* The New Notes have been duly authorized by the Company and, when duly executed by the Company in accordance with the terms of the Indenture, assuming due authentication of the New Notes by the New Notes Trustee, upon delivery to the Investors in accordance with the terms of the Exchange, will be validly issued and delivered and will constitute valid and binding obligations of the Company entitled to the benefits of the Indenture, enforceable against the Company in accordance with their terms, except as such enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium, and other laws relating to or affecting creditors’ rights generally and by general equitable principles (regardless of whether such enforceability is considered in a proceeding in equity or at law).

(d) *Indenture.* The indenture governing the New Notes, dated as of November 17, 2014 between the Company and the New Notes Trustee (as amended, modified or otherwise supplemented, the “**Indenture**”) has been duly and validly authorized, executed and delivered by the Company, and assuming due authorization, execution and delivery by the New Notes Trustee, constitutes the valid and binding agreement of the Company, enforceable against the Company in accordance with its terms, except as such enforceability may be limited by bankruptcy, fraudulent conveyance, insolvency, reorganization, moratorium, and other laws relating to or affecting creditors’ rights generally and by general equitable principles (regardless of whether such enforceability is considered in a proceeding in equity or at law).

(e) *Exemption from Registration.* Assuming the accuracy of the representations and warranties of the Investor and each other Investor executing an Exchange Agreement, (1) the issuance of the Exchanged New Notes in connection with the Exchange pursuant to this Exchange Agreement is exempt from the registration requirements of the Securities Act; and (2) the Indenture is not required to be qualified under the Trust Indenture Act of 1939, as amended.

(f) *New Class.* The New Notes, when issued, will not be of the same class as securities listed on a national securities exchange registered under Section 6 of the Securities Exchange Act of 1934, as amended (the “**Exchange Act**”), or quoted in a U.S. automated inter-dealer quotation system, within the meaning of Rule 144A(d)(3)(i) under the Securities Act.

5. Representations and Warranties of the Investor. The Investor hereby represents and warrants to and covenants with the Company that:

(a) The Investor is a corporation, limited partnership, limited liability company or other entity, as the case may be, duly formed, validly existing and in good standing under the laws of the jurisdiction of its formation.

(b) The Investor has full power and authority to (i) subscribe for and purchase from the Company the Exchanged New Notes, (ii) exchange, sell, assign and transfer the Exchanged Old Notes exchanged hereby and (iii) to enter into this Exchange Agreement and perform all obligations required to be performed by the Investor hereunder. This Exchange Agreement and the consummation of the Exchange will not violate, conflict with or result in a breach of or default under (i) the Investor’s organizational documents, (ii) any agreement or instrument to which the Investor is a party or by which the Investor or any of its assets are bound, or (iii) any laws, regulations or governmental or judicial decrees, injunctions or orders applicable to the Investor.

(c) The Investor is the current sole legal and beneficial owner of the Exchanged Old Notes set forth opposite its name on Annex A hereto. When the Exchanged Old Notes are exchanged, the Company will acquire good, marketable and unencumbered title thereto, free and clear of all liens, restrictions, charges, encumbrances, adverse claims, rights or proxies. The Investor has not, in whole or in part, other than pledges or security interests that the Investor may have created in favor of a prime broker under and in accordance with its prime brokerage agreement with such broker, (a) assigned, transferred, hypothecated, pledged, exchanged or otherwise disposed of any of its Exchanged Old Notes or its rights in its Exchanged Old Notes (other than to the Company pursuant hereto), or (b) given any person or entity any transfer order, power of attorney or other authority of any nature whatsoever with respect to its Exchanged Old Notes.

(d) The Investor is a resident of the state set forth on its signature page hereto and is not acquiring the Exchanged New Notes as a nominee or agent or otherwise for any other person.

(e) The Investor will comply with all applicable laws and regulations in effect in any jurisdiction in which the undersigned purchases, otherwise acquires or sells New Notes and will obtain any consent, approval or permission required for such purchases, acquisitions or sales under the laws and regulations of any jurisdiction to which the undersigned is subject or in which the undersigned makes such purchases, acquisitions or sales, and the Company shall have no responsibility therefor.

(f) The Investor has received a copy of the Indenture. The Investor acknowledges that no person has been authorized to give any information or to make any representation concerning the Exchange or the Company and its subsidiaries and the information given by the Company's duly authorized officers and employees in connection with the Investor's examination of the Company and its subsidiaries and the terms of the Exchange and the Company and its subsidiaries do not take any responsibility for, and neither the Company nor its subsidiaries can provide any assurance as to the reliability of, any other information that may have been provided to the Investor. The Investor hereby acknowledges that J. Wood Capital Advisors LLC (the "**Placement Agent**") does not take any responsibility for, and can provide no assurance as to the reliability of, the information set forth in the Indenture or any such other information.

(g) The Investor understands and accepts that acquiring the New Notes in the Exchange involves risks including, but not limited to, those that are customary in a convertible notes offering, and risks described in the Company's reports filed with the Securities and Exchange Commission (the "**SEC**"). The Investor has such knowledge, skill and experience in business, financial and investment matters that the Investor is capable of evaluating the merits and risks of the Exchange and an investment in the New Notes. With the assistance of the Investor's own professional advisors, to the extent that the Investor has deemed appropriate, the Investor has made its own legal, tax, accounting and financial evaluation of the merits and risks of an investment in the New Notes and the consequences of the Exchange and this Exchange Agreement. The Investor has considered the suitability of the New Notes as an investment in light of its own circumstances and financial condition, and the Investor is able to bear the risks associated with an investment in the New Notes.

(h) The Investor confirms that it is not relying on any communication (written or oral) of the Company, the Placement Agent or any of their respective agents or affiliates as investment advice or as a recommendation to participate in the Exchange and receive the New Notes pursuant to the terms hereof. It is understood that information provided in the Indenture, or by the Company, the Placement Agent or any of their respective agents or affiliates, shall not be considered investment advice or a recommendation with respect to the Exchange, and that none of the Company, the Placement Agent or any of their respective agents or affiliates is acting or has acted as an advisor to the Investor in deciding whether to participate in the Exchange. The Investor is not relying, and has not relied, upon any statement, advice (whether accounting, tax, financial, legal or other), representation or warranty made by the Company or any of its affiliates or representatives including, without limitation, the Placement Agent, except for the representations and warranties made by the Company in this Exchange Agreement.

(i) The Investor confirms that neither the Company nor the Placement Agent has (1) given any guarantee or representation as to the potential success, return, effect or benefit (either legal, regulatory, tax, financial, accounting or otherwise) of an investment in the New Notes; or (2) made any representation to the Investor regarding the legality of an investment in the New Notes under applicable investment guidelines, laws or regulations. In deciding to participate in the Exchange, the Investor is not relying on the advice or recommendations of the Company or the Placement Agent, and the Investor has made its own independent decision that the investment in the New Notes is suitable and appropriate for the Investor.

(j) The Investor is a sophisticated participant in the transactions contemplated hereby and has such knowledge, skill and experience in financial, business and investment matters as to be capable of evaluating the merits and risks of an investment in the New Notes, is experienced in investing in capital markets and is able to bear the economic risk of an investment in the New Notes, including sustaining any loss resulting therefrom without material injury. The Investor is familiar with the business and financial condition and operations of the Company, has conducted its own investigation of the Company and the New Notes and has consulted with its own advisors concerning such matters and shall be responsible for making its own independent investigation and appraisal of the transactions contemplated hereby. The Investor has had access to all materials it deems necessary to enable it to make an informed investment decision concerning the Exchange and has had the opportunity to review the Company's filings and submissions with the SEC, including, without limitation, all information filed or furnished pursuant to the Exchange Act. The Investor acknowledges and agrees that no statement or written material contrary to this Exchange Agreement has been made or given to the Investor by or on behalf of the Company. The Investor has had a full opportunity to ask questions of the Company and its representatives concerning the Company, its business, operations, financial performance, financial condition and prospects, and the terms and conditions of the Exchange and has received answers thereto as the Investor deems necessary to enable it to make an informed investment decision concerning the Exchange and the New Notes.

(k) The Investor understands that no federal, state, local or foreign agency has passed upon the merits or risks of an investment in the New Notes or the common stock of the Company (the "**Common Stock**") issuable upon conversion of the Notes, if any, or made any finding or determination concerning the fairness or advisability of such investment.

(l) The Investor is an "accredited investor" as defined in Rule 501(a) under the Securities Act and a "qualified institutional buyer" as defined in Rule 144A under the Securities Act and is acquiring the New Notes hereunder for investment for its own respective account and not with a view to, or for resale in connection with, any distribution thereof in a manner that would violate the registration requirements of the Securities Act. The Investor agrees to furnish any additional information reasonably requested by the Company or any of its affiliates to assure compliance with applicable U.S. federal and state securities laws in connection with the Exchange.

(m) The Investor is not directly, or indirectly through one or more intermediaries, controlling or controlled by, or under direct or indirect common control with, the Company and is not, and has not been for the immediately preceding three months, an “affiliate” (within the meaning of Rule 144 under the Securities Act) (an “**Affiliate**”) of the Company. To its knowledge, the Investor did not acquire any of the Exchanged Old Notes, directly or indirectly, from an Affiliate of the Company. The Investor and its Affiliates collectively beneficially own and will beneficially own as of the Closing (but without giving effect to the Exchange) (i) less than 5% of the outstanding Common Stock of the Company and (ii) less than 5% of the aggregate number of votes that may be cast by holders of those outstanding securities of the Company that entitle the holders thereof to vote generally on all matters submitted to the Company’s stockholders for a vote (the “**Voting Power**”). Immediately after the receipt by the Investor of New Notes in the Exchange, the aggregate number of shares of Common Stock owned by the Investor and its Affiliates, together with the aggregate number of shares equal to the notional value of any “long” derivative transaction relating to such Common Stock to which the Investor or its Affiliate is a party (excluding derivative transactions relating to broad based indices and any interest in the Old Notes), will not exceed 4.9% of the outstanding Common Stock.

(n) The Investor is acquiring the New Notes solely for the Investor’s own beneficial account, or for an account with respect to which the Investor exercises sole investment discretion, for investment purposes, and not with a view to, or for resale in connection with, any distribution of the New Notes. The Investor understands that the offer of the New Notes has not been registered under the Securities Act or any state securities laws by reason of specific exemptions under the provisions thereof that depend in part upon the investment intent of the Investor and the accuracy of the other representations made by the Investor in this Exchange Agreement.

(o) The Investor understands that the Company is relying upon the representations and agreements contained in this Exchange Agreement (and any supplemental information) for the purpose of determining whether the Investor’s participation in the Exchange meets the requirements for the exemptions referenced in clause (l) above. In addition, the Investor acknowledges and agrees that it has not transacted, and will not transact, in any securities of the Company, including, but not limited to, any hedging transactions, from the time the Investor was first contacted by the Company or the Placement Agent with respect to the Exchange until after the confidential information (as described in the confirmatory email received by the Investor from the Placement Agent (the “**Wall Cross Email**”)) is made public (the “**Public Announcement**”).

(p) The Investor acknowledges that the New Notes have not been registered under the Securities Act. As a result, the New Notes may not be offered or sold within the United States or to, or for the account or benefit of, U.S. persons, except pursuant to an exemption from, or in a transaction not subject to, the registration requirements of the Securities Act as described in Section 2.05 of the Indenture and the Investor hereby agrees that it will not sell the New Notes other than in compliance with such transfer restrictions.

(q) The Investor acknowledges and agrees that no public market exists for the New Notes and that there is no assurance that a public market will ever develop for the New Notes.

(r) The Investor acknowledges that the terms of the Exchange have been mutually negotiated between the Investor and the Company. The Investor was given a meaningful opportunity to negotiate the terms of the Exchange.

(s) The Investor specifically acknowledges that the Company would not enter into this Exchange Agreement or any related documents in the absence of such Investor's representations and acknowledgments set out in this Exchange Agreement, and that this Exchange Agreement, including such representations and acknowledgments, are a fundamental inducement to the Company, and a substantial portion of the consideration provided by such Investor, in this transaction, and that the Company would not enter into this transaction but for this inducement.

(t) The Investor acknowledges the Company intends to pay a fee to the Placement Agent in respect of the Exchange.

(u) The Investor will, simultaneously with the execution and delivery of this Agreement, execute and deliver to the Placement Agent, a non-reliance letter in the form attached as Annex C hereto.

(v) The Investor will, upon request, execute and deliver any additional documents, information or certifications reasonably requested by the Company, the Old Notes Trustee or the New Notes Trustee to complete the Exchange.

(w) The Investor understands that, unless the Investor notifies the Company in writing to the contrary before the Closing, each of the Investor's representations and warranties contained in this Exchange Agreement will be deemed to have been reaffirmed and confirmed as of the Closing Date, taking into account all information received by the Investor.

(x) The Investor's participation in the Exchange was not conditioned by the Company on the Investor's exchange of a minimum principal amount of Old Notes.

(y) The Investor acknowledges that it had a sufficient amount of time to consider whether to participate in the Exchange and that neither the Company nor the Placement Agent has placed any pressure on the Investor to respond to the opportunity to participate in the Exchange. The Investor acknowledges that it did not become aware of the Exchange through any form of general solicitation or advertising within the meaning of Rule 502 under the Securities Act.

(z) The operations of the Investor have been conducted in material compliance with the rules and regulations administered or conducted by the U.S. Department of Treasury Office of Foreign Assets Control ("**OFAC**") applicable to the Investor. The Investor has performed due diligence necessary to reasonably determine that its beneficial owners are not named on the lists of denied parties or blocked persons administered by OFAC, resident in or organized under the laws of a country that is the subject of comprehensive economic sanctions and embargoes administered or conducted by OFAC ("**Sanctions**"), or otherwise the subject of Sanctions.

6. Conditions to Obligations of the Investor and the Company. The obligations of the Investor to deliver the Exchanged Old Notes and of the Company to deliver the New Notes are subject to the satisfaction at or prior to the Closing of the condition precedent that the representations and warranties of the Company and the Investor contained in Sections 4 and 5, respectively, shall be true and correct as of the Closing in all material respects with the same effect as though such representations and warranties had been made as of the Closing.

7. Covenant and Acknowledgment of the Company. At or prior to 8:00 a.m., New York City time, on the first business day after the date hereof, the Company shall file with the SEC a current report on Form 8-K announcing the Exchange, which current report the Company acknowledges and agrees will disclose all confidential information (as described in the Wall Cross Email) to the extent the Company believes such confidential information constitutes material non-public information, if any, with respect to the Exchange or otherwise communicated by the Company to the Investor in connection with the Exchange.

8. Waiver, Amendment. Neither this Exchange Agreement nor any provisions hereof shall be modified, changed, discharged or terminated except by an instrument in writing, signed by the party against whom any waiver, change, discharge or termination is sought.

9. Assignability. Neither this Exchange Agreement nor any right, remedy, obligation or liability arising hereunder or by reason hereof shall be assignable by the Company or the Investor without the prior written consent of the other party.

10. Taxation. The Investor acknowledges that, if the Investor is a United States person for U.S. federal income tax purposes, either (1) the Company must be provided with a correct taxpayer identification number (“**TIN**”), generally a person’s social security or federal employer identification number, and certain other information on Internal Revenue Service (“**IRS**”) Form W-9, which is provided as an attachment hereto, and a certification, under penalty of perjury, that such TIN is correct, that the Investor is not subject to backup withholding (at a rate of 28%) and that the Investor is a United States person, or (2) another basis for exemption from backup withholding must be established. The Investor further acknowledges that, if the Investor is not a United States person for U.S. federal income tax purposes, (1) the Company must be provided the appropriate IRS Form W-8 signed under penalties of perjury, attesting to that non-U.S. Investor’s foreign status, and (2) the Investor may be subject to 30% U.S. federal withholding or 28% U.S. federal backup withholding tax on certain payments made to such Investor unless such Investor properly establishes an exemption from, or a reduced rate of, withholding or backup withholding.

11. Waiver of Jury Trial. EACH OF THE COMPANY AND THE INVESTOR IRREVOCABLY WAIVES ANY AND ALL RIGHT TO TRIAL BY JURY WITH RESPECT TO ANY LEGAL PROCEEDING ARISING OUT OF THE TRANSACTIONS CONTEMPLATED BY THIS EXCHANGE AGREEMENT.

12. Governing Law. THIS EXCHANGE AGREEMENT SHALL BE GOVERNED BY THE LAWS OF THE STATE OF NEW YORK WITHOUT REGARD TO CONFLICT OF LAW PRINCIPLES THAT WOULD RESULT IN THE APPLICATION OF ANY LAW OTHER THAN THE LAW OF THE STATE OF NEW YORK.

13. Submission to Jurisdiction. Each of the Company and the Investor (a) agrees that any legal suit, action or proceeding arising out of or relating to this agreement or the transactions contemplated hereby shall be instituted exclusively in the courts of the State of New York located in the City and County of New York or in the United States District Court for the Southern District of New York; (b) waives any objection that it may now or hereafter have to the venue of any such suit, action or proceeding; and (c) irrevocably consents to the jurisdiction of the aforesaid courts in any such suit, action or proceeding. Each of the Company and the Investor agrees that a final judgment in any such action or proceeding shall be conclusive and may be enforced in other jurisdictions by suit on the judgment or in any other manner provided by law.

14. Venue. Each of the Company and the Investor irrevocably and unconditionally waives, to the fullest extent it may legally and effectively do so, any objection which it may now or hereafter have to the laying of venue of any suit, action or proceeding arising out of or relating to this Exchange Agreement in any court referred to in Section 13. Each of the Company and the Investor irrevocably waives, to the fullest extent permitted by law, the defense of an inconvenient forum to the maintenance of such action or proceeding in any such court.

15. Section and Other Headings. The section and other headings contained in this Exchange Agreement are for reference purposes only and shall not affect the meaning or interpretation of this Exchange Agreement.

16. Counterparts. This Exchange Agreement may be executed by one or more of the parties hereto in any number of separate counterparts (including by facsimile or other electronic means, including telecopy, email or otherwise), and all of said counterparts taken together shall be deemed to constitute one and the same instrument. Delivery of an executed signature page of this Exchange Agreement by facsimile or other transmission (*e.g.*, “pdf” or “tif” format) shall be effective as delivery of a manually executed counterpart hereof.

17. Notices. All notices and other communications to the Company provided for herein shall be in writing and shall be deemed to have been duly given if delivered personally or sent by registered or certified mail, return receipt requested, postage prepaid to the following addresses, or, in the case of the Investor, the address provided on the signature page below (or such other address as either party shall have specified by notice in writing to the other):

If to the Company:

Ionis Pharmaceuticals, Inc.
2855 Gazelle Court
Carlsbad, CA 92010
Attention: Chief Operating Officer

18. Binding Effect. The provisions of this Exchange Agreement shall be binding upon and accrue to the benefit of the parties hereto and their respective heirs, legal representatives, successors and permitted assigns.

19. Notification of Changes. The Investor hereby covenants and agrees to notify the Company upon the occurrence of any event prior to the Closing that would cause any representation, warranty, or covenant of the Investor contained in this Exchange Agreement to be false or incorrect in any material respect.

20. Reliance by Placement Agent. The Placement Agent may rely on each representation and warranty of the Company and the Investor made herein or pursuant to the terms hereof (including, without limitation, in any officer's certificate delivered pursuant to the terms hereof) with the same force and effect as if such representation or warranty were made directly to the Placement Agent. The Placement Agent shall be a third party beneficiary to this Exchange Agreement to the extent provided in this Section 20.

21. Severability. If any term or provision (in whole or in part) of this Exchange Agreement is invalid, illegal or unenforceable in any jurisdiction, such invalidity, illegality or unenforceability shall not affect any other term or provision of this Exchange Agreement or invalidate or render unenforceable such term or provision in any other jurisdiction.

[SIGNATURE PAGES FOLLOW]

Investor:

By _____

Name: _____

Title: _____

Legal Name of Investor: _____

Address: _____

Telephone: _____

State/Country of Residence: _____

Taxpayer Identification Number: _____

Exchanged Old Notes

DTC Participant Number: _____

DTC Participant Name: _____

DTC Participant Phone Number: _____

DTC Participant Contact Email: _____

FFC Account #: _____

Account # at Bank/Broker: _____

Exchanged New Notes (if different from Exchanged Old Notes)

DTC Participant Number: _____

DTC Participant Name: _____

DTC Participant Phone Number: _____

DTC Participant Contact Email: _____

FFC Account #: _____

Account # at Bank/Broker: _____

[Signature Page to Exchange Agreement]

IONIS PHARMACEUTICALS, INC.

By _____

Name:

Title:

[Signature Page to Exchange Agreement]

ANNEX A

Exchange Terms

Aggregate principal amount of Old Notes to be exchanged: \$ _____.

The Exchange Ratio shall be calculated as follows:

Exchange Ratio = (VON + AION)/(VNN' + AINN), where:

VON	=	CRON x VWAP
VNN'	=	VNN + ((VWAP – SP) x DNN x CRNN)
VNN	=	\$1,012.50
DNN	=	0.70
CRON	=	The “conversion rate” as defined in the indenture, dated as of August 13, 2012, between the Company and Wells Fargo Bank, National Association, relating to the Old Notes.
CRNN	=	The “conversion rate” as defined in the Indenture
AION	=	\$6.80
AINN	=	\$1.25
SP	=	\$49.30

“VWAP” means the average of the Daily VWAPs over the Adjustment Period.

“Daily VWAP” has the meaning assigned to such term in the Indenture.

“Adjustment Period” means the period of five consecutive Trading Days (as defined in the Indenture) commencing on and including December 21, 2016.

ANNEX B
Exchange Procedures

NOTICE OF INVESTOR EXCHANGE PROCEDURES

Attached are Investor Exchange Procedures for the settlement of the exchange of 2.75% Convertible Senior Notes due 2019 (the "Old Notes") of Ionis Pharmaceuticals, Inc. (the "Company") for newly issued 1.00% Convertible Senior Notes due 2021 (the "New Notes") pursuant to the Exchange Agreement, dated as of December 20, 2016, between you and the Company which is expected to occur on or about December 30, 2016. To ensure timely settlement, please follow the instructions for exchanging your Old Notes for New Notes as set forth on the following page.

These instructions supersede any prior instructions you received. Your failure to comply with the attached instructions may delay your receipt of New Notes for your Old Notes.

If you have any questions, please contact Katy Neumer at (407) 617-9991.

Thank you.

EXCHANGING OLD NOTES FOR NEW NOTES

Delivery of Old Notes

You must direct the eligible DTC participant through which you hold a beneficial interest in the Old Notes to post **on December 30, 2016, no later than 9:00 a.m., New York City time**, a one-sided withdrawal instruction through DTC via DWAC for the aggregate principal amount of Old Notes (CUSIP/ISIN # 464337AG9/US464337AG95) set forth on Annex A to your Exchange Agreement. **It is important that this instruction be submitted and the DWAC posted on December 30, 2016.**

To receive New Notes

You must direct your eligible DTC participant through which you wish to hold a beneficial interest in the New Notes to post **on December 30, 2016, no later than 9:00 a.m., New York City time**, a one-sided deposit instruction through DTC via DWAC for the aggregate principal amount⁵ of New Notes (CUSIP/ISIN # 464337AJ3/US464337AJ35) set forth next to the caption "Aggregate Principal Amount of New Notes to be Issued to Investor" on Annex A to your Exchange Agreement. **It is important that this instruction be submitted and the DWAC posted on December 30, 2016.**

You must complete both of the steps described above in order to complete the exchange of Old Notes for New Notes.

SETTLEMENT

On December 30, 2016, after the Company receives your Old Notes and your delivery instructions as set forth above, and subject to the satisfaction of the conditions to closing as set forth in your Exchange Agreement, the Company will deliver your New Notes in accordance with the delivery instructions set forth above.

ANNEX C

[NON-RELIANCE LETTER]

J. Wood Capital Advisors LLC

[●]

Re: Exchange of 2.75% Convertible Senior Notes due 2019 (the “Old Notes”) for 1.00% Convertible Senior Notes due 2021 (the “New Notes”) and, together with the Old Notes, the “Securities”) issued by Ionis Pharmaceuticals, Inc. (the “Company”) and, such exchange of the Old Notes for the New Notes, the “Exchange”)

Ladies and Gentlemen:

In connection with the Exchange, we represent, warrant, agree and acknowledge as follows:

1. No disclosure or offering document has been prepared in connection with the Exchange by J. Wood Capital Advisors LLC or any of its affiliates (“J. Wood Capital Advisors”).
 2. (a) We have conducted our own investigation of the Company and the Securities and we have not relied on any statements or other information provided by J. Wood Capital Advisors concerning the Company or the New Notes or the Exchange, (b) we have had access to, and an adequate opportunity to review, financial and other information as we deem necessary to make our decision to subscribe to the Exchange, (c) we have been offered the opportunity to ask questions of the Company and received answers thereto, as we deemed necessary in connection with our decision to subscribe to the Exchange; and (d) we have made our own assessment and have satisfied ourselves concerning the relevant tax and other economic considerations relevant to our investment in the New Notes.
 3. J. Wood Capital Advisors and its directors, officers, employees, representatives and controlling persons have made no independent investigation with respect to the Company or the Securities or the accuracy, completeness or adequacy of any information supplied to us by the Company.
 4. In connection with the Exchange, J. Wood Capital Advisors has not acted as our financial advisor or fiduciary.
 5. We are (x) a qualified institutional buyer (as defined in Rule 144A of the Securities Act of 1933 as amended (the “Securities Act”)) and (y) an accredited investor (as defined in Rule 501 of the Securities Act) and, in the case of (y), either (i) an institutional account as defined in FINRA Rule 4512(c) or (ii) a qualified purchaser, as defined in Section 2(a)(51)(A) of the Investment Company Act. Accordingly, we understand that the Exchange meets the exemptions from filing under FINRA Rule 5123(b)(1)(A)(B), (C) or (J). We are aware that the issuance and delivery to us of the New Notes are being made in reliance on a private placement exemption from registration under the Securities Act and are acquiring the New Notes for our own account or for an account over which we exercise sole discretion for another qualified institutional buyer or accredited investor.
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6. We are able to fend for ourselves in the transactions contemplated herein; have such knowledge and experience in financial and business matters as to be capable of evaluating the merits and risks of our prospective investment in the New Notes; and have the ability to bear the economic risks of our prospective investment and can afford the complete loss of such investment.

7. The New Notes have not been registered under the Securities Act or any other applicable securities laws, are being offered for resale in transactions not requiring registration under the Securities Act, and unless so registered, may not be offered, sold or otherwise transferred except in compliance with the registration requirements of the Securities Act or any other applicable securities laws, pursuant to any exemption therefrom or in a transaction not subject thereto.

Very truly yours,

[NAME OF INVESTOR]

By: _____
Name:
Title:

Date: December 20, 2016
