

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

FORM S-8

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

IONIS PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State of Incorporation)

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

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

Ionis Pharmaceuticals, Inc. 2020 Equity Incentive Plan
(Full title of the plan)

Brett Monia
Chief Executive Officer
IONIS PHARMACEUTICALS, INC.
2855 Gazelle Court
Carlsbad, California 92010
(760) 931-9200
(Name, address, and telephone number, including area code, of agent for service)

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

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

Large accelerated filer
Non-accelerated filer

Accelerated filer
Smaller reporting company
Emerging growth company

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

CALCULATION OF REGISTRATION FEE

Title of Securities to be Registered	Amount to be Registered (1)(2)	Proposed Maximum Offering Price per Share (3)	Proposed Maximum Aggregate Offering Price (3)	Amount of Registration Fee
Common Stock, par value \$.001 per share	2,603,429 shares	\$57.50	\$149,697,168	\$16,331.96

- (1) In accordance with Rule 416 under the Securities Act of 1933, as amended (the "Securities Act"), this Registration Statement on Form S-8 (this "Registration Statement") shall be deemed to cover any additional securities that may from time to time be offered or issued by Ionis Pharmaceuticals, Inc. ("Ionis," the "Registrant," "we," "our" and "us") to prevent dilution resulting from stock splits, stock dividends or similar transactions.
- (2) Represents the number of shares of the Registrant's Common Stock reserved for issuance under the Ionis Pharmaceuticals, Inc. 2020 Equity

Incentive Plan.

- (3) Estimated solely for the purpose of calculating the amount of the registration fee pursuant to Rule 457(c) and Rule 457(h) of the Securities Act. The price per share and the aggregate offering price are calculated on the basis of \$57.50, the average of the high and low sales prices of Registrant's Common Stock on December 29, 2020, as reported on the Nasdaq Global Market.
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EXPLANATORY NOTE

On August 30, 2020, the Registrant entered into an Agreement and Plan of Merger among Akcea Therapeutics, Inc., a Delaware corporation (“Akcea”), the Registrant and Avalanche Merger Sub, Inc., a Delaware corporation and a wholly owned subsidiary of the Registrant (“Purchaser”), pursuant to which Purchaser commenced a tender offer to purchase all of the issued and outstanding shares of common stock, par value \$0.001 per share, of Akcea. On October 12, 2020, the Registrant and Purchaser completed the acquisition of Akcea by consummating the merger of Purchaser with and into Akcea (the “Merger”). In connection with the Merger, the Registrant assumed the unallocated portion of the available share reserve under the Akcea 2015 Equity Incentive Plan, and on December 28, 2020, amended and restated such plan (as amended and restated, the “Plan”) to, among other things, rename such prior plan as the Ionis Pharmaceuticals, Inc. 2020 Equity Incentive Plan and provide for the issuance of up to 2,603,429 shares of the Registrant’s Common Stock to employees, directors and consultants of the Registrant who were employees of Akcea prior to October 12, 2020, pursuant to equity awards to be granted under the Plan.

PART I

INFORMATION REQUIRED IN THE SECTION 10(A) PROSPECTUS

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

INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

Item 3. Incorporation of Documents by Reference.

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

- (a) the Registrant's Annual Report on Form 10-K for the year ended [December 31, 2019](#), as filed with the Commission on March 2, 2020, and the information specifically incorporated by reference into the Registrant's Annual Report on Form 10-K for the year ended December 31, 2019, from the Registrant's Definitive Proxy Statement on Schedule 14A, as filed with the Commission on [April 24, 2020](#);
- (b) the Registrant's Quarterly Report on Form 10-Q for the quarterly period ended [March 31, 2020](#), as filed with the Commission on May 6, 2020, Quarterly Report on Form 10-Q for the quarterly period ended [June 30, 2020](#), as filed with the Commission on August 5, 2020, and Quarterly Report on Form 10-Q for the quarterly period ended [September 30, 2020](#), as filed with the Commission on November 4, 2020;
- (c) the Registrant's Current Reports on Form 8-K filed with the Commission on [January 10, 2020](#), [January 17, 2020](#), [June 10, 2020](#), [August 31, 2020](#), [October 13, 2020](#), [December 9, 2020](#) and [December 18, 2020](#); and
- (d) the description of the Registrant's Common Stock contained in the Registrant's registration statement on Form 8-A filed with the SEC on April 12, 1991, as updated by its Certificate of Amendment of its Restated Certificate of Incorporation filed with its Definitive Proxy Statement on Schedule 14A filed on [April 25, 2014](#), and its Certificate of Amendment of its Restated Certificate of Incorporation filed with its current report on Form 8-K filed on [December 18, 2015](#).

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

Item 5. Interests of Named Experts and Counsel.

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

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

Item 6. Indemnification of Directors and Officers.

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

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

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

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

Item 8. Exhibits.

Exhibit Number	Description
5.1	Opinion of Patrick R. O'Neil.
23.1	Consent of Independent Registered Public Accounting Firm.
23.2	Consent of Patrick R. O'Neil. Reference is made to Exhibit 5.1.
24.1	Power of Attorney is contained on the signature pages.
99.1	Ionis Pharmaceuticals, Inc. 2020 Equity Incentive Plan.
99.2	Form of Global Option Agreement for options granted under the Ionis Pharmaceuticals, Inc. 2020 Equity Incentive Plan.
99.3	Form of Global Restricted Stock Unit Agreement for restricted stock units granted under the Ionis Pharmaceuticals, Inc. 2020 Equity Incentive Plan.
99.4	Forms of Restricted Stock Unit Grant Notice, Stock Option Grant Notice and Stock Option Exercise Notice for options granted under the Ionis Pharmaceuticals, Inc. 2020 Equity Incentive Plan.

Item 9. Undertakings.

(a) The undersigned Registrant hereby undertakes:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Carlsbad, State of California, on December 31, 2020.

IONIS PHARMACEUTICALS, INC.

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

POWER OF ATTORNEY

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

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

Signature	Title	Date
<u>/s/ Brett Monia</u> Brett Monia	Chief Executive Officer (Principal Executive Officer)	December 31, 2020
<u>/s/ Elizabeth Hougen</u> Elizabeth Hougen	Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)	December 31, 2020
<u>/s/ Stanley T. Crooke</u> Stanley T. Crooke	Executive Chairman	December 31, 2020
<u>/s/ Breaux B. Castleman</u> Breaux B. Castleman	Director	December 31, 2020
<u>/s/ Spencer R. Berthelsen</u> Spencer R. Berthelsen	Director	December 31, 2020
<u>/s/ Joseph Klein, III</u> Joseph Klein, III	Director	December 31, 2020
<u>/s/ Joseph Loscalzo</u> Joseph Loscalzo	Director	December 31, 2020
<u>/s/ Frederick T. Muto</u> Frederick T. Muto	Director	December 31, 2020
<u>/s/ Joseph H. Wender</u> Joseph H. Wender	Director	December 31, 2020

/s/ B. Lynne Parshall
B. Lynne Parshall

Director

December 31, 2020

/s/ Peter Reikes
Peter Reikes

Director

December 31, 2020

/s/ Michael Hayden
Michael Hayden

Director

December 31, 2020

/s/ Joan E. Herman
Joan E. Herman

Director

December 31, 2020

December 31, 2020

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

Ladies and Gentlemen:

You have requested my opinion with respect to certain matters in connection with the filing by Ionis Pharmaceuticals, Inc. (the “Company”) of a Registration Statement on Form S-8 (the “Registration Statement”) with the Securities and Exchange Commission, covering the offering of 2,603,429 shares of the Company’s Common Stock, \$.001 par value (the “Shares”), of which, 2,603,429 Shares are issuable pursuant to its Ionis Pharmaceuticals, Inc. 2020 Equity Incentive Plan (the “2020 Plan”) as described in the Registration Statement.

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

On the basis of the foregoing, and in reliance thereon, I am of the opinion that the Shares, when issued and sold in accordance with the 2020 Plan and related prospectuses, will be validly issued, fully paid and nonassessable.

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

Very truly yours,

/s/ Patrick R. O’Neil

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

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement (Form S-8) pertaining to the Ionis Pharmaceuticals, Inc. 2020 Equity Incentive Plan of Ionis Pharmaceuticals, Inc. of our reports dated March 2, 2020, with respect to the consolidated financial statements of Ionis Pharmaceuticals, Inc. and the effectiveness of internal control over financial reporting of Ionis Pharmaceuticals, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2019, filed with the Securities and Exchange Commission.

/s/ Ernst & Young LLP

San Diego, California
December 31, 2020

**IONIS PHARMACEUTICALS, INC.
2020 EQUITY INCENTIVE PLAN**

**ADOPTED BY THE BOARD OF DIRECTORS: DECEMBER 28, 2020
TERMINATION DATE: DECEMBER 15, 2025**

1. GENERAL.

(a) Eligible Stock Award Recipients. The persons eligible to receive Stock Awards are those persons who were employees of Akcea Therapeutics, Inc. and its subsidiaries (collectively “*Akcea*”) immediately prior to the Closing.

(b) Available Stock Awards. The Plan provides for the grant of the following Stock Awards: (i) Options, (ii) Restricted Stock Awards, (iii) Restricted Stock Unit Awards, and (iv) Stock Appreciation Rights.

(c) Purpose. The Company, by means of the Plan, seeks to secure and retain the services of the group of persons eligible to receive Stock Awards as set forth in Section 1(a), to provide incentives for such persons to exert maximum efforts for the success of the Company and any Affiliate, and to provide a means by which such eligible recipients may be given an opportunity to benefit from increases in value of the Common Stock through the granting of Stock Awards.

2. ADMINISTRATION.

(a) Administration by Board. The Board shall administer the Plan unless and until the Board delegates administration of the Plan to a Committee, as provided in Section 2(c).

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

(i) To determine from time to time (A) which of the persons eligible under the Plan shall be granted Stock Awards; (B) when and how each Stock Award shall be granted; (C) what type or combination of types of Stock Award shall be granted; (D) the provisions of each Stock Award granted (which need not be identical), including the time or times when a person shall be permitted to receive cash or Common Stock pursuant to a Stock Award; (E) the number of shares of Common Stock with respect to which a Stock Award shall be granted to each such person; and (F) the Fair Market Value applicable to a Stock Award.

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

(iii) To settle all controversies regarding the Plan and Stock Awards granted under it.

(iv) To accelerate the time at which a Stock Award may first be exercised or the time during which a Stock Award or any part thereof will vest in accordance with the Plan, notwithstanding the provisions in the Stock Award stating the time at which it may first be exercised or the time during which it will vest.

(v) To suspend or terminate the Plan at any time. Suspension or termination of the Plan shall not impair rights and obligations under any Stock Award granted while the Plan is in effect except with the written consent of the affected Participant.

(vi) To amend the Plan in any respect the Board deems necessary or advisable, including, without limitation, relating to certain nonqualified deferred compensation under Section 409A of the Code and/or to bring the Plan or Stock Awards granted under the Plan into compliance therewith, subject to the limitations, if any, of applicable law. However, except as provided in Section 9(a) relating to Capitalization Adjustments, to the extent required by applicable law, stockholder approval shall be required for any amendment of the Plan that either (i) materially increases the number of shares of Common Stock available for issuance under the Plan, (ii) materially expands the class of individuals eligible to receive Stock Awards under the Plan, (iii) materially increases the benefits accruing to Participants under the Plan or materially reduces the price at which shares of Common Stock may be issued or purchased under the Plan, (iv) materially extends the term of the Plan, or (v) expands the types of Stock Awards available for issuance under the Plan. Except as provided above, rights under any Stock Award granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (i) the Company requests the consent of the affected Participant, and (ii) such Participant consents in writing.

(vii) To submit any amendment to the Plan for stockholder approval, including, but not limited to, amendments to the Plan intended to satisfy the requirements of Section 422 of the Code regarding incentive stock options.

(viii) To approve forms of Stock Award Agreements for use under the Plan and to amend the terms of any one or more Stock Awards, including, but not limited to, amendments to provide terms more favorable than previously provided in the Stock Award Agreement, subject to any specified limits in the Plan that are not subject to Board discretion; *provided however*, that, the rights under any Stock Award shall not be impaired by any such amendment unless (i) the Company requests the consent of the affected Participant, and (ii) such Participant consents in writing. Notwithstanding the foregoing, subject to the limitations of applicable law, if any, and without the affected Participant's consent, the Board may amend the terms of any one or more Stock Awards if necessary to bring the Stock Award into compliance with Section 409A of the Code and the related guidance thereunder.

(ix) 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 that are not in conflict with the provisions of the Plan or Stock Awards.

(x) To adopt such procedures and sub-plans as are necessary or appropriate to permit participation in the Plan by Employees, Directors or Consultants who are foreign nationals or employed outside the United States.

(c) **Delegation to Committee.** The Board may delegate some or all of the administration of the Plan to a Committee or Committees. If administration of the Plan is delegated to a Committee, the Committee shall have, in connection with the administration of the Plan, the powers theretofore possessed by the Board that have been delegated to the Committee, including the power to delegate to a subcommittee of the Committee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board shall thereafter be to the Committee or subcommittee), 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 retain the authority to concurrently administer the Plan with the Committee and may, at any time, revert in the Board some or all of the powers previously delegated.

(d) **Delegation to an Officer.** The Board may delegate to one or more Officers of the Company the authority to do one or both of the following: (i) designate Officers (other than Officers of a Vice President level or senior thereto) and Employees who were employees of Akcea prior to the Closing to be recipients of Options (and, to the extent permitted by applicable law, other Stock Awards) and the terms thereof, and (ii) determine the number of shares of Common Stock to be subject to such Stock Awards granted to such Officers and Employees; provided, however, that the Board resolutions regarding such delegation shall specify the total number of shares of Common Stock that may be subject to the Stock Awards granted by such Officer and that such Officer may not grant a Stock Award to himself or herself. Notwithstanding the foregoing, the Board may not delegate authority to an Officer to determine the Fair Market Value of the Common Stock pursuant to Section 13(t) below.

(e) **Effect of Board's Decision.** All determinations, interpretations and constructions made by the Board in good faith shall not be subject to review by any person and shall be final, binding and conclusive on all persons.

(f) **Arbitration.** Any dispute or claim concerning any Stock Awards granted (or not granted) pursuant to the Plan or any disputes or claims relating to or arising out of the Plan shall be fully, finally and exclusively resolved by binding and confidential arbitration conducted pursuant to the Commercial Arbitration Rules of the American Arbitration Association in San Diego, California. The Company shall pay all arbitration fees. In addition to any other relief, the arbitrator may award to the prevailing party recovery of its attorneys' fees and costs. By accepting a Stock Award, Participants and the Company waive their respective rights to have any such disputes or claims tried by a judge or jury.

3. SHARES SUBJECT TO THE PLAN.

(a) **Share Reserve.** Subject to Section 9(a) relating to Capitalization Adjustments, the aggregate number of shares of Common Stock of the Company that may be issued pursuant to Stock Awards after the Effective Date shall not exceed 2,603,429 shares. For clarity, the limitation in this Section 3(a) is a limitation in the number of shares of Common Stock that may be issued pursuant to the Plan. Accordingly, this Section 3(a) does not limit the granting of Stock Awards except as provided in Section 7(a).

(b) Reversion of Shares to the Share Reserve. If any shares of Common Stock issued pursuant to a Stock Award are forfeited back to the Company because of the failure to meet a contingency or condition required to vest such shares in the Participant, then the shares which are forfeited shall revert to and again become available for issuance under the Plan. Also, any shares reacquired by the Company pursuant to Section 8(g) or as consideration for the exercise of an Option shall again become available for issuance under the Plan. Furthermore, if a Stock Award (i) expires or otherwise terminates without having been exercised in full or (ii) is settled in cash (i.e., the holder of the Stock Award receives cash rather than stock), such expiration, termination or settlement shall not reduce (or otherwise offset) the number of shares of Common Stock that may be issued pursuant to the Plan.

(c) Source of Shares. The stock issuable under the Plan shall be shares of authorized but unissued or reacquired Common Stock, including shares repurchased by the Company on the open market.

4. ELIGIBILITY FOR STOCK AWARDS. Stock Awards may be granted only to those Employees, Directors and Consultants who were employees of Akcea immediately prior to the Closing.

5. OPTION PROVISIONS.

Each Option shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The provisions of separate Options need not be identical; *provided, however*, that each Option Agreement shall include (through incorporation of provisions hereof by reference in the Option Agreement or otherwise) the substance of each of the following provisions:

(a) Term. No Option shall be exercisable after the expiration of ten (10) years from the date of its grant or such shorter period specified in the Option Agreement.

(b) Exercise Price. The exercise price of each Option shall be not less than one hundred percent (100%) of the Fair Market Value of the Common Stock subject to the Option on the date the Option is granted.

(c) Consideration. The purchase price of Common Stock acquired pursuant to the exercise of an Option shall be paid, to the extent permitted by applicable law and as determined by the Board in its sole discretion, by any combination of the methods of payment set forth below. The Board shall have the authority to grant Options that do not permit all of the following methods of payment (or otherwise restrict the ability to use certain methods) and to grant Options that require the consent of the Company to utilize a particular method of payment. The permitted methods of payment are as follows:

(i) by cash, check, bank draft or money order payable to the Company;

(ii) pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board that, prior to the issuance of the stock subject to the Option, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sales proceeds;

(iii) by delivery to the Company (either by actual delivery or attestation) of shares of Common Stock;

(iv) by a “net exercise” arrangement pursuant to which the Company will reduce the number of shares of Common Stock issued upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; *provided, however*, that the Company shall accept a cash or other payment from the Participant to the extent of any remaining balance of the aggregate exercise price not satisfied by such reduction in the number of whole shares to be issued; *provided, further*, that shares of Common Stock will no longer be outstanding under an Option and will not be exercisable thereafter to the extent that (A) shares are used to pay the exercise price pursuant to the “net exercise,” (B) shares are delivered to the Participant as a result of such exercise, and (C) shares are withheld to satisfy tax withholding obligations;

(v) according to a deferred payment or similar arrangement approved by the Board between the Company and the Optionholder; *provided, however*, that interest shall compound at least annually and shall be charged at the minimum rate of interest necessary to avoid (A) the imputation of interest income to the Company and compensation income to the Optionholder under any applicable provisions of the Code, and (B) the classification of the Option as a liability for financial accounting purposes; or

(vi) in any other form of legal consideration that may be acceptable to the Board.

(d) **Transferability of Options.** The Board may, in its sole discretion, impose such limitations on the transferability of Options as the Board shall determine. In the absence of such a determination by the Board to the contrary, the following restrictions on the transferability of Options shall apply:

(i) **Restrictions on Transfer.** An Option shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Optionholder only by the Optionholder; *provided, however*, that the Board may, in its sole discretion, permit transfer of the Option to such extent as permitted by Rule 701 of the Securities Act at the time of the grant of the Option and in a manner consistent with applicable tax and securities laws upon the Optionholder’s request.

(ii) **Domestic Relations Orders.** Notwithstanding the foregoing, an Option may be transferred pursuant to a domestic relations order.

(iii) **Beneficiary Designation.** Notwithstanding the foregoing, the Optionholder may, by delivering written notice to the Company, in a form provided by or otherwise satisfactory to the Company, designate a third party who, in the event of the death of the Optionholder, shall thereafter be the beneficiary of an Option with the right to exercise the Option and receive the Common Stock or other consideration resulting from the Option exercise.

(e) **Vesting of Options Generally.** The total number of shares of Common Stock subject to an Option may vest and therefore become exercisable in periodic installments that may or may not be equal. The Option may be subject to such other terms and conditions on the time or times when it may or may not be exercised (which may be based on the satisfaction of performance goals or other criteria) as the Board may deem appropriate. The vesting provisions of individual Options may vary. The provisions of this Section 5(e) are subject to any Option provisions governing the minimum number of shares of Common Stock as to which an Option may be exercised.

(f) Termination of Continuous Service. Except as otherwise provided in the applicable Option Agreement or other agreement between the Optionholder and the Company, in the event that an Optionholder's Continuous Service terminates (other than upon the Optionholder's death or Disability), the Optionholder may exercise his or her Option (to the extent that the Optionholder was entitled to exercise such Option as of the date of termination of Continuous Service) but only within such period of time ending on the earlier of (i) the date three (3) months following the termination of the Optionholder's Continuous Service (or such longer or shorter period specified in the Option Agreement, which period shall not be less than thirty (30) days), or (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination of Continuous Service, the Optionholder does not exercise his or her Option within the time specified herein or in the Option Agreement (as applicable), the Option shall terminate.

(g) Extension of Termination Date. Except as otherwise provided in the applicable Option Agreement or other agreement between the Optionholder and the Company, if the exercise of the Option following the termination of the Optionholder's Continuous Service (other than upon the Optionholder's death or Disability) would be prohibited at any time solely because the issuance of shares of Common Stock would violate the registration requirements under the Securities Act, then the Option shall terminate on the earlier of (i) the expiration of a period of three (3) months after the termination of the Optionholder's Continuous Service during which the exercise of the Option would not be in violation of such registration requirements, or (ii) the expiration of the term of the Option as set forth in the Option Agreement.

(h) Disability of Optionholder. Except as otherwise provided in the applicable Option Agreement or other agreement between the Optionholder and the Company, in the event that an Optionholder's Continuous Service terminates as a result of the Optionholder's Disability, the Optionholder may exercise his or her Option (to the extent that the Optionholder was entitled to exercise such Option as of the date of termination of Continuous Service), but only within such period of time ending on the earlier of (i) the date twelve (12) months following such termination of Continuous Service (or such longer or shorter period specified in the Option Agreement, which period shall not be less than six (6) months), or (ii) the expiration of the term of the Option as set forth in the Option Agreement. If, after termination of Continuous Service, the Optionholder does not exercise his or her Option within the time specified herein or in the Option Agreement (as applicable), the Option shall terminate.

(i) Death of Optionholder. Except as otherwise provided in the applicable Option Agreement or other agreement between the Optionholder and the Company, in the event that (i) an Optionholder's Continuous Service terminates as a result of the Optionholder's death, or (ii) the Optionholder dies within the period (if any) specified in the Option Agreement after the termination of the Optionholder's Continuous Service for a reason other than death, then the Option may be exercised (to the extent the Optionholder was entitled to exercise such Option as of the date of death) by the Optionholder's estate, by a person who acquired the right to exercise the Option by bequest or inheritance or by a person designated as the beneficiary of the Option upon the Optionholder's death, but only within the period ending on the earlier of (i) the date eighteen (18) months following the date of death (or such longer or shorter period specified in the Option Agreement, which period shall not be less than six (6) months), or (ii) the expiration of the term of such Option as set forth in the Option Agreement. If, after the Optionholder's death, the Option is not exercised within the time specified herein or in the Option Agreement (as applicable), the Option shall terminate. If the Optionholder designates a third party beneficiary of the Option in accordance with Section 5(d)(iii), then upon the death of the Optionholder such designated beneficiary shall have the sole right to exercise the Option and receive the Common Stock or other consideration resulting from the Option exercise.

(j) Non-Exempt Employees. No Option granted to an Employee that is a non-exempt employee for purposes of the Fair Labor Standards Act of 1938, as amended, shall be first exercisable for any shares of Common Stock until at least six months following the date of grant of the Option. The foregoing provision is intended to operate so that any income derived by a non-exempt employee in connection with the exercise or vesting of an Option will be exempt from his or her regular rate of pay.

(k) Early Exercise. The Option may, but need not, include a provision whereby the Optionholder may elect at any time before the Optionholder's Continuous Service terminates to exercise the Option as to any part or all of the shares of Common Stock subject to the Option prior to the full vesting of the Option. Subject to the "Repurchase Limitation" in Section 8(l), any unvested shares of Common Stock so purchased may be subject to a repurchase option in favor of the Company or to any other restriction the Board determines to be appropriate. Provided that the "Repurchase Limitation" in Section 8(l) is not violated, the Company shall not be required to exercise its repurchase option until at least six (6) months (or such longer or shorter period of time required to avoid classification of the Option as a liability for financial accounting purposes) have elapsed following exercise of the Option unless the Board otherwise specifically provides in the Option Agreement.

(l) Right of Repurchase. Subject to the "**Repurchase Limitation**" in Section 8(l), the Option may include a provision whereby the Company may elect to repurchase all or any part of the vested shares of Common Stock acquired by the Optionholder pursuant to the exercise of the Option.

(m) Right of First Refusal. The Option may include a provision whereby the Company may elect to exercise a right of first refusal following receipt of notice from the Optionholder of the intent to transfer all or any part of the shares of Common Stock received upon the exercise of the Option. Such right of first refusal shall be subject to the "**Repurchase Limitation**" in Section 8(l). Except as expressly provided in this Section 5(n) or in the Option Agreement, such right of first refusal shall otherwise comply with any applicable provisions of the Bylaws of the Company.

6. PROVISIONS OF STOCK AWARDS OTHER THAN OPTIONS.

(a) Restricted Stock Awards. Each Restricted Stock Award Agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. To the extent consistent with the Company's Bylaws, at the Board's election, shares of Common Stock may be (x) held in book entry form subject to the Company's instructions until any restrictions relating to the Restricted Stock Award lapse; or (y) evidenced by a certificate, which certificate shall be held in such form and manner as determined by the Board. The terms and conditions of Restricted Stock Award Agreements may change from time to time, and the terms and conditions of separate Restricted Stock Award Agreements need not be identical; *provided, however*, that each Restricted Stock Award Agreement shall include (through incorporation of the provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) Consideration. A Restricted Stock Award may be awarded in consideration for (A) past or future services actually or to be rendered to the Company or an Affiliate, or (B) any other form of legal consideration that may be acceptable to the Board in its sole discretion and permissible under applicable law.

(ii) Vesting. Subject to the “Repurchase Limitation” in Section 8(l), shares of Common Stock awarded under the Restricted Stock Award Agreement may be subject to forfeiture to the Company in accordance with a vesting schedule to be determined by the Board.

(iii) Termination of Participant’s Continuous Service. In the event a Participant’s Continuous Service terminates, the Company may receive via a forfeiture condition, any or all of the shares of Common Stock held by the Participant which have not vested as of the date of termination of Continuous Service under the terms of the Restricted Stock Award Agreement.

(iv) Transferability. Rights to acquire shares of Common Stock under the Restricted Stock Award Agreement shall be transferable by the Participant only upon such terms and conditions as are set forth in the Restricted Stock Award Agreement, as the Board shall determine in its sole discretion, so long as Common Stock awarded under the Restricted Stock Award Agreement remains subject to the terms of the Restricted Stock Award Agreement.

(b) Restricted Stock Unit Awards. Each Restricted Stock Unit Award Agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. The terms and conditions of Restricted Stock Unit Award Agreements may change from time to time, and the terms and conditions of separate Restricted Stock Unit Award Agreements need not be identical, *provided, however*, that each Restricted Stock Unit Award Agreement shall include (through incorporation of the provisions hereof by reference in the Agreement or otherwise) the substance of each of the following provisions:

(i) Consideration. At the time of grant of a Restricted Stock Unit Award, the Board will determine the consideration, if any, to be paid by the Participant upon delivery of each share of Common Stock subject to the Restricted Stock Unit Award. The consideration to be paid (if any) by the Participant for each share of Common Stock subject to a Restricted Stock Unit Award may be paid in any form of legal consideration that may be acceptable to the Board in its sole discretion and permissible under applicable law.

(ii) Vesting. At the time of the grant of a Restricted Stock Unit Award, the Board may impose such restrictions or conditions to the vesting of the Restricted Stock Unit Award as it, in its sole discretion, deems appropriate.

(iii) Payment. A Restricted Stock Unit Award may be settled by the delivery of shares of Common Stock, their cash equivalent, any combination thereof or in any other form of consideration, as determined by the Board and contained in the Restricted Stock Unit Award Agreement.

(iv) Additional Restrictions. At the time of the grant of a Restricted Stock Unit Award, the Board, as it deems appropriate, may impose such restrictions or conditions that delay the delivery of the shares of Common Stock (or their cash equivalent) subject to a Restricted Stock Unit Award to a time after the vesting of such Restricted Stock Unit Award.

(v) Dividend Equivalents. Dividend equivalents may be credited in respect of shares of Common Stock covered by a Restricted Stock Unit Award, as determined by the Board and contained in the Restricted Stock Unit Award Agreement. At the sole discretion of the Board, such dividend equivalents may be converted into additional shares of Common Stock covered by the Restricted Stock Unit Award in such manner as determined by the Board. Any additional shares covered by the Restricted Stock Unit Award credited by reason of such dividend equivalents will be subject to all the terms and conditions of the underlying Restricted Stock Unit Award Agreement to which they relate.

(vi) Termination of Participant's Continuous Service. Except as otherwise provided in the applicable Restricted Stock Unit Award Agreement, such portion of the Restricted Stock Unit Award that has not vested will be forfeited upon the Participant's termination of Continuous Service.

(vii) Compliance with Section 409A of the Code. Notwithstanding anything to the contrary set forth herein, any Restricted Stock Unit Award granted under the Plan that is not exempt from the requirements of Section 409A of the Code shall contain such provisions so that such Restricted Stock Unit Award will comply with the requirements of Section 409A of the Code. Such restrictions, if any, shall be determined by the Board and contained in the Restricted Stock Unit Award Agreement evidencing such Restricted Stock Unit Award. For example, such restrictions may include, without limitation, a requirement that any Common Stock that is to be issued in a year following the year in which the Restricted Stock Unit Award vests must be issued in accordance with a fixed pre-determined schedule.

(c) Stock Appreciation Rights. Each Stock Appreciation Right Agreement shall be in such form and shall contain such terms and conditions as the Board shall deem appropriate. Stock Appreciation Rights may be granted as stand-alone Stock Awards or in tandem with other Stock Awards. The terms and conditions of Stock Appreciation Right Agreements may change from time to time, and the terms and conditions of separate Stock Appreciation Right Agreements need not be identical; provided, however, that each Stock Appreciation Right Agreement shall include (through incorporation of the provisions hereof by reference in the agreement or otherwise) the substance of each of the following provisions:

(i) Term. No Stock Appreciation Right shall be exercisable after the expiration of ten (10) years from the date of grant or such shorter period specified in the Stock Appreciation Right Agreement.

(ii) Strike Price. Each Stock Appreciation Right will be denominated in shares of Common Stock equivalents. The strike price of each Stock Appreciation Right granted as a stand-alone or tandem Stock Award shall not be less than one hundred percent (100%) of the Fair Market Value of the Common Stock equivalents subject to the Stock Appreciation Right on the date of grant.

(iii) Calculation of Appreciation. The appreciation distribution payable on the exercise of a Stock Appreciation Right will be not greater than an amount equal to the excess of (A) the aggregate Fair Market Value (on the date of the exercise of the Stock Appreciation Right) of a number of shares of Common Stock equal to the number of shares of Common Stock equivalents in which the Participant is vested under such Stock Appreciation Right, and with respect to which the Participant is exercising the Stock Appreciation Right on such date, over (B) the strike price that will be determined by the Board on the date of grant.

(iv) **Vesting.** At the time of the grant of a Stock Appreciation Right, the Board may impose such restrictions or conditions to the vesting of such Stock Appreciation Right as it, in its sole discretion, deems appropriate.

(v) **Exercise.** To exercise any outstanding Stock Appreciation Right, the Participant must provide written notice of exercise to the Company in compliance with the provisions of the Stock Appreciation Right Agreement evidencing such Stock Appreciation Right.

(vi) **Non-Exempt Employees.** No Stock Appreciation Right granted to an Employee that is a non-exempt employee for purposes of the Fair Labor Standards Act of 1938, as amended, shall be first exercisable for any shares of Common Stock until at least six months following the date of grant of the Stock Appreciation Right. The foregoing provision is intended to operate so that any income derived by a non-exempt employee in connection with the exercise of a Stock Appreciation Right will be exempt from his or her regular rate of pay.

(vii) **Payment.** The appreciation distribution in respect to a Stock Appreciation Right may be paid in Common Stock, in cash, in any combination of the two or in any other form of consideration, as determined by the Board and contained in the Stock Appreciation Right Agreement evidencing such Stock Appreciation Right.

(viii) **Termination of Continuous Service.** Except as otherwise provided in the applicable Stock Appreciation Right Agreement or other agreement between the Participant and the Company, in the event that a Participant's Continuous Service terminates (other than upon the Participant's death or Disability), the Participant may exercise his or her Stock Appreciation Right (to the extent that the Participant was entitled to exercise such Stock Appreciation Right as of the date of termination of Continuous Service) but only within such period of time ending on the earlier of (A) the date three (3) months following the termination of the Participant's Continuous Service (or such longer or shorter period specified in the Stock Appreciation Right Agreement, which period shall not be less than thirty (30) days), or (B) the expiration of the term of the Stock Appreciation Right as set forth in the Stock Appreciation Right Agreement. If, after termination of Continuous Service, the Participant does not exercise his or her Stock Appreciation Right within the time specified herein or in the Stock Appreciation Right Agreement (as applicable), the Stock Appreciation Right shall terminate.

(ix) **Disability of Participant.** Except as otherwise provided in the applicable Stock Appreciation Right Agreement or other agreement between the Participant and the Company, in the event that a Participant's Continuous Service terminates as a result of the Participant's Disability, the Participant may exercise his or her Stock Appreciation Right (to the extent that the Participant was entitled to exercise such Stock Appreciation Right as of the date of termination of Continuous Service), but only within such period of time ending on the earlier of (A) the date twelve (12) months following such termination of Continuous Service (or such longer or shorter period specified in the Stock Appreciation Right Agreement, which period shall not be less than six (6) months), or (B) the expiration of the term of the Stock Appreciation Right as set forth in the Stock Appreciation Right Agreement. If, after termination of Continuous Service, the Participant does not exercise his or her Stock Appreciation Right within the time specified herein or in the Stock Appreciation Right Agreement (as applicable), the Stock Appreciation Right shall terminate.

(x) **Death of Participant.** Except as otherwise provided in the applicable Stock Appreciation Right Agreement or other agreement between the Participant and the Company, in the event that (i) a Participant's Continuous Service terminates as a result of the Participant's death, or (ii) the Participant dies within the period (if any) specified in the Stock Appreciation Right Agreement after the termination of the Participant's Continuous Service for a reason other than death, then the Stock Appreciation Right may be exercised (to the extent the Participant was entitled to exercise such Stock Appreciation Right as of the date of death) by the Participant's estate, by a person who acquired the right to exercise the Stock Appreciation Right by bequest or inheritance or by a person designated as the beneficiary of the Stock Appreciation Right upon the Participant's death, but only within the period ending on the earlier of (i) the date eighteen (18) months following the date of death (or such longer or shorter period specified in the Stock Appreciation Right Agreement, which period shall not be less than six (6) months), or (ii) the expiration of the term of such Stock Appreciation Right as set forth in the Stock Appreciation Right Agreement. If, after the Participant's death, the Stock Appreciation Right is not exercised within the time specified herein or in the Stock Appreciation Right Agreement (as applicable), the Stock Appreciation Right shall terminate.

(xi) **Compliance with Section 409A of the Code.** Notwithstanding anything to the contrary set forth herein, any Stock Appreciation Rights granted under the Plan that are not exempt from the requirements of Section 409A of the Code shall contain such provisions so that such Stock Appreciation Rights will comply with the requirements of Section 409A of the Code. Such restrictions, if any, shall be determined by the Board and contained in the Stock Appreciation Right Agreement evidencing such Stock Appreciation Right. For example, such restrictions may include, without limitation, a requirement that a Stock Appreciation Right that is to be paid wholly or partly in cash must be exercised and paid in accordance with a fixed pre-determined schedule.

7. COVENANTS OF THE COMPANY.

(a) **Availability of Shares.** During the terms of the Stock Awards, the Company shall keep available at all times the number of shares of Common Stock reasonably required to satisfy such Stock Awards.

(b) **Securities Law Compliance.** The Company shall seek to obtain from each regulatory commission or agency having jurisdiction over the Plan such authority as may be required to grant Stock Awards and to issue and sell shares of Common Stock upon exercise of the Stock Awards; *provided, however*, that this undertaking shall not require the Company to register under the Securities Act the Plan, any Stock Award or any Common Stock issued or issuable pursuant to any such Stock Award. If, after reasonable efforts, the Company is unable to obtain from any such regulatory commission or agency the authority that counsel for the Company deems necessary for the lawful issuance and sale of Common Stock under the Plan, the Company shall be relieved from any liability for failure to issue and sell Common Stock upon exercise of such Stock Awards unless and until such authority is obtained.

(c) **No Obligation to Notify.** The Company shall have no duty or obligation to any holder of a Stock Award to advise such holder as to the time or manner of exercising such Stock Award. Furthermore, the Company shall have no duty or obligation to warn or otherwise advise such holder of a pending termination or expiration of a Stock Award or a possible period in which the Stock Award may not be exercised. The Company has no duty or obligation to minimize the tax consequences of a Stock Award to the holder of such Stock Award.

8. MISCELLANEOUS.

(a) **Use of Proceeds from Sales of Common Stock.** Proceeds from the sale of shares of Common Stock pursuant to Stock Awards shall constitute general funds of the Company.

(b) **Corporate Action Constituting Grant of Stock Awards.** Corporate action constituting a grant by the Company of a Stock Award to any Participant shall be deemed completed as of the date of such corporate action, unless otherwise determined by the Board, regardless of when the instrument, certificate, or letter evidencing the Stock Award is communicated to, or actually received or accepted by, the Participant.

(c) **Stockholder Rights.** No Participant shall be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Common Stock subject to such Stock Award unless and until such Participant has satisfied all requirements for exercise of the Stock Award pursuant to its terms and the Participant shall not be deemed to be a stockholder of record until the issuance of the Common Stock pursuant to such exercise has been entered into the books and records of the Company.

(d) **No Employment or Other Service Rights.** Nothing in the Plan, any Stock Award Agreement or any other instrument executed thereunder or in connection with any Stock Award granted pursuant thereto shall confer upon any Participant any right to continue to serve the Company or an Affiliate in the capacity in effect at the time the Stock Award was granted or shall affect the right of the Company or an Affiliate to terminate (i) the employment of an Employee with or without notice and with or without cause, (ii) the service of a Consultant pursuant to the terms of such Consultant's agreement with the Company or an Affiliate, or (iii) the service of a Director pursuant to the Bylaws of the Company or an Affiliate, and any applicable provisions of the corporate law of the state in which the Company or the Affiliate is incorporated, as the case may be.

(e) **Investment Assurances.** The Company may require a Participant, as a condition of exercising or acquiring Common Stock under any Stock Award, (i) to give written assurances satisfactory to the Company as to the Participant's knowledge and experience in financial and business matters and/or to employ a purchaser representative reasonably satisfactory to the Company who is knowledgeable and experienced in financial and business matters and that he or she is capable of evaluating, alone or together with the purchaser representative, the merits and risks of exercising the Stock Award; and (ii) to give written assurances satisfactory to the Company stating that the Participant is acquiring Common Stock subject to the Stock Award for the Participant's own account and not with any present intention of selling or otherwise distributing the Common Stock. The foregoing requirements, and any assurances given pursuant to such requirements, shall be inoperative if (x) the issuance of the shares upon the exercise or acquisition of Common Stock under the Stock Award has been registered under a then currently effective registration statement under the Securities Act, or (y) as to any particular requirement, a determination is made by counsel for the Company that such requirement need not be met in the circumstances under the then applicable securities laws. The Company may, upon advice of counsel to the Company, place legends on stock certificates issued under the Plan as such counsel deems necessary or appropriate in order to comply with applicable securities laws, including, but not limited to, legends restricting the transfer of the Common Stock.

(f) Withholding Obligations. To the extent provided by the terms of a Stock Award Agreement, the Company may, in its sole discretion, satisfy any federal, state or local tax withholding obligation relating to a Stock Award by any of the following means (in addition to the Company's right to withhold from any compensation paid to the Participant by the Company) or by a combination of such means: (i) causing the Participant to tender a cash payment; (ii) withholding shares of Common Stock from the shares of Common Stock issued or otherwise issuable to the Participant in connection with the Stock Award; *provided, however*, that no shares of Common Stock are withheld with a value exceeding the minimum amount of tax required to be withheld by law (or such lower amount as may be necessary to avoid classification of the Stock Award as a liability for financial accounting purposes); (iii) withholding payment from any amounts otherwise payable to the Participant; (iv) withholding cash from a Stock Award settled in cash; or (v) by such other method as may be set forth in the Stock Award Agreement.

(g) Electronic Delivery. Any reference herein to a "written" agreement or document shall include any agreement or document delivered electronically or posted on the Company's intranet.

(h) Deferrals. To the extent permitted by applicable law, the Board, in its sole discretion, may determine that the delivery of Common Stock or the payment of cash, upon the exercise, vesting or settlement of all or a portion of any Stock Award may be deferred and may establish programs and procedures for deferral elections to be made by Participants. Deferrals by Participants will be made in accordance with Section 409A of the Code. Consistent with Section 409A of the Code, the Board may provide for distributions while a Participant is still an employee. The Board is authorized to make deferrals of Stock Awards and determine when, and in what annual percentages, Participants may receive payments, including lump sum payments, following the Participant's termination of employment or retirement, and implement such other terms and conditions consistent with the provisions of the Plan and in accordance with applicable law.

(i) Compliance with Section 409A. To the extent that the Board determines that any Stock Award granted hereunder is subject to Section 409A of the Code, the Stock Award Agreement evidencing such Stock Award shall incorporate the terms and conditions necessary to avoid the consequences specified in Section 409A(a)(1) of the Code. To the extent applicable, the Plan and Stock Award Agreements shall be interpreted in accordance with Section 409A of the Code and Department of Treasury regulations and other interpretive guidance issued thereunder, including without limitation any such regulations or other guidance that may be issued or amended after the Effective Date. Notwithstanding any provision of the Plan to the contrary, in the event that following the Effective Date the Board determines that any Stock Award may be subject to Section 409A of the Code and related Department of Treasury guidance (including such Department of Treasury guidance as may be issued after the Effective Date), the Board may adopt such amendments to the Plan and the applicable Stock Award Agreement or adopt other policies and procedures (including amendments, policies and procedures with retroactive effect), or take any other actions, that the Board determines are necessary or appropriate to (1) exempt the Stock Award from Section 409A of the Code and/or preserve the intended tax treatment of the benefits provided with respect to the Stock Award, or (2) comply with the requirements of Section 409A of the Code and related Department of Treasury guidance.

(j) Repurchase Limitation. The terms of any repurchase option shall be specified in the Stock Award Agreement. The repurchase price for vested shares of Common Stock shall be the Fair Market Value of the shares of Common Stock on the date of repurchase. The repurchase price for unvested shares of Common Stock shall be the lower of (i) the Fair Market Value of the shares of Common Stock on the date of repurchase or (ii) their original purchase price. However, the Company shall not exercise its repurchase option until at least six (6) months (or such longer or shorter period of time necessary to avoid classification of the Stock Award as a liability for financial accounting purposes) have elapsed following delivery of shares of Common Stock subject to the Stock Award, unless otherwise specifically provided by the Board.

9. ADJUSTMENTS UPON CHANGES IN COMMON STOCK; OTHER CORPORATE EVENTS.

(a) Capitalization Adjustments. In the event of a Capitalization Adjustment, the Board shall proportionately and appropriately adjust: (i) the class(es) and maximum number of securities subject to the Plan pursuant to Section 3(a), and (ii) the class(es) and number of securities and price per share of stock subject to outstanding Stock Awards. The Board shall make such adjustments, and its determination shall be final, binding and conclusive.

(b) Dissolution or Liquidation. Except as otherwise provided in the Stock Award Agreement, in the event of a dissolution or liquidation of the Company, all outstanding Stock Awards (other than Stock Awards consisting of vested and outstanding shares of Common Stock not subject to the Company's right of repurchase) shall terminate immediately prior to the completion of such dissolution or liquidation, and the shares of Common Stock subject to the Company's repurchase option may be repurchased by the Company notwithstanding the fact that the holder of such Stock Award is providing Continuous Service, *provided, however*, that the Board may, in its sole discretion, cause some or all Stock Awards to become fully vested, exercisable and/or no longer subject to repurchase or forfeiture (to the extent such Stock Awards have not previously expired or terminated) before the dissolution or liquidation is completed but contingent on its completion.

(c) Corporate Transaction. The following provisions shall apply to Stock Awards in the event of a Corporate Transaction unless otherwise provided in the instrument evidencing the Stock Award or any other written agreement between the Company or any Affiliate and the holder of the Stock Award or unless otherwise expressly provided by the Board at the time of grant of a Stock Award.

(i) Stock Awards May Be Assumed. Except as otherwise stated in the Stock Award Agreement, in the event of a Corporate Transaction, any surviving corporation or acquiring corporation (or the surviving or acquiring corporation's parent company) may assume or continue any or all Stock Awards outstanding under the Plan or may substitute similar stock awards for Stock Awards outstanding under the Plan (including but not limited to, awards to acquire the same consideration paid to the stockholders of the Company pursuant to the Corporate Transaction), and any reacquisition or repurchase rights held by the Company in respect of Common Stock issued pursuant to Stock Awards may be assigned by the Company to the successor of the Company (or the successor's parent company, if any), in connection with such Corporate Transaction. A surviving corporation or acquiring corporation (or its parent) may choose to assume or continue only a portion of a Stock Award or substitute a similar stock award for only a portion of a Stock Award. The terms of any assumption, continuation or substitution shall be set by the Board in accordance with the provisions of Section 2.

(ii) Stock Awards Held by Current Participants. Except as otherwise stated in the Stock Award Agreement, in the event of a Corporate Transaction in which the surviving corporation or acquiring corporation (or its parent company) does not assume or continue such outstanding Stock Awards or substitute similar stock awards for such outstanding Stock Awards, then with respect to Stock Awards that have not been assumed, continued or substituted and that are held by Participants whose Continuous Service has not terminated prior to the effective time of the Corporate Transaction (referred to as the “**Current Participants**”), the vesting of such Stock Awards (and, if applicable, the time at which such Stock Awards may be exercised) shall (contingent upon the effectiveness of the Corporate Transaction) be accelerated in full to a date prior to the effective time of such Corporate Transaction as the Board shall determine (or, if the Board shall not determine such a date, to the date that is five (5) days prior to the effective time of the Corporate Transaction), and such Stock Awards shall terminate if not exercised (if applicable) at or prior to the effective time of the Corporate Transaction, and any reacquisition or repurchase rights held by the Company with respect to such Stock Awards shall lapse (contingent upon the effectiveness of the Corporate Transaction).

(iii) Stock Awards Held by Persons other than Current Participants. Except as otherwise stated in the Stock Award Agreement, in the event of a Corporate Transaction in which the surviving corporation or acquiring corporation (or its parent company) does not assume or continue such outstanding Stock Awards or substitute similar stock awards for such outstanding Stock Awards, then with respect to Stock Awards that have not been assumed, continued or substituted and that are held by persons other than Current Participants, the vesting of such Stock Awards (and, if applicable, the time at which such Stock Award may be exercised) shall not be accelerated and such Stock Awards (other than a Stock Award consisting of vested and outstanding shares of Common Stock not subject to the Company’s right of repurchase) shall terminate if not exercised (if applicable) prior to the effective time of the Corporate Transaction; *provided, however*, that any reacquisition or repurchase rights held by the Company with respect to such Stock Awards shall not terminate and may continue to be exercised notwithstanding the Corporate Transaction.

(iv) Payment for Stock Awards in Lieu of Exercise. Notwithstanding the foregoing, in the event a Stock Award will terminate if not exercised prior to the effective time of a Corporate Transaction, the Board may provide, in its sole discretion, that the holder of such Stock Award may not exercise such Stock Award but will receive, in the Board’s discretion, such cash consideration (including no consideration) as the Board may consider appropriate, in such form as may be determined by the Board, including a payment equal in value to the excess, if any, of (A) the value of the property the holder of the Stock Award would have received upon the exercise of the Stock Award, over (B) any exercise price payable by such holder in connection with such exercise.

(d) Change in Control. A Stock Award may be subject to additional acceleration of vesting and exercisability upon or after a Change in Control as may be provided in the Stock Award Agreement for such Stock Award or as may be provided in any other written agreement approved by the Board between the Company or any Affiliate and the Participant, but in the absence of such provision, no such acceleration shall occur.

10. TERMINATION OR SUSPENSION OF THE PLAN.

(a) **Plan Term.** The Board may suspend or terminate the Plan at any time. Unless sooner terminated by the Board pursuant to Section 2, the Plan shall automatically terminate on December 15, 2025. No Stock Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

(b) **No Impairment of Rights.** Suspension or termination of the Plan shall not impair rights and obligations under any Stock Award granted while the Plan is in effect except with the written consent of the affected Participant.

11. EFFECTIVE DATE OF PLAN.

This Plan shall become effective on the Effective Date.

12. CHOICE OF LAW.

The law of the State of Delaware shall govern all questions concerning the construction, validity and interpretation of this Plan, without regard to that state's conflict of laws rules.

13. DEFINITIONS. As used in the Plan, the following definitions shall apply to the capitalized terms indicated below:

(a) **"Affiliate"** means, at the time of determination, any "parent" or "majority-owned subsidiary" of the Company, as such terms are defined in Rule 405 of the Securities Act. The Board shall have the authority to determine the time or times at which "parent" or "majority-owned subsidiary" status is determined within the foregoing definition.

(b) **"Board"** means the Board of Directors of the Company.

(c) **"Capitalization Adjustment"** means any change that is made in, or other events that occur with respect to, the Common Stock subject to the Plan or subject to any Stock Award after the Effective Date without the receipt of consideration by the Company (through merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or other transaction not involving the receipt of consideration by the Company). Notwithstanding the foregoing, the conversion of any convertible securities of the Company shall not be treated as a transaction "without the receipt of consideration" by the Company.

(d) **"Change in Control"** means the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:

(i) any Exchange Act Person becomes the Owner, directly or indirectly, of securities of the Company representing more than fifty percent (50%) of the combined voting power of the Company's then outstanding securities other than by virtue of a merger, consolidation or similar transaction. Notwithstanding the foregoing, a Change in Control shall not be deemed to occur (A) on account of the acquisition of securities of the Company by an investor, any affiliate thereof or any other Exchange Act Person that acquires the Company's securities in a transaction or series of related transactions the primary purpose of which is to obtain financing for the Company through the issuance of equity securities or (B) solely because the level of Ownership held by any Exchange Act Person (the "**Subject Person**") exceeds the designated percentage threshold of the outstanding voting securities as a result of a repurchase or other acquisition of voting securities by the Company reducing the number of shares outstanding, provided that if a Change in Control would occur (but for the operation of this sentence) as a result of the acquisition of voting securities by the Company, and after such share acquisition, the Subject Person becomes the Owner of any additional voting securities that, assuming the repurchase or other acquisition had not occurred, increases the percentage of the then outstanding voting securities Owned by the Subject Person over the designated percentage threshold, then a Change in Control shall be deemed to occur;

(ii) there is consummated a merger, consolidation or similar transaction involving (directly or indirectly) the Company and, immediately after the consummation of such merger, consolidation or similar transaction, the stockholders of the Company immediately prior thereto do not Own, directly or indirectly, either (A) outstanding voting securities representing more than fifty percent (50%) of the combined outstanding voting power of the surviving Entity in such merger, consolidation or similar transaction or (B) more than fifty percent (50%) of the combined outstanding voting power of the parent of the surviving Entity in such merger, consolidation or similar transaction, in each case in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such transaction;

(iii) the stockholders of the Company approve or the Board approves a plan of complete dissolution or liquidation of the Company, or a complete dissolution or liquidation of the Company shall otherwise occur, except for a liquidation into a parent corporation; or

(iv) there is consummated a sale, lease, exclusive license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries (in each case as determined by the Board in its sole discretion), other than a sale, lease, license or other disposition of all or substantially all of the consolidated assets of the Company and its Subsidiaries to an Entity, more than fifty percent (50%) of the combined voting power of the voting securities of which are Owned by stockholders of the Company in substantially the same proportions as their Ownership of the outstanding voting securities of the Company immediately prior to such sale, lease, license or other disposition.

Notwithstanding the foregoing definition or any other provision of this Plan, (A) the term Change in Control shall not include a sale of assets, merger or other transaction effected exclusively for the purpose of changing the domicile of the Company, and (B) the definition of Change in Control (or any analogous term) in an individual written agreement between the Company or any Affiliate and the Participant shall supersede the foregoing definition with respect to Stock Awards subject to such agreement; provided, however, that if no definition of Change in Control or any analogous term is set forth in such an individual written agreement, the foregoing definition shall apply.

(e) "**Closing**" means the closing of the Agreement and Plan of Merger, among Akcea Therapeutics, Inc., a Delaware corporation, the Company, and Avalanche Merger Sub, Inc., a Delaware corporation and a wholly owned subsidiary of the Company.

- (f) “**Code**” means the Internal Revenue Code of 1986, as amended.
- (g) “**Committee**” means a committee of one or more Directors to whom authority has been delegated by the Board in accordance with Section 2(c).
- (h) “**Common Stock**” means the common stock of the Company.
- (i) “**Company**” means Ionis Pharmaceuticals, Inc., a Delaware corporation.
- (j) “**Consultant**” means any person, including an advisor, who is (i) engaged by the Company or an Affiliate to render consulting or advisory services and is compensated for such services, or (ii) serving as a member of the board of directors of an Affiliate and is compensated for such services. However, service solely as a Director, or payment of a fee for such service, shall not cause a Director to be considered a “**Consultant**” for purposes of the Plan.
- (k) “**Continuous Service**” means that the Participant’s service with the Company or an Affiliate, whether as an Employee, Director or Consultant, is not interrupted or terminated. A change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee, Director, or Consultant or a change in the Entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant’s service with the Company or an Affiliate, shall not terminate a Participant’s Continuous Service; provided, however, if the Entity for which a Participant is rendering service ceases to qualify as an Affiliate, as determined by the Board in its sole discretion, such Participant’s Continuous Service shall be considered to have terminated on the date such Entity ceases to qualify as an Affiliate. For example, a change in status from an employee of the Company to a consultant of an Affiliate or to a Director shall not constitute an interruption of Continuous Service. To the extent permitted by law, the Board or the chief executive officer of the Company, in that party’s sole discretion, may determine whether Continuous Service shall be considered interrupted in the case of any leave of absence approved by that party, including sick leave, military leave or any other personal leave. Notwithstanding the foregoing, a leave of absence shall be treated as Continuous Service for purposes of vesting in a Stock Award only to such extent as may be provided in the Company’s leave of absence policy, in the written terms of any leave of absence agreement or policy applicable to the Participant, or as otherwise required by law.
- (l) “**Corporate Transaction**” means the occurrence, in a single transaction or in a series of related transactions, of any one or more of the following events:
- (i) the consummation of a sale or other disposition of all or substantially all, as determined by the Board in its sole discretion, of the consolidated assets of the Company and its Subsidiaries;
 - (ii) the consummation of a sale or other disposition of at least ninety percent (90%) of the outstanding securities of the Company;
 - (iii) the consummation of a merger, consolidation or similar transaction following which the Company is not the surviving corporation; or
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(iv) the consummation of a merger, consolidation or similar transaction following which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger, consolidation or similar transaction are converted or exchanged by virtue of the merger, consolidation or similar transaction into other property, whether in the form of securities, cash or otherwise.

(m) “**Director**” means a member of the Board.

(n) “**Disability**” means the inability of a Participant to engage in any substantially gainful activity by reason of any medically determinable physical or mental impairment which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than twelve (12) months, and shall be determined by the Board on the basis of such medical evidence as the Board deems warranted under the circumstances.

(o) “**Effective Date**” means the effective date of this Plan, which is the date of the Closing.

(p) “**Employee**” means any person employed by the Company or an Affiliate. However, service solely as a Director, or payment of a fee for such services, shall not cause a Director to be considered an “**Employee**” for purposes of the Plan.

(q) “**Entity**” means a corporation, partnership, limited liability company or other entity.

(r) “**Exchange Act**” means the Securities Exchange Act of 1934, as amended.

(s) (r) “**Exchange Act Person**” means any natural person, Entity or “group” (within the meaning of Section 13(d) or 14(d) of the Exchange Act), except that “**Exchange Act Person**” shall not include (i) the Company or any Subsidiary of the Company, (ii) any employee benefit plan of the Company or any Subsidiary of the Company or any trustee or other fiduciary holding securities under an employee benefit plan of the Company or any Subsidiary of the Company, (iii) an underwriter temporarily holding securities pursuant to an offering of such securities, (iv) an Entity Owned, directly or indirectly, by the stockholders of the Company in substantially the same proportions as their Ownership of stock of the Company; or (v) any natural person, Entity or “group” (within the meaning of Section 13(d) or 14(d) of the Exchange Act) that, as of the Effective Date of the Plan as set forth in Section 11, is the Owner, directly or indirectly, of securities of the Company representing more than fifty percent (50%) of the combined voting power of the Company’s then outstanding securities.

(t) “**Fair Market Value**” means, as of any date, the value of the Common Stock determined as follows:

(i) If the Common Stock is listed on any established stock exchange or traded on any established market, the Fair Market Value of a share of Common Stock will be, unless otherwise determined by the Board, the closing sales price for such stock as quoted on such exchange or market (or the exchange or market with the greatest volume of trading in the Common Stock) on the date of determination, as reported in a source the Board deems reliable.

(ii) Unless otherwise provided by the Board, if there is no closing sales price for the Common Stock on the date of determination, then the Fair Market Value will be the closing sales price on the last preceding date for which such quotation exists.

(iii) In the absence of such markets for the Common Stock, the Fair Market Value will be determined by the Board in good faith and in a manner that complies with Sections 409A and 422 of the Code.

(u) “**Officer**” means any person designated by the Company as an officer.

(v) “**Option**” means an option to purchase shares of Common Stock granted pursuant to the Plan that is not intended to qualify as an “incentive stock option” within the meaning of Section 422 of the Code and the regulations promulgated thereunder.

(w) “**Option Agreement**” means a written agreement between the Company and an Optionholder evidencing the terms and conditions of an Option grant. Each Option Agreement shall be subject to the terms and conditions of the Plan.

(x) “**Optionholder**” means a person to whom an Option is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Option.

(y) “**Own,**” “**Owned,**” “**Owner,**” “**Ownership**” A person or Entity shall be deemed to “Own,” to have “Owned,” to be the “Owner” of, or to have acquired “Ownership” of securities if such person or Entity, directly or indirectly, through any contract, arrangement, understanding, relationship or otherwise, has or shares voting power, which includes the power to vote or to direct the voting, with respect to such securities.

(z) “**Participant**” means a person to whom a Stock Award is granted pursuant to the Plan or, if applicable, such other person who holds an outstanding Stock Award.

(aa) “**Plan**” means this Ionis Pharmaceuticals, Inc. 2020 Equity Incentive Plan.

(bb) “**Restricted Stock Award**” means an award of shares of Common Stock which is granted pursuant to the terms and conditions of Section 6(a).

(cc) “**Restricted Stock Award Agreement**” means a written agreement between the Company and a holder of a Restricted Stock Award evidencing the terms and conditions of a Restricted Stock Award. Each Restricted Stock Award Agreement shall be subject to the terms and conditions of the Plan.

(dd) “**Restricted Stock Unit Award**” means a right to receive shares of Common Stock which is granted pursuant to the terms and conditions of Section 6(b).

(ee) “**Restricted Stock Unit Award Agreement**” means a written agreement between the Company and a holder of a Restricted Stock Unit Award evidencing the terms and conditions of a Restricted Stock Unit Award grant. Each Restricted Stock Unit Award Agreement shall be subject to the terms and conditions of the Plan.

(ff) “*Securities Act*” means the Securities Act of 1933, as amended.

(gg) “*Stock Appreciation Right*” means a right to receive the appreciation on Common Stock that is granted pursuant to the terms and conditions of Section 6(c).

(hh) “*Stock Appreciation Right Agreement*” means a written agreement between the Company and a holder of a Stock Appreciation Right evidencing the terms and conditions of a Stock Appreciation Right grant. Each Stock Appreciation Right Agreement shall be subject to the terms and conditions of the Plan.

(ii) “*Stock Award*” means any right to receive Common Stock granted under the Plan, including an Option, a Restricted Stock Award, a Restricted Stock Unit Award, or a Stock Appreciation Right.

(jj) “*Stock Award Agreement*” means a written agreement between the Company and a Participant evidencing the terms and conditions of a Stock Award grant. Each Stock Award Agreement shall be subject to the terms and conditions of the Plan.

(kk) “*Subsidiary*” means, with respect to the Company, (i) any corporation of which more than fifty percent (50%) of the outstanding capital stock having ordinary voting power to elect a majority of the board of directors of such corporation (irrespective of whether, at the time, stock of any other class or classes of such corporation shall have or might have voting power by reason of the happening of any contingency) is at the time, directly or indirectly, Owned by the Company, and (ii) any partnership, limited liability company or other entity in which the Company has a direct or indirect interest (whether in the form of voting or participation in profits or capital contribution) of more than fifty percent (50%) .

IONIS PHARMACEUTICALS, INC.

2020 EQUITY INCENTIVE PLAN

GLOBAL OPTION AGREEMENT

(INCENTIVE STOCK OPTION OR NONSTATUTORY STOCK OPTION)

Pursuant to your Option Grant Notice (“**Grant Notice**”) and this Global Option Agreement, including all appendices hereto (this “**Agreement**”), Ionis Pharmaceuticals, Inc. (the “**Company**”) has granted you an option under its 2020 Equity Incentive Plan (the “**Plan**”) to purchase the number of shares of the Company’s Common Stock (the “**Option**”) indicated in your Grant Notice at the exercise price indicated in your Grant Notice. Defined terms not explicitly defined in this Agreement but defined in the Plan shall have the same definitions as in the Plan, or in the Grant Notice, as applicable.

The terms of your option are as follows:

1. VESTING. Subject to the limitations contained herein, your Option will vest as provided in your Grant Notice, provided that vesting will cease upon the termination of your Continuous Service.

2. NUMBER OF SHARES AND EXERCISE PRICE. The number of shares of Common Stock subject to your Option and your exercise price per share referenced in your Grant Notice may be adjusted from time to time for Capitalization Adjustments.

3. EXERCISE RESTRICTION FOR NON-EXEMPT EMPLOYEES. In the event that you are an Employee eligible for overtime compensation under the Fair Labor Standards Act of 1938, as amended (*i.e.*, a “**Non-Exempt Employee**”), you may not exercise your Option until you have completed at least six (6) months of Continuous Service measured from the Date of Grant specified in your Grant Notice, notwithstanding any other provision of your Option.

4. METHOD OF PAYMENT. Payment of the exercise price is due in full upon exercise of all or any part of your Option. You may elect to make payment of the exercise price in cash or by check or in any other manner *permitted by your Grant Notice*, which may include one or more of the following:

(a) Bank draft, check, wire transfer or money order payable to the Company.

(b) Pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board that, prior to the issuance of Common Stock, results in either the receipt of cash (or check) by the Company or the receipt of irrevocable instructions to pay the aggregate exercise price to the Company from the sale proceeds.

(c) By a “net exercise” arrangement pursuant to which the Company will reduce the number of shares of Common Stock issued upon exercise by the largest whole number of shares with a Fair Market Value that does not exceed the aggregate exercise price; *provided, however*, that the Company shall accept a cash or other payment from you to the extent of any remaining balance of the aggregate exercise price not satisfied by such reduction in the number of whole shares to be issued; *provided, further*, that shares of Common Stock will no longer be outstanding under an Option and will not be exercisable thereafter to the extent that (A) shares are used to pay the exercise price pursuant to the “net exercise,” (B) shares are delivered to you as a result of such exercise, and (C) shares are withheld to satisfy tax withholding obligations;

(d) For U.S. taxpayers only, by delivery to the Company (either by actual delivery or attestation) of already-owned shares of Common Stock that are owned free and clear of any liens, claims, encumbrances or security interests, and that are valued at Fair Market Value on the date of exercise. Notwithstanding the foregoing, you may not exercise your Option by tender to the Company of Common Stock to the extent such tender would violate the provisions of any law, regulation or agreement restricting the redemption of the Company's stock.

5. **WHOLE SHARES.** You may exercise your Option only for whole shares of Common Stock.

6. **COMPLIANCE WITH LAW.** Notwithstanding any other provision of the Plan or this Agreement, unless there is an exemption from any registration, qualification or other legal requirement applicable to the shares of Common Stock, the Company shall not be required to allow you to exercise the Option and deliver any shares subject to the Option prior to the completion of any registration or qualification of the shares under any U.S. or non-U.S. local, state or federal securities or exchange control law or under rulings or regulations of the U.S. Securities and Exchange Commission ("**SEC**") or of any other governmental regulatory body, or prior to obtaining any approval or other clearance from any U.S. or non-U.S. local, state or federal governmental agency, which registration, qualification or approval the Company shall, in its absolute discretion, deem necessary or advisable. You understand that the Company is under no obligation to register or qualify the shares with the SEC or any state or foreign securities commission or to seek approval or clearance from any governmental authority for the issuance or sale of the shares. Further, you agree that the Company shall have unilateral authority to amend the Agreement without your consent to the extent necessary to comply with securities or other laws applicable to issuance of shares.

7. **TERM.** You may not exercise your Option before the commencement or after the expiration of its term. The term of your Option commences on the Date of Grant and expires upon the earliest of the following:

(a) three (3) months after the termination of your Continuous Service for any reason (other than your Disability, retirement or death); provided, however, that (i) if during any part of such three (3) month period your Option is not exercisable solely because of the condition set forth in Section 6, your Option shall not expire until the earlier of the Expiration Date or until it shall have been exercisable for an aggregate period of three (3) months after the termination of your Continuous Service and (ii) if (x) you are a Non-Exempt Employee, (y) you terminate your Continuous Service within six (6) months after the Date of Grant specified in your Grant Notice, and (z) you have vested in a portion of your Option at the time of your termination of Continuous Service, your Option shall not expire until the earlier of (A) the later of the date that is seven (7) months after the Date of Grant specified in your Grant Notice or the date that is three (3) months after the termination of your Continuous Service or (B) the Expiration Date;

(b) twelve (12) months after the termination of your Continuous Service due to your Disability;

(c) subject to applicable law, eighteen (18) months after the termination of your Continuous Service due to your retirement; provided that (i) you were over the age of 55 at the time of such retirement and (ii) you had been providing Continuous Service to the Company as an Employee, Director or Consultant (or any combination thereof) for a continuous and uninterrupted period of at least five years prior to such retirement;

(d) eighteen (18) months after your death if you die either during your Continuous Service or within three (3) months after your Continuous Service terminates for any reason;

(e) the Expiration Date indicated in your Grant Notice; or

(f) the day before the tenth (10th) anniversary of the Date of Grant.

If your option is an Incentive Stock Option and you are a U.S. taxpayer, note that to obtain the U.S. federal income tax advantages associated with an Incentive Stock Option, the Code requires that at all times beginning on the date of grant of your Option and ending on the day three (3) months before the date of your Option's exercise, you must be an employee of the Company or an Affiliate, except in the event of your death or your permanent and total disability, as defined in Section 22(e) of the Code. (The definition of disability in Section 22(e) of the Code is different from the definition of Disability under the Plan). The Company has provided for extended exercisability of your Option under certain circumstances for your benefit but cannot guarantee that your Option will necessarily be treated as an Incentive Stock Option if you continue to provide services to the Company or an Affiliate as a Consultant or Director after your employment terminates or if you otherwise exercise your Option more than three (3) months after the date your employment with the Company or an Affiliate terminates.

8. EXERCISE.

(a) You may exercise the vested portion of your Option during its term by delivering a Notice of Exercise (in a form designated by the Company) together with the exercise price to the Secretary of the Company, or to such other person as the Company may designate, during regular business hours, together with such additional documents as the Company may then require.

(b) If your option is an Incentive Stock Option, by exercising your Option you agree that you will notify the Company in writing within fifteen (15) days after the date of any disposition of any of the shares of the Common Stock issued upon exercise of your Option that occurs within two (2) years after the date of your Option grant or within one (1) year after such shares of Common Stock are transferred upon exercise of your Option.

9. TRANSFERABILITY.

(a) Restrictions on Transfer. Your Option shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during your lifetime only by you; provided, however, that if you reside in the United States, the Board may, in its sole discretion, permit you to transfer your Option in a manner consistent with applicable tax and securities laws upon your request. Additionally, if your option is an Incentive Stock Option, the Board may permit you to transfer your Option only to the extent permitted by Sections 421, 422 and 424 of the Code and the regulations and other guidance thereunder.

(b) Domestic Relations Orders. Notwithstanding the foregoing, your Option may be transferred pursuant to a domestic relations order issued by a court in the United States; provided, however, that if your Option is an Incentive Stock Option, your Option shall be deemed to be a Nonstatutory Stock Option as a result of such transfer.

(c) Beneficiary Designation. Notwithstanding the foregoing, you may, by delivering written notice to the Company, in a form provided by or otherwise satisfactory to the Company, designate a third party who, in the event of your death, shall thereafter be entitled to exercise your Option (to the extent vested) and receive the Common Stock or other consideration resulting from an Option exercise. In the absence of such designation, the executor or administrator of your estate shall be entitled to exercise the Option (to the extent vested) and receive the Common Stock or other consideration resulting from an Option exercise. If you reside outside the United States, the Company will not be required to honor a beneficiary designation unless it is valid under applicable law; if not valid, then your Option may be exercised only by the executor or administrator of your estate.

10. **OPTION NOT A SERVICE CONTRACT.** Your Option is not an employment or service contract, and nothing in your Option shall be deemed to create in any way whatsoever any obligation on your part to continue in the employ of the Company or an Affiliate, or of the Company or an Affiliate to continue your employment. In addition, nothing in your Option shall obligate the Company or an Affiliate, their respective stockholders, Boards of Directors, Officers or Employees to continue any relationship that you might have as a Director or Consultant for the Company or an Affiliate.

11. TAX OBLIGATIONS.

(a) You acknowledge that, regardless of any action taken by the Company, or if different, your employer (the “**Employer**”), the ultimate liability for all income tax, social insurance, payroll tax, fringe benefit tax, payment on account or other tax-related items related to your participation in the Plan and legally applicable to you (“**Tax-Related Items**”) is and remains your responsibility and may exceed the amount (if any) withheld by the Company or the Employer. You further acknowledge that the Company and/or the Employer (a) make no representations or undertakings regarding the treatment of any Tax-Related Items in connection with any aspect of the Option, including, but not limited to, the grant, vesting or exercise of the Option, the subsequent sale of shares of Common Stock acquired pursuant to such exercise and the receipt of any dividends, and (b) do not commit to structure the terms of the grant or any aspect of the Option to reduce or eliminate your liability for Tax-Related Items or achieve any particular tax result. Further, if you are subject to Tax-Related Items in more than one jurisdiction, you acknowledge that the Company and/or the Employer (or former employer, as applicable) may be required to withhold or account for Tax-Related Items in more than one jurisdiction.

(b) Prior to the relevant taxable or tax withholding event, as applicable, you agree to pay or make arrangements satisfactory to the Company and/or the Employer to fulfill all obligations for Tax-Related Items. In this regard, you authorize the Company and/or the Employer, or their respective agents, at their discretion, to satisfy any withholding obligations for Tax-Related Items by any of the following or a combination thereof:

(i) withholding from your wages or other cash compensation paid to you by the Company and/or the Employer;

(ii) requiring you to tender a cash payment to the Company and/or the Employer;

(iii) withholding from proceeds of the sale of shares of Common Stock acquired upon exercise of your Option either through a voluntary sale or through a mandatory sale arranged by the Company (on your behalf pursuant to this authorization without further consent); or

(iv) any other method acceptable to the Company and permitted under the Plan.

(c) The Company may withhold or account for Tax-Related Items by considering statutory withholding rates or other applicable withholding rates, including up to the maximum applicable rate for your jurisdiction(s). If the maximum applicable rate for your jurisdiction(s) is used, you may receive a refund of any over-withheld amount in cash and will have no entitlement to the equivalent amount in shares. The Company may refuse to honor the exercise of the Option or refuse to issue or deliver the shares of Common Stock or the proceeds from the sale of shares of Common Stock if you fail to comply with your obligations in connection with the Tax-Related Items as described in this Section 11.

12. INSIDER TRADING/MARKET ABUSE LAWS. You acknowledge that you may be subject to insider trading restrictions and/or market abuse laws in applicable jurisdictions including, but not limited to, the United States and, if different, your country, which may affect your ability to acquire or sell shares of Common Stock or rights to shares of Common Stock (e.g., the Option) during such times when you are considered to have “inside information” regarding the Company (as defined by the laws in the applicable jurisdictions). Any restrictions under these laws or regulations are separate from and in addition to any restrictions that may be imposed under any applicable insider trading policy of the Company. You acknowledge that you are responsible for ensuring compliance with any applicable restrictions and understand that you should consult your personal legal advisor on these matters.

13. IMPOSITION OF OTHER REQUIREMENTS. The Company reserves the right to impose other requirements on the Option and any shares of Common Stock underlying or acquired upon exercise of the Option, to the extent the Company determines it necessary or advisable for legal or administrative reasons, and to require you to sign additional agreements or undertakings that may be necessary to accomplish the foregoing.

14. NOTICES. Any notices provided for in the Grant Notice, this Agreement or the Plan shall be given in writing and shall be deemed effectively given upon receipt or, in the case of notices delivered by mail by the Company to you, five (5) days after deposit in the United States mail, postage prepaid, addressed to you at the last address you provided to the Company.

15. GOVERNING PLAN DOCUMENT. Your Option is subject to all the provisions of the Plan, the provisions of which are hereby made a part of your Option, and is further subject to all interpretations, amendments, rules and regulations, which may from time to time be promulgated and adopted pursuant to the Plan. In the event of any conflict between the provisions of your Option and those of the Plan, the provisions of the Plan shall control.

16. ENTIRE AGREEMENT. The Plan and the Grant Notice are incorporated herein by reference. This Agreement, the Grant Notice, and the Plan constitute the entire agreement of the parties with respect to the subject matter hereof and supersede all prior undertakings and agreements with respect to such subject matter.

17. GOVERNING LAW/VENUE. This Agreement shall be governed by and interpreted in accordance with the laws of the State of Delaware, disregarding the choice-of-law principles of the State of Delaware and any other state requiring the application of a jurisdiction's laws other than the State of Delaware. For purposes of any action, lawsuit or other proceedings brought to enforce this Agreement, relating to it, or arising from it, the parties hereby submit to and consent to the sole and exclusive jurisdiction of the courts of Suffolk County, Massachusetts, or the federal courts for the United States for the District of Massachusetts, and no other courts, where this grant is made and/or is to be performed.

18. NON-U.S. RESIDENTS. If you reside outside the United States, the Option shall be subject to the additional terms and conditions set forth in Appendix A. Moreover, if you relocate to a country outside the United States or between the countries included in Appendix A, the terms and conditions for such country will apply to you, to the extent the Company determines that the application of such terms and conditions is necessary or advisable for legal or administrative reasons. Appendix A constitutes part of this Agreement.

19. WAIVER. A waiver by the Company of a breach of any provision of this Agreement shall not operate or be construed as a waiver of any other provision of this Agreement, or any subsequent breach by you or any other person.

20. SEVERABILITY. In the event that any provision of this Agreement is held illegal or invalid, the provision will be severable from, and the illegality or invalidity of the provision will not be construed to have any effect on, the remaining provisions of this Agreement.

21. ELECTRONIC DELIVERY AND ACCEPTANCE. The Company may, in its sole discretion, decide to deliver any documents related to current or future participation in the Plan by electronic means. You hereby consent to receive such documents by electronic delivery and agree to participate in the Plan through an online or electronic system established and maintained by the Company or a third party designated by the Company.

22. NO ADVICE REGARDING GRANT. The Company is not providing any tax, legal, or financial advice, nor is the Company making recommendations regarding your participation in the Plan or your acquisition or sale of the underlying shares of Common Stock. You understand and agree that you should consult with your own personal tax, legal, and financial advisors regarding participation in the Plan before taking any action related to the Option.

OPTIONEE

Signature

Print Name

Residence Address

IONIS PHARMACEUTICALS, INC.

By

Print Name

Title

Additional Provisions for Optionees Based Outside the United States

Ionis Pharmaceuticals, Inc.

2020 Equity Incentive Plan

Capitalized terms not defined in this Appendix A shall have the meaning ascribed to them in the Plan, the Global Option Agreement (the “*Agreement*”), or the Grant Notice, as applicable.

Terms and Conditions

This Appendix A to the Agreement includes additional or different terms and conditions that govern the grant of Options to you if you are based outside the U.S. Moreover, if you have received the Agreement with this Appendix A while inside the U.S. and subsequently relocate outside of the U.S., the terms and conditions set forth in this Appendix A will apply, to the extent the Company determines that the application of such terms and conditions is necessary or advisable for legal or administrative reasons.

If you are a citizen or resident of a country other than the one in which you are currently working and/or residing, or if you transfer employment and/or residency to another country after being granted the Option, the country-specific terms and conditions contained herein may not be applicable in the same manner. The Company, in its discretion and in accordance with applicable law, will determine whether and how the country-specific terms and conditions will apply to you in such a case.

Notifications

This Appendix A also includes information regarding certain issues of which you should be aware with respect to your participation in the Plan. Such laws are often complex and change frequently. As a result, you should not rely on the information in this Appendix A as the only source of information relating to the consequences of participation in the Plan because the information may be out of date at the time you exercise the Option or sell shares of Common Stock acquired under the Plan.

In addition, the information contained herein is general in nature and may not apply to your particular situation, and the Company is not in a position to assure you of a particular result. Accordingly, you should seek appropriate professional advice as to how the relevant laws in your country may apply to your individual situation.

If you are a citizen or resident of a country other than the one in which you are currently working and/or residing, or if you transfer employment and/or residency to another country after being granted the Option, the information herein may not be applicable in the same manner.

ALL COUNTRIES OUTSIDE THE UNITED STATES

1. TERMINATION. This provision supplements Sections 1 and 7 of the Agreement:

For purposes of this Option, your Continuous Service will terminate on the date you are no longer actively providing services to the Company or a Subsidiary or Affiliate (regardless of the reason for the termination and whether or not the termination is later found to be invalid or in breach of employment laws in the jurisdiction where you are employed or engaged or the terms of your employment or service agreement, if any) and, unless otherwise determined by the Company, (a) your right to vest in this Option, if any, will terminate as of such date, and (b) your right to exercise this Option after termination, if any, will be measured from such date, and in both cases, will not be extended by any notice period or “garden leave” or similar period established under employment laws or statutes in the jurisdiction where you are employed or engaged or the terms of your employment or service agreement, if any. The Committee will have the sole discretion to determine when your Continuous Services ends for purposes of the Option (including whether you may still be considered to be providing services while on a leave of absence).

2. TRANSFERABILITY. Notwithstanding the terms of Section 9 of the Agreement, your Option is not transferable, except to your personal representative on your death, and is exercisable during your life only by you or by your personal representative after your death.

3. NATURE OF GRANT. In accepting the Option, you acknowledge, understand, and agree that:

(a) the Plan is established voluntarily by the Company, it is discretionary in nature, and may be modified, amended, altered, or discontinued by the Company at any time to the extent permitted by the Plan;

(b) the grant of the Option is exceptional, voluntary and occasional and does not create any contractual or other right to receive future grants of options, or benefits in lieu of options, even if options have been granted in the past;

(c) all decisions with respect to future option or other grants, if any, will be at the sole discretion of the Board;

(d) you are voluntarily participating in the Plan;

(e) the Option and the shares of Common Stock subject to the Option, and the income from and value of same, are not intended to replace any pension rights or compensation;

(f) the Option and the shares of Common Stock subject to the Option, and the income from and value of same, are not part of normal or expected compensation or salary for any purpose, including, but not limited to, calculating any severance, resignation, termination, redundancy, dismissal, end of service payments, holiday pay, bonuses, long-service awards, pension or retirement or welfare benefits or similar payments;

(g) unless otherwise agreed with the Company, the Option and the shares of Common Stock subject to the Option, and the income from and value of same, are not granted as consideration for, or in connection with, services you may provide as a director of a Subsidiary or Affiliate;

(h) no claim or entitlement to compensation or damages shall arise from forfeiture of the Option resulting from your termination of Continuous Service (regardless of the reason for the termination and whether or not the termination is later found to be invalid or in breach of employment laws in the jurisdiction where you are employed or engaged or the terms of your employment or service agreement, if any), and in consideration of the grant of this Option to which you are otherwise not entitled, you irrevocably agree never to institute any claim against the Company or any Affiliate, waive your ability, if any, to bring any such claim, and release the Company and any Affiliate from any such claim; if, notwithstanding the foregoing, any such claim is allowed by a court of competent jurisdiction, then, by participating in the Plan, you shall be deemed irrevocably to have agreed not to pursue such claim and agree to execute any and all documents necessary to request dismissal or withdrawal of such claim;

(i) the future value of the shares of Common Stock underlying the Option is unknown, indeterminable, and cannot be predicted with certainty;

(j) if the shares of Common Stock underlying the Option do not increase in value, the Option will have no value;

(k) if you exercise the Option and acquire shares of Common Stock, the value of the shares may increase or decrease, even below the exercise price; and

(l) neither the Company nor any Subsidiary or Affiliate shall be liable for any foreign exchange rate fluctuation between your local currency and the U.S. dollar that may affect the value of the Option or the value of any amount due to you pursuant to the exercise of the Option or the subsequent sale of any shares of Common Stock acquired upon exercise.

4. DATA PRIVACY.

(a) You explicitly and unambiguously acknowledge and consent to the collection, use and transfer, in electronic or other form, of your personal data as described in this document by and among, as applicable, your employer, the Company and its Affiliates for the exclusive purpose of implementing, administering and managing your participation in the Plan. You understand that the Company, its Affiliates and your employer hold certain personal information about you, including, but not limited to, name, home address and telephone number, date of birth, social security number (or other identification number), salary, nationality, job title, any shares of stock or directorships held in the Company, details of all options or any other entitlement to shares of Common Stock awarded, canceled, purchased, exercised, vested, unvested or outstanding in your favor for the purpose of implementing, managing and administering the Plan (“*Data*”). You understand that the Data may be transferred to any third parties assisting in the implementation, administration and management of the Plan, that these recipients may be located in your country or elsewhere, in particular in the US, and that the recipient country may have different data privacy laws providing less protections of your personal data than your country. You may request a list with the names and addresses of any potential recipients of the Data by contacting as the stock plan administrator at the Company (the “*Stock Plan Administrator*”). You acknowledge that the recipients may receive, possess, process, use, retain and transfer the Data, in electronic or other form, for the purposes of implementing, administering and managing your participation in the Plan, including any requisite transfer of such Data, as may be required to a broker or other third party with whom you may elect to deposit any shares of Common Stock acquired upon the exercise of your Option. You understand that Data will be held only as long as is necessary to implement, administer and manage your participation in the Plan. You may, at any time, view the Data, request additional information about the storage and processing of the Data, require any necessary amendments to the Data or refuse or withdraw the consents herein, in any case without cost, by contacting the Stock Plan Administrator in writing.

(b) For the purposes of operating the Plan in the European Union, Switzerland and the United Kingdom, the Company will collect and process information relating to you in accordance with the privacy notice from time to time in force.

5. **LANGUAGE.** You acknowledge that you are sufficiently proficient in English to understand the terms and conditions of this Agreement, or have consulted with an advisor who is sufficiently proficient in English, so as to allow you to understand the terms and conditions of this Agreement. Furthermore, if you have received this Agreement or any other document related to the Option or the Plan translated into a language other than English and if the meaning of the translated version is different from the English version, the English version will control.

6. **FOREIGN ASSET/ACCOUNT, EXCHANGE CONTROL AND TAX REPORTING.** Depending on your country, you may be subject to foreign asset/account, exchange control and/or tax reporting and payment requirements in connection with the Option, the acquisition, holding and/or transfer of shares of Common Stock or cash resulting from participation in the Plan and/or the opening and maintaining of a brokerage or bank account in connection with the Plan. You may be required to report such assets, accounts, account balances and values, and/or related transactions to the applicable authorities in his or her country. You may also be required to repatriate any funds received in connection with the Option to your country and you may be required to use a specific account for doing so and/or to convert the funds to local currency. You acknowledge that you are responsible for ensuring compliance with any applicable foreign asset/account, exchange control and tax requirements. You further understand that you should consult your personal legal advisor on these matters.

CANADA

Data Privacy. The following provision supplements Section 4 of this Appendix A:

You hereby authorize the Company and its representatives to discuss with and obtain all relevant information from all personnel, professional or not, involved in the administration and operation of the Plan. You further authorize the Company, any Affiliates and any stock plan service provider that may be selected by the Company to assist with the Plan to disclose and discuss the Plan with their respective advisors. You further authorize the Company and any Affiliates to record such information and to keep such information in your employee file.

Language Consent. The parties to the Agreement acknowledge that it is their express wish that the Agreement, as well as all documents, notices, and legal proceedings entered into, given or instituted pursuant hereto or relating directly or indirectly hereto, be drawn up in English.

Consentement relatif à la langue utilisée

Les parties reconnaissent avoir exigé que cette convention («Agreement») soit rédigée en anglais, ainsi que tous les documents, avis et procédures judiciaires, exécutés, donnés ou intentés en vertu de, ou liés directement ou indirectement à la présente.

Continuous Service. Notwithstanding anything else in the Plan or the Agreement, your Continuous Service will be deemed to end on the date when you cease to be actively providing services to the Company or an Affiliate, regardless of whether the cessation of your employment was lawful, and shall not include any period of statutory, contractual, common law, civil law or other reasonable notice of termination of employment or any period of salary continuance or deemed employment. As a result, if you receive notice of termination for a reason other than cause, and the Company or its Affiliate does not require you to continue to attend at work and elects to provide you with a payment in lieu of notice, your Continuous Service will end on the date you receive such notice, as opposed any later date when severance payments to you cease.

Employment Matters.

No Fractions. No fractional shares of Common Stock shall be issued under the Agreement and no cash amount shall be payable in respect thereof.

Voluntary Participation. Your participation in the Plan is voluntary, and you acknowledge and agree that you have not been induced to enter into the Agreement or acquire any Option or shares of Common Stock by expectation of employment, engagement or appointment or continued employment, engagement or appointment.

Securities Law Information.

The definition of “Affiliate” is modified such that the following supplements the existing definition in the Plan:

“For purposes of issuances of securities under the Plan to Directors, Employees and Consultants in Canada, an Affiliate means a person (which includes a corporation) that controls the Company or is controlled by the Company or is controlled by the same person that controls the Company. For this purpose, a person (first person) is considered to control a person (second person) if the first person, directly or indirectly, has the power to direct the management and policies of the second person by virtue of ownership of or direction over voting securities in the second person (over 50%); or a written agreement or indenture.”

The definition of “Consultant” is modified such that the following supplements the existing definition in the Plan:

“For purposes of issuances of securities under the Plan to Consultants in Canada, a Consultant means a person, any person, including an advisor, who (a) is (i) engaged by the Company or an Affiliate to render consulting or advisory services and is compensated for such services, or (ii) serving as a member of the board of directors of an Affiliate and is compensated for such services; (b) provides the services under a written contract with the Company or an Affiliate; and (c) spends or will spend a significant amount of time and attention on the affairs and business of the Company or an Affiliate and includes (d) for an individual consultant, a corporation of which the individual consultant is an employee or shareholder, and a partnership of which the individual consultant is an employee or partner, and (e) for a consultant that is not an individual, an employee, executive officer, or director of the consultant, provided that the individual employee, executive officer, or director spends or will spend a significant amount of time and attention on the affairs and business of the Company or an Affiliate. However, service solely as a Director, or payment of a fee for such service, shall not cause a Director to be considered a “*Consultant*” for purposes of the Plan.”

You understand that you are permitted to sell the shares of Common Stock acquired pursuant to any Awards, provided that the Company is a “foreign issuer” that is not a public company in any jurisdiction of Canada and the sale of the shares of Common Stock acquired pursuant to the Plan takes place: (i) through an exchange, or a market, outside of Canada on the distribution date; or (ii) to a person or company outside of Canada. For purposes hereof, in addition to not being a reporting issuer in any jurisdiction of Canada, a “foreign issuer” is an issuer that: (i) is not incorporated or existing pursuant to the laws of Canada or any jurisdiction of Canada; (ii) does not have its head office in Canada; and (iii) does not have a majority of its executive officers or directors ordinarily resident in Canada. If any designated broker is appointed under the Plan, you shall sell such securities through the designated broker.

Foreign Asset/Account Reporting Information. Canadian residents are required to report any foreign property on form T1135 (Foreign Income Verification Statement) if the total cost of their foreign property exceeds C\$100,000 at any time in the year. It is your responsibility to comply with these reporting obligations, and you should consult with your own personal tax advisor in this regard.

IRELAND

Director Notification Requirement. If you are a director, shadow director, or secretary of an Irish Affiliate of the Company, pursuant to Part 5, Chapter 5 of the Companies Act 2014, you must notify that Affiliate in writing when receiving or disposing of an interest in the Company (e.g., the Option, shares of Common Stock), or when becoming aware of the event giving rise to the notification requirement, or when becoming a director or secretary if such an interest exists at the time. This notification requirement also applies with respect to the interests of a spouse or minor children (whose interests will be attributed to the director, shadow director, or secretary). The foregoing requirements apply only if your securities represent one percent (1%) or more of the Company.

Data Privacy. Section 4 (Data Privacy) of this Appendix A is deleted and replaced with the following:

This section is intended to provide information about the collection and processing of your personal data by the Company.

- (a) **Data Collection and Usage.** The Company collect, process and use certain personal information about you, including, but not limited to, your name, home address, telephone number, email address, date of birth, social insurance number or other identification number, salary, nationality, job title, any shares or directorships held in the Company and details of all options or any other entitlement to shares of Common Stock awarded, cancelled, purchased, exercised, vested, unvested or outstanding in your favor for the purpose of implementing, managing and administering the Plan (“**Data**”), for purposes of implementing, administering and managing the Plan and for compliance with the Company’s legal obligations. The Company is the controller of such Data. The legal basis, where required, for the processing of Data is that the processing is contractually necessary for the performance of the Plan. The Company will share Data with third parties, including brokers or any other third party with whom you elect to deposit any shares of Common Stock acquired upon the exercise of your choice under the Plan, law firms, accountants and information technology service providers, for purposes of implementing, administering and managing the Plan. You may request a list with the names and addresses of any potential recipients of the Data by contacting the stock plan administrator at the Company (the “**Stock Plan Administrator**”). The Company is based in the United States, which means the recipients of Data may be located in the United States or elsewhere. You acknowledge and understand that Data will be transferred, processed and stored in the United States, as it is necessary for the performance of the Plan. Where required for purposes of implementing, administering and managing the Plan, the Company may transfer data elsewhere and on the basis of standard contractual clauses. For more information or to obtain a copy of the standard contractual clauses, you can contact the Stock Plan Administrator. The Company will hold and use Data for as long as is necessary to implement, administer and manage your participation in the Plan; as required to comply with legal or regulatory obligations, including under tax, exchange control, labour and securities laws; and as otherwise necessary in connection with legal rights, claims or proceedings. This period may extend beyond the period of your employment with the Company. When the Company no longer needs Data for any of the above purposes, it will cease processing it in this context and remove it from all of its systems used for such purposes to the fullest extent practicable. You may have a number of rights under *Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (“GDPR”)* and applicable Irish data protection legislation. Such rights include the right to (i) request access to Data the Company processes, (ii) request rectification of inaccurate Data, (iii) request the deletion of Data, (iv) request the restriction of processing of Data, (v) request the portability of Data, and (vi) lodge a complaint with the Irish Data Protection Commission or any competent supervisory authority. To receive clarification regarding these rights or to exercise these rights, you can contact the Stock Plan Administrator.
- (b) For the purposes of operating the Plan in Ireland, the Company will collect and process information relating to you in accordance with the privacy notice from time to time in force.

Optionholder Self-Assessment. The following section supplements Section 11 of the Agreement (Tax Obligations):

Under current Irish law, the Company is not under any obligation to operate withholding tax on the grant or exercise of your Options and is not required to account to the Irish Revenue Commissioners (“**Revenue**”) for any tax in connection with the grant or exercise of the Options. You are responsible for accounting for the tax to Revenue. If you are within the charge to Irish tax, you must account for income tax, universal social charge (“**USC**”) and employee pay related social insurance (“**PRSI**”) under the self-assessment system. You are required to file a Form RTSO1 with the Revenue and pay the associated tax on any gain realised in connection with the exercise (or in certain cases, in connection with the grant) of the Option within 30 days of exercise (or grant).

SWITZERLAND

Securities Law Information. The Option grant is not intended to be publicly offered in or from Switzerland. Because it is considered a private offering, it is not subject to securities registration in Switzerland. Neither this document nor any other materials relating to the Option (i) constitutes a prospectus as such term is understood pursuant to article 652a of the Swiss Code of Obligations, (ii) may be publicly distributed nor otherwise made publicly available in Switzerland or (iii) has been or will be filed with, approved or supervised by any Swiss regulatory authority, including the Swiss Financial Market Supervisory Authority (FINMA).

UNITED KINGDOM

Nature of Grant. The following supplements Section 3 of this Appendix A (Nature of Grant):

You waive all rights to compensation or damages in consequence of the termination of your office or employment with the Company or any Affiliate for any reason whatsoever (whether lawful or unlawful and including, without prejudice to the foregoing, in circumstances giving rise to a claim for wrongful dismissal) in so far as those rights arise or may arise from you ceasing to hold or being able to vest your Option, or from the loss or diminution in value of any rights or entitlements in connection with the Plan.

Withholding Obligations. The following supplements Section 11 of the Agreement (Tax Obligations):

As a condition of the vesting of your Option, you unconditionally and irrevocably agree:

(i) to place the Company in funds and indemnify the Company in respect of (1) all liability to UK income tax which the Company is liable to account for on your behalf directly to HM Revenue & Customs; and (2) all liability to employee’s national insurance contributions which the Company is liable to account for on your behalf to HM Revenue & Customs, which arises as a consequence of or in connection with the exercise of your Option (the “**UK Tax Liability**”); or

(ii) to permit the Company to sell at the best price which it can reasonably obtain such number of shares of Common Stock allocated or allotted to you following exercise as will provide the Company with an amount equal to the UK Tax Liability; and to permit the Company to withhold an amount not exceeding the UK Tax Liability from any payment made to you (including, but not limited to salary); and

(iii) if so required by the Company, and, to the extent permitted by law, to enter into a joint election or other arrangements under which the liability for all or part of such employer's national insurance contributions liability is transferred to you; and

(iv) if so required by the Company, to enter into a joint election within Section 431 of (UK) Income Tax (Earnings and Pensions) Act 2003 ("*ITEPA*") in respect of computing any tax charge on the acquisition of "restricted securities" (as defined in Section 423 and 424 of *ITEPA*); and

(v) to sign, promptly, all documents required by the Company to effect the terms of this provision, and references in this provision to "the Company" shall, if applicable, be construed as also referring to any Affiliate.

IONIS PHARMACEUTICALS, INC.

2020 EQUITY INCENTIVE PLAN

GLOBAL RESTRICTED STOCK UNIT AGREEMENT

Pursuant to the Restricted Stock Unit Grant Notice (“**Grant Notice**”) and this Global Restricted Stock Unit Agreement, including any appendices thereto (the “**Agreement**”), Ionis Pharmaceuticals, Inc. (the “**Company**”) has awarded you a Restricted Stock Unit Award (the “**Award**”) under its 2020 Equity Incentive Plan (the “**Plan**”). Your Award is granted to you effective as of the Date of Grant set forth in the Grant Notice for this Award. If not otherwise accepted by you, this Agreement shall be deemed to be agreed to by the Company and you upon the earlier of (i) signing (or electronic acceptance) by you of the Restricted Stock Unit Grant Notice to which it is attached, and (ii) your receipt of shares of Common Stock under this Agreement. Capitalized terms not explicitly defined in this Agreement shall have the same meanings given to them in the Plan or the Grant Notice, as applicable. In the event of any conflict between the terms in this Agreement and the Plan, the terms of the Plan shall control. The details of your Award, in addition to those set forth in the Grant Notice and the Plan, are as follows.

1. GRANT OF THE AWARD. This Award represents the right to be issued on a future date the number of shares of the Company’s Common Stock that is equal to the number of stock units indicated in the Grant Notice (the “**Stock Units**”). As of the Date of Grant, the Company will credit to a bookkeeping account maintained by the Company for your benefit (the “**Account**”) the number of Stock Units subject to the Award. Except as otherwise provided herein, you will not be required to make any payment to the Company with respect to your receipt of the Award, the vesting of the Stock Units or the delivery of the Common Stock which may be issued in respect of the Award.

2. VESTING.

(a) In General. Subject to the limitations contained herein, your Award will vest, if at all, in accordance with the vesting schedule provided in the Grant Notice, provided that vesting will cease upon the termination of your Continuous Service. Upon such termination of your Continuous Service, the Stock Units credited to the Account that were not vested on the date of such termination will be forfeited at no cost to the Company and you will have no further right, title or interest in the Stock Units or the shares of Common Stock to be issued in respect of the Award.

3. NUMBER OF SHARES.

(a) The number of Stock Units subject to your Award may be adjusted from time to time for Capitalization Adjustments, as provided in the Plan.

(b) Any additional Stock Units that become subject to the Award pursuant to this Section [3](#) and Section [7](#), if any, shall be subject, in a manner determined by the Board, to the same forfeiture restrictions, restrictions on transferability, and time and manner of delivery as applicable to the other Stock Units covered by your Award.

(c) Notwithstanding the provisions of this Section 3, no fractional shares or rights to fractional shares of Common Stock shall be created pursuant to this Section 3. The Board shall, in its discretion, determine an equivalent benefit for any fractional shares that might be created by the adjustments referred to in this Section 3.

4. **SECURITIES LAW COMPLIANCE.** You may not be issued any shares in respect of your Award unless either (i) the shares are registered under the U.S. Securities Act; or (ii) the Company has determined that such issuance would be exempt from the registration requirements of the U.S. Securities Act. Your Award also must comply with other applicable laws and regulations governing the Award, and you will not receive such shares if the Company determines that such receipt would not be in material compliance with such laws and regulations.

5. **TRANSFER RESTRICTIONS.** Prior to the time that shares of Common Stock have been delivered to you, you may not transfer, pledge, sell or otherwise dispose of this Award or the shares issuable in respect of your Award, except that your Award may be transferred to your personal representative on your death, as expressly provided in this Section 5. For example, you may not use shares that may be issued in respect of your Award as security for a loan. The restrictions on transfer set forth herein will lapse upon delivery to you of shares in respect of your vested Award.

6. **DATE OF ISSUANCE.**

(a) If the Award is exempt from application of Section 409A of the Code and the regulations and other guidance thereunder and any state law of similar effect (collectively "**Section 409A**"), the Company will deliver to you a number of shares of the Common Stock equal to the number of vested Stock Units subject to your Award, including any additional Stock Units received pursuant to Section 3 above that relate to those vested Stock Units on the applicable vesting date(s). However, if a scheduled delivery date falls on a date that is not a business day, such delivery date shall instead fall on the next following business day. Notwithstanding the foregoing, in the event that (i) you are subject to the Company's policy permitting officers and directors to sell shares only during certain "window" periods, in effect from time to time (the "**Policy**") or you are otherwise prohibited from selling shares of the Common Stock in the public market and any shares covered by your Award are scheduled to be delivered on a day (the "**Original Distribution Date**") that does not occur during an open "window period" applicable to you or a day on which you are permitted to sell shares of the Common Stock pursuant to a written plan that meets the requirements of Rule 10b5-1 under the Exchange Act (a "**Rule 10b5-1 Plan**"), in each case as determined by the Company in accordance with the Policy, or does not occur on a date when you are otherwise permitted to sell shares of the Common Stock on the open market, and (ii) the Company is unable under applicable tax or securities laws to satisfy its tax Withholding Taxes obligations by withholding shares from your distribution, then such shares shall not be delivered on such Original Distribution Date and shall instead be delivered on the first business day of the next occurring open "window period" applicable to you pursuant to such policy (regardless of whether you are still providing continuous services at such time) or the next business day when you are not prohibited from selling shares of the Common Stock in the open market, but (if you are subject to taxation in the U.S.) in no event later than the fifteenth day of the third calendar month of the calendar year following the calendar year in which the shares covered by the Award vest. If you are subject to taxation in the U.S., delivery of the shares pursuant to the provisions of this Section 6(a) is intended to comply with the requirements for the short-term deferral exemption available under Treasury Regulation 1.409A-1(b)(4) and shall be construed and administered in such manner. The form of such delivery of the shares (e.g., a stock certificate or electronic entry evidencing such shares) shall be determined by the Company.

(b) If you are subject to taxation in the U.S., the provisions of this Section **6(b)** are intended to apply if the Award is subject to Section 409A because of the terms of a severance arrangement or other agreement between you and the Company, if any, that provides for acceleration of vesting of the Award upon your separation from service (as such term is defined in section 409A(a)(2)(A)(i) of the Code and applicable guidance thereunder (“**Separation From Service**”) and such severance benefit does not satisfy the requirements for an exemption from application of Section 409A provided under Treasury Regulations Sections 1.409A-1(b)(4) or 1.409A-1(b)(9) (“**Non-Exempt Severance Arrangement**”). If the Award is subject to and not exempt from application of Section 409A due to application of a Non-Exempt Severance Arrangement, the following provisions in this Section **6(b)** shall supersede anything to the contrary in Section **6(a)**.

(i) If the Award vests in ordinary course during your Continuous Service in accordance with the vesting schedule set forth in the Grant Notice, in no event will the shares to be issued in respect of your Award be issued any later than the later of: (i) December 31st of the calendar year that includes the applicable vesting date, or (ii) the 60th day that follows the applicable vesting date.

(ii) If the Award accelerates vesting under the terms of your Non-Exempt Severance Arrangement in connection with your Separation From Service, and such vesting acceleration provisions of your Non-Exempt Severance Arrangement were in effect as of the Date of Grant of the Award and therefore part of the terms of the Award as of the Date of Grant, then the shares will be earlier issued in respect of your Award upon your Separation From Service in accordance with the terms of the Non-Exempt Severance Arrangement, but in no event later than the 60th day that follows the date of your Separation From Service. However, if at the time the shares would otherwise be issued you are subject to the distribution limitations contained in section 409A of the Code applicable to “specified employees” as defined in section 409A(a)(2)(B)(i) of the Code and applicable guidance thereunder, such share issuances shall not be made before the date which is six months following the date of your Separation From Service, or, if earlier, the date of your death that occurs within such six month period.

(iii) If the Award accelerates vesting under the terms of your Non-Exempt Severance Arrangement in connection with your Separation From Service, and such vesting acceleration provisions of your Non-Exempt Severance Arrangement were not in effect as of the Date of Grant of the Award and therefore not a part of the terms of the Award on the Date of Grant, then such acceleration of vesting of the Award shall not accelerate the issuance date of the shares, but the shares shall instead be issued on the same schedule as set forth on the Grant Notice as if they had vested in ordinary course during your Continuous Service, notwithstanding the vesting acceleration of the Award; provided, however, that in no event will the shares be issued any later than the later of: (i) December 31st of the calendar year that includes the applicable vesting date, or (ii) the 60th day that follows the applicable vesting date. Such issuance schedule is intended to satisfy the requirements of payment on a specified date or pursuant to a fixed schedule, as provided under Treas. Reg. 1.409A-3(a)(4).

(iv) In the event that vesting of the Award upon your Separation From Service pursuant to Section 6(b)(ii) or Section 6(b)(iii) is contingent on your execution of a release of claims or other agreement (together, a “**Release**”) and the period in which to provide such Release spans two calendar years, issuance of the shares will occur in the second such year (subject to your execution of the required Release) or on such later scheduled date specified in Section 6(b)(iii), regardless of when you execute the Release.

(c) If you are subject to taxation in the U.S., the provisions in this Agreement for delivery of the shares in respect of the Award are intended either to comply with the requirements of Section 409A or to provide a basis for exemption from such requirements so that the delivery of the shares will not trigger the additional tax imposed under Section 409A, and any ambiguities herein will be so interpreted. Notwithstanding any other provision of this Agreement, the Company reserves the right, to the extent the Company deems necessary or advisable, in its sole discretion, to unilaterally amend the Plan and/or this Agreement to ensure that all Stock Units qualify for exemption from or comply with Section 409A. However, the Company has no obligation to modify the terms of this Agreement or the Plan and does not guarantee that the Stock Units or the delivery of shares in respect of the Award will not be subject to taxes, interest and penalties or any other adverse tax consequences under Section 409A. The Company will have no liability to you or any other party if the Award that is intended to be exempt from, or compliant with, Section 409A, is not so exempt or compliant or for any action taken by the Board with respect thereto.

7. **DIVIDEND EQUIVALENTS.** You shall be entitled to receive payments equal to any cash dividends and other distributions paid with respect to a corresponding number of shares to be issued in respect of the Stock Units covered by your Award, provided that if any such dividends or distributions are paid in shares, the Fair Market Value of such shares shall be converted into additional Stock Units covered by the Award, and further provided that such additional Stock Units shall be subject to the same forfeiture restrictions and restrictions on transferability and time and manner of delivery as apply to the Stock Units subject to the Award with respect to which they relate.

8. **RESTRICTIVE LEGENDS.** The shares issued in respect of your Award shall be endorsed with appropriate legends determined by the Company.

9. **AWARD NOT A SERVICE CONTRACT.**

(a) Your Continuous Service with the Company or an Affiliate may be terminated by you or by the Company or an Affiliate in accordance with applicable law and the terms of your employment agreement, if any. Nothing in this Agreement (including, but not limited to, the vesting of your Award pursuant to the schedule set forth in Section 2 herein or the issuance of the shares in respect of your Award), the Plan or any covenant of good faith and fair dealing that may be found implicit in this Agreement or the Plan shall: (i) confer upon you any right to continue in the employ of, or affiliation with, the Company or an Affiliate; (ii) constitute any promise or commitment by the Company or an Affiliate regarding the fact or nature of future positions, future work assignments, future compensation or any other term or condition of employment or affiliation; (iii) confer any right or benefit under this Agreement or the Plan unless such right or benefit has specifically accrued under the terms of this Agreement or Plan; or (iv) deprive the Company or your Employer of any right it may have to terminate your employment and without regard to any future vesting opportunity that you may have.

(b) By accepting this Award, you acknowledge and agree that the right to continue vesting in the Award pursuant to the schedule set forth in Section 2 is earned only by continuing as an Employee, Director or Consultant (not through the act of being hired, being granted this Award or any other award or benefit) and that the Company has the right to reorganize, sell, spin-out or otherwise restructure one or more of its businesses or Affiliates at any time or from time to time, as it deems appropriate (a “**reorganization**”). You further acknowledge and agree that such a reorganization could result in the termination of your Continuous Service, or the termination of Affiliate status of the Employer and the loss of benefits available to you under this Agreement, including but not limited to, the termination of the right to continue vesting in the Award. You further acknowledge and agree that this Agreement, the Plan, the transactions contemplated hereunder and the vesting schedule set forth herein or any covenant of good faith and fair dealing that may be found implicit in any of them do not constitute an express or implied promise of continued engagement as an Employee or Consultant for the term of this Agreement, for any period, or at all, and shall not interfere in any way with your right or the Company’s right to terminate your Continuous Service in accordance with applicable law and the terms of your employment agreement, if any.

10. WITHHOLDING OBLIGATIONS.

(a) You acknowledge that, regardless of any action taken by the Company or, if different, your employer (the “**Employer**”), the ultimate liability for all federal, state, local and foreign tax income tax, social insurance, payroll tax, fringe benefits tax, payment on account or other tax-related items related to your participation in the Plan and legally applicable to you (“**Tax-Related Items**”) is and remains your responsibility and may exceed the amount, if any, actually withheld by the Company or the Employer. You further acknowledge that the Company and/or the Employer (i) make no representations or undertakings regarding the treatment of any Tax-Related Items in connection with any aspect of the Stock Units, including, but not limited to, the grant, vesting or settlement of the Stock Units, the subsequent sale of shares of Common Stock acquired pursuant to such settlement and the receipt of any dividends and/or any dividend equivalents; and (ii) do not commit to and are under no obligation to structure the terms of the grant or any aspect of the Stock Units to reduce or eliminate your liability for Tax-Related Items or achieve any particular tax result. Further, if you are subject to Tax-Related Items in more than one jurisdiction, you acknowledge that the Company and/or the Employer (or former employer, as applicable) may be required to withhold or account for Tax-Related Items in more than one jurisdiction.

(b) On or before the time you receive a distribution of the shares subject to your Award, or at any time thereafter as requested by the Company, you hereby agree to make adequate arrangements satisfactory to the Company and/or the Employer to satisfy all withholding obligations for Tax-Related Items (the “**Withholding Taxes**”). In this regard, the Company or, as applicable, the Employer, may, in its sole discretion, satisfy all or any portion of the Withholding Taxes relating to your Award by any of the following means or by a combination of such means: (i) withholding from any compensation otherwise payable to you by the Company or the Employer; (ii) causing you to tender a cash payment; (iii) withholding shares of Common Stock from the shares of Common Stock issued or otherwise issuable to you in connection with the Award with a Fair Market Value (measured as of the date that the liability for Withholding Taxes is determined) equal to the amount of such Withholding Taxes; provided, however, that the number of such shares of Common Stock so withheld shall not exceed the amount necessary to satisfy the required Withholding Taxes calculated using the minimum amount of Tax-Related Items that are required to be withheld under applicable law (or such higher amount as may be permitted by the Plan); or (iv) withholding from proceeds of the sale of shares of Common Stock acquired upon settlement of the Stock Units either through a voluntary sale or through a mandatory sale arranged by the Company (on your behalf pursuant to this authorization without further consent), provided that either (1) you are not subject to the Policy or (2) the date of the applicable tax withholding event occurs during an open “window period” under the Policy or on a date on which you are otherwise permitted to sell shares of the Common Stock on the open market, whether pursuant to a Rule 10b5-1 Plan or otherwise, as determined by the Company in accordance with the Policy.

(c) Unless the Withholding Taxes of the Company and/or the Employer are satisfied, the Company shall have no obligation to deliver to you any Common Stock.

(d) In the event the Company’s or the Employer’s obligation to withhold Tax-Related Items arises prior to the delivery to you of Common Stock or it is determined after the delivery of Common Stock to you that the amount of the Company’s or the Employer’s withholding obligation was greater than the amount withheld by the Company or the Employer, you agree to indemnify and hold the Company and the Employer harmless from any failure by the Company or the Employer to withhold the proper amount. Further (if you are subject to taxation in the U.S.), notwithstanding anything in this Section 10 to the contrary, to avoid a prohibited acceleration under Section 409A, if shares of Common Stock underlying the Stock Units will be withheld to satisfy any Withholding Taxes arising prior to the date of settlement of the Stock Units for any portion of the Award that is considered an item of “nonqualified deferred compensation” subject to Section 409A, then the number of shares of Common Stock withheld shall not exceed the number of shares that equals the liability for the Tax-Related Items.

(e) If specified in your Grant Notice and permitted by the Company, you may direct the Company to withhold shares of Common Stock with a Fair Market Value (measured as of the date that the liability for Withholding Taxes is determined) equal to the amount of such Withholding Taxes; provided, however, that the number of such shares of Common Stock so withheld shall not exceed the amount necessary to satisfy the required Withholding Taxes calculated using the minimum amount of Tax-Related Items that are required to be withheld under applicable law (or such higher amount as may be permitted by the Plan).

(f) Notwithstanding anything to the contrary in this Section [10](#), if you are a Section 16 officer or director of the Company under the Exchange Act, then the Company will satisfy any applicable Withholding Taxes by withholding in shares of Common Stock upon the relevant taxable event, unless the use of such withholding method is not feasible under applicable tax or securities law, in which case the Withholding Taxes may be satisfied by one or a combination of the other methods set forth in Section [10\(b\)](#) above.

(g) No fractional shares of Common Stock will be sold or withheld to cover Tax-Related Items. If the obligation for Withholding Taxes is satisfied by withholding a number of shares of Common Stock as described in subsection (b) (iii) or (e) above, for tax purposes you will be deemed to have been issued the full number of shares subject to the vested Stock Units, notwithstanding that a number of shares are held back solely for the purpose of satisfying the Withholding Taxes.

11. NATURE OF GRANT. In accepting the Award, you acknowledge, understand, and agree that:

(a) the Plan is established voluntarily by the Company, it is discretionary in nature, and it may be modified, amended, suspended or terminated by the Company at any time, to the extent permitted by the Plan;

(b) the grant of the Award is voluntary and occasional and does not create any contractual or other right to receive future grants of Awards, or benefits in lieu of Awards, even if Awards have been granted in the past;

(c) all decisions with respect to future grants of Awards, if any, will be at the sole discretion of the Company;

(d) you are voluntarily participating in the Plan;

(e) unless otherwise agreed with the Company, the Award and any shares subject to the Award, and the income and value of the same, are not granted as consideration for, or in connection with, any service you may provide as a director of an Affiliate;

(f) the Award and any shares subject to the Award, and the income and value of same, are not intended to replace any pension rights or compensation;

(g) the Award and any shares subject to the Award, and the income and value of same, are not part of normal or expected compensation or salary for purposes of (including but not limited to) calculating any severance, resignation, termination, redundancy, dismissal, end of service payments, bonuses, long-service awards, leave-related payments, holiday pay, pension or retirement or welfare benefits or similar payments or for purposes of calculating your benefits under any employee benefit plan sponsored by the Company or any Affiliate, except as such plan otherwise expressly provides. The Company expressly reserves its rights to amend, modify, or terminate any of the Company's employee benefit plans;

(h) the future value of the shares subject to the Award is unknown, indeterminable, and cannot be predicted with certainty;

(i) no claim or entitlement to compensation or damages shall arise from forfeiture of the Award resulting from you ceasing to provide Continuous Service to the Company, the Employer or any Affiliate (for any reason whatsoever and whether or not later found to be invalid or in breach of employment laws in the jurisdiction where you are employed or providing services or the terms of your employment agreement or service contract, if any) and in consideration of the grant of this Award to which you are otherwise not entitled, you irrevocably agree never to institute any claim against the Company, your Employer or any Affiliate, waive your ability, if any, to bring any such claim, and release the Company, your Employer and any Affiliate from any such claim; if, notwithstanding the foregoing, any such claim is allowed by a court of competent jurisdiction, then, by participating in the Plan, you shall be deemed irrevocably to have agreed not to pursue such claim and agree to execute any and all documents necessary to request dismissal or withdrawal of such claim;

(j) except as otherwise provided in the Agreement, the date your Continuous Service terminates is the date that you are no longer providing active service and will not be extended by any notice period (e.g., Continuous Service would not include any contractual notice period or any period of “garden leave” or similar period under employment laws in the jurisdiction where you are employed or providing Continuous Service or the terms of your employment agreement or service contract, if any), regardless of the reason for your termination and whether or not later found to be invalid or in breach of employment laws in the jurisdiction where you are employed or providing services or the terms of your employment agreement or service contract, if any. The Board or the chief executive officer of the Company, in that party’s sole discretion, may determine when you are no longer providing Continuous Service for purposes of the Award; and

(k) neither the Company, the Employer nor any Affiliate will be liable for any foreign exchange rate fluctuation between your local currency and the United States dollar that may affect the value of the Stock Units or any amounts due to you pursuant to the vesting of the Stock Units or the subsequent sale of any shares of Common Stock acquired under the Plan.

12. NO ADVICE REGARDING GRANT. The Company is not providing any tax, legal or financial advice, nor is the Company making any recommendations regarding participation in the Plan, or your acquisition or sale of shares of Common Stock. You understand and agree that you should consult with your own personal tax, legal and financial advisors regarding your participation in the Plan before taking any action related to the Plan.

13. DATA PRIVACY.

(a) You explicitly and unambiguously acknowledge and consent to the collection, use and transfer, in electronic or other form, of your personal data as described in this document by and among, as applicable, your Employer, the Company and its Affiliates for the exclusive purpose of implementing, administering and managing your participation in the Plan. You understand that the Company, its Affiliates and your Employer hold certain personal information about you, including, but not limited to, name, home address and telephone number, date of birth, social security number (or other identification number), salary, nationality, job title, any shares of stock or directorships held in the Company, details of all options or any other entitlement to shares of stock awarded, canceled, purchased, exercised, vested, unvested or outstanding in your favor for the purpose of implementing, managing and administering the Plan (“**Data**”). You understand that the Data may be transferred to any third parties assisting in the implementation, administration and management of the Plan, that these recipients may be located in your country or elsewhere, in particular in the US, and that the recipient country may have different data privacy laws providing less protections of your personal data than your country. You may request a list with the names and addresses of any potential recipients of the Data by contacting the stock plan administrator at the Company (the “**Stock Plan Administrator**”). You acknowledge that the recipients may receive, possess, process, use, retain and transfer the Data, in electronic or other form, for the purposes of implementing, administering and managing your participation in the Plan, including any requisite transfer of such Data, as may be required to a broker or other third party with whom you may elect to deposit any shares of Common Stock acquired upon the vesting of your Award. You understand that Data will be held only as long as is necessary to implement, administer and manage your participation in the Plan. You may, at any time, view the Data, request additional information about the storage and processing of the Data, require any necessary amendments to the Data or refuse or withdraw the consents herein, in any case without cost, by contacting the Stock Plan Administrator in writing.

(b) For the purposes of operating the Plan in the European Union, Switzerland and the United Kingdom, the Company will collect and process information relating to you in accordance with the privacy notice from time to time in force.

14. UNSECURED OBLIGATION. Your Award is unfunded, and as a holder of a vested Award, you shall be considered an unsecured creditor of the Company with respect to the Company's obligation, if any, to issue shares pursuant to this Agreement. You shall not have voting or any other rights as a stockholder of the Company with respect to the shares to be issued pursuant to this Agreement until such shares are issued to you pursuant to Section 6 of this Agreement. Upon such issuance, you will obtain full voting and other rights as a stockholder of the Company. Nothing contained in this Agreement, and no action taken pursuant to its provisions, shall create or be construed to create a trust of any kind or a fiduciary relationship between you and the Company or any other person.

15. OTHER DOCUMENTS. You hereby acknowledge receipt or the right to receive a document providing the information required by Rule 428(b)(1) promulgated under the Securities Act, which includes the Plan prospectus. In addition, you acknowledge receipt of the Policy and agree that you may sell shares only in compliance with such policy, in effect from time to time.

16. NOTICES. Any notices provided for in your Award or the Plan shall be given in writing and shall be deemed effectively given upon receipt or, in the case of notices delivered by the Company to you, five days after deposit in the United States mail, postage prepaid, addressed to you at the last address you provided to the Company. Notwithstanding the foregoing, the Company may, in its sole discretion, decide to deliver any documents related to participation in the Plan and this Award by electronic means or to request your consent to participate in the Plan by electronic means. You hereby consent to receive such documents by electronic delivery and, if requested, to agree to participate in the Plan through an on-line or electronic system established and maintained by the Company or another third party designated by the Company.

17. MISCELLANEOUS.

(a) The rights and obligations of the Company under your Award shall be transferable to any one or more persons or entities, and all covenants and agreements hereunder shall inure to the benefit of, and be enforceable by the Company's successors and assigns. Your rights and obligations under your Award may only be assigned with the prior written consent of the Company.

(b) You agree upon request to execute any further documents or instruments necessary or desirable in the sole determination of the Company to carry out the purposes or intent of your Award.

(c) You acknowledge and agree that you have reviewed your Award in its entirety, have had an opportunity to obtain the advice of counsel prior to executing and accepting your Award, and fully understand all provisions of your Award.

(d) This Agreement and the Award shall be subject to all applicable laws, rules, and regulations, and to such approvals by any governmental agencies or national securities exchanges as may be required.

(e) All obligations of the Company under the Plan and this Agreement shall be binding on any successor to the Company, whether the existence of such successor is the result of a direct or indirect purchase, merger, consolidation, or otherwise, of all or substantially all of the business and/or assets of the Company.

18. GOVERNING PLAN DOCUMENT. Your Award is subject to all the provisions of the Plan, the provisions of which are hereby made a part of your Award, and is further subject to all interpretations, amendments, rules and regulations which may from time to time be promulgated and adopted pursuant to the Plan. Except as expressly provided herein, in the event of any conflict between the provisions of your Award and those of the Plan, the provisions of the Plan shall control.

19. SEVERABILITY. If all or any part of this Agreement or the Plan is declared by any court or governmental authority to be unlawful or invalid, such unlawfulness or invalidity shall not invalidate any portion of this Agreement or the Plan not declared to be unlawful or invalid. Any Section of this Agreement (or part of such a Section) so declared to be unlawful or invalid shall, if possible, be construed in a manner which will give effect to the terms of such Section or part of a Section to the fullest extent possible while remaining lawful and valid.

20. CHOICE OF LAW AND VENUE. The interpretation, performance and enforcement of this Agreement will be governed by the law of the state of California without regard to such state's conflicts of laws rules. For purposes of litigating any dispute that arises directly or indirectly in respect of this Award, the parties hereby submit to and consent to the jurisdiction of the State of Massachusetts and agree that such litigation shall be conducted in the courts of Middlesex County, Massachusetts, or the federal courts for the United States for the District of Massachusetts, and no other courts, where this grant is made and/or to be performed.

21. AMENDMENT. This Agreement may not be modified, amended or terminated except by an instrument in writing, signed by you and by a duly authorized representative of the Company. Notwithstanding the foregoing, this Agreement may be amended solely by the Board by a writing which specifically states that it is amending this Agreement, so long as a copy of such amendment is delivered to you, and provided that no such amendment adversely affecting your rights hereunder may be made without your written consent, except as set forth in Section 6(c) of this Agreement. Without limiting the foregoing, the Board reserves the right to change, by written notice to you, the provisions of this Agreement in any way it may deem necessary or advisable to carry out the purpose of the grant as a result of any change in applicable laws or regulations or any future law, regulation, ruling, or judicial decision, provided that any such change shall be applicable only to rights relating to that portion of the Award which is then subject to restrictions as provided herein.

22. LANGUAGE. You acknowledge that you are sufficiently proficient in English to understand the terms and conditions of this Agreement, or have consulted with an advisor who is sufficiently proficient in English, so as to allow you to understand the terms and conditions of this Agreement. Furthermore, if you have received this Agreement or any other document related to the Plan translated into a language other than English and if the meaning of the translated version is different than the English version, the English version will control.

23. APPENDIX. The Award shall be subject to any special terms and conditions set forth in the Appendix for your country, if any. If you relocate to one of the countries included in the Appendix during the vesting period or while holding shares of Common Stock issued upon vesting of the Stock Units, the special terms and conditions for such country shall apply to you, to the extent the Company determines that the application of such provisions is advisable or necessary for legal or administrative reasons. The Appendix constitutes part of this Agreement.

24. INSIDER TRADING RESTRICTIONS/MARKET ABUSE LAWS. You acknowledge that, depending on your or your broker's country of residence or where the shares of Common Stock are listed, you may be subject to insider trading restrictions and/or market abuse laws, which may affect your ability to accept, acquire, sell, or otherwise dispose of shares of Common Stock, rights to Common Stock (*e.g.*, Stock Units) or rights linked to the value of Common Stock (*e.g.*, phantom awards, futures) during such times as you are considered to have "inside information" regarding the Company (as defined by the laws or regulations in your country). Local insider trading laws and regulations may prohibit the cancellation or amendment of orders you placed before possessing inside information. Furthermore, you could be prohibited from (i) disclosing the inside information to any third party (other than on a "need to know" basis) and (ii) "tipping" third parties or otherwise causing them to buy or sell securities. Keep in mind third parties includes fellow employees. Any restrictions under these laws or regulations are separate from and in addition to any restrictions that may be imposed under the Policy or any other applicable Company insider trading policy. You acknowledge that it is your responsibility to comply with any applicable restrictions, and you should speak to your personal advisor on this matter.

25. FOREIGN ASSET/ACCOUNT REPORTING; EXCHANGE CONTROLS AND TAX REQUIREMENTS. Your country may have certain foreign asset and/or account reporting requirements and/or exchange controls that may affect your ability to acquire or hold shares of Common Stock under the Plan or cash received from participating in the Plan (including from any dividends received or sale proceeds arising from the sale of shares of Common Stock) in a brokerage or bank account outside your country. You may be required to report such accounts, assets, or transactions to the tax or other authorities in your country. You may also be required to repatriate sale proceeds or other funds received as a result of your participation in the Plan to your country through a designated broker or bank and/or within a certain time after receipt. In addition, you may be subject to tax payment and/or reporting obligations in connection with any income realized under the Plan and/or from the sale of shares of Common Stock. You acknowledge that it is your responsibility to be compliant with such regulations and you understand and agree that you should consult your personal legal advisor for any details.

26. WAIVER. You acknowledge that a waiver by the Company of breach of any provision of this Agreement shall not operate or be construed as a waiver of any other provision of this Agreement, or of any subsequent breach by you or any other Participant.

APPENDIX

GLOBAL RESTRICTED STOCK UNIT AGREEMENT IONIS PHARMACEUTICALS, INC. 2020 EQUITY INCENTIVE PLAN

COUNTRY-SPECIFIC PROVISIONS

This Appendix includes special terms and conditions applicable to you if you reside and/or work in the countries below. These terms and conditions are in addition to those set forth in the Agreement. Any capitalized term used in this Appendix without definition shall have the meaning ascribed to such term in the Plan, the Grant Notice, or the Agreement, as applicable.

This Appendix also includes information relating to exchange control, foreign asset and/or account reporting, and other issues of which you should be aware with respect to your participation in the Plan. Such laws are often complex and change frequently. As a result, the Company strongly recommends that you not rely on the information herein as the only source of information relating to the consequences of participation in the Plan because the information may be out of date at the time the Stock Units vest or shares of Common Stock acquired under the Plan are sold.

In addition, the information is general in nature and may not apply to your particular situation, and the Company is not in a position to assure you of any particular result. Accordingly, you should seek appropriate professional advice as to how the relevant laws in your country may apply to your situation. If you are a citizen or resident of a country other than the one in which you are currently working and/or residing, are considered a resident of another country or transfer employment and/or change residency to another country after the Award has been granted, the terms and conditions and the information contained herein may not be applicable to you. The Company shall, in its sole discretion, determine to what extent the terms and conditions included herein will apply to you in such circumstances. Any references to the "Employer" in this Agreement shall include any entity engaging your services.

CANADA

Grant of the RSU Award. Notwithstanding any other provision governing your Award, except as set forth below under "Withholding Obligations", the Company may not issue you the cash equivalent of Common Stock, in part or in full satisfaction of the delivery of shares of Common Stock upon vesting of your Award.

Data Privacy. The following provision supplements Section 13 (Data Privacy) of the Agreement:

You hereby authorize the Company and its representatives to discuss with and obtain all relevant information from all personnel, professional or not, involved in the administration and operation of the Plan. You further authorize the Company, any Affiliates, your Employer and any stock plan service provider that may be selected by the Company to assist with the Plan to disclose and discuss the Plan with their respective advisors. You further authorize the Company, your Employer and any Affiliates to record such information and to keep such information in your employee file.

Language Consent. The parties acknowledge that it is their express wish that the Agreement, as well as all documents, notices and legal proceedings entered into, given or instituted pursuant hereto or relating directly or indirectly hereto, be drawn up in English.

Les parties reconnaissent avoir exigé la rédaction en anglais de cette convention («Agreement»), ainsi que cette Annexe, ainsi que de tous documents, avis et procédures judiciaires, exécutés, donnés ou intentés en vertu de, ou liés directement ou indirectement à, la présente convention.

Continuous Service. Notwithstanding anything else in the Plan or the Agreement, your Continuous Service will be deemed to end on the date when you cease to be actively providing services to the Company, your Employer or an Affiliate, regardless of whether the cessation of your employment was lawful, and shall not include any period of statutory, contractual, common law, civil law or other reasonable notice of termination of employment or any period of salary continuance or deemed employment. As a result, if you receive notice of termination for a reason other than cause, and the Company, your Employer or any Affiliate does not require you to continue to attend at work and elects to provide you with a payment in lieu of notice, your Continuous Service will end on the date you receive such notice, as opposed any later date when severance payments to you cease.

No Fractions. No fractional shares of Common Stock shall be issued under the Agreement and no cash amount shall be payable in respect thereof.

Voluntary Participation. Your participation in the Plan is voluntary, and you acknowledge and agree that you have not been induced to enter into the Agreement or acquire any Award or shares of Common Stock by expectation of employment, engagement or appointment or continued employment, engagement or appointment.

Securities Law Information.

The definition of “Affiliate” is modified such that the following supplements the existing definition in the Plan:

“For purposes of issuances of securities under the Plan to Directors, Employees and Consultants in Canada, an Affiliate means a person (which includes a corporation) that controls the Company or is controlled by the Company or is controlled by the same person that controls the Company. For this purpose, a person (first person) is considered to control a person (second person) if the first person, directly or indirectly, has the power to direct the management and policies of the second person by virtue of ownership of or direction over voting securities in the second person (over 50%); or a written agreement or indenture.”

The definition of “Consultant” is modified such that the following supplements the existing definition in the Plan:

“For purposes of issuances of securities under the Plan to Consultants in Canada, a Consultant means a person, any person, including an advisor, who (a) is (i) engaged by the Company or an Affiliate to render consulting or advisory services and is compensated for such services, or (ii) serving as a member of the board of directors of an Affiliate and is compensated for such services; (b) provides the services under a written contract with the Company or an Affiliate; and (c) spends or will spend a significant amount of time and attention on the affairs and business of the Company or an Affiliate and includes (d) for an individual consultant, a corporation of which the individual consultant is an employee or shareholder, and a partnership of which the individual consultant is an employee or partner, and (e) for a consultant that is not an individual, an employee, executive officer, or director of the consultant, provided that the individual employee, executive officer, or director spends or will spend a significant amount of time and attention on the affairs and business of the Company or an Affiliate. However, service solely as a Director, or payment of a fee for such service, shall not cause a Director to be considered a “Consultant” for purposes of the Plan.”

You understand that you are permitted to sell the shares of Common Stock acquired pursuant to any Awards, provided that the Company is a “foreign issuer” that is not a public company in any jurisdiction of Canada and the sale of the shares of Common Stock acquired pursuant to the Plan takes place: (i) through an exchange, or a market, outside of Canada on the distribution date; or (ii) to a person or company outside of Canada. For purposes hereof, in addition to not being a reporting issuer in any jurisdiction of Canada, a “foreign issuer” is an issuer that: (i) is not incorporated or existing pursuant to the laws of Canada or any jurisdiction of Canada; (ii) does not have its head office in Canada; and (iii) does not have a majority of its executive officers or directors ordinarily resident in Canada. If any designated broker is appointed under the Plan, you shall sell such securities through the designated broker.

Foreign Asset/Account Reporting Information. Canadian residents are required to report any foreign property on form T1135 (Foreign Income Verification Statement) if the total cost of their foreign property exceeds C\$100,000 at any time in the year. It is your responsibility to comply with these reporting obligations, and you should consult with your own personal tax advisor in this regard.

Withholding Obligations. Section 10(b) of the Agreement is deleted and replaced with the following:

On or before the time you receive a distribution of the shares of Common Stock underlying your Award, and at any other time as reasonably requested by the Company in accordance with applicable tax laws, you agree to make adequate arrangements satisfactory to the Company or adequate provision in cash for any sums required to satisfy the federal, state, local and foreign tax withholding and source deduction obligations of the Company or any Affiliate that arise in connection with your RSU Award (the “**Withholding Taxes**”). Additionally, the Company or any Affiliate may satisfy all or any portion of the Withholding Taxes obligation relating to your RSU Award by any of the following means or by a combination of such means: (i) withholding from any compensation otherwise payable to you by the Company or an Affiliate; (ii) causing you to tender a cash payment; (iii) permitting you to enter into a “same day sale” commitment, if applicable, with a broker-dealer (subject to your written consent) whereby you irrevocably elect to sell a portion of the shares of Common Stock to be delivered in connection with your Stock Units to satisfy the Withholding Taxes and whereby the broker-dealer irrevocably commits to forward the proceeds necessary to satisfy the Withholding Taxes directly to the Company or its Affiliates; or (iv) permitting you (subject to your written consent) to surrender Stock Units to the Company for a cash payment which shall be used to satisfy the Withholding Taxes, whereby the number of Stock Units that may be surrendered for a cash payment shall be equal to the Withholding Taxes divided by a Fair Market Value (measured as of the date shares of Common Stock are otherwise issuable to you pursuant to Section 6). However, the Company does not guarantee that you will be able to satisfy the Withholding Taxes through any of the methods described in the preceding provisions and in all circumstances you remain responsible for timely and fully satisfying the Withholding Taxes.

Dividends. Section 7 of the Agreement is deleted and replaced with the following:

You may become entitled to be granted additional Stock Units equal to any cash dividends and other distributions paid with respect to a corresponding number of shares of Common Stock in respect of the Stock Units covered by your Award. In such event, you will automatically be granted additional Stock Units subject to the Award (the “**Dividend Units**”), and such Dividend Units shall be subject to the same forfeiture restrictions and restrictions on transferability, and same timing requirements for issuance of shares, as apply to the Stock Units subject to the Award with respect to which the Dividend Units relate.

IRELAND

Director Notification Obligation. Directors, shadow directors and secretaries of the Company’s Irish Affiliates whose interest in the Company represents more than 1% of the Company’s voting share capital are subject to certain notification requirements under Part 5, Chapter 5 of the Companies Act 2014. Directors, shadow directors and secretaries must notify the Irish Affiliates in writing of their interest in the Company (e.g., RSUs, shares of Common Stock, etc.) and the number and class of shares or rights to which the interest relates within five days of the acquisition or disposal of shares or within five days of becoming aware of the event giving rise to the notification. This notification requirement also applies with respect to the interests of a spouse or children under the age of 18 (whose interests will be attributed to the director, shadow director or secretary).

This section is intended to provide information about the collection and processing of your personal data by the Company.

(a) Data Collection and Usage. The Company collect, process and use certain personal information about you, including, but not limited to, your name, home address, telephone number, email address, date of birth, social insurance number or other identification number, salary, nationality, job title, any shares or directorships held in the Company and details of all options or any other entitlement to shares of Common Stock awarded, cancelled, purchased, exercised, vested, unvested or outstanding in your favor for the purpose of implementing, managing and administering the Plan (“**Data**”), for purposes of implementing, administering and managing the Plan and for compliance with the Company’s legal obligations. The Company is the controller of such Data. The legal basis, where required, for the processing of Data is that the processing is contractually necessary for the performance of the Plan. The Company will share Data with third parties, including brokers or any other third party with whom you elect to deposit any shares of Common Stock acquired upon the exercise of your choice under the Plan, law firms, accountants and information technology service providers, for purposes of implementing, administering and managing the Plan. You may request a list with the names and addresses of any potential recipients of the Data by contacting the stock plan administrator at the Company (the “**Stock Plan Administrator**”). The Company is based in the United States, which means the recipients of Data may be located in the United States or elsewhere. Participants acknowledge and understand that Data will be transferred, processed and stored in the United States, as it is necessary for the performance of the Plan. Where required for purposes of implementing, administering and managing the Plan, the Company may transfer data elsewhere and on the basis of standard contractual clauses. For more information or to obtain a copy of the standard contractual clauses, you can contact the Stock Plan Administrator. The Company will hold and use Data for as long as is necessary to implement, administer and manage your participation in the Plan; as required to comply with legal or regulatory obligations, including under tax, exchange control, labour and securities laws; and as otherwise necessary in connection with legal rights, claims or proceedings. This period may extend beyond the period of your employment with the Company. When the Company no longer needs Data for any of the above purposes, it will cease processing it in this context and remove it from all of its systems used for such purposes to the fullest extent practicable. The Participants may have a number of rights under *Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (“GDPR”)* and applicable Irish data protection legislation. Such rights include the right to (i) request access to Data the Company processes, (ii) request rectification of inaccurate Data, (iii) request the deletion of Data, (iv) request the restriction of processing of Data, (v) request the portability of Data, and (vi) lodge a complaint with the Irish Data Protection Commission or any competent supervisory authority. To receive clarification regarding these rights or to exercise these rights, you can contact the Stock Plan Administrator.

(b) For the purposes of operating the Plan in Ireland, the Company will collect and process information relating to you in accordance with the privacy notice from time to time in force.

SWITZERLAND

Securities Law Notification. The grant of the Award and the issuance of any shares of Common Stock is not intended to be a public offering in Switzerland. Neither this document nor any other materials relating to the Award constitute a prospectus as such term is understood pursuant to article 652a of the Swiss Code of Obligations, and neither this document nor any other materials relating to the Award may be publicly distributed nor otherwise made publicly available in Switzerland. Neither this document nor any other offering or marketing material relating to the Award have been or will be filed with, or approved or supervised by, any Swiss regulatory authority (in particular, the Swiss Financial Market Supervisory Authority (FINMA)).

UNITED KINGDOM

Nature of Grant. The following supplements Section 11 of the Agreement. You waive all rights to compensation or damages in consequence of the termination of your office or employment with the Company or any Affiliate for any reason whatsoever (whether lawful or unlawful and including, without prejudice to the foregoing, in circumstances giving rise to a claim for wrongful dismissal) in so far as those rights arise or may arise from you ceasing to hold or being able to vest your Award, or from the loss or diminution in value of any rights or entitlements in connection with the Plan.

Withholding Obligations. The following supplements Section 4 of the Agreement:

As a condition of the vesting of your Award, you unconditionally and irrevocably agree:

(i) to place the Company in funds and indemnify the Company in respect of (1) all liability to UK income tax which the Company is liable to account for on your behalf directly to HM Revenue & Customs; and (2) all liability to employee's national insurance contributions which the Company is liable to account for on your behalf to HM Revenue & Customs, which arises as a consequence of or in connection with your participation in the Plan (the "**UK Tax Liability**"); or

(ii) to permit the Company to sell at the best price which it can reasonably obtain such number of shares of Common Stock allocated or allotted to you following vesting as will provide the Company with an amount equal to the UK Tax Liability; and to permit the Company to withhold an amount not exceeding the UK Tax Liability from any payment made to you (including, but not limited to salary); and

(iii) if so required by the Company, to enter into a joint election within Section 431 of (UK) Income Tax (Earnings and Pensions) Act 2003 ("**ITEPA**") in respect of computing any tax charge on the acquisition of "restricted securities" (as defined in Section 423 and 424 of ITEPA); and

(iv) to sign, promptly, all documents required by the Company to effect the terms of this provision, and references in this provision to "the Company" shall, if applicable, be construed as also referring to any Affiliate.

IONIS PHARMACEUTICALS, INC.
RESTRICTED STOCK UNIT GRANT NOTICE
(2020 EQUITY INCENTIVE PLAN)

Ionis Pharmaceuticals, Inc. (the “Company”), pursuant to its 2020 Equity Incentive Plan (the “Plan”), hereby awards to Participant a Restricted Stock Unit Award for the number of stock units set forth below (the “Award”). The Award is subject to all of the terms and conditions as set forth herein; and in the Plan and the Restricted Stock Unit Agreement, both of which are attached hereto and incorporated herein in their entirety. Capitalized terms not otherwise defined herein shall have the meanings set forth in the Plan or the Restricted Stock Unit Agreement. In the event of any conflict between the terms in the Award and the Plan, the terms of the Plan shall control.

Participant: _____
Date of Grant: _____
Vesting Commencement Date: _____
Number of Stock Units Subject to Award: _____
Consideration: Participant’s Services

Vesting Schedule: _____

You must accept this Award prior to the first vesting date. If you do not accept this Award by the first vest date, this Award will automatically expire.

Issuance Schedule: The shares of Common Stock to be issued in respect of the Award will be issued in accordance with the issuance schedule set forth in Section 6 of the Restricted Stock Unit Agreement.

Special Tax

Withholding Right: If permitted by the Company, you may direct the Company (i) to withhold, from shares otherwise issuable in respect of the Award, a portion of those shares with an aggregate fair market value (measured as of the delivery date) equal to the amount of the applicable withholding taxes, and (ii) to make a cash payment equal to such fair market value directly to the appropriate taxing authorities, as provided in Section 10 of the Restricted Stock Unit Agreement. The default mechanism for satisfying tax withholding is Sell-to-Cover where E*Trade automatically sells an amount of shares to cover the taxes.

Additional Terms/Acknowledgements: The undersigned Participant acknowledges receipt of, and understands and agrees to, this Restricted Stock Unit Grant Notice, the Restricted Stock Unit Agreement and the Plan. Participant further acknowledges that as of the Date of Grant, this Restricted Stock Unit Grant Notice, the Restricted Stock Unit Agreement and the Plan set forth the entire understanding between Participant and the Company regarding the Award and supersedes all prior oral and written agreements on that subject, with the exception of any employment or severance arrangement that would provide for vesting acceleration of the Award upon the terms and conditions set forth therein. If you are an Executive Officer of the Company, the shares issued under that Award may be subject to additional holding requirements pursuant to Company Policy

IONIS PHARMACEUTICALS, INC.
By: _____
Signature

PARTICIPANT:

Signature

Title: Duly authorized on behalf of the Board of Directors

Date: _____

Date: _____

ATTACHMENTS: Restricted Stock Unit Agreement, 2020 Equity Incentive Plan



IONIS PHARMACEUTICALS, INC.
OPTION GRANT NOTICE
(2020 EQUITY INCENTIVE PLAN)

Ionis Pharmaceuticals, Inc. (the “*Company*”), pursuant to its **2020 Equity Incentive Plan** (the “*Plan*”), hereby grants to Optionholder an option to purchase the number of shares of the Company’s Common Stock set forth below. This option is subject to all of the terms and conditions as set forth herein and in the Global Option Agreement (including the appendix thereto, if applicable (the “*Appendix*”)), as applicable (the “*Agreement*”), the Plan and the Notice of Exercise, all of which are attached hereto and incorporated herein in their entirety.

Optionholder: _____
Date of Grant: _____
Vesting Commencement Date: _____
Number of Shares Subject to Option: _____
Exercise Price (Per Share) (US\$): _____
Expiration Date: _____

Type of Option: _____

Exercise Schedule: Same as Vesting Schedule Early Exercise Permitted

Vesting Schedule: _____

Payment: By one or a combination of the following items (described in the Agreement):

- By cash or check
- By bank draft or money order payable to the Company
- Pursuant to a Regulation T program if the Shares are publicly traded
- By net exercise if the Company has established a procedure for net exercise at the time of such exercise

Additional Terms/Acknowledgements: The undersigned Optionholder acknowledges receipt of, and understands and agrees to, this Stock Option Grant Notice, the Agreement and the Plan. Optionholder further acknowledges that as of the Date of Grant, this Stock Option Grant Notice, the Agreement and the Plan set forth the entire understanding between Optionholder and the Company regarding the acquisition of stock in the Company and supersede all prior oral and written agreements on that subject with the exception of (i) options previously granted and delivered to Optionholder under the Plan, and (ii) the following agreements only:

OTHER AGREEMENTS: _____

* * *

IONIS PHARMACEUTICALS, INC.

By: _____
Signature

OPTIONHOLDER:

Signature

Title: Duly authorized on behalf of the Board of Directors

ATTACHMENTS: Global Option Agreement (including the Appendix), as applicable, 2020 Equity Incentive Plan and Notice of Exercise

NOTICE OF EXERCISE

IONIS PHARMACEUTICALS
2855 Gazelle Court
Carlsbad, CA 92010

Date of Exercise: _____

Ladies and Gentlemen:

This constitutes notice under my stock option that I elect to purchase the number of shares for the price set forth below.

Number of shares as
to which option is
exercised:

Certificates to be
issued in name of:

Employee ID:

Total Exercise Price (US\$):

Cash payment delivered
herewith:

US\$ _____ US\$ _____

By this exercise, I agree (i) to provide such additional documents as you may require pursuant to the terms of the Ionis Pharmaceuticals, Inc. 2020 Equity Incentive Plan, Option Grant Notice and Global Option Agreement (including the appendix thereto), as applicable, and (ii) to provide for the payment by me (in the manner designated by you) of the withholding obligation, if any, relating to the exercise of this option.

Very truly yours,
