

SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

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

Date of report (Date of earliest event reported): October 18, 2018

IONIS PHARMACEUTICALS, INC.

(Exact Name of Registrant as Specified in Charter)

Delaware

(State or Other Jurisdiction of Incorporation)

000-19125

(Commission File No.)

33-0336973

(IRS Employer Identification No.)

2855 Gazelle Court
Carlsbad, CA 92010

(Address of Principal Executive Offices and Zip Code)

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

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

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

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

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 5.02 Compensatory Arrangements of Certain Officers.

(e)

On October 18, 2018, Ionis Pharmaceuticals, Inc. (the “**Company**”) implemented a Change of Control and Severance Benefit Plan (the “**Plan**”) that provides for change of control and severance benefits to the Company’s executive officers, including the Company’s Chief Executive Officer and Chief Financial Officer. The Plan is designed to provide certain economic benefits to the executive officers if their employment is terminated in the circumstances described below.

A copy of the Plan is attached hereto and incorporated herein as Exhibit 10.1. The below description is qualified in its entirety by reference to the Plan. Capitalized terms not otherwise defined herein have the meaning given to them in the Plan.

The Plan provides that if a Participant is terminated without Cause or resigns for Good Reason, except in connection with a Change in Control of the Company, the Participant will generally be entitled to receive the following severance benefits upon termination:

- (1) A lump sum payment of the Participant’s then-current annual base salary.
- (2) Accelerated vesting of stock options and restricted stock units previously granted by the Company and outstanding as of the termination date that otherwise would have vested over the applicable Severance Period.
- (3) Continued medical group health and dental plan coverage.

The benefits above will be calculated using an 18-month period for the Chief Executive Officer, and a 12-month period for the other executive officers.

If the Participant’s termination or resignation occurs during the period that begins three months before and ends twelve months following a Change in Control of the Company, the Participant will generally be entitled to receive the following severance benefits upon termination:

- (1) A lump sum payment of the Participant’s then-current annual base salary.
- (2) Payment of the Participant’s then-current target bonus (multiplied by 1.5 for the Chief Executive Officer).
- (3) Accelerated vesting of all stock options and restricted stock units previously granted by the Company and outstanding as of the termination date.
- (4) Continued medical group health and dental plan coverage.

Payments of salary and continued medical and dental group coverage will be calculated using an 18-month period for the Chief Executive Officer and a 12-month period for the other executive officers.

Payments under the Plan will be subject to all required taxes. The Plan includes provisions for adjustment to the timing of payments to minimize accelerated or additional tax pursuant to Section 409A of the Internal Revenue Code. The Plan does not include any tax gross-up or other tax indemnity related to payments made to Participants under the Plan; however, payments, benefits or distributions to or for the benefit of the Participant under the Plan may be reduced if doing so would result in a more favorable after-tax position for the Participant.

Payment of the foregoing benefits under the Plan is conditioned upon the Participant executing (and not revoking) a release in favor of the Company, which release will contain standard release from liability, non-solicitation and non-disparagement provisions, and a reaffirmation of the Participant's confidentiality obligations to the Company.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

[10.1](#) Ionis Severance Benefit Plan and Summary Plan Description dated October 18, 2018.

SIGNATURE

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

IONIS PHARMACEUTICALS, INC.

Dated: October 19, 2018

By: /s/ Patrick R. O'Neil

PATRICK R. O'NEIL

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

IONIS PHARMACEUTICALS, INC.

SEVERANCE BENEFIT PLAN

1. **Introduction.** This Ionis Pharmaceuticals, Inc. Severance Benefit Plan (the “**Plan**”) is established by Ionis Pharmaceuticals, Inc. (the “**Company**”) on October 18, 2018 (the “**Effective Date**”). The Plan provides for severance benefits to selected employees of the Company. This document constitutes the Summary Plan Description for the Plan.
2. **Definitions.** For purposes of the Plan, the following terms are defined as follows:
- (a) “**Affiliate**” shall have the meaning given to such term in the Equity Plan.
 - (b) “**Board**” means the Board of Directors of the Company.
 - (c) “**Cause**” means the occurrence of any one or more of the following: (i) any material breach of any written agreement between the Participant and the Company, if such breach causes material harm to the Company or reasonably threatens to cause such harm; (ii) any material failure to comply with the Company’s written policies or rules, as they may be in effect from time to time during the Participant’s employment or any statutory duty to the Company, if such failure causes material harm to the Company or reasonably threatens to cause such harm, and to the extent it is curable by the Participant, is not cured within 30 days after written notice thereof is given to the Participant by the Company; (iii) commission, conviction of, or a plea of “guilty” or “no contest” to, a felony under the laws of the United States or any State; or (iv) any willful, intentional or grossly negligent act having the effect of materially injuring (whether financially or otherwise) the business or reputation of the Company, which to the extent it is curable by the Participant, is not cured within 30 days after written notice thereof is given to the Participant by the Company.
 - (d) “**Change in Control**” for purposes of this Plan shall mean the sale of all or substantially all the assets of the Company; any merger, consolidation or acquisition of the Company with, by or into another corporation, entity or person; or any change in the ownership of more than 50% of the voting capital stock of the Company in one or more related transactions, provided, none of the following events will be a Change in Control: (1) acquisitions of capital stock directly from the Company for cash, whether in a public or private offering, (2) distributions of capital stock by the Company’s stockholders, (3) acquisitions of capital stock by or from any employee benefit plan or related trust, or (4) a merger the sole purpose of which is to change the Company’s name and/or state of incorporation.
 - (e) “**Change in Control Protection Period**” means the period commencing three months prior to, and ending 12 months following, the effective date of a Change of Control.
 - (f) “**Change in Control Termination**” means a Participant’s Qualifying Termination that occurs during the Change in Control Protection Period.
 - (g) “**Code**” means the Internal Revenue Code of 1986, as amended.
 - (h) “**Common Stock**” means the common stock of the Company.

- (i) **“Continuous Service”** shall have the meaning given to such term in the Equity Plan.
- (j) **“Disability”** shall have the meaning given to such term in the Equity Plan.
- (k) **“Employment Agreement”** means any individual employment offer letter, contract or agreement that a Participant has with the Company.
- (l) **“Equity Award”** means each compensatory equity award granted to a Participant, whether under the Equity Plan, or otherwise.
- (m) **“Equity Plan”** means the Company’s 2011 Equity Incentive Plan, as amended from time to time.
- (n) **“ERISA”** means the Employee Retirement Income Security Act of 1974, as amended.
- (o) **“Good Reason”** means the occurrence of any of the following events without the Participant’s consent: (a) a material reduction by the Company of the Participant’s base salary as in effect immediately prior to the reduction; (b) a material reduction by the Company of the Participant’s annual bonus target as in effect immediately prior to the reduction, provided a compensation plan change that affects similarly all employees at similar levels will not constitute Good Reason; (c) a material reduction in the Participant’s authority, duties or responsibilities, provided a change in job title or reporting relationship without a reduction in the Participant’s base salary or annual bonus target will not constitute Good Reason; or (d) relocation of the offices at which the Participant is required to work to a location that is outside San Diego county or would increase the Participant’s one-way commute by more than 40 miles; *provided*, that any resignation by the Participant due to any of the above conditions will only be deemed for Good Reason if: (i) the Participant gives the Company written notice of the intent to terminate for Good Reason within 90 days following the first occurrence of the condition(s) that the Participant believes constitutes Good Reason, which notice will describe such condition(s); (ii) the Company fails to remedy, if remediable, such condition(s) within 30 days following receipt of the Participant’s written notice (the “Cure Period”) of such condition(s) from the Participant; and (iii) the Participant actually resigns his or her employment within the first 15 days after expiration of the Cure Period.
- (p) **“Individual Severance Arrangement”** means any Employment Agreement providing for severance or change in control benefits to a Participant or any other severance arrangement between the Participant and the Company other than the Plan, in each case that remains in effect through the date of a Qualifying Termination.
- (q) **“Non-CiC Termination”** means a Participant’s Qualifying Termination that does not occur during the Change in Control Protection Period.
- (r) **“Participant”** means each individual who is employed by the Company, has been designated as a Participant by the Plan Administrator, and has received and returned a signed Participation Notice.

(s) **“Participation Notice”** means the latest notice delivered by the Company to a Participant informing the Participant that he or she is eligible to participate in the Plan, substantially in the form attached hereto as **EXHIBIT A**.

(t) **“Plan Administrator”** means the Board or any committee of the Board duly authorized to administer the Plan, including the Compensation Committee of the Board, or any member of senior management of the Company designated by the Board (including, for example, the head of Human Resources). The Board may at any time administer the Plan, in whole or in part, notwithstanding that the Board has previously appointed a committee or other person to act as the Plan Administrator. Notwithstanding the foregoing, upon and after the consummation of a Change in Control, the Plan Administrator shall mean the Representative.

(u) **“Person”** means a “person” as such term is used in Sections 13(d) and 14(d) of the United States Securities Exchange Act of 1934, as amended

(v) **“Qualifying Termination”** means a termination of the Participant’s Continuous Service either (x) by the Company without Cause or (y) by the Participant with Good Reason. Termination of Continuous Service due to the Participant’s death or Disability will not constitute a Qualifying Termination. Transferring from the Company to an Affiliate where such transfer does not constitute Good Reason will not constitute a Qualifying Termination. For clarity, if the Participant terminates his or her employment without Good Reason, and the Company unilaterally accelerates the Participant’s date of termination in connection therewith, such acceleration will not result in a termination by the Company without Cause or a Qualifying Termination hereunder. Further, if the Participant is offered an identical or substantially equivalent or comparable position with the Company or an Affiliate, such Participant will not be deemed to have been terminated without Cause. For purposes of the foregoing, a “substantially equivalent or comparable position” is one that provides the Participant substantially the same level of responsibility and compensation. The Participant’s death or disability will not constitute a without Cause termination, Good Reason resignation or a Qualifying Termination under this Agreement.

(w) **“Release Effective Date”** means the date, which must occur during the Release Period, on which the Release becomes effective and is no longer revocable by the Participant.

(x) **“Release”** has the meaning set forth in Section 5.

(y) **“Release Period”** means the sixty-day period following a Participant’s Qualifying Termination during which the Release must be executed (and not revoked) by the Participant.

(z) **“Representative”** means one or more members of the Board or other persons designated by the Board (including a member of senior management such as the head of Human Resources) prior to or in connection with a Change in Control to administer the Plan.

(aa) **“Separation from Service”** means a “separation from service” within the meaning of Treasury Regulations Section 1.409A-1(h), without regard to any alternative definition thereunder.

(bb) **“Severance Period”** means the number of months of severance payable under this Plan to the Participant with respect to the applicable Qualifying Termination, as indicated in the Participant’s Participation Notice, which will be 18 months for the Chief Executive Officer and 12 months for the other Executive Officers.

(cc) “**Target Bonus**” means with respect to a Participant, 100% of the Participant’s target annual bonus under the Company’s annual cash bonus plan or policy then in effect (and without giving effect to any reduction in target bonus that would give rise to the Participant’s right to resign for Good Reason or which is implemented following a Change in Control); provided that, if the Company does not maintain such a plan or policy, then the last target bonus prior to the Change in Control.

3. **Eligibility for Benefits.** Subject to the terms and conditions of the Plan, the Company will provide the benefits described in Section 5 to the affected Participant. A Participant will not receive benefits under the Plan (or will receive reduced benefits under the Plan) in the following circumstances, as determined by the Plan Administrator, in its sole discretion:

(a) The Participant’s employment is terminated by either the Company or the Participant for any reason other than a Qualifying Termination;

(b) The Participant is rehired by the Company or an Affiliate and recommences employment prior to the date benefits under the Plan are scheduled to commence.

(c) The Participant has not entered into the Company’s standard form of Employee Invention Assignment and Confidentiality Agreement or any similar or successor document (the “**Confidentiality Agreement**”);

(d) The Participant has failed to execute and allow to become effective the Release (as defined and described below) within the Release Period; and

(e) The Participant has failed to return all Company Property. For this purpose, “**Company Property**” means all paper and electronic Company documents (and all copies thereof) created and/or received by the Participant during his or her period of employment with the Company and other Company materials and property that the Participant has in his or her possession or control, including, without limitation, Company files, notes, drawings records, plans, forecasts, reports, studies, analyses, proposals, agreements, financial information, research and development information, sales and marketing information, operational and personnel information, specifications, code, software, databases, computer-recorded information, tangible property and equipment (including, without limitation, leased vehicles, computers, computer equipment, software programs, facsimile machines, mobile telephones, servers), credit and calling cards, entry cards, identification badges and keys, and any materials of any kind that contain or embody any proprietary or confidential information of the Company (and all reproductions thereof, in whole or in part). As a condition to receiving benefits under the Plan, a Participant must not make or retain copies, reproductions or summaries of any such Company documents, materials or property. However, a Participant is not required to return his or her personal copies of documents evidencing the Participant’s hire, termination, compensation, benefits and stock options and any other documentation received as a stockholder of the Company.

4. No Duplicative Benefits Provided Under Plan. This Plan does not supersede the terms of any Individual Severance Arrangement or Equity Award in effect as of the Effective Date. Unless otherwise determined by the Plan Administrator in its discretion, if a Participant is otherwise eligible to receive severance benefits under this Plan that are of the same category and would otherwise duplicate the benefits available under the terms of any Individual Severance Arrangement (“*Duplicative Benefits*”), such Participant will receive severance benefits under the Individual Severance Arrangement in lieu of any Plan benefits to the extent such benefits are Duplicative Benefits, and severance benefits will be provided under the Plan only to the extent, if any, that Plan benefits are not Duplicative Benefits.

5. Payments & Benefits Upon a Qualifying Termination. Except as may otherwise be provided in the Participant’s Participation Notice, in the event of a Qualifying Termination, the Company will provide the payments and benefits described in this Section 5, subject to the terms and conditions of the Plan.

(a) Payment of Accrued Obligations. The Company shall pay to each eligible Participant who incurs a Qualifying Termination a lump sum payment in cash, paid in accordance with applicable law, equal to the sum of (i) the Participant’s accrued but unpaid base salary and any accrued but unpaid vacation pay through the date of the Qualifying Termination, and (ii) any earned but unpaid annual bonus for any fiscal year preceding the fiscal year in which the termination occurs.

(b) Non-CiC Termination.

(i) Cash Severance. Subject to the execution (and non-revocation) of the Release, upon a Non-CiC Termination, the Participant will receive as severance an amount equal to the Participant’s Severance Base Pay. Such amount will be payable in accordance with Section 5(b)(i)(2) below.

(1) Severance Base Pay. For this purpose, “*Severance Base Pay*” means an amount equal to the product of (A) the Participant’s annual base salary or annualized wages (excluding incentive pay, premium pay, commissions, overtime, bonuses and other forms of variable compensation) as in effect on the date of the Qualifying Termination and (B) a fraction, the numerator of which is the number of months represented by the Severance Period and the denominator of which is twelve (12).

(2) Payment Schedule. The Company will pay the Severance Base Pay in a lump sum on the first payroll date that occurs more than five (5) days after the Release Effective Date. Notwithstanding the foregoing, to the extent required to comply with Section 409A (as defined below), if the Release Period spans two calendar years such that the Release Effective Date could occur in either of such calendar years, the Severance Base Pay to be paid to the Participant will be made in the second calendar year.

(ii) COBRA Payments; Special Severance Payments.

(1) COBRA Payment Period. If the Participant is eligible for and has made the necessary elections for continuation coverage pursuant to COBRA under a group health, dental or vision plan sponsored by the Company, the Company will pay, as and when due directly to the COBRA carrier, the premiums sufficient to continue the Participant’s COBRA coverage for the Participant and the Participant’s eligible dependents from the date of the Non-CiC Termination until the earliest to occur of (i) end of the Severance Period, (ii) the expiration of the Participant’s eligibility for the continuation coverage under COBRA, and (iii) the date on which the Participant becomes eligible for health insurance coverage in connection with new employment or self-employment (such period, the “*COBRA Payment Period*”). The Participant agrees to promptly notify the Company as soon as the Participant becomes eligible for health insurance coverage in connection with new employment or self-employment.

(2) **Special Severance Payment.** Notwithstanding Section 5(b)(ii)(1) above, if at any time the Company determines, in its sole discretion, that the payment of the COBRA premiums would result in a violation of the nondiscrimination rules of Section 105(h)(2) of the Code or any statute or regulation of similar effect (including, without limitation, the 2010 Patient Protection and Affordable Care Act, as amended by the 2010 Health Care and Education Reconciliation Act and any other subsequent amendments), then in lieu of providing the benefit set forth in Section 5(b)(ii)(1) above, the Company will instead pay the Participant, on the first day of each month of the remainder of the COBRA Payment Period, a fully taxable cash payment equal to the COBRA premiums for that month, subject to applicable tax withholdings and deductions (such amount, the “Special Severance Payment”).

(3) **Payment Schedule.** The Company will make the first payment under this Section 5(b)(ii) (and, in the case of the Special Severance Payment, such payment will be made to the Participant, in a lump sum) within five (5) business days after the Release Effective Date. Notwithstanding the foregoing, to the extent required to comply with Section 409A (as defined below), in the event that the Release Period spans two calendar years such that the Release Effective Date could occur in either of such calendar years, the first payment to be made under this Section 5(b)(ii) will be made in the second calendar year (and, if applicable, will include any amounts that the Company otherwise would have paid through such date), with the balance of the payments (if applicable) paid thereafter on the original schedule.

(iii) **Accelerated Vesting.** Subject to the Participant’s execution (and non-revocation) of the Release, upon a Non-CiC Termination, the vesting and exercisability (if applicable) of all outstanding unvested time-based equity awards granted under the Company’s equity incentive plans that are held by a Participant on the date of the Non-CiC Termination that otherwise would have vested with the passage of time over the entirety of the Severance Period had the Participant remained in Continuous Service with the Company will be accelerated.

(c) **Change in Control Termination.**

(i) **Cash Severance.** Subject to the execution (and non-revocation) of the Release, upon a Change in Control Termination, the Participant will receive as severance an amount equal to the Participant’s Severance Base Pay and Target Bonus Multiple. Such amount will be payable in accordance with Section 5(c)(i)(3) below.

(1) **Severance Base Pay.** For this purpose, “**Severance Base Pay**” means an amount equal to the product of (A) the Participant’s annual base salary or annualized wages (excluding incentive pay, premium pay, commissions, overtime, bonuses and other forms of variable compensation) as in effect on the date of the Change in Control and (B) a fraction, the numerator of which is the number of months represented by the Severance Period and the denominator of which is twelve (12).

(2) **Target Bonus Multiple.** For this purpose, “**Target Bonus Multiple**” means an amount equal to the product of (A) the Participant’s Target Bonus as in effect on the date of the Change in Control and (B) a fraction, the numerator of which is the number of months represented by the Severance Period and the denominator of which is twelve (12).

(3) **Payment Schedule.** The Company will pay the Severance Base Pay and Target Bonus Multiple in a lump sum on the first payroll date that occurs more than five (5) days after the Release Effective Date. Notwithstanding the foregoing, to the extent required to comply with Section 409A (as defined below), if the Release Period spans two calendar years such that the Release Effective Date could occur in either of such calendar years, the Severance Base Pay and Target Bonus Multiple to be paid to the Participant will be made in the second calendar year.

(ii) **COBRA Payments; Special Severance Payments.**

(1) **COBRA Payment Period.** If the Participant is eligible for and has made the necessary elections for continuation coverage pursuant to COBRA under a group health, dental or vision plan sponsored by the Company, the Company will pay, as and when due directly to the COBRA carrier, the premiums sufficient to continue the Participant’s COBRA coverage for the Participant and the Participant’s eligible dependents from the date of the Change in Control Termination until the earliest to occur of (i) end of the Severance Period, (ii) the expiration of the Participant’s eligibility for the continuation coverage under COBRA, and (iii) the date on which the Participant becomes eligible for health insurance coverage in connection with new employment or self-employment (such period, the “**COBRA Payment Period**”). The Participant agrees to promptly notify the Company as soon as the Participant becomes eligible for health insurance coverage in connection with new employment or self-employment.

(2) **Special Severance Payment.** Notwithstanding Section 5(c)(ii)(1) above, if at any time the Company determines, in its sole discretion, that the payment of the COBRA premiums would result in a violation of the nondiscrimination rules of Section 105(h)(2) of the Code or any statute or regulation of similar effect (including, without limitation, the 2010 Patient Protection and Affordable Care Act, as amended by the 2010 Health Care and Education Reconciliation Act and any other subsequent amendments), then in lieu of providing the benefit set forth in Section 5(c)(ii)(1) above, the Company will instead pay the Participant, on the first day of each month of the remainder of the COBRA Payment Period, a fully taxable cash payment equal to the COBRA premiums for that month, subject to applicable tax withholdings and deductions (such amount, the “**Special Severance Payment**”).

(3) **Payment Schedule.** The Company will make the first payment under this Section 5(c)(ii) (and, in the case of the Special Severance Payment, such payment will be made to the Participant, in a lump sum) within five (5) business days after the Release Effective Date. Notwithstanding the foregoing, to the extent required to comply with Section 409A (as defined below), in the event that the Release Period spans two calendar years such that the Release Effective Date could occur in either of such calendar years, the first payment to be made under this Section 5(c)(ii) will be made in the second calendar year (and, if applicable, will include any amounts that the Company otherwise would have paid through such date), with the balance of the payments (if applicable) paid thereafter on the original schedule.

(iii) Accelerated Vesting. Subject to the Participant's execution (and non-revocation) of the Release, upon a Change in Control Termination, the vesting and exercisability (if applicable) of all outstanding unvested time-based equity awards granted under the Company's equity incentive plans that are held by a Participant on the date of the Change in Control Termination will be accelerated in full. Notwithstanding the foregoing, if, in connection with a Change in Control, an equity award will terminate and will not be so assumed or continued by the successor or acquiror entity in such Change in Control or substituted for a similar award of the successor or acquiror entity, then, the Participant will become vested, with respect to 100 percent of any then unvested portion of any applicable equity award, effective immediately prior to, but subject to the consummation of such Change in Control.

6. CONDITIONS AND LIMITATIONS ON BENEFITS.

(a) Release. To be eligible to receive any benefits under the Plan, a Participant must sign a general waiver and release in substantially the form attached hereto as **EXHIBIT B**, **EXHIBIT C**, or **EXHIBIT D**, as appropriate (the "**Release**"), and such release must be executed (and not revoked) by the Participant in accordance with its terms, in each case within the Release Period. The Plan Administrator, in its sole discretion, may modify the form of the required Release to comply with applicable law, and any such Release may be incorporated into a termination agreement or other agreement with the Participant.

(b) Prior Agreements; Certain Reductions. The Plan Administrator will reduce a Participant's benefits under the Plan by any other statutory severance obligations or contractual severance benefits, obligations for pay in lieu of notice, and any other similar benefits payable to the Participant by the Company (or any successor thereto) that are due in connection with the Participant's Qualifying Termination and that are in the same form as the benefits provided under the Plan (e.g., equity award vesting credit). Without limitation, this reduction includes a reduction for any benefits required pursuant to (i) any applicable legal requirement, including, without limitation, the Worker Adjustment and Retraining Notification Act of 1988 and any similar state or local laws (collectively, the "**WARN Act**"), (ii) a written employment, severance or equity award agreement with the Company, (iii) any Company policy or practice providing for the Participant to remain on the payroll for a limited period of time after being given notice of the termination of the Participant's employment, and (iv) any required salary continuation, notice pay, statutory severance payment, or other payments either required by local law, or owed pursuant to a collective labor agreement, as a result of the termination of the Participant's employment. The benefits provided under the Plan are intended to satisfy, to the greatest extent possible, and not to provide benefits duplicative of, any and all statutory, contractual and collective agreement obligations of the Company in respect of the form of benefits provided under the Plan that may arise out of a Qualifying Termination, and the Plan Administrator will so construe and implement the terms of the Plan. Reductions may be applied on a retroactive basis, with benefits previously provided being recharacterized as benefits pursuant to the Company's statutory or other contractual obligations. The payments pursuant to the Plan are in addition to, and not in lieu of, any unpaid salary, bonuses or employee welfare benefits to which a Participant may be entitled for the period ending with the Participant's Qualifying Termination.

(c) **Indebtedness of Participants.** If a Participant is indebted to the Company on the effective date of his or her Qualifying Termination, the Company reserves the right to offset the payment of any benefits under the Plan by the amount of such indebtedness. Such offset will be made in accordance with all applicable laws. The Participant's execution of the Participation Notice constitutes knowing written consent to the foregoing.

(d) **Parachute Payments; No-Gross Ups.**

(i) Except as otherwise expressly provided in an agreement between a Participant and the Company, if any payment or benefit the Participant would receive in connection with a Change in Control from the Company or otherwise (a "Payment") would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the "Excise Tax"), then such Payment will be equal to the Reduced Amount. The "Reduced Amount" will be either (A) the largest portion of the Payment that would result in no portion of the Payment being subject to the Excise Tax, or (B) the largest portion, up to and including the total, of the Payment, whichever amount ((A) or (B)), after taking into account all applicable federal, state, provincial, foreign, and local employment taxes, income taxes, and the Excise Tax (all computed at the highest applicable marginal rate), results in the Participant's receipt, on an after-tax basis, of the greatest economic benefit notwithstanding that all or some portion of the Payment may be subject to the Excise Tax. If a reduction in payments or benefits constituting "parachute payments" is necessary so that the Payment equals the Reduced Amount, reduction in the payments and/or benefits will occur in the manner that results in the greatest economic benefit to the Participant, as determined in this paragraph; *provided*, that if more than one method of reduction will result in the same economic benefit, the portions of the Payment shall be reduced pro rata.

(ii) The professional firm engaged by the Company for general tax purposes as of the day prior to the effective date of the Change in Control shall make all determinations required to be made under this Section 5(d). If the professional firm so engaged by the Company is serving as an accountant or auditor for the individual, entity or group effecting the Change in Control, the Company shall appoint a nationally recognized independent registered public accounting firm to make the determinations required hereunder. The Company shall bear all expenses with respect to the determinations by such professional firm required to be made hereunder. Any good faith determinations of the professional firm made hereunder shall be final, binding and conclusive upon the Company and the Participant.

(iii) Participants are not eligible to receive any tax gross-up payments under this Plan.

(a) **Application of Section 409A of the Code.** It is intended that all of the payments and benefits provided under the Plan satisfy, to the greatest extent possible, the exemptions from the application of Section 409A of the Code and the regulations and other guidance thereunder and any state law of similar effect (collectively, “**Section 409A**”) provided under Treasury Regulations Sections 1.409A-1(b)(4), 1.409A-1(b)(5), and 1.409A-1(b)(9), and the Plan will be construed to the greatest extent possible as consistent with those provisions. To the extent not so exempt, the Plan (and any definitions in the Plan) will be construed in a manner that complies with Section 409A, and will incorporate by reference all required definitions and payment terms. Notwithstanding anything to the contrary herein, to the extent required to comply with Section 409A, a termination of employment shall not be deemed to have occurred for purposes of any provision of the Plan providing for the payments of amounts or benefits upon or following a termination of employment unless such termination is also a “separation from service” within the meaning of Section 409A and, for purposes of any such provision of the Plan, references to a “resignation,” “termination,” “termination of employment” or like terms shall mean separation from service. For purposes of Section 409A (including, without limitation, for purposes of Treasury Regulations Section 1.409A-2(b)(2)(iii)), a Participant’s right to receive any installment payments under the Plan will be treated as a right to receive a series of separate payments and, accordingly, each installment payment under the Plan will at all times be considered a separate and distinct payment. If the Plan Administrator determines that any of the payments upon a Separation from Service provided under the Plan (or under any other arrangement with the Participant) constitute “deferred compensation” under Section 409A and if the Participant is a “specified employee” of the Company, as such term is defined in Section 409A(a)(2)(B)(i), at the time of his or her Separation from Service, then, solely to the extent necessary to avoid the incurrence of the adverse personal tax consequences under Section 409A, the timing of the payments upon a Separation from Service will be delayed as follows: on the earlier to occur of (i) the date that is six (6) months and one (1) day after the effective date of the Participant’s Separation from Service, and (ii) the date of the Participant’s death (such earlier date, the “**Delayed Initial Payment Date**”), the Company will (A) pay to the Participant a lump sum amount equal to the sum of the payments upon Separation from Service that the Participant would otherwise have received through the Delayed Initial Payment Date if the commencement of the payments had not been delayed pursuant to this Section 6(a), and (B) commence paying the balance of the payments in accordance with the applicable payment schedules set forth above. No interest will be due on any amounts so deferred.

(b) **Withholding.** All payments and benefits under the Plan will be subject to all applicable deductions and withholdings, including, without limitation, obligations to withhold for federal, state, provincial, foreign and local income and employment taxes.

(c) **Tax Advice.** By becoming a Participant in the Plan, the Participant agrees to review with Participant’s own tax advisors the federal, state, provincial, local, and foreign tax consequences of participation in the Plan. The Participant will rely solely on such advisors and not on any statements or representations of the Company or any of its agents. The Participant understands that the Participant (and not the Company) will be responsible for the Participant’s own tax liability that may arise as a result of becoming a Participant in the Plan.

8. **Reemployment.** In the event of a Participant’s reemployment by the Company or one of its Affiliates during the Severance Period, the Company, in its sole and absolute discretion, may require such Participant to repay to the Company all or a portion of such severance benefits as a condition of reemployment.

9. Clawback; Recovery. All payments and severance benefits provided under the Plan will be subject to recoupment in accordance with any clawback policy that the Company is required to adopt pursuant to the listing standards of any national securities exchange or association on which the Company's securities are listed or as is otherwise required by the Dodd-Frank Wall Street Reform and Consumer Protection Act or other applicable law. In addition, the Board may impose such other clawback, recovery or recoupment provisions as the Board determines necessary or appropriate, including but not limited to a reacquisition right in respect of previously acquired shares of common stock of the Company or other cash or property upon the occurrence of a termination of employment for Cause.

10. RIGHT TO INTERPRET PLAN; AMENDMENT AND TERMINATION.

(a) Exclusive Discretion. The Plan Administrator (or the Representative, as applicable) will have the exclusive discretion and authority to establish rules, forms, and procedures for the administration of the Plan and to construe and interpret the Plan and to decide any and all questions of fact, interpretation, definition, computation or administration arising in connection with the operation of the Plan, including, without limitation, the eligibility to participate in the Plan, the amount of benefits paid under the Plan and any adjustments that need to be made in accordance with the laws applicable to a Participant. The rules, interpretations, computations and other actions of the Plan Administrator (or the Representative, as applicable) will be binding and conclusive on all persons.

(b) Amendment or Termination. This Plan and any Participation Notice executed hereunder cannot be amended, modified or terminated with respect to a Participant except by a written agreement signed by the Participant and the Company.

11. NO IMPLIED EMPLOYMENT CONTRACT. The Plan will not be deemed (i) to give any employee or other service provider any right to be retained in the employ or services of the Company, or (ii) to interfere with the right of the Company to discharge any employee or other service provider at any time, with or without Cause, which right is hereby reserved.

12. LEGAL CONSTRUCTION. The Plan will be governed by and construed under the laws of the State of California (without regard to principles of conflict of laws), except to the extent preempted by ERISA.

13. CLAIMS, INQUIRIES AND APPEALS.

(A) Applications for Benefits and Inquiries. Any application for benefits, inquiries about the Plan or inquiries about present or future rights under the Plan must be submitted to the Plan Administrator in writing by an applicant (or his or her authorized representative). The Plan Administrator is set forth in Section 14(d).

(b) Denial of Claims. If any application for benefits is denied in whole or in part, the Plan Administrator must provide the applicant with written or electronic notice of the denial of the application, and of the applicant's right to review the denial. Any electronic notice will comply with the regulations of the U.S. Department of Labor. The notice of denial will be set forth in a manner designed to be understood by the applicant and will include the following:

- (1) the specific reason or reasons for the denial;
- (2) references to the specific Plan provisions upon which the denial is based;
- (3) a description of any additional information or material that the Plan Administrator needs to complete the review and an explanation of why such information or material is necessary; and
- (4) an explanation of the Plan's review procedures and the time limits applicable to such procedures, including a statement of the applicant's right to bring a civil action under Section 502(a) of ERISA following a denial on review of the claim, as described in Section 12(d).

The notice of denial will be given to the applicant within ninety (90) days after the Plan Administrator receives the application, unless special circumstances require an extension of time, in which case, the Plan Administrator has up to an additional ninety (90) days for processing the application. If an extension of time for processing is required, written notice of the extension will be furnished to the applicant before the end of the initial ninety (90) day period.

The notice of extension will describe the special circumstances necessitating the additional time and the date by which the Plan Administrator is to render its decision on the application.

(c) Request for a Review. Any person (or that person's authorized representative) for whom an application for benefits is denied, in whole or in part, may appeal the denial by submitting a request for a review to the Plan Administrator within sixty (60) days after the application is denied. A request for a review will be in writing and will be addressed to:

Ionis Pharmaceuticals, Inc.
Attn: Plan Administrator of the Severance Benefit Plan
2855 Gazelle
Carlsbad, California 92010

A request for review must set forth all of the grounds on which it is based, all facts in support of the request and any other matters that the applicant feels are pertinent. The applicant (or the applicant's representative) will have the opportunity to submit (or the Plan Administrator may require the applicant to submit) written comments, documents, records, and other information relating to his or her claim. The applicant (or his or her representative) will be provided, upon request and free of charge, reasonable access to, and copies of, all documents, records and other information relevant to his or her claim. The review will take into account all comments, documents, records and other information submitted by the applicant (or his or her representative) relating to the claim, without regard to whether such information was submitted or considered in the initial benefit determination.

(d) Decision on Review. The Plan Administrator will act on each request for review within sixty (60) days after receipt of the request, unless special circumstances require an extension of time (not to exceed an additional sixty (60) days), for processing the request for a review. If an extension for review is required, written notice of the extension will be furnished to the applicant within the initial sixty (60) day period. This notice of extension will describe the special circumstances necessitating the additional time and the date by which the Plan Administrator is to render its decision on the review. The Plan Administrator will give prompt, written or electronic notice of its decision to the applicant. Any electronic notice will comply with the regulations of the U.S. Department of Labor. If the Plan Administrator confirms the denial of the application for benefits, in whole or in part, the notice will set forth, in a manner designed to be understood by the applicant, the following:

- (1) the specific reason or reasons for the denial;
- (2) references to the specific Plan provisions upon which the denial is based;
- (3) a statement that the applicant is entitled to receive, upon request and free of charge, reasonable access to, and copies of, all documents, records and other information relevant to the applicant's claim; and
- (4) a statement of the applicant's right to bring a civil action under Section 502(a) of ERISA.

(e) Rules and Procedures. The Plan Administrator will establish rules and procedures, consistent with the Plan and with ERISA, as necessary and appropriate in carrying out its responsibilities in reviewing benefit claims. The Plan Administrator may require an applicant who wishes to submit additional information in connection with an appeal from the denial of benefits to do so at the applicant's own expense.

(f) Exhaustion of Remedies. No legal action for benefits under the Plan may be brought until the applicant (i) has submitted a written application for benefits in accordance with the procedures described by Section 12(a), (ii) has been notified by the Plan Administrator that the application is denied, (iii) has filed a written request for a review of the application in accordance with the appeal procedure described in Section 12(c), and (iv) has been notified that the Plan Administrator has denied the appeal. Notwithstanding the foregoing, if the Plan Administrator does not respond to an applicant's claim or appeal within the relevant time limits specified in this Section 12, the applicant may bring legal action for benefits under the Plan pursuant to Section 502(a) of ERISA.

14. Basis Of Payments To And From Plan. All benefits under the Plan will be paid by the Company. The Plan will be unfunded, and benefits hereunder will be paid only from the general assets of the Company.

15. OTHER PLAN INFORMATION.

(a) Employer and Plan Identification Numbers. The Employer Identification Number assigned to the Company (which is the "Plan Sponsor" as that term is used in ERISA) by the Internal Revenue Service is 33-0336973. The Plan Number assigned to the Plan by the Plan Sponsor pursuant to the instructions of the Internal Revenue Service is 511.

31. (b) **Ending Date for Plan's Fiscal Year.** The date of the end of the fiscal year for the purpose of maintaining the Plan's records is December

(c) **Agent for the Service of Legal Process.** The agent for the service of legal process with respect to the Plan is:

Ionis Pharmaceuticals, Inc.
Attn: General Counsel
2855 Gazelle
Carlsbad, California 92010

(d) **Plan Sponsor and Administrator.** The "Plan Sponsor" and the "Plan Administrator" of the Plan is:

Ionis Pharmaceuticals, Inc.
Attn: Plan Administrator of the Severance Benefit Plan
2855 Gazelle
Carlsbad, California 92010

The Plan Sponsor's and Plan Administrator's telephone number is (760) 603-3848. The Plan Administrator is the named fiduciary charged with the responsibility for administering the Plan.

16. STATEMENT OF ERISA RIGHTS.

Participants in the Plan (which is a welfare benefit plan sponsored by Ionis Pharmaceuticals, Inc.) are entitled to certain rights and protections under ERISA. For purposes of this Section 16 and, under ERISA, Participants are entitled to:

Receive Information About the Plan and Benefits

(a) Examine, without charge, at the Plan Administrator's office and at other specified locations, such worksites, all documents governing the Plan and a copy of the latest annual report (Form 5500 Series), if applicable, filed by the Plan with the U.S. Department of Labor and available at the Public Disclosure Room of the Employee Benefits Security Administration;

(b) Obtain, upon written request to the Plan Administrator, copies of documents governing the operation of the Plan and copies of the latest annual report (Form 5500 Series), if applicable, and an updated (as necessary) Summary Plan Description. The Plan Administrator may make a reasonable charge for the copies; and

(c) Receive a summary of the Plan's annual financial report, if applicable. The Plan Administrator is required by law to furnish each Participant with a copy of this summary annual report.

Prudent Actions by Plan Fiduciaries

In addition to creating rights for Participants, ERISA imposes duties upon the people who are responsible for the operation of the employee benefit plan. The people who operate the Plan, called "fiduciaries" of the Plan, have a duty to do so prudently and in the interest of Participants and beneficiaries. No one, including a Participant's employer, union (if applicable) or any other person, may fire a Participant or otherwise discriminate against a Participant in any way to prevent the Participant from obtaining a Plan benefit or exercising a Participant's rights under ERISA.

Enforcement of Participant Rights

If a claim for a Plan benefit is denied or ignored, in whole or in part, a Participant has a right to know why this was done, to obtain copies of documents relating to the decision without charge, and to appeal any denial, all within certain time schedules.

Under ERISA, there are steps a Participant can take to enforce the above rights. For instance, if a Participant requests a copy of Plan documents or the latest annual report from the Plan, if applicable, and does not receive them within thirty (30) days, the Participant may file suit in a federal court. In such a case, the court may require the Plan Administrator to provide the materials and pay the Participant up to \$110 a day until the Participant receives the materials, unless the materials were not sent because of reasons beyond the control of the Plan Administrator.

If a Participant has a claim for benefits that is denied or ignored, in whole or in part, the Participant may file suit in a state or federal court.

If a Participant is discriminated against for asserting the Participant's rights, the Participant may seek assistance from the U.S. Department of Labor, or may file suit in a federal court. The court will decide who should pay court costs and legal fees. If a Participant is successful, the court may order the person the Participant has sued to pay these costs and fees. If the Participant loses, the court may order the Participant to pay these costs and fees, for example, if it finds the Participant's claim is frivolous.

Assistance with Questions

If a Participant has any questions about the Plan, the Participant should contact the Plan Administrator. If a Participant has any questions about this statement or about the Participant's rights under ERISA, or if the Participant needs assistance in obtaining documents from the Plan Administrator, the Participant should contact the nearest office of the Employee Benefits Security Administration, U.S. Department of Labor, listed in the Participant's telephone directory or the Division of Technical Assistance and Inquiries, Employee Benefits Security Administration, U.S. Department of Labor, 200 Constitution Avenue N.W., Washington, D.C. 20210. The Participant may also obtain certain publications about the Participant's rights and responsibilities under ERISA by calling the publications hotline of the Employee Benefits Security Administration.

17. GENERAL PROVISIONS.

(a) **Notices.** Any notice, demand or request required or permitted to be given by either the Company or a Participant pursuant to the terms of the Plan will be in writing and will be deemed given when delivered personally, when received electronically (including email addressed to the Participant's Company email account and to the Company email account of the Company's head of legal affairs), or deposited in the U.S. Mail, First Class with postage prepaid, and addressed to the parties, in the case of the Company, at the address set forth in Section 14(d), in the case of a Participant, at the address as set forth in the Company's employment file maintained for the Participant as previously furnished by the Participant or such other address as a party may request by notifying the other in writing.

(b) **Transfer and Assignment.** The rights and obligations of a Participant under the Plan may not be transferred or assigned without the prior written consent of the Company. The Plan will be binding upon any surviving entity resulting from a Change in Control and upon any other person who is a successor by merger, acquisition, consolidation or otherwise to the business formerly carried on by the Company without regard to whether or not such person or entity actively assumes the obligations hereunder.

(c) **Waiver.** Any party's failure to enforce any provision or provisions of the Plan will not in any way be construed as a waiver of any such provision or provisions, nor prevent any party from thereafter enforcing each and every other provision of the Plan. The rights granted to the parties herein are cumulative and will not constitute a waiver of any party's right to assert all other legal remedies available to it under the circumstances.

(d) **Severability.** Should any provision of the Plan be declared or determined to be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions will not in any way be affected or impaired.

(e) **Section Headings.** Section headings in the Plan are included only for convenience of reference and will not be considered part of the Plan for any other purpose.

18. Effective Date. The Plan shall become effective on the Effective Date.

EXHIBIT A

IONIS PHARMACEUTICALS, INC.

SEVERANCE BENEFIT PLAN
PARTICIPATION NOTICE

To: _____

Date: _____

Ionis Pharmaceuticals, Inc. (the “*Company*”) has adopted the Ionis Pharmaceuticals, Inc. Severance Benefit Plan (the “*Plan*”). The Company is providing you this Participation Notice to inform you that you have been designated as a Participant in the Plan. A copy of the Plan document is attached to this Participation Notice. The terms and conditions of your participation in the Plan are as set forth in the Plan and this Participation Notice, which together constitute the Summary Plan Description for the Plan.

Your Severance Period is [XX months]¹.

Please return to the Company’s head of Human Resources a copy of this Participation Notice signed by you and retain a copy of this Participation Notice, along with the Plan document, for your records.

IONIS PHARMACEUTICALS, INC.

(Signature)

Name:

Title:

PARTICIPANT:

(Signature)

Name:

Date:

¹ 18 months for CEO, 12 months for other Section 16 officers.

EXHIBIT B

RELEASE AGREEMENT
[EMPLOYEES AGE 40 OR OVER; INDIVIDUAL TERMINATION]

I understand and agree completely to the terms set forth in the Ionis Pharmaceuticals, Inc. Severance Benefit Plan (the “Plan”).

I understand that this Release, together with the Plan, constitutes the complete, final and exclusive embodiment of the entire agreement between the Company, affiliates of the Company and me with regard to the subject matter hereof. I am not relying on any promise or representation by the Company or an affiliate of the Company that is not expressly stated therein. Certain capitalized terms used in this Release are defined in the Plan.

I hereby confirm my obligations under my Confidentiality Agreement.

I hereby resign all positions (if any) I hold on the Company’s Board of Directors, including all committees.

Except as otherwise set forth in this Release, I hereby generally and completely release the Company and its affiliates, and their parents, subsidiaries, successors, predecessors and affiliates, and its and their partners, members, directors, officers, employees, stockholders, shareholders, agents, attorneys, predecessors, insurers, affiliates and assigns, from any and all claims, liabilities and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring at any time prior to and including the date I sign this Release. This general release includes, but is not limited to: (a) all claims arising out of or in any way related to my employment with the Company and its affiliates, or their affiliates, or the termination of that employment; (b) all claims related to my compensation or benefits, including salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, or any other ownership interests in the Company and its affiliates, or their affiliates; (c) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (d) all tort claims, including claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (e) all federal, state, provincial and local statutory claims, including claims for discrimination, harassment, retaliation, attorneys’ fees, or other claims arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990 (as amended), the federal Age Discrimination in Employment Act (as amended) (“*ADEA*”), and the federal Employee Retirement Income Security Act of 1974 (as amended).

Notwithstanding the foregoing, I understand that the following rights or claims are not included in my Release: (a) any rights or claims for indemnification I may have pursuant to any written indemnification agreement with the Company or its affiliate to which I am a party; the charter, bylaws, or operating agreements of the Company or its affiliate; or under applicable law; or (b) any rights which cannot be waived as a matter of law. In addition, I understand that nothing in this Release prevents me from filing, cooperating with, or participating in any proceeding before the Equal Employment Opportunity Commission or the Department of Labor, except that I hereby waive my right to any monetary benefits in connection with any such claim, charge or proceeding.

I hereby represent and warrant that, other than the claims identified in this paragraph, I am not aware of any claims I have or might have that are not included in the Release.

I acknowledge that I am knowingly and voluntarily waiving and releasing any rights I may have under the ADEA, and that the consideration given under the Plan for the waiver and release in the preceding paragraph hereof is in addition to anything of value to which I was already entitled. I further acknowledge that I have been advised by this writing, as required by the ADEA, that: (a) my waiver and release do not apply to any rights or claims that may arise after the date I sign this Release; (b) I should consult with an attorney prior to signing this Release (although I may choose voluntarily not to do so); (c) I have twenty-one (21) days to consider this Release (although I may choose voluntarily to sign this Release earlier); (d) I have seven (7) days following the date I sign this Release to revoke the Release by providing written notice to an officer of the Company; and (e) this Release will not be effective until the date upon which the revocation period has expired, which will be the eighth day after I sign this Release.

I hereby represent that I have been paid all compensation owed and for all hours worked; I have received all the leave and leave benefits and protections for which I am eligible pursuant to the Family and Medical Leave Act, or otherwise; and I have not suffered any on-the-job injury for which I have not already filed a workers' compensation claim.

I represent that I am not aware of any claim by me other than the claims that are released by this Release. I acknowledge that I may hereafter discover claims or facts in addition to or different than those which I now know or believe to exist with respect to the subject matter of this Release and which, if known or suspected at the time of entering into this Release, may have materially affected this Release and my decision to enter into it. Nevertheless, I hereby waive any right, claim or cause of action that might arise as a result of such different or additional claims or facts and I hereby expressly waive any and all rights and benefits conferred upon me by the provisions of California Civil Code Section 1542, which provides as set forth below, as well as under any other statute or common law principles of similar effect:

“A GENERAL RELEASE DOES NOT EXTEND TO CLAIMS WHICH THE CREDITOR DOES NOT KNOW OR SUSPECT TO EXIST IN HIS OR HER FAVOR AT THE TIME OF EXECUTING THE RELEASE, WHICH IF KNOWN BY HIM OR HER MUST HAVE MATERIALLY AFFECTED HIS OR HER SETTLEMENT WITH THE DEBTOR.”²

I agree not to disparage the Company and its affiliates, and the Company's and its affiliates' officers, directors, employees, shareholders, investors and agents, in any manner likely to be harmful to them or their business, business reputation or personal reputation; provided that I may respond accurately and fully to any question, inquiry or request for information when required by legal process or as part of a government investigation. Notwithstanding the foregoing, nothing in this Release shall limit my right to voluntarily communicate with the Equal Employment Opportunity Commission, United States Department of Labor, the National Labor Relations Board, the Securities and Exchange Commission, other federal government agency or similar state or local agency or to discuss the terms and conditions of my employment with others to the extent expressly permitted by Section 7 of the National Labor Relations Act.

² For California employees.

I agree that for the one (1) year period after the date my employment ends, I will not, as an officer, director, employee, consultant, owner, partner, or in any other capacity, either directly or through others, solicit, induce, encourage, or participate in soliciting, inducing or encouraging any employee, consultant, or independent contractor of Company to terminate his, her or its relationship with Company or its Affiliates, even if I did not initiate the discussion or seek out the contact.

I acknowledge that to become effective, I must sign and return this Release to the Company so that it is received not later than twenty-one (21) days following the date it is provided to me.

PARTICIPANT:

(Signature)

Name:

Date:

RELEASE AGREEMENT
[EMPLOYEES AGE 40 OR OVER; GROUP TERMINATION]

I understand and agree completely to the terms set forth in the Ionis Pharmaceuticals, Inc. Severance Benefit Plan (the "Plan").

I understand that this Release, together with the Plan, constitutes the complete, final and exclusive embodiment of the entire agreement between the Company, affiliates of the Company and me with regard to the subject matter hereof. I am not relying on any promise or representation by the Company or an affiliate of the Company that is not expressly stated therein. Certain capitalized terms used in this Release are defined in the Plan.

I hereby confirm my obligations under my Confidentiality Agreement.

I hereby resign all positions (if any) I hold on the Company's Board of Directors, including all committees.

Except as otherwise set forth in this Release, I hereby generally and completely release the Company and its affiliates, and their parents, subsidiaries, successors, predecessors and affiliates, and its and their partners, members, directors, officers, employees, stockholders, shareholders, agents, attorneys, predecessors, insurers, affiliates and assigns, from any and all claims, liabilities and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring at any time prior to and including the date I sign this Release. This general release includes, but is not limited to: (a) all claims arising out of or in any way related to my employment with the Company and its affiliates, or their affiliates, or the termination of that employment; (b) all claims related to my compensation or benefits, including salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, or any other ownership interests in the Company and its affiliates, or their affiliates; (c) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (d) all tort claims, including claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (e) all federal, state, provincial and local statutory claims, including claims for discrimination, harassment, retaliation, attorneys' fees, or other claims arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990 (as amended), the federal Age Discrimination in Employment Act (as amended) ("**ADEA**"), and the federal Employee Retirement Income Security Act of 1974 (as amended).

Notwithstanding the foregoing, I understand that the following rights or claims are not included in my Release: (a) any rights or claims for indemnification I may have pursuant to any written indemnification agreement with the Company or its affiliate to which I am a party; the charter, bylaws, or operating agreements of the Company or its affiliate; or under applicable law; or (b) any rights which cannot be waived as a matter of law. In addition, I understand that nothing in this Release prevents me from filing, cooperating with, or participating in any proceeding before the Equal Employment Opportunity Commission, or the Department of Labor, except that I hereby waive my right to any monetary benefits in connection with any such claim, charge or proceeding. I hereby represent and warrant that, other than the claims identified in this paragraph, I am not aware of any claims I have or might have that are not included in the Release.

I acknowledge that I am knowingly and voluntarily waiving and releasing any rights I may have under the ADEA, and that the consideration given under the Plan for the waiver and release in the preceding paragraph hereof is in addition to anything of value to which I was already entitled. I further acknowledge that I have been advised by this writing, as required by the ADEA, that: (a) my waiver and release do not apply to any rights or claims that may arise after the date I sign this Release; (b) I should consult with an attorney prior to signing this Release (although I may choose voluntarily not to do so); (c) I have forty-five (45) days to consider this Release (although I may choose voluntarily to sign this Release earlier); (d) I have seven (7) days following the date I sign this Release to revoke the Release by providing written notice to an officer of the Company; (e) this Release will not be effective until the date upon which the revocation period has expired, which will be the eighth day after I sign this Release; and (f) I have received with this Release a detailed list of the job titles and ages of all employees who were terminated in this group termination and the ages of all employees of the Company in the same job classification or organizational unit who were not terminated.

I hereby represent that I have been paid all compensation owed and for all hours worked; I have received all the leave and leave benefits and protections for which I am eligible pursuant to the Family and Medical Leave Act, or otherwise; and I have not suffered any on-the-job injury for which I have not already filed a workers' compensation claim.

I represent that I am not aware of any claim by me other than the claims that are released by this Release. I acknowledge that I may hereafter discover claims or facts in addition to or different than those which I now know or believe to exist with respect to the subject matter of this Release and which, if known or suspected at the time of entering into this Release, may have materially affected this Release and my decision to enter into it. Nevertheless, I hereby waive any right, claim or cause of action that might arise as a result of such different or additional claims or facts and I hereby expressly waive any and all rights and benefits conferred upon me by the provisions of California Civil Code Section 1542, which provides as set forth below, as well as under any other statute or common law principles of similar effect:

“A GENERAL RELEASE DOES NOT EXTEND TO CLAIMS WHICH THE CREDITOR DOES NOT KNOW OR SUSPECT TO EXIST IN HIS OR HER FAVOR AT THE TIME OF EXECUTING THE RELEASE, WHICH IF KNOWN BY HIM OR HER MUST HAVE MATERIALLY AFFECTED HIS OR HER SETTLEMENT WITH THE DEBTOR.”³

³ For California employees.

I agree not to disparage the Company and its affiliates, and the Company's and its affiliates' officers, directors, employees, shareholders, investors and agents, in any manner likely to be harmful to them or their business, business reputation or personal reputation; provided that I may respond accurately and fully to any question, inquiry or request for information when required by legal process or as part of a government investigation. Notwithstanding the foregoing, nothing in this Release shall limit my right to voluntarily communicate with the Equal Employment Opportunity Commission, United States Department of Labor, the National Labor Relations Board, the Securities and Exchange Commission, other federal government agency or similar state or local agency or to discuss the terms and conditions of my employment with others to the extent expressly permitted by Section 7 of the National Labor Relations Act.

I agree that for the one (1) year period after the date my employment ends, I will not, as an officer, director, employee, consultant, owner, partner, or in any other capacity, either directly or through others, solicit, induce, encourage, or participate in soliciting, inducing or encouraging any employee, consultant, or independent contractor of Company to terminate his, her or its relationship with Company or its Affiliates, even if I did not initiate the discussion or seek out the contact.

I acknowledge that to become effective, I must sign and return this Release to the Company so that it is received not later than forty-five (45) days following the date it is provided to me.

PARTICIPANT:

(Signature)

Name:

Date:

RELEASE AGREEMENT
[EMPLOYEES UNDER AGE 40]

I understand and agree completely to the terms set forth in the Ionis Pharmaceuticals, Inc. Severance Benefit Plan (the “Plan”).

I understand that this Release, together with the Plan, constitutes the complete, final and exclusive embodiment of the entire agreement between the Company, affiliates of the Company and me with regard to the subject matter hereof. I am not relying on any promise or representation by the Company or an affiliate of the Company that is not expressly stated therein. Certain capitalized terms used in this Release are defined in the Plan.

I hereby confirm my obligations under my Confidentiality Agreement.

I hereby resign all positions (if any) I hold on the Company’s Board of Directors, including all committees.

Except as otherwise set forth in this Release, I hereby generally and completely release the Company and its affiliates, and their parents, subsidiaries, successors, predecessors and affiliates, and its and their partners, members, directors, officers, employees, stockholders, shareholders, agents, attorneys, predecessors, insurers, affiliates and assigns, from any and all claims, liabilities and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring at any time prior to and including the date I sign this Release. This general release includes, but is not limited to: (a) all claims arising out of or in any way related to my employment with the Company and its affiliates, or their affiliates, or the termination of that employment; (b) all claims related to my compensation or benefits, including salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, or any other ownership interests in the Company and its affiliates, or their affiliates; (c) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (d) all tort claims, including claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (e) all federal, state, provincial and local statutory claims, including claims for discrimination, harassment, retaliation, attorneys’ fees, or other claims arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990 (as amended), and the federal Employee Retirement Income Security Act of 1974 (as amended).

Notwithstanding the foregoing, I understand that the following rights or claims are not included in my Release: (a) any rights or claims for indemnification I may have pursuant to any written indemnification agreement with the Company or its affiliate to which I am a party; the charter, bylaws, or operating agreements of the Company or its affiliate; or under applicable law; or (b) any rights which cannot be waived as a matter of law. In addition, I understand that nothing in this Release prevents me from filing, cooperating with, or participating in any proceeding before the Equal Employment Opportunity Commission, or the Department of Labor, except that I hereby waive my right to any monetary benefits in connection with any such claim, charge or proceeding. I hereby represent and warrant that, other than the claims identified in this paragraph, I am not aware of any claims I have or might have that are not included in the Release.

I hereby represent that I have been paid all compensation owed and for all hours worked; I have received all the leave and leave benefits and protections for which I am eligible pursuant to the Family and Medical Leave Act, or otherwise; and I have not suffered any on-the-job injury for which I have not already filed a workers' compensation claim.

[I represent that I am not aware of any claim by me other than the claims that are released by this Release. I acknowledge that I may hereafter discover claims or facts in addition to or different than those which I now know or believe to exist with respect to the subject matter of this Release and which, if known or suspected at the time of entering into this Release, may have materially affected this Release and my decision to enter into it. Nevertheless, I hereby waive any right, claim or cause of action that might arise as a result of such different or additional claims or facts and I hereby expressly waive any and all rights and benefits conferred upon me by the provisions of California Civil Code Section 1542, which provides as set forth below, as well as under any other statute or common law principles of similar effect:

“A GENERAL RELEASE DOES NOT EXTEND TO CLAIMS WHICH THE CREDITOR DOES NOT KNOW OR SUSPECT TO EXIST IN HIS OR HER FAVOR AT THE TIME OF EXECUTING THE RELEASE, WHICH IF KNOWN BY HIM OR HER MUST HAVE MATERIALLY AFFECTED HIS OR HER SETTLEMENT WITH THE DEBTOR.”⁴

I agree not to disparage the Company and its affiliates, and the Company's and its affiliates' officers, directors, employees, shareholders, investors and agents, in any manner likely to be harmful to them or their business, business reputation or personal reputation; provided that I may respond accurately and fully to any question, inquiry or request for information when required by legal process or as part of a government investigation. Notwithstanding the foregoing, nothing in this Release shall limit my right to voluntarily communicate with the Equal Employment Opportunity Commission, United States Department of Labor, the National Labor Relations Board, the Securities and Exchange Commission, other federal government agency or similar state or local agency or to discuss the terms and conditions of my employment with others to the extent expressly permitted by Section 7 of the National Labor Relations Act.

I agree that for the one (1) year period after the date my employment ends, I will not, as an officer, director, employee, consultant, owner, partner, or in any other capacity, either directly or through others, solicit, induce, encourage, or participate in soliciting, inducing or encouraging any employee, consultant, or independent contractor of Company to terminate his, her or its relationship with Company or its Affiliates, even if I did not initiate the discussion or seek out the contact.

⁴ For California employees.

I acknowledge that to become effective, I must sign and return this Release to the Company so that it is received not later than fourteen (14) days following the date it is provided to me.

PARTICIPANT:

(Signature)

Name:

Date:
