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

SCHEDULE 14A

Proxy Statement Pursuant to Section 14(a) of the Securities Exchange Act of 1934 (Amendment No.)

Filed by the Registrant ⊠	
File	ed by a Party other than the Registrant \square
Che	eck the appropriate box: Preliminary Proxy Statement Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2)) Definitive Proxy Statement Definitive Additional Materials Soliciting Material under §240.14a-12
	Ionis Pharmaceuticals, Inc.
	(Name of Registrant as Specified In Its Charter)
	(Name of Person(s) Filing Proxy Statement, if other than the Registrant)
Pay ⊠ □	yment of Filing Fee (Check the appropriate box): No fee required. Fee computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11. (1) Title of each class of securities to which transaction applies:
	(2) Aggregate number of securities to which transaction applies:
	Per unit price or other underlying value of transaction computed pursuant to Exchange Act Rule 0-11 (set forth the amount on which the filing fee is calculated and state how it was determined):
	(4) Proposed maximum aggregate value of transaction:
	(5) Total fee paid:
	Fee paid previously with preliminary materials. Check box if any part of the fee is offset as provided by Exchange Act Rule 0-11(a)(2) and identify the filing for which the offsetting fee was paid previously. Identify the previous filing by registration statement number, or the Form or Schedule and the date of its filing. (1) Amount Previously Paid:
	(2) Form, Schedule or Registration Statement No.:
	(3) Filing Party:
	(4) Date Filed:

Dear Stockholders:

Our annual stockholders' meeting will be held on Wednesday, June 2 at 2:00 p.m., Pacific Time, and due to the COVID-19 pandemic, we will be using a virtual meeting format.

We are asking for your vote **FOR Proposal 2** in our Proxy Statement filed with the Securities and Exchange Commission on April 23, 2021, to approve an amendment of the Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan to, among other things, increase the aggregate number of shares of common stock authorized for issuance under such plan by 6,700,000 shares to an aggregate of 29,700,000 shares and add a fungible share counting ratio (the "2011 Equity Incentive Plan" proposal). If approved, the amended 2011 Equity Incentive Plan (as amended, the "Amended 2011 Plan") will allow us to continue granting stock options, restricted stock units, and performance-based restricted stock units to employees at appropriate levels. If Proposal 2 fails, then we will have a significantly reduced ability to use equity to recruit and retain highly qualified personnel and we will be substantially disadvantaged in our ability to compete.

Providing equity to our employees is a critically important tool for recruiting and retaining highly qualified personnel. For this reason, our board of directors (the "Board") unanimously recommends a vote **FOR Proposal 2** in the Proxy Statement.

We are pleased to note that Glass Lewis is supporting the approval of the Amended 2011 Plan. In contrast, Institutional Shareholder Services ("ISS") has issued an unfavorable recommendation on Proposal 2.

In response to ISS' concerns, our Compensation Committee has approved an amendment to the Ionis Pharmaceuticals 2020 Equity Incentive Plan (the "2020 Plan") to reduce the number of shares reserved for issuance under the 2020 Plan by 978,596 shares effective March 31, 2021 so that the number of unallocated shares available for future grants as of March 31, 2021 is equal to 1,100,000. We assumed the 2020 Plan in connection with Ionis' acquisition of all of the outstanding shares of Akcea Therapeutics, Inc. (the "Akcea Acquisition"). Equity awards granted under the 2020 Plan are reserved primarily for legacy employees of Akcea Therapeutics, Inc. who were employed as of October 12, 2020, which was the completion date of the Akcea Acquisition.

Further information about the actions we have taken can be found in the attached materials.

Our Amended 2011 Plan is designed to protect stockholder value by enabling us to compete for talent while protecting stockholder interests.

To enable us to compete effectively, we adopted changes to the Amended 2011 Plan so that it enables us to effectively use equity that is earned based on continued service to Ionis and/or achievement of performance goals to retain and incentivize our workforce while remaining responsible to our stockholders. With more limited ability to grant equity awards to our workforce, it will be difficult for us to compete with other employers who grant equity compensation, which we believe would put us at a significant disadvantage in the labor market.

The Amended 2011 Plan contains provisions that promote stockholder value and are in line with corporate best practices. We have described these provisions in detail in the Proxy Statement, but would again like to briefly highlight the following provisions:

- No repricing of stock options or stock appreciation rights without stockholder approval
- No discounting of stock options or stock appreciation rights
- Minimum vesting requirements for grants with a limited exception for 5% of the shares available under the Amended 2011 Plan

- "Fungible" share reserve by which the share reserve is reduced by 1.7 shares for each share issued pursuant to a full value award
- No dividends or dividend equivalents on unearned stock awards
- *No liberal change in control definition*
- · No liberal share counting provisions with respect to stock options and stock appreciation rights

We have managed our equity grants conservatively.

We have a long track record of managing our equity spend conservatively and to good effect. ISS itself measures equity spend through its "burn rate" metric and has established a benchmark of 7.91% for three-year historical responsible equity spend. Using ISS' methodology, our three-year <u>average adjusted</u> burn rate (which incorporates a volatility multiplier of 2.0 for full value awards) was 3.67% and our three-year <u>average unadjusted</u> burn rate was 2.91%, each well below ISS' benchmark.

Approval of Proposal 2 supports stockholder value creation.

For the reasons we have stated above, we strongly believe that our Amended 2011 Plan is in the best interests of our stockholders and we respectfully ask for your vote **FOR Proposal 2**.

Sincerely,

Ionis Pharmaceuticals, Inc.

SUPPLEMENTAL INFORMATION REGARDING PROPOSAL 2 – APPROVAL OF THE AMENDED 2011 EQUITY INCENTIVE PLAN OF IONIS PHARMACEUTICALS, INC.

As described in Proposal 2 ("Proposal 2") of the proxy statement (the "Proxy Statement") for the 2021 Annual Meeting of Stockholders (the "2021 Annual Meeting") of Ionis Pharmaceuticals, Inc. (the "Company"), we are requesting that our stockholders approve an amendment to our 2011 Equity Incentive Plan (as amended, the "Amended 2011 Plan"). After furnishing the Proxy Statement to our stockholders, we were informed by Institutional Shareholder Services ("ISS") that Proposal 2 received an unfavorable recommendation as determined by ISS. In response, the Compensation Committee (the "Compensation Committee") of our board of directors (the "Board") has approved an amendment to the Ionis Pharmaceuticals 2020 Equity Incentive Plan (the "2020 Plan") to reduce the number of shares reserved for issuance under the 2020 Plan by 978,596 shares effective March 31, 2021 so that the number of unallocated shares available for future grants as of March 31, 2021 is equal to 1,100,000. We assumed the 2020 Plan in connection with Ionis' acquisition of all of the outstanding shares of Akcea Therapeutics, Inc. (the "Akcea Acquisition"). Equity awards granted under the 2020 Plan are reserved primarily for legacy employees of Akcea Therapeutics, Inc. who were employed as of October 12, 2020, which was the completion date of the Akcea Acquisition. The Board amended the Amended 2011 Plan, subject to approval by our stockholders, in order to enable us to have a competitive equity incentive program that aligns the interests of our employees, directors and consultants with the interests of our stockholders. The Board believes that the grant of equity awards is a key element underlying our ability to recruit, retain and motivate our employees, directors and consultants because of the strong competition for highly trained and experienced individuals in the pharmaceutical industry.

ISS issued its recommendation in part because ISS found the cost of the Amended 2011 Plan, when combined with the Ionis Pharmaceuticals, Inc. 1989 Stock Option Plan (the "89 Plan") and the 2020 Plan, excessive. As described in the Proxy Statement, we recognize that equity awards dilute existing stockholders, and, therefore, we are mindful to responsibly manage the growth of our equity compensation program. We believe our historic three-year burn rate is reasonable, and we are committed to effectively monitoring our equity compensation share reserve and burn rate to ensure that we maximize stockholders' value by granting the appropriate number of equity awards necessary to attract, reward, and retain employees, directors and consultants.

Equity compensation has significantly contributed to our growth and success to date, and it is important that we remain able to utilize equity vehicles in the future. Thus, the Board considers approval of the Amended 2011 Plan critical to our ability to continue to execute our strategic plans. If the Amended 2011 Plan is not approved, we will be required to revise our compensation philosophy in a manner that could competitively disadvantage our ability to attract and retain employees, directors and consultants.

The Compensation Committee has decided to reduce the number of shares reserved for issuance under the 2020 Plan. Accordingly, on May 20, 2021, the Compensation Committee approved an amendment to the 2020 Plan to reduce the aggregate number of shares of our common stock that may be issued under the 2020 Plan by 978,596 shares effective March 31, 2021 so that the number of unallocated shares available for future grants as of March 31, 2021 is equal to 1,100,000. This will reduce the potential dilutive impact of the 2020 Plan on other stockholders and the overall cost of our equity plans, including the Amended 2011 Plan. The Board made no other changes to the 2020 Plan, the Amended 2011 Plan or the 89 Plan.

As a result of the Compensation Committee's action, the available reserve of the 2020 Plan has been reduced by 978,596 shares effective March 31, 2021 so that the number of unallocated shares available for future grants as of March 31, 2021 is equal to 1,100,000 and the aggregate proposed increase to the share reserve of the Amended 2011 Plan will continue to be 6,700,000 shares. Except as set forth herein, there are no changes to Proposal 2.

Key Considerations in Approving the Amended 2011 Plan

The Board believes that the Amended 2011 Plan is in the best interests of our business and our stockholders and recommends a vote in favor of Proposal 2. The Amended 2011 Plan includes provisions that are designed to protect our stockholders' interests and to reflect corporate governance best practices, including:

- Repricing is not allowed. The Amended 2011 Plan prohibits the repricing of stock options and stock appreciation rights without prior stockholder approval.
- *No discounted stock options or stock appreciation rights.* All stock options and stock appreciation rights granted under the Amended 2011 Plan must have an exercise price equal to or greater than the fair market value of our common stock on the date the stock option or stock appreciation right is granted.
- *Minimum vesting requirements*. The Amended 2011 Plan provides that no award may vest until at least 12 months following the date of grant of such award, except that shares of our common stock up to 5% of the share reserve of the Amended 2011 Plan may be issued pursuant to awards that do not meet such vesting requirements.
- Restrictions on dividends. The Amended 2011 Plan provides that (i) no dividends or dividend equivalents may be paid with respect to any shares of our common stock subject to an award before the date such shares have vested, (ii) any dividends or dividend equivalents that are credited with respect to any such shares will be subject to all of the terms and conditions applicable to such shares under the terms of the applicable award agreement (including, but not limited to, any vesting conditions), and (iii) any dividends or dividend equivalents that are credited with respect to any such shares will be forfeited to us on the date, if any, such shares are forfeited to or repurchased by us due to a failure to vest.
- *No liberal change in control definition*. The change in control definition in the Amended 2011 Plan is not a "liberal" definition. A change in control transaction must actually occur in order for the change in control provisions in the Amended 2011 Plan to be triggered.
- *Fungible Reserve.* The Amended 2011 Plan includes a "fungible" share counting structure, whereby the number of shares of common stock available for issuance under the Amended 2011 Plan will be reduced by (i) one share for each share issued pursuant to a stock option or stock appreciation right with an exercise price that is at least 100% of the fair market value of our common stock on the date of grant (an "Appreciation Award") granted under the Amended 2011 Plan, and (ii) 1.7 shares for each share issued pursuant to a stock award that is not an Appreciation Award.
- No liberal share counting provisions for stock options and stock appreciation rights. We prohibit the recycling of shares we reacquire
 pursuant to our withholding obligations in connection with a stock option or SAR or as consideration for the exercise of a stock option or
 SAR and such reacquired shares will not become available for issuance under the Amended 2011 Plan.

Vote Required

At the 2021 Annual Meeting, we are asking the stockholders to approve the Amended 2011 Plan. The affirmative vote of the holders of a majority of the shares present and entitled to vote either in person or by proxy is required to approve the Amended 2011 Plan.

THE BOARD OF DIRECTORS RECOMMENDS VOTING "FOR" THE APPROVAL OF THE AMENDED 2011 PLAN.

Additional Information

If you have already returned your proxy card or voted over the internet or by telephone, you do not need to vote again unless you wish to change your vote. Your vote will be tabulated as you instructed. If you have not yet voted, please do so as soon as possible by following the instructions set forth in the Proxy Statement. If you have already returned your proxy card or already voted over the internet or by telephone and wish to change your vote in view of the supplemental information contained herein, you may do so by following the instructions below. You may vote on all the proposals by submitting a proxy card or submitting a proxy via the internet or by telephone by following the procedures previously sent to you. Votes already cast by stockholders will remain valid and will be voted at the 2021 Annual Meeting unless changed or revoked.

How do I vote on Proposal No. 2 if I have not yet voted?

For Proposal No. 2, you may vote "FOR" or "AGAINST", or abstain from voting.

The procedures for voting are fairly simple:

Stockholder of Record: Shares Registered in Your Name. If you are a stockholder of record, you may vote at the virtual 2021 Annual Meeting, vote by proxy on the internet, vote by proxy over the telephone or vote by proxy by requesting a proxy card in the mail. Whether or not you plan to attend the virtual 2021 Annual Meeting, we urge you to vote by proxy to ensure your vote is counted. You may still attend the virtual 2021 Annual Meeting and vote at the meeting if you have already voted by proxy.

- To vote in person, attend the virtual 2021 Annual Meeting and cast your vote by clicking on the "Voting" button in the bottom right-hand corner of the virtual meeting platform.
- To vote via the internet, go to "www.voteproxy.com" to complete an electronic proxy card and follow the steps outlined on the secured website. Your vote must be received by 11:59 P.M. Eastern Time on June 1, 2021, to be counted.
- To vote by telephone, dial toll-free +1-800-690-6903 within the United States, Canada and Puerto Rico using a touch-tone phone and follow the instructions provided by the recorded message. Your vote must be received by 11:59 P.M. Eastern Time on June 1, 2021, to be counted.
- To vote by mail, you may do so by first requesting printed copies of the proxy materials by mail and then filling out the proxy card and sending it back in the envelope provided. If you return your signed proxy card to us before the 2021 Annual Meeting, we will vote your shares as you direct.

Beneficial Owner: Shares Registered in the Name of a Broker or Bank. If you are a beneficial owner of shares registered in the name of your broker, bank or other nominee, you should have received a Notice containing voting instructions from that organization rather than from Ionis. Simply follow the voting instructions in the Notice to ensure that your vote is counted. To vote at the virtual 2021 Annual Meeting, log in to the virtual meeting using your control number and cast your vote by clicking on the "Voting" button in the bottom right-hand corner of the virtual meeting platform.

How do I change my vote on Proposal No. 2 if I have already submitted my proxy?

You can revoke your proxy before the final vote at the 2021 Annual Meeting. If you are the record holder of your shares, you may revoke your proxy in any one of four ways:

- You may grant a subsequent proxy by telephone or through the internet, provided that your subsequent proxy must be received by 11:59 P.M. Eastern Time on June 1, 2021;
- You may submit another properly completed proxy bearing a later date, which must be received before the final vote;
- You may send a written notice of revocation to our principal executive offices at 2855 Gazelle Court, Carlsbad, CA 92010 USA, attention Patrick O'Neil, Corporate Secretary, which must be received before the final vote; or
- You may attend the virtual 2021 Annual Meeting and re-cast your vote by clicking on the "Voting" button in the bottom right-hand corner of the virtual meeting platform. Simply attending the virtual 2021 Annual Meeting will not, by itself, revoke your proxy.

Your most current proxy card or internet proxy or telephone proxy timely provided to us is the one that is counted.

If your shares are held by your broker or bank as a nominee or agent, you should follow the instructions provided by your broker or bank.

Only stockholders of record at the close of business on the record date, April 5, 2021, are entitled to vote the shares for which they are stockholders of record on that date at the 2021 Annual Meeting, or any postponement or adjournment of the 2021 Annual Meeting.

Our definitive proxy statement, including these additional proxy materials and our Annual Report on Form 10-K/A for the fiscal year ended December 31, 2020, as filed with the Securities and Exchange Commission, are available at https://ir.ionispharma.com/financial-information/sec-filings.