# SCHEDULE 14A

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

Filed by the Registrant ☒

Filed by a party other than the Registrant ☐

Check 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)

Payment of Filing Fee (Check all boxes that apply):

☒ No fee required

☐ Fee paid previously with preliminary materials

☐ Fee computed on table in exhibit required by Item 25(b) per Exchange Act Rules 14a-6(i)(1) and 0-11



# NOTICE OF 2026 ANNUAL MEETING OF STOCKHOLDERS AND PROXY STATEMENT

Dear Stockholders,

I am pleased to invite you to Ionis Pharmaceuticals, Inc.'s 2026 Annual Meeting of Stockholders to be held on June 4, 2026. The Annual Meeting will be held in a virtual meeting format only, via live webcast on the Internet, with no physical in-person meeting. You can attend and participate in the Annual Meeting online by visiting www.virtualshareholdermeeting.com/IONS2026, where you will be able to listen to the meeting live, submit questions and vote. As always, we encourage you to vote your shares prior to the Annual Meeting.

This document includes the agenda for this year's Annual Meeting and the Proxy Statement. We will cover the formal items on the agenda during the Annual Meeting. Following the formal Annual Meeting, we will review the major developments of the past year and our plans for 2026 via webcast. You can find information regarding how to join the webcast on our website at ir.ionis.com. The Proxy Statement explains the matters we will discuss in the meeting and provides additional information about us.

Your vote is very important. Whether or not you plan to attend the meeting, please vote your shares as soon as possible to ensure your representation at the meeting. We are distributing our proxy materials under a Securities and Exchange Commission rule that allows us to furnish proxy materials to our stockholders over the Internet rather than in paper form. We believe this method of distribution reduces our environmental impact and costs without hindering our stockholders' timely access to such important material. As a result, if you are a stockholder of record (that is, if your stock is registered with us in your own name) you will receive a Notice Regarding the Availability of Proxy Materials in the mail, which contains instructions on how to access our proxy materials and vote electronically through the Internet or to request printed proxy materials so you may vote by telephone or mail.

If your shares are registered in the name of a broker or other nominee, that nominee will forward the Notice Regarding the Availability of Proxy Materials to you and you can direct that nominee to vote your shares. Alternatively, if your nominee participates in a program provided through Broadridge Financial Solutions, Inc. that allows you to vote by telephone or through the Internet, your nominee will send you a voting form with telephone and Internet voting instructions.

If you plan to attend the virtual meeting and prefer to vote online, you may still do so even if you have already returned your proxy.

**PLEASE NOTE, HOWEVER, THAT IF A BROKER, BANK OR OTHER NOMINEE HOLDS YOUR SHARES OF RECORD AND YOU WISH TO VOTE AT THE MEETING, *YOU MUST OBTAIN A PROXY ISSUED IN YOUR NAME* FROM THE BROKER, BANK OR OTHER NOMINEE.**

In this document, unless the context requires otherwise, the words "Ionis," "Company," "we," "our" and "us" refer only to Ionis Pharmaceuticals, Inc. and its subsidiaries and not to any other person or entity.

Sincerely,

*Patrick R. O'Neil*
Corporate Secretary

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## NOTICE OF 2026 ANNUAL MEETING OF STOCKHOLDERS

| | |
|---|---|
| Date: | June 4, 2026 |
| Time: | 2:00 p.m. Pacific Time |
| Place: | Online only: www.virtualshareholdermeeting.com/IONS2026 |
| Record Date: | April 7, 2026. If you were an Ionis stockholder of record at the close of business on April 7, 2026, you may vote at the Annual Meeting. |
| Items of Business: | We are holding the Annual Meeting for the following purposes, as more fully described in the accompanying Proxy Statement: |

1. To elect our nominees, Spencer R. Berthelsen and Joan E. Herman, to our Board of Directors to serve as directors for a three-year term;
2. To make an advisory vote on executive compensation;
3. To approve an amendment of the Amended and Restated Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan to increase the aggregate number of shares of common stock authorized for issuance under such plan by 9,500,000 shares to an aggregate of 52,000,000 shares;
4. To approve an amendment of the Amended and Restated 2000 Employee Stock Purchase Plan to increase the number of shares of common stock authorized for purchase under such plan by 750,000 shares and remove the termination date of the plan;
5. To ratify the Audit Committee's selection of Ernst & Young LLP as independent auditors for our 2026 fiscal year; and
6. To transact any other business that may be properly presented at the Annual Meeting.

| | |
|---|---|
| Virtual Meeting: | To participate in the Annual Meeting, please visit www.virtualshareholdermeeting.com/IONS2026. You will need the 16-digit control number included on your Notice of Internet Availability of Proxy Materials or your proxy card or voting instruction form that accompanied your proxy materials. Stockholders will be able to vote and submit questions during the Annual Meeting. |
| Voting: | WHETHER OR NOT YOU EXPECT TO ATTEND THE MEETING, PLEASE VOTE BY TELEPHONE OR INTERNET BY FOLLOWING THE INSTRUCTIONS INCLUDED IN THIS PROXY STATEMENT AND YOUR NOTICE REGARDING THE AVAILABILITY OF PROXY MATERIALS OR PROXY CARD. ALTERNATIVELY, YOU MAY REQUEST A WRITTEN PROXY STATEMENT, AND COMPLETE, DATE, SIGN AND RETURN YOUR PROXY AS PROMPTLY AS POSSIBLE TO ENSURE YOUR REPRESENTATION AT THE MEETING. IF YOU RECEIVE YOUR PROXY MATERIALS BY MAIL, WE WILL INCLUDE A RETURN ENVELOPE (WHICH IS POSTAGE PREPAID IF MAILED IN THE UNITED STATES) FOR THAT PURPOSE. EVEN IF YOU HAVE GIVEN YOUR PROXY, YOU MAY STILL VOTE AT THE VIRTUAL MEETING VIA LIVE WEBCAST. PLEASE NOTE, HOWEVER, THAT IF YOUR SHARES ARE HELD OF RECORD BY A BROKER, BANK OR OTHER NOMINEE AND YOU WISH TO VOTE AT THE MEETING, YOU MUST OBTAIN FROM THE BROKER, BANK OR OTHER NOMINEE A PROXY ISSUED IN YOUR NAME. |

By order of the Board of Directors,

*Patrick R. O'Neil*
Corporate Secretary
Carlsbad, California
April 23, 2026

**ALL STOCKHOLDERS ARE CORDIALLY INVITED TO ATTEND THE VIRTUAL MEETING VIA LIVE WEBCAST.**

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**IONIS PHARMACEUTICALS, INC.**
**2855 Gazelle Court**
**Carlsbad, CA 92010**

# PROXY STATEMENT
# FOR THE 2026 ANNUAL MEETING OF STOCKHOLDERS

**To Be Held on June 4, 2026**

## QUESTIONS AND ANSWERS ABOUT THESE PROXY MATERIALS AND VOTING

### Why did I receive a Notice Regarding the Availability of Proxy Materials on the Internet?

The Board of Directors (the "***Board***") of Ionis Pharmaceuticals, Inc. (the "***Company***") is soliciting your proxy to vote at the 2026 Annual Meeting of Stockholders, including at any adjournments or postponements of the meeting. We are distributing our Notice of Annual Meeting and Proxy Materials (the "***Notice***") by mail using the Notice and Access procedures established by the United States Securities and Exchange Commission (the "***SEC***"). The Notice is important because it contains a control number and instructions that will allow you to access our proxy materials and vote electronically through the Internet or to request printed proxy materials so you may vote by telephone or mail. Your vote is very important. Whether or not you plan to attend the meeting, please be sure to vote your shares as soon as possible to ensure your representation at the meeting. All stockholders will have the ability to access the proxy materials on the website referred to in the Notice or request to receive a printed set of the proxy materials. You can find instructions on how to access the proxy materials over the Internet or to request a printed copy in the Notice.

We intend to mail the Notice on April 23, 2026 to all stockholders of record entitled to vote at the Annual Meeting.

### Will I receive any other proxy materials by mail?

We may send you a proxy card, along with a second Notice, on or after May 5, 2026.

### Where and when is the Annual Meeting?

The Annual Meeting will be held on Thursday, June 4, 2026, at 2:00 p.m. Pacific Time sharp. The Annual Meeting will be held in a virtual meeting format only, via live webcast on the Internet, with no physical in-person meeting. To participate, vote or submit questions during the Annual Meeting via live webcast, please visit www.virtualshareholdermeeting.com/IONS2026.

If you cannot attend, please note that we will make a webcast of the presentation that follows the Annual Meeting available on the day of the meeting and for a limited time following the meeting at www.ionis.com.[1]

If you plan to attend the virtual meeting and prefer to vote online, you may still do so even if you have already returned your proxy.

### How do I attend the Annual Meeting?

We will be hosting the Annual Meeting via live webcast on the Internet. **You will not be able to attend the Annual Meeting in person.** All stockholders at the close of business on April 7, 2026 can listen to and participate in the Annual Meeting live via the internet at www.virtualshareholdermeeting.com/IONS2026. **The webcast will begin at 2:00 p.m. Pacific Time sharp on June 4, 2026. Stockholders may vote and submit questions while connected to the Annual Meeting on the Internet.** A summary of the information you need to attend the Annual Meeting online is provided below.

### What do I need in order to be able to participate in the Annual Meeting online?

You will need the 16-digit control number included on your Notice of Internet Availability of Proxy Materials, proxy card or voting instruction form that accompanied your proxy materials to be able to vote your shares or submit questions during the virtual Annual Meeting. **Instructions on how to connect and participate in the Annual Meeting via the Internet, including how to demonstrate proof of stock ownership, are posted at www.virtualshareholdermeeting.com/IONS2026.**

[1] Any information that is included on or linked to our website is not part of this Proxy Statement or any registration statement or report that incorporates this Proxy Statement by reference.

### What if I have technical difficulties or trouble accessing the live webcast of the Annual Meeting?

If you encounter any difficulties accessing the live webcast of the Annual Meeting or during the Annual Meeting, please call the telephone number that is listed at www.virtualshareholdermeeting.com/IONS2026 for assistance. If you misplace the 16-digit control number that is required to enter the Annual Meeting webcast and are a stockholder of record, operators providing assistance at this telephone number will be able to provide it to you. However, if you need your 16-digit control number and hold your shares in an account at a brokerage firm, bank, dealer, or other similar organization, you must contact that organization to obtain your 16-digit control number prior to the Annual Meeting.

### Who can attend and vote at the Annual Meeting?

Only stockholders at the close of business on April 7, 2026 may attend and vote at the Annual Meeting. On this record date, there were 165,102,174 shares of common stock outstanding and entitled to vote.

*Stockholder of Record: Shares Registered in Your Name*

If on April 7, 2026 your shares were registered directly in your name with our transfer agent, Equiniti Trust Company, then you are a stockholder of record. As a stockholder of record, you may vote online at the virtual meeting or vote by proxy over the telephone, by mail, or the Internet as instructed under the section below titled "How do I vote?" Whether or not you plan to attend the meeting, we urge you to fill out and return the proxy card or vote over the telephone or Internet to ensure your vote is counted.

*Beneficial Owner: Shares Registered in the Name of a Broker or Bank*

If on April 7, 2026 you did not own shares in your name, but rather in an account at a brokerage firm, bank, dealer or other similar organization, then you are the beneficial owner of shares held in "street name" and that organization is forwarding the Notice to you. The organization holding your account is the stockholder of record for purposes of voting at the Annual Meeting. As a beneficial owner, you may direct your broker or other agent regarding how to vote the shares in your account. If your shares are registered in the name of a broker or other nominee, your nominee may be participating in a program provided through Broadridge Financial Solutions, Inc. ("***Broadridge***") that also allows you to vote by telephone or through the Internet. If so, the voting form your nominee sends you will provide telephone and Internet instructions. You are also invited to attend the virtual Annual Meeting via live webcast.

**PLEASE NOTE, HOWEVER, THAT IF A BROKER, BANK OR OTHER NOMINEE HOLDS YOUR SHARES OF RECORD AND YOU WISH TO VOTE AT THE MEETING, *YOU MUST OBTAIN A PROXY ISSUED IN YOUR NAME* FROM THE BROKER, BANK OR OTHER NOMINEE.**

### What am I voting on?

The following matters are scheduled for a vote:

1. Proposal 1: elect our nominees, Spencer R. Berthelsen and Joan E. Herman, to our Board of Directors to serve as directors for a three-year term;
2. Proposal 2: make an advisory vote on executive compensation;
3. Proposal 3: approve an amendment of the Amended and Restated Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan to increase the aggregate number of shares of common stock authorized for issuance under such plan by 9,500,000 shares to an aggregate of 52,000,000 shares;
4. Proposal 4: approve an amendment of the Amended and Restated 2000 Employee Stock Purchase Plan to increase the number of shares of common stock authorized for purchase under such plan by 750,000 shares and remove the termination date of the plan; and
5. Proposal 5: ratify the Audit Committee's selection of Ernst & Young LLP as independent auditors for our 2026 fiscal year.

### What if another matter is properly brought before the meeting?

The Board knows of no other matters that will be presented for consideration at the Annual Meeting. If any other matters are properly brought before the meeting, the persons named in the accompanying proxy intend to vote on those matters in accordance with their best judgment. Discretionary authority for them to do so is provided for in the proxy card.

## How do I vote?

You may vote in one of the following ways:

1. vote through the Internet by following the instructions included with your Notice or proxy card;
2. vote by telephone by following the instructions included with your proxy card if you have received proxy materials electronically or by mail;
3. vote by mail by completing, signing, dating, and returning your proxy card in the postage paid envelope provided; or
4. vote during the virtual Annual Meeting by following the instructions posted at www.virtualshareholdermeeting.com/IONS2026.

The procedures for voting are fairly simple:

*For Shares Registered in Your Name:*

If you are a stockholder of record, you may go to www.proxyvote.com to vote your shares through the Internet up until 11:59 p.m. Eastern Time on June 3, 2026. The votes represented by your proxy will be displayed on the computer screen and you will be prompted to submit or revise your votes as desired.

To vote your shares by telephone, you must first request that we send proxy materials to you by following the instructions included in your Notice. Once you have received your proxy materials, you may vote using a touch-tone telephone by calling 1-800-690-6903 up until 11:59 p.m. Eastern Time on June 3, 2026, and following the recorded instructions. Please have your proxy card available at the time you vote.

To vote using the proxy card, simply complete, sign and date the proxy card that may be delivered to you and return it promptly in the envelope provided. If we receive your signed proxy card before the Annual Meeting, we will vote your shares as you direct.

*For Shares Registered in the Name of a Broker or Bank:*

If your broker or bank holds your shares in "street name," you will need to obtain a proxy form from the institution that holds your shares and follow the instructions included on that form regarding how to instruct your broker to vote your shares. If you do not give instructions to your broker, your broker can vote your shares with respect to "discretionary" items, but not with respect to "non-discretionary" items. Discretionary items are proposals considered routine under the rules of the New York Stock Exchange ("***NYSE***") on which a broker may vote shares held in street name in the absence of your voting instructions. While Ionis is listed with the Nasdaq Stock Market ("***Nasdaq***"), NYSE rules affect how brokers licensed by the NYSE can vote in a director election of any company, including companies listed with Nasdaq. The proposal to ratify Ernst & Young LLP as independent auditors is a discretionary item. Proposals 1 through 4 regarding (1) the election of directors, (2) an advisory vote on our executive compensation, (3) approval of an amendment of the Amended and Restated Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan to increase the aggregate number of shares of common stock authorized for issuance under such plan by 9,500,000 shares to an aggregate of 52,000,000 shares, and (4) approval of an amendment of the Amended and Restated 2000 Employee Stock Purchase Plan to increase the number of shares of common stock authorized for purchase under such plan by 750,000 shares and remove the termination date of the plan, are non-discretionary items. If you do not give your broker instructions for a non-discretionary item your broker cannot vote your shares, which will result in what is commonly referred to as a "broker non-vote." Broker non-votes will have no effect.

A number of brokers and banks are participating in a program provided by Broadridge that allows proxies to vote shares by means of the telephone and Internet. If your shares are held in an account with a broker or bank participating in the Broadridge program, you may vote your shares by telephone or through the Internet by having the voting form in hand and calling the number or going to the website indicated on the form and following the instructions.

## What if I return a proxy card or otherwise vote but do not make specific choices?

If you return a signed and dated proxy card or otherwise vote without marking voting selections, one of the individuals named on your proxy card will vote your shares as follows:

1. "For" the election of the nominees for director named in the Proxy Statement;
2. "For" an advisory vote on our executive compensation;

3. "For" the approval of an amendment of the Amended and Restated Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan to increase the aggregate number of shares of common stock authorized for issuance under such plan by 9,500,000 shares to an aggregate of 52,000,000 shares;

4. "For" the approval of an amendment of the Amended and Restated 2000 Employee Stock Purchase Plan to increase the number of shares of common stock authorized for purchase under such plan by 750,000 shares and remove the termination date of the plan; and

5. "For" the ratification of the Audit Committee's selection of Ernst & Young LLP as independent auditors for our 2026 fiscal year.

If any other matter is properly presented at the meeting, one of the individuals named on your proxy card will vote your shares using their best judgment.

### Who is paying for this proxy solicitation?

Our Board is soliciting your proxy to vote at the Annual Meeting. We will bear the entire cost of soliciting proxies, including preparing, assembling, making available on the Internet and printing and mailing this Proxy Statement, the proxy card and any additional information furnished to stockholders. We will furnish copies of solicitation materials to banks, brokerage houses, fiduciaries and custodians holding our common stock in "street name" on behalf of beneficial owners of such shares. We may reimburse persons representing beneficial owners of our common stock for their costs of forwarding solicitation materials to such beneficial owners. Our directors, officers or other employees may supplement original solicitation of proxies by telephone, electronic mail, or personal solicitation. We will not pay our directors, officers, or employees any additional compensation for soliciting proxies. However, please be aware that you must bear any costs associated with your Internet service, such as usage charges from Internet access providers or telephone companies. In addition, we have hired Alliance Advisors, LLC to perform solicitation services. In 2026, we expect to pay Alliance Advisors, LLC a fee of $26,000 plus reasonable expenses for these services.

### What does it mean if I receive more than one Notice?

If you receive more than one Notice or proxy card, your shares are registered in more than one name or are registered in different accounts. Please complete, sign, date and return *each* separate proxy card or vote by telephone or through the Internet by following the instructions included with *each* Notice or proxy card to properly vote your shares.

### Can I change my vote after submitting my proxy?

Yes. Once you have submitted your proxy by mail, Internet, or telephone, you may revoke it at any time before we exercise it at the Annual Meeting. You may revoke your proxy by any one of the following four ways:

1. you may mail another proxy marked with a later date;

2. you may revoke it through the Internet;

3. you may notify our corporate secretary in writing sent to 2855 Gazelle Court, Carlsbad, California 92010 that you wish to revoke your proxy before the Annual Meeting takes place; or

4. you may vote during the virtual Annual Meeting. *Attending* the meeting *will not*, by itself, revoke a proxy.

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

### When are stockholder proposals due for next year's Annual Meeting?

If you have a proposal that you would like us to include in our proxy materials for next year's Annual Meeting of Stockholders, you must send the proposal to us in writing by no later than December 24, 2026, and comply with all applicable requirements of Rule 14a-8 ("***Rule 14a-8***") promulgated under the Securities Exchange Act of 1934, as amended (the "***Exchange Act***"). Stockholders wishing to submit proposals or director nominations that are not to be included in such proxy materials for next year's Annual Meeting of Stockholders pursuant to Rule 14a-8 must do so no later than the close of business on February 4, 2027, as required by our bylaws. Stockholders should also review our bylaws, which contain additional requirements with respect to advance notice of stockholder proposals and director nominations. In addition to satisfying the foregoing requirements under our bylaws, stockholders who intend to solicit proxies in support of director nominees other than the Company's nominees must also comply with the additional requirements of Rule 14a-19(b).

### What is the quorum requirement?

A quorum of stockholders is necessary to hold a valid meeting. A quorum will be present at the meeting if at least a majority of the outstanding shares entitled to vote are represented at the meeting or by proxy. We will count your shares towards the quorum only if you submit a valid proxy vote (or one is submitted on your behalf by your broker, bank, or other nominee) or vote at the meeting. We will count abstentions and broker non-votes towards the quorum requirement.

If there is no quorum, either the chair of the meeting or the holders of a majority of shares present at the meeting or represented by proxy may adjourn the meeting to another date.

### How are votes counted?

Each share of our common stock you own entitles you to one vote. Your Notice and proxy card indicates the number of shares of our common stock you owned at the close of business on April 7, 2026. The inspector of elections will count votes for the meeting and will separately count "For" and "Against" votes, abstentions, and, if applicable, broker non-votes for Proposals 1-5. Abstentions will have no effect on Proposals 1, 3, and 4. Abstentions will count towards the vote total for Proposals 2 and 5 and will have the same effect as "Against" votes. Broker non-votes have no effect and the inspector of elections will not count them towards the vote total for Proposals 1-4.

### What are "broker non-votes"?

Broker non-votes occur when a beneficial owner of shares held in "street name" does not give instructions to the broker or nominee holding the shares as to how to vote on matters deemed "non-routine." If your broker holds your shares in "street name," and you do not give instructions to your broker, your broker can vote your shares with respect to "discretionary" items, but not with respect to "non-discretionary" items. The proposal to ratify Ernst & Young LLP as independent auditors is a discretionary item. Proposals 1 through 4 regarding (1) the election of directors, (2) an advisory vote on our executive compensation, (3) approval of an amendment of the Amended and Restated Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan to increase the aggregate number of shares of common stock authorized for issuance under such plan by 9,500,000 shares to an aggregate of 52,000,000 shares, and (4) approval of an amendment of the Amended and Restated 2000 Employee Stock Purchase Plan to increase the number of shares of common stock authorized for purchase under such plan by 750,000 shares and remove the termination date of the plan, are all non-discretionary items.

### How many votes are needed to approve each proposal?

1. Proposal 1: For the election of directors in an uncontested election, a director nominee must receive a majority of the votes cast in the election such that the number of shares voted "For" the nominee must exceed 50% of the votes cast with respect to that director. Only "For" and "Against" votes will affect the outcome. Abstentions and broker non-votes, if any, will have no effect.

2. Proposal 2: We will consider the advisory vote on the compensation of our executive officers to be approved if it receives "For" votes from a majority of the holders of shares present or represented by proxy and entitled to vote on the matter. If you "Abstain" from voting, it will have the same effect as an "Against" vote. Broker non-votes, if any, will have no effect.

3. Proposal 3: Pursuant to the rules of the Nasdaq Stock Market, to be approved, the amendment of the Amended and Restated 2011 Equity Incentive Plan must receive "For" votes from the holders of a majority of the votes cast on the proposal, voting virtually or by proxy at the meeting. Abstentions and broker non-votes, if any, will have no effect.

4. Proposal 4: Pursuant to the rules of the Nasdaq Stock Market, to be approved, the amendment of the Amended and Restated 2000 Employee Stock Purchase Plan must receive "For" votes from the holders of a majority of the votes cast on the proposal, voting virtually or by proxy at the meeting. Abstentions and broker non-votes, if any, will have no effect.

5. Proposal 5: To be approved, the ratification of the selection of Ernst & Young LLP as our independent auditors for our 2026 fiscal year must receive "For" votes from a majority of the holders of shares present or represented by proxy and entitled to vote on the matter. If you "Abstain" from voting, it will have the same effect as an "Against" vote. Because brokers have discretionary authority to vote on the ratification of the selection of Ernst & Young LLP, we do not expect any broker non-votes in connection with the ratification.

### How can I find out the results of the voting at the Annual Meeting?

We will announce preliminary voting results at the Annual Meeting. In addition, we will publish final voting results in a current report on Form 8-K that we expect to file within four business days after the Annual Meeting. If final voting results are not available to us in time to file as part of a Form 8-K within four business days after the Annual Meeting, we intend to file a Form 8-K to publish preliminary results and, within four business days after we know the final results, file an additional Form 8-K to publish final results.

## How can I elect to receive materials for future Annual Meetings electronically?

We are pleased to offer to our stockholders the benefits and convenience of electronic delivery of Annual Meeting materials, including:

1. delivering the Proxy Statement, Annual Report on Form 10-K, and related materials by email to our stockholders;
2. stockholder voting online;
3. helping the environment by decreasing the use of paper documents;
4. reducing the number of bulky documents stockholders receive; and
5. reducing our printing and mailing costs associated with more traditional delivery methods.

We encourage you to conserve natural resources and to reduce printing and mailing costs by signing up for electronic delivery of our stockholder communications after you place your current vote at www.proxyvote.com.

## List of Shareholders

A list of stockholders entitled to vote at the Annual Meeting will be available for examination at our principal executive offices at the address listed above for a period of 10 days prior to the Annual Meeting.

# PROPOSAL 1

# ELECTION OF DIRECTORS

## Information about our Board

The Board is divided into three classes. Presently, the Board has ten members with two classes consisting of four directors each and one class consisting of two directors. Each class serves a three-year term and we hold elections each year at the Annual Meeting to elect the directors whose terms are expiring. Our Nominating, Governance and Review Committee of the Board reviews the Company's classified Board structure every year to evaluate whether it continues to be the appropriate structure for the Company. Following such evaluation, we believe maintaining this structure is critical at this time to enable us to execute on our new commercial strategy, which we believe will generate long-term sustainable value for stockholders.

In addition, the Board may elect a new director to fill any vacant spot, including a vacancy caused by an increase in the size of the Board. However, the Board believes it is important for our stockholders to ratify any member of the Board whom the Board appoints. As a result, whenever the Board appoints a new member, the Board will submit such new member's directorship for ratification or election at the next regularly scheduled Annual Meeting of Stockholders.

The Board represents the interests of our stockholders by overseeing the Chief Executive Officer and other executive officers in our operations. The Board's goal is to optimize long-term value by providing guidance and strategic oversight to Ionis' management on our stockholders' behalf.

## Information about the 2026 Elections

The class of directors with a term expiring at the Annual Meeting consists of four directors. As previously announced in our Current Report on Form 8-K filed with the SEC on March 9, 2026, B. Lynne Parshall and Joseph H. Wender are not seeking re-election at the Annual Meeting, and their terms as directors will end at the closing of the polls at the Annual Meeting. The Board has nominated the two remaining individuals in this class, Spencer R. Berthelsen and Joan E. Herman, for election at the Annual Meeting. Also as previously announced, Peter N. Reikes will be rejoining the Board following the Annual Meeting. Each of the nominees currently serves as one of our directors. Spencer R. Berthelsen and Joan E. Herman have each served as a director for the periods set forth in the table below.

| Name | Commencement of Ionis Directorship |
|---|---|
| Spencer R. Berthelsen | May 2002 |
| Joan E. Herman | June 2019 |

Dr. Berthelsen and Ms. Herman have been previously re-elected by our stockholders. If re-elected, Dr. Berthelsen and Ms. Herman will serve until the 2029 Annual Meeting or, in each case, until their respective successor is elected and has qualified, or until their earlier death, resignation or removal.

Our bylaws provide a majority vote standard for the election of directors in uncontested elections. In an uncontested election, the majority vote standard means that to be elected, a director nominee must receive a majority of the votes cast in the election such that the number of shares voted "For" the nominee must exceed 50% of the votes cast with respect to that director. The number of votes cast with respect to a director's election excludes abstentions and broker non-votes. In contested elections where the number of nominees exceeds the number of directors to be elected, the vote standard will be a plurality of the shares present or represented by proxy and entitled to vote.

If a nominee who already serves as a director is not elected, and no successor is elected, the director will offer to tender their resignation to the Board. The Nominating, Governance and Review Committee will make a recommendation to the Board on whether to accept or reject the resignation, or whether to take other action. The Board will act on the Nominating, Governance and Review Committee's recommendation and publicly disclose its decision and the rationale behind it within 90 days from the date of the certification of the election results. The director who tenders their resignation will not participate in the recommendation of the Nominating, Governance and Review Committee or in the Board's decision. If a nominee's failure to be elected at the Annual Meeting results in a vacancy on the Board, then the Board can fill the vacancy.

On March 3, 2026, the Nominating, Governance and Review Committee provided its recommendations to the Board for director nominees to stand for election at the Annual Meeting. Following such recommendations, the Board determined it would be in the best interests of Ionis and its stockholders to nominate Dr. Berthelsen and Ms. Herman to be re-elected as directors at the Annual Meeting. Below we provide a short biography for each nominee. Dr. Berthelsen and Ms. Herman have agreed to serve if re-elected, and we have no reason to believe that they cannot or will not serve. However, if they cannot or will not serve, the proxy holders may vote your proxy for another nominee proposed by the Board, or the Board may leave a vacancy on the Board or reduce the number of authorized directors.

## Board Skills Matrix

The following tables illustrate (i) the core skills the Nominating, Governance and Review Committee considers to be the most relevant to the Board's oversight role with respect to our business, and (ii) each director's skills in such areas indicated by check mark. The lack of a check mark for a particular item for a director does not mean the director lacks that skill; rather, a check mark indicates a specific area of focus or expertise for which the Board relies on such director. Additional information about each director's background, business experience and other matters, including a description of how each individual's experience qualifies the director to serve on the Board, is provided below beginning on the following page of this Proxy Statement.

| | |
|---|---|
| **Industry Experience** | Provides the Board with industry knowledge to support effective oversight of, and contributions to, our business and strategy |
| **Executive/Leadership Experience** | Equips directors to successfully advise on and oversee the Company's performance and represent stockholders' interests |
| **Corporate Governance and Public Company Board Experience** | Ensures directors have the background and knowledge to perform oversight and governance roles |
| **Accounting, Financial or Investment Experience** | Enables our directors to analyze our financial statements, oversee our capital structure and consider financial transactions |
| **Scientific, Research or Development Experience** | Facilitates the constant improvement of our science and technology to enable us to continue to drive innovation in RNA therapies |
| **Commercial, Marketing, Reimbursement or Sales Experience** | Ensures we have appropriate Board expertise to continue to advance our commercial strategy |

| Director Skills and Qualifications | Spencer R. Berthelsen | Allene M. Diaz | Michael Hayden | Joan E. Herman | Joseph Klein III | Joseph Loscalzo | Brett P. Monia | B. Lynne Parshall | Joseph H. Wender | Michael Yang |
|---|---|---|---|---|---|---|---|---|---|---|
| **Industry Experience** | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| **Executive/Leadership Experience** | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| **Corporate Governance and Public Company Board Experience** | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ | ✓ |
| **Accounting, Financial or Investment Experience** | | ✓ | ✓ | ✓ | ✓ | | ✓ | ✓ | ✓ | ✓ |
| **Scientific, Research or Development Experience** | ✓ | ✓ | ✓ | | | ✓ | ✓ | ✓ | | ✓ |
| **Commercial, Marketing, Reimbursement or Sales Experience** | | ✓ | | ✓ | | | ✓ | ✓ | | ✓ |

## Biographies of the Nominees for Election for a Three-Year Term Expiring at the 2029 Annual Meeting

***Spencer R. Berthelsen***, M.D., age 73[2], has served as a director of Ionis since May 2002. Dr. Berthelsen practiced Internal Medicine with the Kelsey Seybold Clinic, a 400-physician medical group based in the Texas Medical Center in Houston, until March 2017. Dr. Berthelsen began at Kelsey Seybold in 1980 and served in various senior leadership positions throughout his nearly four-decade career at the clinic, including Chairman of the Department of Internal Medicine, Medical Director and Managing Director. He also served as Chairman of its board of directors from October 2001 through April 2016. He has served as Clinical Professor of Medicine at both Baylor College of Medicine and The University of Texas Health Science Center. Previously, Dr. Berthelsen served on the boards of the Texas Academy of Internal Medicine and the Caremark National Pharmacy and Therapeutics Committee from 1999 through 2005.

The Board believes Dr. Berthelsen is uniquely suited to serve on the Board because of his experience advising a large multispecialty group practice and almost 40 years of experience as a practicing physician.

***Joan E. Herman***, age 72, has served as a director of Ionis since June 2019. Since 2008, Ms. Herman has served as President and Chief Executive Officer of Herman & Associates, a management consulting firm that specializes in advising private equity firms investing in healthcare. She has experience leading healthcare and payor companies, serving in several executive positions at Elevance (formerly Anthem, which was formerly WellPoint), including as President and Chief Executive Officer of several different business units. Ms. Herman also served as a Senior Vice President of Phoenix Life Insurance Company. Since January 2013, Ms. Herman has served on the board of directors of Encompass Health. Ms. Herman also serves on the board of managers of Fifth Avenue Private Equity 17 and Fifth Avenue Private Equity 18. She previously served on the boards of both Convergys and AARP Services, Inc.

The Board believes Ms. Herman is uniquely suited to serve on the Board because of her experience leading healthcare and payor companies. Ms. Herman also brings valuable cybersecurity experience to the Board through her cybersecurity certification from the National Association of Corporate Directors ("***NACD***").

**THE BOARD UNANIMOUSLY RECOMMENDS A VOTE "FOR" THE ELECTION OF THE ABOVE NOMINEES.**

## Biographies of the Directors Not Seeking Re-Election

***B. Lynne Parshall***, age 72, has served as a director of Ionis since September 2000. Ms. Parshall is CEO of Lyme Pinnacle Consulting, which provides strategic advisory services to biotechnology companies. Ms. Parshall was a Senior Strategic Advisor to Ionis from January 2018 to December 2022. Previously she served as our Chief Operating Officer from December 2007 through January 2018 and as our Chief Financial Officer from June 1994 through December 2012. She also served as our Corporate Secretary through 2014 and served with the Company in various executive roles from November 1991 through December 2022. Prior to joining Ionis, Ms. Parshall practiced law at Cooley LLP, outside counsel to Ionis, where she was a partner from 1986 to 1991. Ms. Parshall is a member of the American Bar Association. Ms. Parshall has served on the boards of directors of Foghorn Therapeutics Inc, a public biopharmaceutical company, since August 2022, Cytokinetics, Inc., a public biopharmaceutical company, since February 2013, and Akcea Therapeutics, Inc., from January 2015 until the completion of the Company's merger with Akcea Therapeutics, Inc. (the "***Akcea Merger***"). Ms. Parshall also serves on the Board of Directors of several private biotechnology companies.

Ms. Parshall is not seeking re-election at the 2026 Annual Meeting of Stockholders. Ionis thanks Ms. Parshall for her 35 years of service to the Company as a former executive officer and Board member.

***Joseph H. Wender***, age 81, has served as a director of Ionis since January 1994 and our Independent Lead Director since December 2020. Mr. Wender began with Goldman, Sachs & Co. in 1971 and became a General Partner of that firm in 1982, where he headed the Financial Institutions Group for over a decade. Since January 2022 he has been a Senior Consultant to Goldman Sachs & Co., from January 2019 to December 2021 he was an Advisory Director to Goldman Sachs & Co. and from January 2008 to December 2018 was a Senior Consultant to Goldman Sachs & Co. He is a former Independent Trustee of the Schwab Family of Funds and director of Grandpoint Capital, a bank holding company. Mr. Wender also is co-CEO and partner of Colgin Cellars. Mr. Wender was a director of Outfront Media, a lessor of advertising space on out-of-home advertising structures from 2014 to 2025.

Mr. Wender is not seeking re-election at the 2026 Annual Meeting of Stockholders. Ionis thanks Mr. Wender for his 32 years of service to the Company as a Board member.

[2] The ages of all our directors are as of March 1, 2026.

## Biographies of the Directors Whose Terms Expire at the 2027 Annual Meeting

***Brett P. Monia***, Ph.D., age 64, has served as a director of Ionis since March 2019. Dr. Monia was promoted to Chief Executive Officer in January 2020. From January 2018 to December 2019, Dr. Monia served as our Chief Operating Officer, from January 2012 to January 2018, as our Senior Vice President, Drug Discovery, from February 2009 to January 2012, as our Vice President, Drug Discovery, and from October 2000 to February 2009, as our Vice President, Preclinical Drug Discovery. From October 1989 to October 2000, he held various positions within our Molecular Pharmacology department. Dr. Monia has served on the board of directors of Cognition Therapeutics, Inc., a public clinical stage neuroscience company, since October 2020.

The Board believes Dr. Monia is uniquely suited to serve on the Board primarily because, as an executive officer of the Company since 2012 and a founder of Ionis, he has dedicated more than 35 years to discovering and developing RNA-based drugs. Dr. Monia is the inventor on over 100 issued patents and has published more than 200 scientific manuscripts.

***Michael Yang***, age 64, has served as a director of Ionis since December 2023. Mr. Yang served as President and Chief Executive Officer of ViaCyte, Inc., a regenerative medicine company focused on the discovery, development, and commercialization of novel cell replacement therapies to treat human diseases, from February 2021 until it was acquired by Vertex Pharmaceuticals in October 2022. From March 2017 to February 2021, Mr. Yang served as Executive Vice President and Chief Commercial Officer of Acadia Pharmaceuticals Inc. Mr. Yang joined Acadia from Janssen Pharmaceutical Companies of Johnson & Johnson, where he served as President of Janssen Biotech Inc. and was responsible for building Janssen's U.S. Immunology business. Mr. Yang began his career at Johnson & Johnson in 1997 and held numerous senior commercial positions such as President, CNS where he was responsible for growing the anti-psychotic long-acting therapy portfolio. His broad background of commercialization and general management experience also includes roles as the Worldwide General Manager of the medical device companies of Therakos, Inc and Veridex, LLC, where he launched new platforms, expanded global revenues and diversified the product lines. Prior to that, Mr. Yang was Vice President of Sales and Marketing, Oncology at Ortho Biotech Inc. Mr. Yang currently serves on the board of directors of Pacira Pharmaceuticals, Inc. and previously served on the board of ViaCyte as well as Akcea Therapeutics, Inc. from September 2019 until the completion of the Akcea Merger.

The Board believes Mr. Yang is uniquely suited to serve on the Board because of his extensive strategic and operational experience in the pharmaceutical, medical device and diagnostic markets and his broad commercial and general management experience across multiple therapeutic categories, lifecycle stages and commercial environments.

## Biographies of the Directors Whose Terms Expire at the 2028 Annual Meeting

***Allene M. Diaz***, age 61, has served as a director of Ionis since June 2021. Since 2022 Ms. Diaz has served as a Senior Advisor to Bain Capital Life Sciences, a venture capital firm based in Boston, Massachusetts, and since 2020, she has led AMD Consulting, a new product strategy and portfolio management consulting practice based in Tampa, FL. Previously, Ms. Diaz served as Senior Vice President, Research and Development Portfolio Management at GlaxoSmithKline, a global pharmaceutical company based in Brentwood, UK, from September 2019 through June 2020 and as Senior Vice President, Global Commercial Development and Program Strategy at TESARO Inc., a biotechnology company based in Waltham, MA, from May 2015 through August 2019. Prior to that she held a variety of commercial leadership roles in the Merck Serono and EMD Serono divisions of Merck KGaA. Earlier in her career, Ms. Diaz held management, operating, sales, and medical affairs roles at various biopharmaceutical companies, including Pfizer, Parke-Davis, Biogen, and Amylin Pharmaceuticals. She has contributed to the global development, launch or commercialization of multiple transformative products across several therapeutic areas. Ms. Diaz served on the board of directors of Mersana Therapeutics from March 2021 to January 2026. Ms. Diaz served on the board of directors of Allena Pharmaceuticals from April 2019 to September 2022, BCLS Acquisition Corporation from October 2020 to October 2022, and Erytech Pharma SA from September 2016 to September 2019.

The Board believes Ms. Diaz is uniquely suited to serve on the Board primarily because of her deep expertise in product development, commercial strategy, market access, and portfolio management.

***Michael Hayden***, CM, OBC, MB, ChB, Ph.D., FRCP(C), FRSC, age 74, has served as a director of Ionis since September 2018. Dr. Hayden has been Chief Executive Officer and director of Prilenia Therapeutics, a private clinical stage biotech company, since September 2018. Dr. Hayden is also a Killam Professor at the University of British Columbia ("***UBC***"), the highest honor UBC can confer on any faculty member. In addition, he is an accomplished scientist and physician. He was the President of Global R&D and Chief Scientific Officer at Teva Pharmaceuticals from 2012 to 2017. During this time approximately 35 new products were approved in major markets with many for diseases of the central nervous system. In 2015 Teva R&D was recognized as one of the 100 most exciting innovators in the pharmaceutical industry by IDEA Pharma, and in 2017 Teva R&D ranked top of the industry for central nervous system development and clinical trial success rate by Pharma Intelligence. Dr. Hayden has founded five biotechnology companies and has been the recipient of numerous prestigious honors and awards, including being inducted into the Canadian Medical Hall of Fame and receiving the July 2012 Diamond Jubilee Medal on behalf of HRH Queen Elisabeth II. He has also received the Canada Gairdner Wightman Award. Dr. Hayden was awarded the Order of Canada, the Order of British Columbia, named Canada's Health Researcher of the Year by Canadian Institutes of Health Research, and received the Prix Galien Award in 2007. Dr. Hayden has also been awarded honorary degrees of science and medicine from the University of Alberta in 2009, University Gottingen in 2014, and University of Cape Town in 2023. Dr. Hayden served on the board of Aurinia Pharmaceuticals, Inc. until August 2021, Xenon Pharmaceuticals until June 2022, Oxford Biomedica until June 2024 and 89Bio until November 2025. Dr. Hayden currently serves on the board of AbCellera Biologics.

The Board believes Dr. Hayden is uniquely suited to serve on the Board because he has significant expertise in pharmaceutical research and development, both in academia and in commercial settings. In addition, Dr. Hayden has made substantial research contributions to advance treatments for brain diseases, which is particularly valuable as we grow our neurologic disease franchise, a key focus of ours. Dr. Hayden also serves as the Chair of our Medical and Science Committee, providing invaluable guidance on the key scientific and development issues facing our technology and medicines in development.

***Joseph "Skip" Klein, III***, age 64, has served as a director of Ionis since December 2005 and is Chairman of the Audit Committee. Mr. Klein is currently Managing Director of Gauss Capital Advisors, LLC, a financial consulting and investment advisory firm focused on biopharmaceuticals, which he founded in March 1998. From September 2003 to December 2008, Mr. Klein also served as a Venture Partner of Red Abbey Venture Partners, L.P., a life science private equity fund. From September 2001 to September 2002, Mr. Klein was a Venture Partner of MPM Capital, a healthcare venture capital firm. From June 1999 to September 2000 when it merged with WebMD Corporation, Mr. Klein served as Vice President, Strategy, for Medical Manager Corporation, a leading developer of physician office management information systems. For over nine years from 1989 to 1998, Mr. Klein was a health care investment analyst at T. Rowe Price Associates, Inc., where he was the founding portfolio manager of the T. Rowe Price Health Sciences Fund. Mr. Klein has served on the boards of directors of The Prospector Funds, Inc., an SEC Registered Investment Company that manages two no-load mutual funds, from September 2007 to September 2024, and Akcea Therapeutics, Inc., from September 2019 until the completion of the Akcea Merger. Mr. Klein has also served on the boards of private and non-profit entities.

The Board believes Mr. Klein is uniquely suited to serve on the Board and as Chairman of the Audit Committee because he is a Chartered Financial Analyst and has extensive public company, venture investment, board, and financial advisory expertise in the life sciences industry, including previously serving as chairman of the audit committee at several public biopharmaceutical companies.

***Joseph Loscalzo***, M.D., Ph.D., age 74, has served as a director of Ionis since February 2014 and as Chairman of the Board since June 2021. Dr. Loscalzo is the Hersey Distinguished Professor of the Theory and Practice of Medicine, the Samuel A. Levine Professor of Medicine at Harvard Medical School and Physician-in-Chief Emeritus at Brigham and Women's Hospital. Dr. Loscalzo is also a co-founder and member of the Scientific Advisory Board of Scipher Medicine, a private network medicine-based company matching patients with their most effective therapy. Dr. Loscalzo received his A.B. degree, *summa cum laude*, his Ph.D. in biochemistry, and his M.D. from the University of Pennsylvania. He completed his clinical training at Brigham and Women's Hospital and Harvard Medical School, where he served as Resident and Chief Resident in medicine and Fellow in cardiovascular medicine. Post-training, Dr. Loscalzo joined the Harvard faculty and staff at Brigham and Women's Hospital in 1984. He rose to the rank of Associate Professor of Medicine, Chief of Cardiology at the West Roxbury Veterans Administration Medical Center, and director of the Center for Research in Thrombolysis at Brigham and Women's Hospital. He joined the faculty of Boston University in 1994, first as Chief of Cardiology and, in 1997, Wade Professor and Chair of Medicine, Professor of Biochemistry, and director of the Whitaker Cardiovascular Institute. He returned to Harvard and Brigham and Women's Hospital in 2005. Since January 2016, Dr. Loscalzo has served on the board of directors of Leap Therapeutics, Inc., a public biopharmaceutical company.

The Board believes Dr. Loscalzo is uniquely suited to serve on the Board and as our Chairman primarily because of his extensive scientific expertise, including 32 years of research in the areas of vascular biology, thrombosis, and atherosclerosis, and practical knowledge as a practicing physician. Dr. Loscalzo's expertise and role as a leading cardiologist is particularly valuable as we advance and grow our cardiovascular franchise.

## Executive Officers

The following table sets forth certain information regarding our executive officers as of March 1, 2026:

| Name | Age | Position |
|---|---|---|
| Brett P. Monia, Ph.D. | 64 | Chief Executive Officer |
| Joseph T. Baroldi, M.B.A. | 48 | Executive Vice President, Chief Business Officer |
| Brian Birchler | 60 | Executive Vice President, Corporate Development and Operations |
| C. Frank Bennett, Ph.D. | 69 | Executive Vice President, Chief Scientific Officer |
| Shannon L. Devers, M.B.A. | 55 | Executive Vice President, Chief Human Resources Officer |
| Holly Kordasiewicz, Ph.D. | 46 | Executive Vice President, Chief Development Officer |
| Elizabeth L. Hougen | 64 | Executive Vice President, Finance and Chief Financial Officer |
| Kyle Jenne | 50 | Executive Vice President, Chief Global Product Strategy Officer |
| Patrick R. O'Neil, Esq. | 52 | Executive Vice President, Chief Legal Officer, General Counsel and Corporate Secretary |
| Eugene Schneider, M.D. | 54 | Executive Vice President, Chief Clinical Development and Operations Officer |
| Eric E. Swayze, Ph.D. | 60 | Executive Vice President, Research |

Set forth below is biographical information for each of our executive officers other than Dr. Monia, whose biographical information is provided above:

***Joseph T. Baroldi***, M.B.A., has served as Ionis' Executive Vice President, Chief Business Officer since January 2022. Prior to rejoining Ionis in 2022, Mr. Baroldi was the chief operating officer at Avidity Biosciences, a biotechnology company focused on oligonucleotide-based therapies. Prior to Avidity, Mr. Baroldi was Vice President, Business Development at Ionis, where he held several roles of increasing responsibility from 2009 to 2020. Mr. Baroldi has also held positions in strategic planning and scientific research for Gen-Probe Inc.

***Brian Birchler*** has served as Ionis' Executive Vice President, Corporate and Development Operations since March 2022. From April 2020 to March 2022, Mr. Birchler served as our Senior Vice President, Drug Development Operations. From September 2004 to April 2020, he served as our Vice President, Development Operations, and from March 2003 to September 2004, as our Vice President, Development Chemistry Operations. Mr. Birchler joined Ionis in 1995 and held roles of increasing responsibility in Development Chemistry Operations until his promotion to Vice President in March 2003. Prior to joining Ionis, Mr. Birchler was employed by CIBA Vision Corp. and Burroughs Wellcome Pharmaceuticals in various engineering, development and commercial positions.

***C. Frank Bennett***, Ph.D., has served as Ionis' Executive Vice President, Chief Scientific Officer since April 2020. In January 2020, Dr. Bennett was promoted to Chief Scientific Officer. From January 2006 to December 2019, Dr. Bennett served as Senior Vice President, Antisense Research. From June 1995 to January 2006, Dr. Bennett served as our Vice President, Research. From March 1993 to June 1995, he was Director, Molecular Pharmacology, and from May 1992 to March 1993, he was an Associate Director in our Molecular and Cellular Biology department. Prior to joining Ionis in 1989, Dr. Bennett was employed by SmithKline and French Laboratories in various research positions. He is a member of the board of directors of the Hereditary Disease Foundation.

***Shannon L. Devers***, M.B.A., has served as Ionis' Chief Human Resources Officer since September 2024. From April 2020 to September 2024, Ms. Devers served as our Senior Vice President, Human Resources. From August 2013 to March 2020, Ms. Devers served as our Vice President, Human Resources. Ms. Devers joined Ionis in 2001 as Senior Human Resources Manager. Prior to joining Ionis, Ms. Devers was employed by Target Corporation, Nike, Inc. and Taco Bell Corporation in various human resources roles.

***Holly Kordasiewicz***, Ph.D., has served as Ionis' Executive Vice President, Chief Development officer since December 2025. From December 2022 to December 2025, Dr. Kordasiewicz served as our Senior Vice President, Head of Neurology Research and Neurology Franchise, and from December 2019 to December 2022 as our Vice President, Neurology Research. Dr. Kordasiewicz joined Ionis in 2011 and was a member of the Neurology Research group until taking over leadership of the Neurology Research team in December 2019.

***Elizabeth L. Hougen*** has served as Ionis' Executive Vice President and Chief Financial Officer since April 2020. From January 2013 to March 2020, Ms. Hougen served as our Senior Vice President, Finance and Chief Financial Officer. From January 2007 to December 2012, Ms. Hougen served as our Vice President, Finance and Chief Accounting Officer and from May 2000 to January 2007, she served as our Vice President, Finance. Prior to joining Ionis in 2000, Ms. Hougen was Executive Director, Finance and Chief Financial Officer for Molecular Biosystems, Inc., a public biotechnology company. She is a member of the board of directors and audit committee chair for Artiva Biotherapeutics.

***Kyle Jenne*** has served as Ionis' Executive Vice President, Chief Global Product Strategy Officer since February 2024. Prior to rejoining Ionis in 2024, Mr. Jenne served as chief executive officer at Elsie Biotechnologies from September 2022 until its acquisition by GlaxoSmithKline in May 2023, and from June 2023 until February 2024 served as chief commercial officer at TauRx. Mr. Jenne served in senior commercial leadership roles at Ionis and Akcea from May 2017 to August 2022. Prior to joining Akcea in 2017, Mr. Jenne was employed by Schering Plough, King Pharmaceuticals, and Acorda Therapeutics in various commercial roles.

***Patrick R. O'Neil***, Esq., has served as Ionis' Executive Vice President, Chief Legal Officer and General Counsel since September 2021. Mr. O'Neil also serves as our Corporate Secretary. From March 2020 to September 2021, Mr. O'Neil served as our Executive Vice President, Legal & General Counsel and Chief Compliance Officer. From January 2013 to March 2020, Mr. O'Neil served as our Senior Vice President, Legal and General Counsel. From September 2010 to January 2013, Mr. O'Neil served as our Vice President, Legal and General Counsel and from January 2009 to September 2010, he served as our Vice President, Legal and Senior Transactions Counsel. From October 2001 to January 2009 he held various positions within our Legal department. Prior to joining Ionis, Mr. O'Neil was an associate at Cooley LLP.

***Eugene Schneider***, M.D., has served as Ionis' Executive Vice President and Chief Clinical Development and Operations Officer since September 2023. From January 2021 to September 2023, Dr. Schneider served as our Executive Vice President and Chief Clinical Development Officer. From August 2018 to December 2020, Dr. Schneider served as our Senior Vice President, Head of Clinical Development. From April 2015 to July 2018, Dr. Schneider was our Vice President, Clinical Development, Severe and Rare Diseases. Dr. Schneider joined Ionis in December 2013 as Executive Director, Clinical Development. Dr. Schneider has two decades of experience in clinical development primarily in the rare diseases space. Prior to joining Ionis, Dr. Schneider was senior medical director at both Synageva BioPharma and Biovail Technologies Ltd.

***Eric E. Swayze***, Ph.D., has served as Ionis' Executive Vice President, Research since April 2020 and is responsible for leading preclinical antisense drug discovery and antisense technology research. In January 2020, Dr. Swayze was promoted to Senior Vice President of Research. Previously, Dr. Swayze was Vice President of Chemistry and Neuroscience Drug Discovery at Ionis, overseeing the advancement of multiple programs to clinical development. He joined Ionis in 1994 and has contributed to key technology advancements, including Ionis' Generation 2.5 chemistry and LICA technology.

# INFORMATION REGARDING THE BOARD AND CORPORATE GOVERNANCE

## Independence of the Board of Directors

As required under Nasdaq listing standards, a majority of the members of a listed company's board of directors must qualify as "independent," as evaluated by our Nominating, Governance and Review Committee and affirmatively determined by our Board. Our Nominating, Governance and Review Committee consults with our legal counsel to ensure that the Committee's determinations are consistent with all relevant securities and other laws and regulations regarding the definition of "independent," including those set forth in the applicable Nasdaq listing standards and applicable SEC rules and regulations, as in effect from time to time.

Consistent with these considerations, after review of all relevant transactions or relationships between each director, or any of their family members, and Ionis, its executive officers and its independent auditors, the Board affirmatively has determined that all of our directors are independent directors within the meaning of the applicable Nasdaq listing standards and SEC rules and regulations, except Dr. Monia, our current Chief Executive Officer. In making this determination, the Board found that none of these independent directors has a material or other disqualifying relationship with us. Notably, although the Company does business with Goldman Sachs & Co. and Brigham and Women's Hospital, neither Mr. Wender nor Dr. Loscalzo, respectively, receives any personal compensation directly from revenue received from Ionis.

## Information Regarding the Board and its Committees

### *Leadership Structure*

Dr. Loscalzo, an independent director, has served as Chair of our Board since June 2021. We believe that having an independent Board Chair encourages active participation by the independent directors in the work of our Board, enhances our Board's role of representing stockholders' interests, and improves our Board's ability to supervise and evaluate our CEO and other executive officers. Further, separation of the Chair and CEO roles allows our CEO to focus on operating and managing the company while leveraging our independent Chair's experience and perspectives.

### *Risk Oversight*

Our Board administers its risk oversight function directly and through all of its current committees. We provide a complete description of each committee and its respective roles and responsibilities on pages 15 through 19 of this Proxy Statement. While each of these committees is responsible for evaluating certain risks and overseeing how we manage risk, these committees inform the entire Board about such risks through committee reports.

The Audit Committee oversees management of financial risks. In 2019, the Audit Committee authorized the formation of an internal audit function known as "Advisory Services" that reports to the Audit Committee. Advisory Services strives to accomplish its mission of adding value to and improving the Company's operations through sustaining a systematic, disciplined, and transparent approach to evaluating the effectiveness of governance, risk management, and control processes. The scope of Advisory Services is to determine if the control environment and internal control structure, as designed and represented by Company management, are adequate and functioning in a manner to enable the Company to meet its business objectives and satisfy its responsibilities. The Audit Committee is also responsible for reviewing and discussing the Company's cybersecurity risks.

The Nominating, Governance and Review Committee manages risks associated with the independence of the Board and potential conflicts of interests at the Board level, including review of related party transactions. The Nominating, Governance and Review Committee also periodically reviews our policies and procedures and makes recommendations when appropriate. In addition, the Nominating, Governance and Review Committee oversees our corporate responsibility and environmental, social and governance matters. The Compensation Committee reviews risks to the Company related to our executive compensation program and our general compensation philosophies. The Finance Committee evaluates risks to the Company associated with our corporate finance matters. The Medical and Science Committee reviews risks to the Company related to our technology platform and medicines in development. The Compliance Committee is responsible for evaluating risks to the Company in connection with the commercialization of our medicines and good practice guidelines and regulations.

The Company maintains an enterprise risk management program that the Board oversees with specific risk categories assigned to the appropriate Board committee. As part of the risk management program the Company maintains a risk dashboard that management updates on a quarterly basis and distributes to the Board prior to each Board meeting. In addition to the formal enterprise risk management program, the Board and its committees encourage management to promote a corporate culture that understands risk management and incorporates it into the overall corporate strategy and day-to-day business operations. Our risk management structure also includes an ongoing effort to assess and analyze the most likely areas of future risk for Ionis. As a result, the Board and most of its committees periodically ask our executives to discuss the most likely sources of material future risks and how we are addressing any significant potential vulnerability.

*Board Committees*

The Board has six committees: an Audit Committee, a Compensation Committee, a Nominating, Governance and Review Committee, a Medical and Science Committee, a Finance Committee, and a Compliance Committee. Below is a description of each committee of our Board. Each of the committees has authority to engage legal counsel or other experts or consultants as it deems appropriate to carry out its responsibilities. The Board has determined that each member of our Audit Committee, Compensation Committee, and Nominating, Governance and Review Committee:

- meets the applicable rules and regulations regarding "independence," including, but not limited to, Rule 5605(a)(2) of the Nasdaq listing standards and applicable SEC rules and regulations;
- is not an officer or employee of Ionis; and
- is free of any relationship that would interfere with their individual exercise of independent judgment with regard to Ionis.

## Meetings and Attendance; Committee Members

The Board met four times in 2025. Each director attended 75% or more of the aggregate number of meetings of the Board and the committees on which such director served during 2025. We encourage each member of the Board to attend the Annual Meeting of Stockholders.

Executive sessions, which are meetings at which only independent directors are present, are regularly scheduled throughout the year, typically at the time of each regular Board meeting and as frequently as such independent directors deem appropriate. Our Board met in executive session four times in 2025.

### Board Committee Members

The table below provides membership and meeting information for each of the Board committees in 2025.

| Name | Audit | Compensation | Compliance | Finance | Nominating, Governance and Review | Medical and Science** | Attended 2025 Annual Meeting |
|---|---|---|---|---|---|---|---|
| Dr. Spencer R. Berthelsen | — | X* | — | — | X | X | — |
| Ms. Allene M. Diaz | X | — | X | — | — | — | X |
| Dr. Michael Hayden | — | — | — | — | — | X* | X |
| Ms. Joan E. Herman | X | X | X | — | — | — | — |
| Mr. Joseph Klein, III | X* | — | — | X | — | — | X |
| Dr. Joseph Loscalzo | — | — | — | — | X | X | X |
| Dr. Brett P. Monia | — | — | — | — | — | — | X |
| Ms. B. Lynne Parshall | — | — | X* | X | — | — | — |
| Mr. Joseph H. Wender | — | X | — | X* | X* | — | — |
| Mr. Michael Yang | — | — | X | — | — | — | — |
| Total meetings in fiscal year 2025 | 8 | 8 | 7 | 8 | 2 | 3 | |

* Committee Chairperson
** Dr. Frank Bennett, the Company's EVP and Chief Scientific Officer, is the executive sponsor of the committee.

## Audit Committee

The Audit Committee of the Board oversees our corporate accounting and financial reporting process, including audits of our financial statements. For this purpose, the Audit Committee performs several functions.

The Audit Committee:

- reviews the annual and quarterly financial statements, including the disclosures contained under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations," and oversees the annual and quarterly financial reporting processes, including sessions with the independent auditors and internal auditors in which Ionis' employees and management are not present;
- selects and hires our independent auditors;

- oversees the independence of our independent auditors;
- evaluates our independent auditors' performance; and
- has the authority to hire its own outside consultants and advisors, if necessary.

In addition to the responsibilities listed above, the Audit Committee has the following functions:

- receiving and considering our independent auditors' comments as to the audit of the financial statements and internal controls, adequacy of staff and management performance and procedures in connection with internal controls;
- establishing and enforcing procedures for the receipt, retention, and treatment of complaints regarding accounting or auditing improprieties;
- pre-approving all audit and non-audit services provided by our independent auditors that are not prohibited by law;
- reviewing and discussing the Company's cybersecurity risks; and
- meeting regularly with members of the internal audit/Advisory Services team.

Our Audit Committee utilizes an Audit Committee calendar to manage and track its key duties and responsibilities throughout each year.

Our Audit Committee charter requires that each member must be independent. We consider the members to be independent as long as they:

- do not accept any consulting, advisory or other compensatory fee from us, except in connection with their service as a director;
- are not an affiliate of Ionis or one of its subsidiaries; and
- meet all of the other Nasdaq and SEC rules independence requirements.

In addition, all Audit Committee members must be financially literate and at least one member must be an "audit committee financial expert," as defined by SEC regulations. Our Board has determined that the Audit Committee's financial expert is Mr. Klein based on, among other things, his experience as a Chartered Financial Analyst and his extensive public company, venture investment, board, and financial advisory expertise in the life sciences industry, including previously serving as chairman of the audit committee at several public biopharmaceutical companies. We provide the Audit Committee with the funding it needs to perform its duties.

The Audit Committee is responsible for reviewing and discussing the Company's cybersecurity risks. The Audit Committee receives reports from our Senior Vice President, Information Technology concerning our significant cybersecurity threats and risks (including certain cybersecurity threats) and the processes we have implemented that are designed to address them. The Audit Committee also meets with the Company's independent auditors regarding their annual audit procedures, which include information technology. Two of our Board members, Ms. Herman and Ms. Parshall, have obtained cybersecurity certifications from the NACD. In addition, we utilize an information security awareness training program that is available to all employees.

In 2025, the Audit Committee met twice each quarter: once in connection with quarterly Board of Directors meetings, and once to review quarterly financial results and Form 10-Q or annual financial results and Form 10-K. The Board has adopted a written Audit Committee charter, which you can find on our corporate website at www.ionis.com.[3] Each member meets the membership criteria set forth in the Audit Committee charter and as stated above.

### Compensation Committee

The primary function of the Compensation Committee of the Board is to review, modify (as needed) and approve our overall compensation strategy and policies for our executive officers and recommend that the Board approve the compensation and other terms of employment for our Chief Executive Officer. We include a full list of the Compensation Committee's responsibilities as part of the Compensation Discussion and Analysis ("***CD&A***") set forth on pages 43 through 68 of this Proxy Statement. The charter of the Compensation Committee grants the Compensation Committee full access to our books, records, facilities and personnel, and authority to obtain, at our expense, advice and assistance from internal and external legal, accounting or other advisors and consultants and other external resources that the Compensation Committee considers necessary or appropriate in the performance of its duties. In particular, the Compensation Committee has the sole authority to retain independent compensation consultants to help the Compensation Committee evaluate executive and director compensation, including the authority to approve the consultants' reasonable fees and other retention terms.

[3] Any information that is included on or linked to our website is not part of this Proxy Statement or any registration statement or report that incorporates this Proxy Statement by reference.

We also have a Non-Management Stock Option Committee that, as delegated by the Compensation Committee, may award stock options and RSUs to employees who are below director level in accordance with guidelines adopted by the Compensation Committee. The Non-Management Stock Option Committee has one member, Dr. Monia.

The Compensation Committee met eight times in 2025. The Compensation Committee acted by unanimous written consent 20 times. The Board has adopted a written Compensation Committee charter, which you can find on our corporate website at www.ionis.com.[4]

The Compensation Committee reviews with management Ionis' CD&A to consider whether to recommend that we include the CD&A in our Proxy Statements and other filings.

## Compensation Committee Interlocks and Insider Participation

As noted above, during the fiscal year ended December 31, 2025, our Compensation Committee was composed of Dr. Berthelsen, Mr. Wender, and Ms. Herman. In each case, none of the members of the Compensation Committee has ever been an employee or officer of Ionis. None of our executive officers serves as a member of the board of directors or compensation committee of any other entity that has one or more executive officers serving as a member of our Board or Compensation Committee. Except as disclosed under "Certain Relationships and Related Transactions," no person who served as a member of the Compensation Committee during 2025 had any relationship requiring disclosure by us under Item 404 of Regulation S-K.

## Nominating, Governance and Review Committee

The Nominating, Governance and Review Committee of the Board is responsible for:

- interviewing, evaluating, nominating, and recommending individuals for membership on our Board, and considering proposed changes to the Board for approval;
- managing risks associated with the independence of the Board and potential conflicts of interests at the Board and executive level, including reviewing and, if appropriate, approving related party transactions;
- periodically reviewing our policies and procedures and making recommendations when appropriate;
- overseeing environmental, social and governance matters; and
- performing such other functions as may be necessary or convenient for the efficient discharge of the foregoing.

The Nominating, Governance and Review Committee met two times during 2025. You can find our Nominating, Governance and Review Committee charter on our corporate website at www.ionis.com.[5]

### *Director Nominations - Minimum Qualifications*

The Nominating, Governance and Review Committee believes that candidates for director should have certain minimum qualifications. As a result, the Board adopted membership standards (that may be revised from time to time) and believes that the Board members should meet the minimum membership requirements listed below.

The minimum membership requirements are as follows:

- members must be able to read and understand basic financial statements;
- members must demonstrate high personal integrity and ethics;
- members cannot serve as a director on the boards of more than five total publicly traded companies (including Ionis);
- members cannot serve more than ten consecutive three-year terms on the Board; and
- members cannot run for re-election to the Board once they have reached the age of 80.

In addition to these minimum standards, the Nominating, Governance and Review Committee will consider such factors as:

- possessing relevant expertise to offer advice and guidance to management;

[4] Any information that is included on or linked to our website is not part of this Proxy Statement or any registration statement or report that incorporates this Proxy Statement by reference.

[5] Any information that is included on or linked to our website is not part of this Proxy Statement or any registration statement or report that incorporates this Proxy Statement by reference.

- having sufficient time to devote to Ionis' affairs;
- demonstrating excellence in their field;
- having sound business judgment; and
- being committed to vigorously representing the long-term interests of our stockholders.

*Director Nominations*

In considering director nominations, the Nominating, Governance and Review Committee considers the total mix of competencies represented on the Board as a whole, as well as the competencies each member, or nominee, brings to the Board. In general, our Board members' experience falls into three large categories: (1) investment banking, financial accounting, and corporate governance experience; (2) medical and scientific expertise; and (3) experience with the commercialization of pharmaceutical products. By selecting individuals who have investment banking, financial accounting, and corporate governance backgrounds, we gain valuable experience that ensures we are managing our financial resources appropriately, reporting our financial results fairly and accurately, and generally running our business consistent with current good corporate practices. As a pioneer in RNA-targeted medicines, we also greatly benefit from Board members who themselves are scientists and medical doctors and can help set and adjust our strategy and objectives based on the results we generate from our research and development efforts. In addition, as a fully integrated commercial-stage biotechnology company, we benefit from Board members with backgrounds in the commercialization of pharmaceutical products. In different ways, these categories allow us to effectively manage our cash and make prudent investments in our technology to achieve the greatest likelihood of success. We have an even balance of Board members across these three categories of experience.

Our Board currently consists of three directors who self-identify as female and two directors who self-identify as ethnically diverse. We do not discriminate against nominees on the basis of gender, race, religion, national origin, sexual orientation, disability, or any other protected basis.

*Director Nominations – Tenure*

Our drug technology is a "platform technology," which means the more knowledge and experience an individual has with our technology platform, the better equipped that individual is to create value at Ionis. This is no different for our non-employee directors. While we believe it's important to add new non-employee directors who will bring fresh ideas and perspectives, given the uniqueness and complexity of our technology, it is also critical to retain the knowledge and experience of an appropriate number of outstanding long service non-employee directors who can contribute to our future business decisions while understanding our history.

*Director Nominations - Process*

The Nominating, Governance and Review Committee will consider director candidates our stockholders recommend. The Nominating, Governance and Review Committee does not intend to alter the manner in which it evaluates candidates, including the minimum criteria set forth above, based on whether or not a stockholder recommended the candidate.

The Nominating, Governance and Review Committee reviews new candidates for director in the context of the Board's composition, our operating requirements, and our stockholders' long-term interests. In conducting this assessment, the Nominating, Governance and Review Committee considers the minimum membership requirements discussed above, character, diversity of skills, background, experience and perspective and such other factors as it deems appropriate given the current needs of the Board and Ionis, to maintain a balance of knowledge, experience and capability. The Nominating, Governance and Review Committee then uses its network of contacts to compile a list of potential candidates, but may also engage, if it deems appropriate, a paid professional search firm. The Nominating, Governance and Review Committee conducts any appropriate and necessary inquiries into the backgrounds and qualifications of possible candidates after considering the function and needs of the Board. In the case of incumbent directors whose terms of office are set to expire, the Nominating, Governance and Review Committee reviews such directors' overall service to Ionis during their term, including the number of meetings attended, level of participation, quality of performance, and any other relationships and transactions that might impair such directors' independence.

The Nominating, Governance and Review Committee meets to discuss and consider the candidates' qualifications and determines whether each candidate is independent based upon applicable Nasdaq listing standards, SEC rules and regulations, and the advice of counsel, if necessary. Finally, the Nominating, Governance and Review Committee then selects a nominee for recommendation to the Board by majority vote.

*Stockholder Recommendations for Directors*

Stockholders who wish to recommend individuals for consideration by the Nominating, Governance and Review Committee to become nominees for election to the Board may do so by delivering a written recommendation to Ionis' corporate secretary at the following address: 2855 Gazelle Court, Carlsbad, California 92010. Submissions must include:

- the name, age, business address and residence address of the nominee;
- the principal occupation or employment of the nominee;
- the stock ownership in Ionis of the nominee;
- the stock ownership in Ionis of the stockholder making the nomination, including any trading in derivative securities that may disguise ownership occurring within the last 12 months;
- the information relating to the nominee that is required to be disclosed in solicitations of proxies under applicable securities laws;
- the nominee's written consent to being named in the Proxy Statement as a nominee and to serving as a director if elected;
- other information as we may reasonably require to determine the eligibility of the proposed nominee to serve as an independent director or that could be material to a reasonable stockholder's understanding of the independence of the proposed nominee; and
- any voting commitments the nominee has to third parties.

In addition, the nominee will need to complete a written questionnaire regarding the background and qualifications of the nominee, and the background of any other person or entity on whose behalf the nomination is being made. The nominee must also agree to comply with all of our applicable publicly disclosed corporate governance, conflict of interest, confidentiality and stock ownership and trading policies and guidelines. The description of the requirements for director nomination set forth above is qualified in its entirety by reference to our full and complete bylaws, which is an exhibit to our Current Report on Form 8-K filed with the SEC on March 29, 2021, a copy of which is available by contacting our corporate secretary. To date, the Board has not received or rejected a timely director nominee for election at the upcoming stockholder meeting from a stockholder or stockholders holding more than 5% of our voting stock.

## Medical and Science Committee

The primary functions of the Medical and Science Committee of the Board are to focus on the key scientific and development issues facing our technology and medicines in development and help set our strategy in such areas. The Medical and Science Committee met three times in 2025.

## Finance Committee

The primary function of the Finance Committee of the Board is to advise the Board and management on certain corporate finance matters for the Company and its subsidiaries, including its capital structure, strategic financial plan, financings, investments, and share repurchase activities. The Finance Committee met eight times in 2025.

## Compliance Committee

The Compliance Committee is primarily responsible for overseeing and reviewing the Company's healthcare compliance program and the status of the Company's compliance with laws, regulations (including good practice guidelines and regulations), industry standards, and internal procedures. The primary function of the Compliance Committee is to oversee the development and implementation of compliance and ethics policies and practices at the Company; however, management is responsible for designing and implementing such policies and practices. The Compliance Committee met seven times in 2025.

## Stockholder Communications with the Board

We make every effort to ensure that our Board or individual directors, as applicable, hear our stockholders' views, and provide appropriate responses to stockholders in a timely manner. Stockholders who wish to communicate with the Board, or individual directors, may do so by sending written communications addressed to Ionis' corporate secretary at 2855 Gazelle Court, Carlsbad, California 92010. If you wish to communicate with the independent directors about your concerns or issues, you may address correspondence to a particular director or to the independent directors generally. If you do not name a particular director, depending on the subject matter, we will forward the letter to the Chair of the appropriate committee of the Board. One or more of our employees designated by the Board will review these communications and will determine whether to present the materials to the Board. The purpose of this screening is to allow the Board to avoid having to consider irrelevant or inappropriate communications, such as advertisements, commercial solicitations, and hostile

communications. In accordance with our Code of Ethics and Business Conduct, all communications that relate to questionable accounting or auditing matters involving Ionis will be promptly and directly forwarded to the Audit Committee. Other than the processes described above, our Board has not adopted a formal written process for stockholder communications with the Board. We believe our Board's responsiveness to stockholder communications has been excellent.

### Code of Ethics and Business Conduct

We have adopted a Code of Ethics and Business Conduct that applies to all officers, directors, and employees. Our Code of Ethics and Business Conduct is posted on our website at www.ionis.com.[6] We intend to make all required disclosures regarding any amendments to, or waivers from, provisions of our Code of Ethics and Business Conduct on our website.

### Corporate Governance Guidelines

The Board has adopted corporate governance guidelines to ensure that the Board will have the necessary authority and practices in place to review and evaluate our business operations as needed and to make decisions that are independent of our management. The guidelines are also intended to align our directors' and management's interests with those of our stockholders. The corporate governance guidelines set forth the practices the Board intends to follow with respect to Board composition and selection, Board meetings and involvement of executive officers, Chief Executive Officer performance evaluation, succession planning for Board committees and compensation, "clawbacks" of executive compensation, and share retention guidelines for our executive officers and directors. The Board adopted the corporate governance guidelines to, among other things, reflect changes to the Nasdaq listing standards and SEC rules adopted to implement provisions of the Sarbanes-Oxley Act of 2002. You may view our corporate governance guidelines, as well as the charters for the Audit, Compensation, Nominating, Governance and Review, Finance and Compliance committees at www.ionis.com.[7]

### Anti-Hedging Policy and Anti-Pledging Policy

All directors and employees, including our named executive officers, are prohibited from taking a "short" position in our stock and otherwise hedging their position in our stock against a future drop in our stock price including short sales and derivatives such as put or call options, swaps, forwards, and futures, or other inherently speculative transactions with respect to Ionis' securities at any time. In addition, we also prohibit all directors and employees, including our named executive officers, from pledging our stock as collateral.

### Corporate Responsibility Initiatives

At Ionis, we are driven by a sense of urgency to discover, develop and deliver medicines to create a better future for people with serious diseases. We believe operating responsibly and sustainably creates long-term value for the Company and our stakeholders. We encourage you to view our 2025 Corporate Responsibility Report published on our website for more detailed information regarding our corporate responsibility initiatives. Nothing in the report or on our website shall be deemed incorporated by reference into this Proxy Statement.

Our approach to corporate responsibility strategy and disclosure is informed by our stakeholders and third-party frameworks such as the Sustainability Accounting Standards Board Health Care – Biotechnology and Pharmaceuticals Standard and the Task Force on Climate Related Financial Disclosures. In addition, our corporate responsibility strategy is aligned with the United Nations Sustainable Development Goals, which represent the international community's plan of action to address the most pressing challenges facing our world today.

Our corporate responsibility initiatives are driven by our Chief Executive Officer and executive-level Corporate Responsibility Steering Committee. The Corporate Responsibility Steering Committee consists of senior leaders in key functions across the company, including Legal, Finance, Investor Relations, Human Resources, Research and Development, Manufacturing, Commercial, Compliance and Corporate Affairs.

Our Board of Directors, specifically the Nominating, Governance and Review Committee, maintains oversight of our overall corporate responsibility strategy and sustainability risks and opportunities as outlined in the Nominating, Governance and Review Committee's charter. The Nominating, Governance and Review Committee receives updates at least once annually and is engaged on specific topics as needed.

[6] Any information that is included on or linked to our website is not part of this Proxy Statement or any registration statement or report that incorporates this Proxy Statement by reference.

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## PROPOSAL 2

## ADVISORY VOTE ON EXECUTIVE COMPENSATION

The Dodd-Frank Wall Street Reform and Consumer Protection Act of 2010, called the "Dodd-Frank Act," entitles Ionis' stockholders to make an advisory (nonbinding) vote on the compensation of our Chief Executive Officer, Chief Financial Officer and our four[8] other most highly compensated executive officers (at December 31, 2025), called our "named executive officers" as disclosed in this Proxy Statement in accordance with Section 14A of the Exchange Act.

We are asking our stockholders to indicate their support for our named executive officers' compensation as described in this Proxy Statement. This Proposal 2, commonly known as a "say on pay" proposal, gives our stockholders the opportunity to express their views on the compensation paid to our named executive officers. This vote is not intended to address any specific item of compensation, but rather the overall compensation of our named executive officers and the philosophy, policies and practices described in this Proxy Statement. Accordingly, we are asking our stockholders to vote "FOR" the following resolution at the Annual Meeting:

**"RESOLVED, that Ionis' stockholders approve, on an advisory (nonbinding) basis, the compensation of the named executive officers, as disclosed in this Proxy Statement for the 2026 Annual Meeting of Stockholders pursuant to the compensation disclosure rules of the Securities and Exchange Commission."**

We recommend you carefully review the EXECUTIVE COMPENSATION section of this Proxy Statement located on pages 43 through 68. Below is a high-level summary of some of our compensation practices. This summary is qualified by the detailed disclosure contained in the EXECUTIVE COMPENSATION section of this Proxy Statement.

Unless the Board decides to modify its policy regarding the frequency of soliciting advisory votes on the compensation of our named executives, the next scheduled "say on pay" vote will be at the 2027 Annual Meeting of Stockholders.

[8] Dr. Geary was no longer serving as an executive officer as of December 31, 2025. Had Dr. Geary been serving in that capacity on December 31, 2025, he would have been a named executive officer, and as such, is included as a named executive officer in this Proxy Statement.

The table below summarizes some of our executive compensation practices, both the practices we implement because we believe they are consistent with our vision and long-term stockholder value, and those that we choose not to implement as we believe they are counter to our vision and long-term stockholder value:

| | |
|---|---|
| ✓ General compensation principles | We design our compensation structure to drive the creation of long-term stockholder value and mitigate unnecessary or imprudent business risk taking. Specifically, we:<br>• Use a combination of compensation vehicles that provide a balanced mix of fixed and variable cash incentives, and long-term stock incentives;<br>• Require a 12-month minimum vesting period for equity awards;<br>• Set explicit and demanding objectives at the beginning of each year from which we measure performance for the year;<br>• Set a strict budget for equity awards and salary increases;<br>• Do *not* provide perquisites for any employees; and<br>• Do *not* provide "gross-up" payments, other than for relocation. |
| ✓ Align executive compensation with Company performance and design performance-based awards to drive creation of long-term stockholder value | We tie a significant portion of our executive officers' compensation to Company performance and design performance-based awards to drive the creation of long-term stockholder value. For example, we:<br>• Increased the proportion of performance-based restricted stock units ("***PRSUs***") to be awarded to our executive officers beginning in 2026 as follows: from 33% to 40% of our CEO's total equity awards and from 20% to 40% of our other executive officers' total equity awards;<br>• Allocated approximately 60% of our Chief Executive Officer's 2025 compensation in the form of performance-based compensation, which we consider to consist of cash bonuses, stock options and PRSUs;<br>• Revised our PRSU structure for grants made beginning in 2023 such that:<br>  ○ awards have a single vesting period at the end of three years; and<br>  ○ the relative total shareholder return ("***TSR***") percentile rank for maximum payout of the awards increased from the 75th percentile to the 90th percentile.<br>• Place a maximum limit on cash bonuses and do not guarantee a cash bonus – cash bonuses can be, and have been, zero; and<br>• Empower our Compensation Committee with the ability to reduce the Company Performance Factor (used to determine cash bonuses) for our executive officers based on Company performance. |
| ✓ Stock ownership and holding guidelines | We maintain stock ownership and holding guidelines that require our executive officers and non-employee directors to meet certain ownership thresholds. We increased such ownership requirements for our non-employee directors in 2023. |
| ✓ Clawback policy | We use an executive "clawback" policy that applies to all Section 16 officers and is consistent with the clawback policy rules adopted by the SEC and Nasdaq in 2023. |
| ✓ Disallow hedging and pledging | We do not allow pledging, shorting, or hedging against our stock by directors or employees. |
| ✓ No option re-pricing or cash buyouts | We do not reprice or "cash-out" stock options without stockholder approval. |
| ✓ Engage an independent compensation consultant | The Compensation Committee has retained a compensation consultant whose relationship with the Company was confirmed to be independent for 2025.<br><br>The compensation consultant, among other things, assists us in selecting an appropriate peer group and annually reviews our compensation levels, policies, practices, and procedures for our employees and non-employee directors compared to our peer group. |
| ✓ Use a "double trigger" for change in control for our executive officers | We use a "double trigger" for cash payments and equity acceleration for change in control for our executive officers. |
| ✓ Hold a "say on pay" vote annually | Provides an effective way for us to obtain information on stockholder sentiment about our executive compensation program each year. |

The affirmative vote of a majority of the holders of shares present or represented by proxy at the Annual Meeting and entitled to vote on the matter is required to adopt the resolution. If you indicate on your proxy to "Abstain" from voting, it will have the same effect as a vote "Against" this Proposal 2. Brokers do not have discretion to vote uninstructed shares with respect to this Proposal 2. Accordingly, if brokers do not receive voting instructions from beneficial owners of the shares, they cannot vote the shares. Therefore, broker non-votes will not affect the outcome of the voting on this Proposal 2.

The "say on pay" vote is advisory, and therefore is not binding on Ionis, the Compensation Committee or the Board. However, Ionis' management, the Board and the Compensation Committee value the opinions of the stockholders. As such, if there is any significant vote against the named executive officers' compensation as disclosed in this Proxy Statement, the Board will consider the stockholders' concerns and the Board and Compensation Committee will evaluate whether any actions are necessary to address those concerns.

**THE BOARD UNANIMOUSLY RECOMMENDS A VOTE "FOR" PROPOSAL 2.**

## PROPOSAL 3

## APPROVAL OF AN AMENDMENT OF OUR AMENDED AND RESTATED IONIS PHARMACEUTICALS, INC 2011 EQUITY INCENTIVE PLAN

In March 2011, the Compensation Committee of the Board, and the Board, adopted the Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan (the "***2011 Plan***") and the stockholders approved the 2011 Plan on June 16, 2011. Since its adoption, the stockholders have approved several amendments to the 2011 Plan to increase the aggregate number of shares of common stock authorized for issuance under the 2011 Plan, most recently in June 2025, to increase by 4,000,000 shares to an aggregate of 42,500,000 shares.

In this Proposal 3, we are requesting stockholders to approve an amendment of the 2011 Plan to increase the aggregate number of shares of common stock authorized for issuance under the 2011 Plan by 9,500,000 shares to an aggregate of 52,000,000 shares.

Our management, Board and Compensation Committee believe that stock options, restricted stock units ("***RSUs***") and PRSUs are a key aspect of our ability to attract and retain qualified personnel in the face of intense competition for experienced scientists and other personnel among many pharmaceutical and health care companies. On March 4, 2026, the Board, upon the recommendation of the Compensation Committee, approved an amendment to the 2011 Plan to increase the aggregate number of shares of common stock authorized for issuance under the 2011 Plan by 9,500,000 shares to an aggregate of 52,000,000 shares, to ensure that, based on our current business plans, we can continue to grant stock options, RSUs and PRSUs to employees at appropriate levels as determined by the Compensation Committee. If the stockholders do not approve this Proposal 3, and as a consequence, we cannot continue to grant options, RSUs and PRSUs at competitive levels, we believe that it will negatively affect our ability to recruit and retain highly qualified personnel and our ability to manage future growth. Without these additional shares, management expects that the current shares available for grant under the 2011 Plan will not be sufficient to maintain our stock award practices for new employees or for promotions or merit awards for current employees.

Each year the Compensation Committee approves a budget that sets the number of stock options, RSUs and PRSUs we can grant our employees for annual merit awards. We do not grant options, RSUs or PRSUs that exceed this budget without the Compensation Committee's approval. Over the past three years, the average merit award stock budget set by the Compensation Committee has been approximately 2.36% of our outstanding common stock on an issued and outstanding basis. This stock compensation budget, and therefore our equity compensation burn rate, is below the 3.4% average of our peers over the same period.

The 2011 Plan is our primary means of offering stock options, RSUs and PRSUs to our employees. There were only approximately 2.6 million shares available as of March 31, 2026 for grant under the 2011 Plan. The 2011 Plan also allows us to utilize a broad array of equity incentives and performance cash incentives to secure and retain the services of our employees and to provide long-term incentives that align the interests of our employees with the interests of our stockholders.

Until December 2025, we also made grants to eligible employees from the Ionis Pharmaceuticals, Inc. 2020 Equity Incentive Plan (the "***2020 Plan***"), which we assumed in connection with the Akcea Merger. Equity awards granted under the 2020 Plan were reserved solely for legacy employees of Akcea who were employed as of October 12, 2020, which was the completion date of the Akcea Merger. The 2020 Plan terminated in December 2025.

The table below provides certain information regarding the 2011 Plan and 2020 Plan as of March 31, 2026.

| Employee Equity Incentive Plans (as of March 31, 2026) | | |
|---|---|---|
| | 2011 Plan | 2020 Plan |
| Total number of shares of common stock subject to outstanding stock options | 9,562,483 | 372,387 |
| Weighted-average exercise price of outstanding stock options | $50.51 | $41.96 |
| Weighted-average remaining term in years of outstanding stock options | 6.32 | 7.08 |
| Total number of shares of common stock subject to outstanding full value awards | 5,580,930 | 199,002 |
| Total number of shares of common stock available for grant under the plan | 2,609,480 | 0 |
| Total number of shares of common stock available for grant to non-employee Directors under the Non-Employee Director Plan[(1)] | | 348,350 |
| Total number of shares of common stock available for grant under other equity incentive plans | | — |
| Total number of shares of common stock outstanding | | 165,902,064 |
| Per-share closing price of common stock as reported on Nasdaq Capital Market | | $75.09 |

(1) This amount reflects the number of shares of common stock available as of March 31, 2026 for grant under our 2002 Amended and Restated Non-Employee Directors' Stock Option Plan ("***Non-Employee Directors' Stock Option Plan***"), which we use solely to offer equity awards to our non-employee directors. With respect to the Non-Employee Directors' Stock Option Plan, the total number of shares of common stock subject to outstanding stock options is 750,232, the weighted-average exercise price of outstanding stock options is $47.45, the weighted-average remaining term in years of outstanding stock options is 5.46, the total number of shares of common stock subject to outstanding full value awards is 62,343, and the total number of shares of common stock available for grant under the Non-Employee Directors' Stock Option Plan is 348,350. We have no equity incentive plans other than the 2011 Plan and the Non-Employee Directors' Stock Option Plan. The 2020 Plan expired on December 15, 2025.

### Required Vote and Board of Directors Recommendation

Pursuant to the rules of the Nasdaq Stock Market, approval of this Proposal 3 requires "For" votes from the holders of a majority of the votes cast on the proposal, voting virtually or by proxy at the meeting. Abstentions are not treated as votes cast and, therefore, will have no effect. Broker non-votes will have no effect on the outcome of the vote.

Our Board believes that approval of Proposal 3 is in our best interests and the best interests of our stockholders for the reasons stated above.

**THE BOARD UNANIMOUSLY RECOMMENDS A VOTE "FOR" APPROVAL OF PROPOSAL 3.**

## DESCRIPTION OF THE AMENDED AND RESTATED IONIS PHARMACEUTICALS, INC. 2011 EQUITY INCENTIVE PLAN

Below is a high-level summary of the terms of the 2011 Plan. This summary is qualified in its entirety by reference to the complete text of the 2011 Plan. We encourage our stockholders to read the actual text of the 2011 Plan, in its entirety, a copy of which we filed with this Proxy Statement as Appendix A.

The 2011 Plan:

- is administered by our Compensation Committee, which is composed entirely of independent directors;
- has a term ending on June 15, 2031;
- contains a "fungible share counting" structure, whereby the number of shares of our common stock available for issuance under the 2011 Plan is 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 2011 Plan, and (ii) 1.7 shares for each share issued pursuant to a stock award that is not an Appreciation Award (a "***Full Value Award***"). As part of such fungible share counting structure, the number of shares of our common stock available for issuance under the 2011 Plan is increased by (i) one share for each share that becomes available again for issuance under the terms of the 2011 Plan subject to an Appreciation Award, and (ii) 1.7 shares for each share that is granted after June 2, 2021 under the 2011 Plan that becomes available again for issuance under the terms of the 2011 Plan subject to a Full Value Award;

- prohibits the repricing of any option or stock appreciation rights outstanding under the 2011 Plan, or "cashing out" underwater awards unless approved by our stockholders;
- is limited to the granting of stock options, SARs, restricted stock awards, RSUs, PRSUs, and performance cash awards;
- prohibits the payment of dividends and dividend equivalents with respect to shares subject to an award until such shares have vested in accordance with the terms of the corresponding award agreement;
- prohibits the recycling of shares forfeited to cover the exercise price or withholding taxes for all stock awards;
- requires that each newly granted stock option, restricted stock award, RSU, SAR and PRSU award not become fully vested until a date at least one year after the date of grant, except in the case of (1) a sale of all or substantially all of the assets of the Company, (2) a disposition of at least 90% of the Company's securities, a merger or other similar transaction after which the Company is not the surviving corporation, (3) a merger or other similar transaction after which the Company is the surviving corporation but the shares of common stock immediately preceding the transaction are exchanged into other property, (4) an award granted in exchange for previously granted awards of a company acquired by the Company and (5) awards to non-employee directors that vest on the earlier of the one-year anniversary of the date of grant or the next annual meeting of stockholders, provided that such vesting period may not be less than 50 weeks; and Ionis may grant up to 2,600,000 shares (i.e., 5% of the share reserve) worth of stock options, restricted stock awards, RSUs, SARs or PRSU awards that vest earlier than the minimum period described above;
- provides that if any stock awards held by participants who haven't terminated service prior to a corporate transaction are not assumed, continued or substituted for by the acquiror (or its parent) in the transaction, then, contingent on the closing of the transaction, the vesting (and exercisability, if applicable) of such awards will be accelerated in full, and with respect to any awards subject to performance-based vesting conditions, vesting will be deemed satisfied at the greater of actual performance or target level; and
- requires all options and SARs outstanding under the 2011 Plan to have an exercise or strike price of not less than 100% of the fair market value of our common stock on the date of grant.

### Purpose

The main purpose of the 2011 Plan is to allow us to give our employees (including officers), directors and consultants an opportunity to benefit from increases in value of our common stock through the granting of a combination of stock options and RSUs. We believe providing our employees a combination of stock options and RSUs allows us to:

- retain the highest quality employees while motivating all employees to achieve key drivers of stock value;
- issue fewer shares, thereby reducing dilution;
- better align employee and stockholder interests; and
- encourage long-term holding.

In 2025, we granted our non-executive officer employees a combination of stock options and RSUs under our 2011 Plan, where we allocated 25% of the grant date dollar value to stock options and allocated 75% of the value to RSUs; and assumed that each share subject to an RSU was worth two shares subject to a stock option.

### Background

The terms of the 2011 Plan provide for the grant of stock options, SARs, restricted stock awards, RSUs, PRSU awards and performance cash awards that may be settled in cash, stock, or other property.

### Shares Available for Awards

If this Proposal 3 is approved, there will be a total of 52,000,000 shares of our common stock authorized for issuance under the 2011 Plan. If this Proposal 3 is not approved, there will only be approximately 2.6 million shares available for issuance under the 2011 Plan as of March 31, 2026, which, given our future hiring projections, we expect will not be sufficient to maintain our stock award practices for new employees or for promotions or merit awards for current employees.

The following table summarizes the equity awards granted over the last three years, and through March 31, 2026, to our employees under our equity plans. We grant most of our equity awards for each year in January of such year as part of the annual merit compensation process.

| Equity Award Grant History Under Employee Equity Plans[1] | | | | |
|---|---|---|---|---|
| | 2023 | 2024 | 2025 | 2026 (through March 31st) |
| Shares subject to equity awards granted | 5,549,603 | 6,528,855 | 6,525,163 | 5,305,079 |
| Shares subject to equity awards canceled or forfeited | (2,106,879) | (2,112,280) | (2,580,266) | (185,355) |
| Net shares subject to equity awards[2] | 3,442,724 | 4,416,575 | 3,944,897 | 5,119,724 |

(1) Amounts shown reflect grants under our 2011 Plan and 2020 Plan. We currently grant equity awards to our non-employee directors separately under our Non-Employee Directors' Stock Option Plan.

(2) Shares subject to equity awards that are canceled or forfeited become available for re-issuance under the applicable equity plan.

*No Share Recycling*

Under the 2011 Plan, we prohibit the recycling of shares we reacquire pursuant to our withholding obligations or as consideration for the exercise of all stock awards and such reacquired shares will *not* become available for issuance under the 2011 Plan.

## Eligibility

All of our employees and our directors and consultants are eligible to participate in the 2011 Plan. As of March 31, 2026, we had a total of 1,410 employees who were eligible to participate in the 2011 Plan.

## Administration

Our Board has the authority to administer the 2011 Plan. The Board may delegate authority to administer the 2011 Plan to a committee but may retain the authority to concurrently administer the 2011 Plan with the committee and may, at any time, revest in itself some or all of the powers previously delegated to the committee. Our Board has delegated administration of the 2011 Plan to the Compensation Committee. Subject to the terms of the 2011 Plan, the Compensation Committee may determine the recipients, numbers, and types of stock awards to be granted, and terms and conditions of the stock awards, including the period of their exercisability and vesting. Subject to the limitations set forth below, the Compensation Committee also determines the fair market value applicable to a stock award and the exercise price of stock options and SARs granted under the 2011 Plan.

At the discretion of the Board, the Compensation Committee may consist solely of two or more "non-employee directors" within the meaning of Rule 16b-3 of the Exchange Act. We also have a Non-Management Stock Award Committee that, as delegated by the Compensation Committee, awards stock awards to employees who are below director level in accordance with guidelines adopted by the Compensation Committee. The Non-Management Stock Award Committee has one member, Dr. Monia. As used herein, except as explicitly stated otherwise, with respect to the 2011 Plan, the "Board" refers to any committee the Board appoints or, if applicable, any subcommittee, as well as to the Board itself.

## No Repricing, "Cash-Out," or Cancellation and Re-Grant of Stock Awards without Stockholder Approval

Under the 2011 Plan, the Board cannot reprice any outstanding options or SARs by reducing the exercise price of the stock award or cancel any outstanding options or SARs in exchange for cash or other stock awards without obtaining the approval of our stockholders within 12 months prior to the repricing or cancellation and re-grant event.

## Minimum Vesting; Restrictions on Accelerated Vesting

Under the 2011 Plan, no stock award granted to an employee or member of the Board will become 100% vested in a period of less than one year after the grant of such award, *except that* the vesting of a stock award may accelerate (or may be accelerated by the Board or Compensation Committee) in the case of (1) a sale of all or substantially all of the assets of the Company, (2) a disposition of at least 90% of the Company's securities, a merger or other similar transaction after which the Company is not the surviving corporation, (3) a merger or other similar transaction after which the Company is the surviving corporation but the shares of common stock immediately preceding the transaction are exchanged into other property, (4) an award granted in exchange for previously granted awards of a company acquired by the Company and (5) awards to non-employee directors that vest on the earlier of the one-year anniversary of the date of grant or the next annual meeting of stockholders, provided in such case that such vesting period may not be less than 50 weeks; and Ionis may grant up to 2,600,000 shares worth of stock options, restricted stock awards, RSUs, SARs or PRSU awards that vest earlier than the minimum period described above.

### Dividends and Dividend Equivalents

The 2011 Plan prohibits the payment of dividends and dividend equivalents with respect to shares subject to an award until such shares have vested in accordance with the terms of the corresponding award agreement.

### No Evergreen

The 2011 Plan does not include an automatic share reserve increase provision (i.e., an evergreen provision).

### Stock Options

The Board grants stock options under the 2011 Plan pursuant to stock option agreements. The 2011 Plan permits the grant of stock options that qualify as nonstatutory stock options ("***NSOs***"). Individual stock option agreements may be more restrictive as to any or all of the permissible terms described in this section.

#### *Exercise Price; Payment*

The exercise price of stock options may not be less than 100% of the fair market value of the common stock subject to the stock option on the date of grant. As of March 31, 2026, the closing price of our common stock as reported on the Nasdaq Global Select Market was $75.09 per share.

#### *Vesting*

Stock options granted under the 2011 Plan may become exercisable in cumulative increments, or "vest," as determined by our Board at the rate specified in the stock option agreement, subject to the minimum vesting requirements described above. Shares covered by different stock options granted under the 2011 Plan may be subject to different vesting schedules as our Board may determine.

#### *Term*

In general, the term of stock options granted under the 2011 Plan was previously seven years, which we increased to ten years beginning with grants made in January 2022. The 2011 Plan does not allow stock options to have a term that exceeds ten years. Unless the terms of an option holder's stock option agreement or other agreement with the Company provides for earlier or later termination:

- if an option holder's service relationship with us, or any affiliate of ours, ceases due to disability, the option holder may exercise any vested stock options for up to 12 months after the date the service relationship ends;
- if an option holder's service relationship with us, or any affiliate of ours, ceases due to death, the option holder's beneficiary may exercise any vested stock options for up to 18 months after the date the service relationship ends; and
- if an option holder's service relationship with us, or any affiliate of ours, ceases for any reason, other than as described above, the option holder may exercise any vested stock options for up to three months after the date the service relationship ends.

Under the 2011 Plan, the stock option term may be extended if exercise of the stock option following termination of service is prohibited by applicable securities laws or if the sale of stock received upon exercise of a stock option would violate the Company's insider trading policy. In no event may a stock option be exercised after its expiration date.

#### *Consideration*

Our Board determines the acceptable forms of consideration for the purchase of our common stock pursuant to the exercise of a stock option under the 2011 Plan, which may include cash, check, bank draft or money order made payable to us, shares of our common stock, payment pursuant to a program developed under Regulation T as promulgated by the Federal Reserve Board, or a net exercise feature.

#### *Transferability*

Generally, an option holder may not transfer a stock option other than by will or the laws of descent and distribution or a domestic relations order. However, to the extent permitted under the terms of the applicable stock option agreement, an option holder may designate a beneficiary who may exercise the stock option following the option holder's death.

### Restricted Stock Unit Awards

RSUs are granted under the 2011 Plan pursuant to restricted stock unit award agreements. Payment of any purchase price is made in any legal form acceptable to the Board. We settle a payment due to a recipient of a restricted stock unit award by delivery of shares of our common stock, by cash, by a combination of cash and stock, or in any other form of consideration determined by our Board and set forth in the restricted stock unit award agreement. We may credit dividend equivalents in respect of shares of our common stock covered by a restricted stock unit award; however, no dividend equivalents may be paid with respect to such shares before the date such shares have vested in accordance with the terms of the corresponding award agreement. RSUs are subject to vesting in accordance with a vesting schedule determined by our Board, subject to the minimum vesting requirements described earlier. Except as otherwise provided in the applicable RSU award agreement, RSUs that have not vested will be forfeited upon the participant's termination of continuous service for any reason.

### Restricted Stock Awards

The Board may grant restricted stock awards under the 2011 Plan pursuant to restricted stock award agreements. The Board may grant a restricted stock award in consideration for cash, check, bank draft or money order payable to us, the recipient's services performed for us, or any other form of legal consideration acceptable to the Board. Shares of our common stock acquired under a restricted stock award are subject to forfeiture to us in accordance with a vesting schedule determined by our Board. Holders of awards may only transfer their rights to acquire shares of our common stock under a restricted stock award upon such terms and conditions as are set forth in the restricted stock award agreement. We may credit dividend equivalents in respect of shares of our common stock covered by a restricted stock award; however, no dividend equivalents may be paid with respect to such shares before the date such shares have vested in accordance with the terms of the corresponding award agreement. Except as otherwise provided in the applicable restricted stock award agreement, restricted stock awards that have not vested will be forfeited upon the participant's termination of continuous service for any reason.

### Stock Appreciation Rights

The Board may grant SARs under the 2011 Plan pursuant to SAR agreements. Each SAR is denominated in common stock share equivalents. The Board will determine the strike price of each stock appreciation right but the strike price cannot be less than 100% of the fair market value of the stock subject to the SAR at the time of grant. Our Board may also impose restrictions or conditions upon the vesting of SARs that it deems appropriate, subject to the minimum vesting requirements described earlier. We may settle SARs in our common stock, in cash, in a combination of cash and stock, or in any other form of legal consideration approved by our Board and set forth in the stock appreciation right agreement. SARs will be subject to the same conditions upon termination and restrictions on transfer as stock options under the 2011 Plan.

### Performance Awards

The 2011 Plan provides for the grant of two types of performance awards: PRSU awards and performance cash awards. The Board may grant, vest, or settle performance awards based upon the attainment of specified performance goals during a specified period of time. The Compensation Committee will determine the length of any performance period, the performance goals to be achieved during the performance period, and the measure of whether and to what degree such performance goals have been attained.

In granting a performance award, the Compensation Committee will set a period of time, called a performance period, over which the attainment of one or more performance goals will be measured for the purpose of determining whether the award recipient has a vested right in or to such award. The Compensation Committee will establish the performance goals, based upon one or more criteria, called performance criteria enumerated in the 2011 Plan. As soon as administratively practicable following the end of the performance period, the Compensation Committee will determine whether the performance goals have been satisfied.

The Board is authorized to determine whether, when calculating the attainment of performance goals for a performance period, as follows:

- to exclude restructuring and/or other nonrecurring charges;
- to exclude exchange rate effects, as applicable, for non-U.S. dollar denominated performance goals;
- to exclude the effects of changes to generally accepted accounting principles;
- to exclude the effects of any statutory adjustments to corporate tax rates;
- to exclude the effects of items that are "unusual" in nature or occur "infrequently," as determined under generally accepted accounting principles; and
- to exclude accounting expenses relating to share-based compensation.

### Changes to Capital Structure

If certain capitalization adjustments occur, the Board will appropriately adjust:

- the class(es) and maximum number of securities subject to the 2011 Plan; and
- the class(es) and number of securities and price per share of stock subject to outstanding stock awards.

### Corporate Transactions

Unless otherwise provided in the stock award agreement, any other written agreement between the Company or any of its affiliates and the participant, or in any director compensation policy of the Company, in the event of a corporate transaction (as specified in the 2011 Plan and described below), all outstanding stock awards under the 2011 Plan will be assumed, continued or substituted for by any surviving or acquiring entity (or its parent company). If the surviving or acquiring entity (or its parent company) elects not to assume, continue or substitute for such stock awards, then (i) with respect to any such stock awards that are held by individuals whose continuous service with us or an affiliate has not terminated prior to the effective date of the corporate transaction, the vesting and exercisability provisions of such stock awards will be accelerated in full (and with respect to any performance stock awards, vesting will be deemed satisfied at the greater of actual performance or target level) and such awards will terminate if not exercised prior to the effective date of the corporate transaction, and (ii) with respect to any stock awards that are held by individuals whose continuous service with the Company or an affiliate of the Company has terminated prior to the effective date of the corporate transaction, the vesting and exercisability provisions of such stock awards will not be accelerated and such awards will terminate if not exercised prior to the effective date of the corporate transaction (except that any reacquisition or repurchase rights held by the Company with respect to such stock awards will not terminate and may continue to be exercised notwithstanding the corporate transaction).

For purposes of the 2011 Plan, a corporate transaction will be deemed to occur in the event of the consummation of:

- a sale of all or substantially all of our consolidated assets;
- a sale of at least 90% of our outstanding securities;
- a merger or consolidation in which we are not the surviving corporation; or
- a merger or consolidation in which we are the surviving corporation but shares of our outstanding common stock are converted into other property by virtue of the transaction.

The acceleration of vesting of an award in the event of a corporate transaction under the 2011 Plan may be viewed as an anti-takeover provision, which may have the effect of discouraging a proposal to acquire or otherwise obtain control of the Company.

### Change in Control

A stock award will not be subject to additional acceleration of vesting and exercisability in connection with a change in control (as defined in the 2011 Plan), except upon certain termination events that are in connection with a change in control as provided in the stock award agreement for such stock award or as otherwise may be provided in any other written agreement between us or any affiliate and the participant. In such a case, the stock award agreement or other written agreement may provide that vesting (and, if applicable, exercisability) of time-based awards will be accelerated in full and performance-based stock awards will be deemed to have been satisfied at the greater of actual performance or target level.

The acceleration of vesting of an award in the event of a change in control event under the 2011 Plan may be viewed as an anti-takeover provision, which may have the effect of discouraging a proposal to acquire or otherwise obtain control of the Company.

### Plan Amendments

Our Board has the authority to amend or terminate the 2011 Plan. However, no amendment or termination of the 2011 Plan will adversely affect any rights under awards already granted to a participant unless agreed to by the affected participant. We will obtain stockholder approval of any amendment to the 2011 Plan as required by applicable law and listing requirements. We will not seek to amend the prohibition on option repricing or "cashing-out" without obtaining such stockholder approval.

### Plan Termination

Unless sooner terminated by our Board, the 2011 Plan will automatically terminate on June 15, 2031.

## Federal Income Tax Information

The information set forth below is a summary only and does not purport to be complete. The information is based upon current federal income tax rules and therefore is subject to change when those rules change. Because the tax consequences to any recipient may depend on their particular situation, each recipient should consult the recipient's tax adviser regarding the federal, state, local, and other tax consequences of the grant or exercise of an award or the disposition of stock acquired as a result of an award. The 2011 Plan is not qualified under the provisions of Section 401(a) of the Internal Revenue Code (the "***Code***") and is not subject to any of the provisions of the Employee Retirement Income Security Act of 1974. Our ability to realize the benefit of any tax deductions described below depends on our generation of taxable income, as well as the requirement of reasonableness and the satisfaction of our tax reporting obligations.

### *Nonstatutory Stock Options*

Generally, there is no taxation upon the grant of an NSO if the stock option is granted with an exercise price equal to the fair market value of the underlying stock on the grant date. On exercise, an option holder will recognize ordinary income equal to the excess, if any, of the fair market value of the underlying stock on the date of exercise of the stock option over the exercise price. If the option holder is employed by us or one of our affiliates, that income will be subject to withholding taxes. The option holder's tax basis in those shares will be equal to their fair market value on the date of exercise of the stock option, and the option holder's capital gain holding period for those shares will begin on that date.

Subject to the requirement of reasonableness, the provisions of Section 162(m) of the Code ("***Section 162(m)***"), and the satisfaction of our tax reporting obligation, we will generally be entitled to a tax deduction equal to the taxable ordinary income realized by the option holder.

### *Restricted Stock Unit Awards*

Generally, the recipient of a restricted stock unit award structured to comply with the requirements of Section 409A of the Code or an exemption to Section 409A of the Code will recognize ordinary income at the time the stock is delivered equal to the excess, if any, of the fair market value of the shares of our common stock received over any amount paid by the recipient in exchange for the shares of our common stock. To comply with the requirements of Section 409A of the Code, the shares of our common stock subject to a restricted stock unit award may generally only be delivered upon one of the following events: a fixed calendar date (or dates), separation from service, death, disability or a change in control. If delivery occurs on another date, unless the restricted stock unit award otherwise complies with or qualifies for an exemption to the requirements of Section 409A of the Code, in addition to the tax treatment described above, the recipient will owe an additional 20% federal tax and interest on any taxes owed.

The recipient's basis for the determination of gain or loss upon the subsequent disposition of shares acquired from a restricted stock unit award will be the amount paid for such shares plus any ordinary income recognized when the stock is delivered.

Subject to the requirement of reasonableness, the provisions of Section 162(m), and the satisfaction of our tax reporting obligation, we will generally be entitled to a tax deduction equal to the taxable ordinary income realized by the recipient of the restricted stock unit award.

### *Restricted Stock Awards*

Generally, the recipient of a restricted stock award will recognize ordinary income at the time the stock is received equal to the excess, if any, of the fair market value of the stock received over any amount paid by the recipient in exchange for the stock. If, however, the stock is not vested when it is received (for example, if the employee is required to work for a period of time in order to have the right to sell the stock), the recipient generally will not recognize income until the stock becomes vested, at which time the recipient will recognize ordinary income equal to the excess, if any, of the fair market value of the stock on the date it becomes vested over any amount paid by the recipient in exchange for the stock. A recipient may, however, file an election with the Internal Revenue Service, within 30 days following their receipt of the stock award, to recognize ordinary income, as of the date the recipient receives the award, equal to the excess, if any, of the fair market value of the stock on the date the award is granted over any amount paid by the recipient for the stock.

The recipient's basis for the determination of gain or loss upon the subsequent disposition of shares acquired from a restricted stock award will be the amount paid for such shares plus any ordinary income recognized either when the stock is received or when the stock becomes vested.

Subject to the requirement of reasonableness, the provisions of Section 162(m), and the satisfaction of our tax reporting obligation, we will generally be entitled to a tax deduction equal to the taxable ordinary income realized by the recipient of the restricted stock award.

*Stock Appreciation Rights*

We may grant stock appreciation rights under the 2011 Plan separate from any other award or together with other awards under the 2011 Plan.

Generally, if a stock appreciation right is granted with an exercise price equal to the fair market value of the underlying stock on the grant date, the recipient will recognize ordinary income equal to the fair market value of the stock or cash received upon such exercise.

Subject to the requirement of reasonableness, the provisions of Section 162(m), and the satisfaction of our tax reporting obligation, we will generally be entitled to a tax deduction equal to the taxable ordinary income realized by the recipient of the stock appreciation right.

*Section 162(m) Limitations*

Section 162(m) disallows a deduction to any publicly held corporation and its affiliates for certain compensation paid to "covered employees" in a taxable year to the extent that compensation paid to a covered employee exceeds $1 million. The exemption from Section 162(m)'s deduction limit for performance-based compensation has been repealed, effective for taxable years beginning after December 31, 2017, such that compensation paid to our covered employees in excess of $1 million will not be deductible unless it qualifies for transition relief applicable to certain arrangements in place as of November 2, 2017, and not modified in any material respect on or after such date. As a result, compensation (including compensation pursuant to awards granted under the 2011 Plan) paid to any of our "covered employees" under Section 162(m) in excess of $1 million per taxable year generally will not be deductible.

**New Plan Benefits**

Awards granted under the 2011 Plan to our executive officers and other employees are discretionary and are not subject to set benefits or amounts under the terms of the 2011 Plan, and our Board and our Compensation Committee have not granted any awards under the 2011 Plan subject to stockholder approval of this Proposal 3. Accordingly, the future benefits or amounts that will be received by or allocated to our executive officers and other employees under the 2011 Plan are not determinable.

## Plan Benefits

The following table sets forth, for each individual and group indicated, the total number of shares subject to awards that have been granted under the 2011 Plan as of March 31, 2026.

| PLAN BENEFITS<br>2011 PLAN | | | | |
|---|---|---|---|---|
| **Name of Employee** | **Total Number of Shares** | **Options** | **RSUs** | **PRSUs[1]** |
| Brett P. Monia<br>Chief Executive Officer | 1,220,517 | 658,287 | 348,540 | 213,690 |
| Elizabeth L. Hougen<br>Executive Vice President, Chief Financial Officer | 283,341 | 125,916 | 111,245 | 46,180 |
| Richard S. Geary<br>Executive Vice President, Chief Development Officer | 234,741 | 122,059 | 80,282 | 32,400 |
| Brian Birchler<br>EVP, Corporate and Development Operations | 294,237 | 174,055 | 87,782 | 32,400 |
| Eric Swayze<br>Executive Vice President, Research | 315,365 | 202,683 | 80,282 | 32,400 |
| Patrick R. O'Neil<br>EVP, Chief Legal Officer & General Counsel | 234,741 | 122,059 | 80,282 | 32,400 |
| All Executive Officers as a Group[2] | 3,982,049 | 2,227,510 | 1,221,719 | 532,820 |
| All Non-Employee Directors as a Group | — | — | — | — |
| All Non-Executive Officer Employees as a Group | 14,921,574 | 8,776,888 | 6,144,686 | — |

(1) Reflects the target payout of shares under the PRSU awards.

(2) Includes shares subject to awards granted under the 2011 Plan to executive officers as of March 31, 2026.

Please see page 42 for information regarding outstanding options and shares reserved for future issuance under our equity compensation plans as of March 31, 2026.

# PROPOSAL 4

# APPROVAL OF AN AMENDMENT OF OUR AMENDED AND RESTATED 2000 EMPLOYEE STOCK PURCHASE PLAN

In January 2000, the Compensation Committee recommended, and the Board adopted, the 2000 Employee Stock Purchase Plan (the "***ESPP***") and the stockholders approved the ESPP on June 8, 2000. The Board adopted, and in June 2009 the stockholders approved, an amendment to the ESPP, which extended the term, limited the evergreen provision to add 150,000 shares each year, limited the offering periods to six months, and imposed a minimum six-month holding period on shares purchased under the ESPP. On March 22, 2019 (the "***A&R ESPP Effective Date***"), we amended and restated the ESPP to remove the evergreen provision.

In this Proposal 4, we are requesting stockholders to approve an amendment of the ESPP to increase the number of shares of common stock authorized for purchase under the ESPP by 750,000 shares and remove the termination date of the plan.

The ESPP provides employees with an opportunity to acquire shares of common stock at a price below market value and to pay for the purchases through voluntary payroll deductions, thereby enabling the Company to attract, retain and reward employees and strengthen the mutuality of interests between employees and other Company stockholders. The Board believes that the ESPP is an integral part of our long-term compensation philosophy and is necessary to continue providing the appropriate levels and types of equity compensation for our employees.

## Why We Are Asking Our Stockholders to Approve the ESPP

As of December 31, 2025, 130,884 shares were available for future issuance under the ESPP. Without replenishment, we believe such amount may be insufficient to meet our anticipated employee recruiting and retention needs before the 2027 Annual Meeting. If this Proposal 4 is not approved by our stockholders, our ability to recruit and retain employees could be negatively impacted.

## Important Aspects of the ESPP

The ESPP includes certain provisions that are designed to protect our stockholders' interests and to reflect corporate governance best practices, including:

- *Submission of amendments to the ESPP to stockholders.* The ESPP requires stockholder approval for material amendments, including any increase in the number of shares reserved for issuance under the ESPP. Our ESPP does not contain an annual "evergreen" provision.
- *Broad-based eligibility for equity awards.* The vast majority of our employees are eligible to participate in the ESPP. By doing so, we tie our employee's interests with stockholder interests and motivate our employees to act as owners of the business.
- *Our ESPP contains a holding period for shares of stock purchased under the ESPP.* The ESPP includes a holding period of six months for shares purchased on any given purchase date in a future offering.

## Required Vote and Board of Directors Recommendation

Pursuant to the rules of the Nasdaq Stock Market, approval of this Proposal 4 requires "For" votes from the holders of a majority of the votes cast on the proposal, voting virtually or by proxy at the meeting. Abstentions are not treated as votes cast and, therefore, will have no effect. Broker non-votes will have no effect on the outcome of the vote.

Our Board believes that approval of this Proposal 4 is in our best interests and the best interests of our stockholders for the reasons stated above.

**THE BOARD UNANIMOUSLY RECOMMENDS A VOTE "FOR" APPROVAL OF PROPOSAL 4.**

## DESCRIPTION OF THE IONIS PHARMACEUTICALS, INC. 2000 EMPLOYEE STOCK PURCHASE PLAN

Below is a high-level summary of the terms of the ESPP. This summary is qualified in its entirety by reference to the complete text of the ESPP. We encourage our stockholders to read the actual text of the ESPP, in its entirety, a copy of which we filed with this Proxy Statement as Appendix B.

## Purpose

The purpose of the ESPP is to retain the services of our employees and to provide incentives to exert maximum efforts for the success of the Company by allowing eligible employees to purchase Ionis common stock on favorable terms through payroll deductions.

### Administration

The Board has the authority to administer the ESPP. The Board can construe and interpret the ESPP and, subject to the provisions of the ESPP, determine when and how rights to purchase our common stock under the ESPP are granted to eligible employees, determine the provisions of each offering, and designate which of our affiliates will be eligible to participate in the ESPP. The Board can delegate administration of the ESPP to a committee composed of at least two members of the Board. The Board has delegated administration of the ESPP to the Compensation Committee. The "Board" refers to the Compensation Committee as well as to the Board of Directors itself throughout the remainder of this Proposal 4.

### Eligibility and Participation

Ionis employees based in the U.S. who work at least 20 hours a week and have been employed for a continuous period set by the Board, no more than two years, are eligible to participate in an offering. As of March 31, 2026, we had approximately 1,205 employees who were eligible to participate in the ESPP. An employee's participation in an offering will terminate automatically upon termination of employment. Ionis' officers may participate in an offering, but the Board may limit the participation of certain highly compensated employees. An employee's participation in the ESPP may not exceed $25,000 in any calendar year. In addition, any employee owning 5% or more of our total combined voting power may not participate. Employees desiring to participate in an offering must provide appropriate notice to the Company. Employees may terminate participation in any offering at any time, except as limited by the Board.

### Terms of Offering

Each eligible employee can designate a percentage of their earnings up to 10%, or such lower percentage designated by the Board, during the offering period to be deducted and used to purchase Ionis common stock in the offering. We deposit the payroll deductions with the general funds of the Company. The Board may allow certain changes to payroll deduction amounts for an offering. The Board may also designate a maximum dollar amount for purchases during an offering.

The Board may also specify a maximum number of shares that (i) each employee can purchase per offering, and (ii) all employees together can purchase per offering. The purchase price of stock purchased under the ESPP will be the lesser of (i) an amount equal to 85% of the fair market value of the stock on the first day of the offering; or (ii) an amount equal to 85% of the fair market value of the stock on the purchase date. On each purchase date under an offering, we will apply each participant's accumulated payroll deductions to purchase our Common Stock. We currently have two offerings a year under the ESPP, each of which lasts approximately six months.

### Minimum Holding Period

Participants must hold the stock they purchase under the ESPP for a minimum of six months from the date of purchase.

### Duration, Amendment, and Termination

The Board may suspend or terminate the ESPP at any time. No rights may be granted under the ESPP while the ESPP is suspended or after it is terminated. Unless sooner terminated, the ESPP will terminate on March 21, 2029. Under the proposed amendments described in this Proposal 4, the termination date of the ESPP will be removed.

### Shares Subject to the ESPP

As of March 31, 2026, there were 56,118 shares subject to the ESPP. We expect to issue these shares as part of the remaining offering this year under the ESPP.

### Adjustments Upon Change in Stock

If any change is made in the stock under the ESPP due to a change in corporate capitalization through reincorporation, stock dividend, stock split, reverse stock split, combination or reclassification of shares, the ESPP will be appropriately adjusted in the class(es) and maximum number of securities subject to the ESPP and price of shares under the offering. The Board will make the adjustment and its determination will be final, binding and conclusive.

In the event of: (1) a dissolution, liquidation or sale of all or substantially all of the assets of Ionis, (2) a merger or consolidation in which Ionis is not the surviving corporation, or (3) a reverse merger in which Ionis is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger are converted by virtue of the merger into other property, whether in the form of securities, cash or otherwise or (4) any other capital reorganization in which more than fifty percent (50%) of the securities of Ionis entitled to vote are sold or otherwise exchanged, then any surviving corporation may assume outstanding rights or substitute similar rights for those under the

ESPP. If the surviving corporation does not assume the outstanding rights or substitutes similar rights, participants' accumulated payroll deductions will be used to purchase Common Stock immediately prior to the transaction described above and the participants' rights under the ongoing offering will be terminated immediately following that purchase.

### Tax Information

Participation in the ESPP is intended to qualify for the favorable federal tax treatment accorded employee stock purchase plans under Section 423 of the Internal Revenue Code. Under these provisions, a participant will be taxed on amounts withheld as if actually received. However, no income will be taxable to a participant until disposition of the shares acquired.

If the stock is disposed of more than two years after the beginning of the offering and more than one year after the stock is transferred to the participant, the lesser of (i) the excess of the fair market value of the stock at the time of the disposition over the exercise price or (ii) the excess of the fair market value of the stock as of the beginning of the offering over the exercise price (determined as of the beginning of the offering period) will be treated as ordinary income. Any further gain or any loss will be taxed as a capital gain or loss.

If the stock is sold or disposed of before the expiration of either of the holding periods described above, the excess of the fair market value of the stock on the exercise date over the exercise price generally will be treated as ordinary income at the time of the disposition, and Ionis may, in the future, be required to withhold income taxes relating to the ordinary income from other payments made to the participant. The balance of any gain will be treated as capital gain. Even if the stock is later disposed of for less than its fair market value on the exercise date, the same amount of ordinary income is attributed to the participant and a capital loss is recognized equal to the difference between the sales price and the fair market value of the stock on the exercise date.

Any capital gain or loss realized by a participant upon the disposition of stock acquired under the ESPP will be long- or short-term depending on whether the stock has been held for more than one year.

There are no federal income tax consequences to Ionis by reason of the grant or exercise of rights under the ESPP. Ionis generally is entitled to a deduction for amounts taxed as ordinary income to a participant upon disposition by a participant of stock before the expiration of the holding periods described above.

### New Plan Benefits

Because benefits under the ESPP will depend on employees' elections to participate and to purchase shares under the ESPP at various future dates, it is not possible to determine the benefits that our executive officers and other employees will receive under the ESPP. Non-employee directors are not eligible to participate in the ESPP.

## Plan Benefits

The following table presents certain information with respect to the aggregate number of shares purchased through our ESPP as of March 31, 2026 by each executive officer named in the Summary Compensation Table since the A&R ESPP Effective Date. This information is for illustration only and may not be indicative of purchases that the officers will make in the future under the ESPP. Shares from our ESPP are purchased on February 28 (or 29 in a leap year) and August 31 of each year.

| PLAN BENEFITS<br>2000 EMPLOYEE STOCK PURCHASE PLAN | |
|---|---|
| **Name and Position** | **Number of Shares Purchased** |
| Brett P. Monia<br>Chief Executive Officer | 3,407 |
| Elizabeth L. Hougen<br>EVP Finance, Chief Financial Officer | 1,404 |
| Richard S. Geary<br>EVP, Chief Development Officer | — |
| Brian Birchler<br>EVP, Corporate and Development Operations | 3,232 |
| Eric Swayze<br>EVP, Research | 3,261 |
| Patrick R. O'Neil<br>EVP, Chief Legal Officer & General Counsel | 3,400 |
| All Executive Officers as a Group | 17,551 |
| All Non-Employee Directors as a Group[(1)] | — |
| All Non-Executive Officer Employees as a Group | 601,264 |

(1) Non-employee Directors are not eligible to participate in the ESPP.

# PROPOSAL 5

# RATIFICATION OF SELECTION OF INDEPENDENT AUDITORS

The Audit Committee has selected Ernst & Young LLP as our independent registered public accounting firm for our 2026 fiscal year and has requested management to ask for stockholder ratification at the Annual Meeting. Ernst & Young LLP has audited our financial statements since we were founded in 1989. Representatives of Ernst & Young LLP will be at the Annual Meeting to answer appropriate questions and make a statement should they desire to do so.

Although our bylaws do not require stockholders to ratify our independent registered public accounting firm, the Audit Committee would like our stockholders' opinion as a matter of good corporate practice. If the stockholders do not ratify the selection of Ernst & Young LLP, the Audit Committee will reconsider whether to keep the firm. However, even if the stockholders ratify the selection, the Audit Committee may choose to appoint a different independent accounting firm at any time during the year if it believes that a change would be in the best interests of our stockholders and Ionis.

The affirmative vote of the holders of a majority of the shares present or represented by proxy at the Annual Meeting and entitled to vote on the matter will be required to ratify the selection of Ernst & Young LLP. If you indicate on your proxy to "Abstain" from voting, it will have the same effect as an "Against" vote for this Proposal 5. Because brokers have discretionary authority to vote on the ratification of the selection of Ernst & Young LLP, we do not expect any broker non-votes in connection with the ratification.

## Independent Auditors' Fees; Pre-Approval Policies and Procedures

The Audit Committee has adopted a policy and procedure for the pre-approval of audit and permissible non-audit services rendered by our independent registered public accounting firm, Ernst & Young LLP. The policy generally pre-approves specific services in the defined categories of audit services, audit-related services, and tax services up to pre-determined amounts. The Audit Committee may pre-approve services as part of its approval of the scope of the engagement of the independent auditor or on an individual explicit case-by-case basis before the Audit Committee engages the independent registered public accounting firm to provide each service. The Audit Committee pre-approved all of the services described below.

### Audit Fees

For the fiscal years ended December 31, 2025 and 2024, Ernst & Young LLP billed us approximately $2.4 million and $2.2 million, respectively, primarily related to the integrated audit of our financial statements and reviews of our interim financial statements. In addition, Ernst & Young LLP billed us approximately $490,000 and approximately $320,000 in 2025 and 2024, respectively, related to corporate transactions.

### Audit Related Fees

For the fiscal years ended December 31, 2025, Ernst & Young LLP billed us approximately $606,000 for fees related to professional services in connection with a pre-implementation assessment of a new enterprise resource planning software platform. For the fiscal year ended December 31, 2024, there were no audit related fees billed by Ernst & Young LLP.

### Tax Fees

For the fiscal years ended December 31, 2025 and 2024, Ernst & Young LLP billed us approximately $110,000 and $120,000 for each year, respectively, primarily related to professional services on tax projects.

### All Other Fees

During the fiscal years ended December 31, 2025 and 2024, all other fees billed by Ernst & Young LLP were approximately $7,000 for each year. These fees were for a subscription to an online accounting and tax information service. The Audit Committee has determined that the rendering of all non-audit services by Ernst & Young LLP is compatible with maintaining the auditor's independence. During the fiscal years ended December 31, 2025 and 2024, none of the total hours expended on our financial audit by Ernst & Young LLP were provided by persons other than Ernst & Young LLP's employees.

**THE BOARD UNANIMOUSLY RECOMMENDS A VOTE "FOR" APPROVAL OF PROPOSAL 5.**

## SECURITY OWNERSHIP OF CERTAIN BENEFICIAL OWNERS AND MANAGEMENT

This table outlines the ownership of our common stock as of March 31, 2026 by (1) each director and nominee for director; (2) each named executive officer; and (3) all directors and executive officers as a group. For every entity that we know beneficially owns more than five percent of our common stock, the table below reflects ownership of our common stock as of the most recent Schedule 13D or 13G filed with the SEC.

Except as otherwise indicated below, the address of each beneficial owner listed in this table is c/o Ionis Pharmaceuticals, Inc., 2855 Gazelle Court, Carlsbad, California 92010.

| | Beneficial Ownership[1] | |
|---|---|---|
| Beneficial Owner | Number of Shares | Percent of Total[2] |
| FMR LLC[3]<br>245 Summer Street<br>Boston, MA 02210 | 21,520,872 | 12.97% |
| Capital World Investors[4]<br>333 South Hope Street, 55th Floor<br>Los Angeles, CA 90071 | 17,961,299 | 10.83% |
| The Vanguard Group[5]<br>100 Vanguard Boulevard<br>Malvern, PA 19355 | 16,472,539 | 9.93% |
| T. Rowe Price Investment Management, Inc.[6]<br>1307 Point Street<br>Baltimore, MD 21231 | 9,108,019 | 5.49% |
| BlackRock Inc.[7]<br>50 Hudson Yards<br>New York, NY 10001 | 9,066,517 | 5.46% |
| Spencer R. Berthelsen[8] | 276,515 | * |
| Allene M. Diaz[9] | 13,922 | * |
| Michael Hayden[10] | 160,730 | * |
| Joan Herman[11] | 106,518 | * |
| Joseph Klein, III[12] | 59,546 | * |
| Joseph Loscalzo[13] | 123,730 | * |
| B. Lynne Parshall[14] | 144,776 | * |
| Joseph H. Wender[15] | 156,467 | * |
| Michael Yang[16] | 26,289 | * |
| Brian Birchler[17] | 191,478 | * |
| Richard S. Geary[18] | 132,541 | * |
| Elizabeth L. Hougen[19] | 119,274 | * |
| Brett P. Monia[20] | 586,330 | * |
| Patrick R. O'Neil[21] | 84,795 | * |
| Eric Swayze[22] | 163,874 | * |
| All Directors and executive officers as a group (twenty-one persons)[23] | 3,008,231 | 1.81% |

* Less than one percent

(1) We base this table upon information supplied by officers, directors, principal stockholders, and Form 3s, Form 4s, Form 5s, Schedules 13D and 13G filed with the SEC. Unless otherwise indicated in the footnotes to this table and subject to community property laws where applicable, we believe that each of the stockholders named in this table has sole voting and investment power with respect to the shares indicated as beneficially owned.

(2) Applicable percentages are based on 165,902,064 shares of common stock outstanding on March 31, 2026, adjusted as required by rules promulgated by the SEC.

(3) FMR LLC has sole voting power to direct the vote of 21,519,114 shares and sole power to dispose or direct the disposition of 21,520,872 shares. The Fidelity Growth Company Commingled Pool holds the interest of 9,268,403 shares of our common stock, which amounts to 5.49% of our total outstanding as of March 31, 2026. Abigail P. Johnson is a director, the Chairman, and the Chief Executive Officer of FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC.

(4) Capital World Investors has sole voting power to direct the vote of 17,961,299 shares and sole power to dispose or direct the disposition of 17,961,299 shares.

(5) The Vanguard Group has shared voting power to direct the vote of 69,305 shares, sole power to dispose or direct the disposition of 16,225,634 shares, and shared dispositive power for 246,905 shares. The Vanguard Group subsequently reported that due to an internal realignment it no longer has, or is deemed to have, beneficial ownership over Company securities beneficially owned by various Vanguard subsidiaries and/or business divisions. The Vanguard Group also reported that certain subsidiaries or business divisions that formerly had, or were deemed to have, beneficial ownership with The Vanguard Group, will report beneficial ownership separately (on a disaggregated basis).

(6) T. Rowe Price Investment Management, Inc. has sole voting power to direct the vote of 9,083,319 shares and sole power to dispose or direct the disposition of 9,108,019 shares.

(7) BlackRock Inc. is a parent holding company and various persons have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of shares of our common stock. BlackRock has sole voting power to direct the vote of 8,800,496 shares and sole power to dispose or direct the disposition of 9,066,517 shares.

(8) Includes 70 shares owned by Dr. Berthelsen's daughter for which he disclaims beneficial ownership. Includes 120,432 shares of common stock issuable upon exercise of options held by Dr. Berthelsen that are exercisable on or before May 30, 2026.

(9) Includes 10,111 shares of common stock issuable upon exercise of options held by Ms. Diaz that are exercisable on or before May 30, 2026.

(10) Includes 104,432 shares of common stock issuable upon exercise of options held by Dr. Hayden that are exercisable on or before May 30, 2026.

(11) Includes 60,432 shares of common stock issuable upon exercise of options held by Ms. Herman that are exercisable on or before May 30, 2026.

(12) Includes, 40,432 shares of common stock issuable upon exercise of options held by Mr. Klein that are exercisable on or before May 30, 2026, and 8,000 shares of common stock issuable upon exercise of options held in trusts for the benefit of Mr. Klein's three children that are exercisable on or before May 30, 2026.

(13) Includes 87,400 shares of common stock issuable upon exercise of options held by Dr. Loscalzo that are exercisable on or before May 30, 2026.

(14) Includes 88,432 shares of common stock issuable upon exercise of options held by Ms. Parshall that are exercisable on or before May 30, 2026.

(15) Includes 52,035 shares of common stock held by Mr. Wender in a trust, and 104,432 shares of common stock issuable upon exercise of options held by Mr. Wender that are exercisable on or before May 30, 2026.

(16) Includes 18,349 shares of common stock issuable upon exercise of options held by Mr. Yang that are exercisable on or before May 30, 2026.

(17) Includes 124,880 shares of common stock issuable upon exercise of options held by Mr. Birchler that are exercisable on or before May 30, 2026.

(18) Includes 72,884 shares of common stock issuable upon exercise of options held by Dr. Geary that are exercisable on or before May 30, 2026.

(19) Includes 36,614 shares of common stock issuable upon exercise of options held by Ms. Hougen that are exercisable on or before May 30, 2026.

(20) Includes 343,668 shares of common stock issuable upon exercise of options held by Dr. Monia that are exercisable on or before May 30, 2026.

(21) Includes 22,584 shares of common stock issuable upon exercise of options held by Mr. O'Neil that are exercisable on or before May 30, 2026.

(22) Includes 131,195 shares of common stock issuable upon exercise of options held by Dr. Swayze that are exercisable on or before May 30,2026.

(23) Includes an aggregate of 1,791,967 shares issuable upon exercise of options held by all directors and executive officers as a group that are exercisable on or before May 30, 2026.

## Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires our directors, executive officers, and persons who own more than ten percent of a registered class of our equity securities, to file with the SEC initial reports of ownership and reports of changes in ownership of our common stock and other equity securities. Officers, directors and greater than ten percent stockholders are required by SEC regulations to furnish us with copies of all Section 16(a) forms they file.

To our knowledge, based on a review of Section 16 reports submitted on EDGAR and written representations from the reporting persons that no Form 5s were required during the fiscal year ended December 31, 2025, our officers, directors and greater than ten percent beneficial owners have complied with all applicable Section 16(a) filing requirements.

## Securities Authorized for Issuance Under Equity Compensation Plans

The following table sets forth information regarding outstanding options and shares reserved for future issuance under our equity compensation plans as of December 31, 2025:

| Plan Category | Number of Shares to be Issued Upon Exercise of Outstanding Options, Warrants and Rights | Weighted Average Exercise Price of Outstanding Options, Warrants and Rights[1] | Number of Shares Remaining Available for Future Issuance |
|---|---|---|---|
| Equity compensation plans approved by stockholders[2] | 15,528,253 | $45.93 | 8,136,194[3] |
| Equity compensation plans not approved by stockholders | — | — | — |
| Total | 15,528,253 | $45.93 | 8,136,194[3] |

(1) Does not include PRSU awards.

(2) Consists of four Ionis plans: Non-Employee Directors' Stock Option Plan, 2011 Equity Incentive Plan, 2020 Equity Incentive Plan, and 2000 Employee Stock Purchase Plan.

(3) Of these shares, 130,884 remained available for purchase under the ESPP as of December 31, 2025.

# EXECUTIVE COMPENSATION

## Compensation Discussion and Analysis

### 2025 NEOs, 2025 "Say on Pay" Vote and Summary of Recent Compensation and Governance Changes

*Named Executive Officers*. On December 31, 2025, our Chief Executive Officer, Chief Financial Officer, and our four[9] other most highly compensated executive officers, called our "named executive officers" or "NEOs," were as follows:

| Name | Title |
|---|---|
| Brett P. Monia | Chief Executive Officer |
| Elizabeth L. Hougen | Executive Vice President, Chief Financial Officer |
| Richard S. Geary | Executive Vice President, Chief Development Officer |
| Brian Birchler | Executive Vice President, Corporate and Development Operations |
| Eric Swayze | Executive Vice President, Research |
| Patrick R. O'Neil | Executive Vice President, Chief Legal Officer and General Counsel |

*"Say on Pay" Vote*. In June 2025, we held a stockholder advisory vote on the compensation of our named executive officers. Our stockholders overwhelmingly approved, on an advisory (nonbinding) basis, the compensation of our named executive officers, with approximately 96% of stockholder votes cast in favor of our "say on pay" resolution. In evaluating our general compensation practices during 2025 and in early 2026, we were mindful of the strong support our stockholders expressed for our compensation philosophies and practices. We remain committed to considering stockholder feedback on an ongoing basis and ensuring that our compensation practices align with market trends.

*Compensation and Governance Changes*. As reflected in the following table, we have made several compensation and governance-related changes responsive to feedback we received over the past several years. We believe these changes continue to align the Company with peer companies and incentivize management to enhance long-term stockholder value.

| Year Implemented | Compensation or Governance Change |
|---|---|
| 2026 | Revised our Non-Employee Director Compensation Policy to reduce the cap on annual equity awards such that incumbent non-employee directors will receive no more than $400,000 in annual equity compensation per year and newly appointed non-employee directors will receive no more than $600,000 in initial equity compensation, in both cases based on the aggregate grant date fair value |
| 2026 | Increased the proportion of PRSUs to be awarded to our executive officers beginning in 2026 as follows: from 33% to 40% of our CEO's total equity awards and from 20% to 40% of our other executive officers' total equity awards |
| 2023 | Increased the vesting term of initial equity awards granted to our non-employee directors upon joining the Board such that all initial awards vest equally over three years instead of vesting in one year |
| 2023 | Modified our executive clawback policy to align with the SEC's clawback policy rules |
| 2023 | Revised the structure of our performance-based equity awards such that they have a single vesting period at the end of three years and require a higher relative TSR percentile rank for maximum payout of the awards (increased from the 75th percentile to the 90th percentile) |
| 2023 | Increased the ownership requirements in our stock ownership and holding guidelines applicable to our non-employee directors |
| 2022 | Implemented PRSUs for our other executive officers |
| 2020 | Implemented PRSUs for our CEO |

[9] Dr. Geary was no longer serving as an executive officer as of December 31, 2025. Had Dr. Geary been serving in that capacity on December 31, 2025, he would have been a named executive officer, and as such, is included as a named executive officer in this Proxy Statement.

## Business Overview and Recent Achievements

*Overview*. For over three decades, we have invented medicines that bring better futures to people with serious diseases. As a pioneer in RNA-targeted medicines with a deep understanding of disease biology and an industry-leading drug discovery technology, we are driven to deliver innovative, life-changing advances for patients. With two independent commercial launches now underway, we have transitioned into a fully integrated commercial-stage biotechnology company.

*Our Medicines*. We currently have seven marketed medicines: TRYNGOLZA® (olezarsen), DAWNZERA™ (donidalorsen), WAINUA® (eplontersen), SPINRAZA® (nusinersen), QALSODY® (tofersen), TEGSEDI® (inotersen) and WAYLIVRA® (volanesorsen). We also have a rich innovative pipeline across our focus areas of neurology, cardiometabolic diseases and select areas of high patient need. We currently have ten medicines in Phase 3 development and multiple additional medicines in early and mid-stage development.

*Our Recent Achievements*. 2025 was a defining year for Ionis, marked by the execution of our first two independent launches and multiple positive data readouts across our rich pipeline.

Our first launch was for TRYNGOLZA following approval in December 2024 for adults with familial chylomicronemia syndrome ("***FCS***"), as an adjunct to diet. Our second launch was for DAWNZERA following approval in August 2025 for patients 12 years of age and older with hereditary angioedema ("***HAE***"). In addition, we are positioned to independently launch two additional medicines in 2026 assuming regulatory approval: olezarsen for the treatment of severe hypertriglyceridemia ("***sHTG***"), our first anticipated launch in a broad patient population, and zilganersen for Alexander disease ("***AxD***"), our first launch from our wholly owned neurology portfolio.

Focusing on our Ionis-owned pipeline, we advanced numerous medicines in development. We currently have three wholly-owned medicines in late-stage development, including obudanersen for Angelman syndrome, which we advanced into a Phase 3 study in the second quarter of 2025. We are advancing additional wholly-owned medicines in early and mid-stage development.

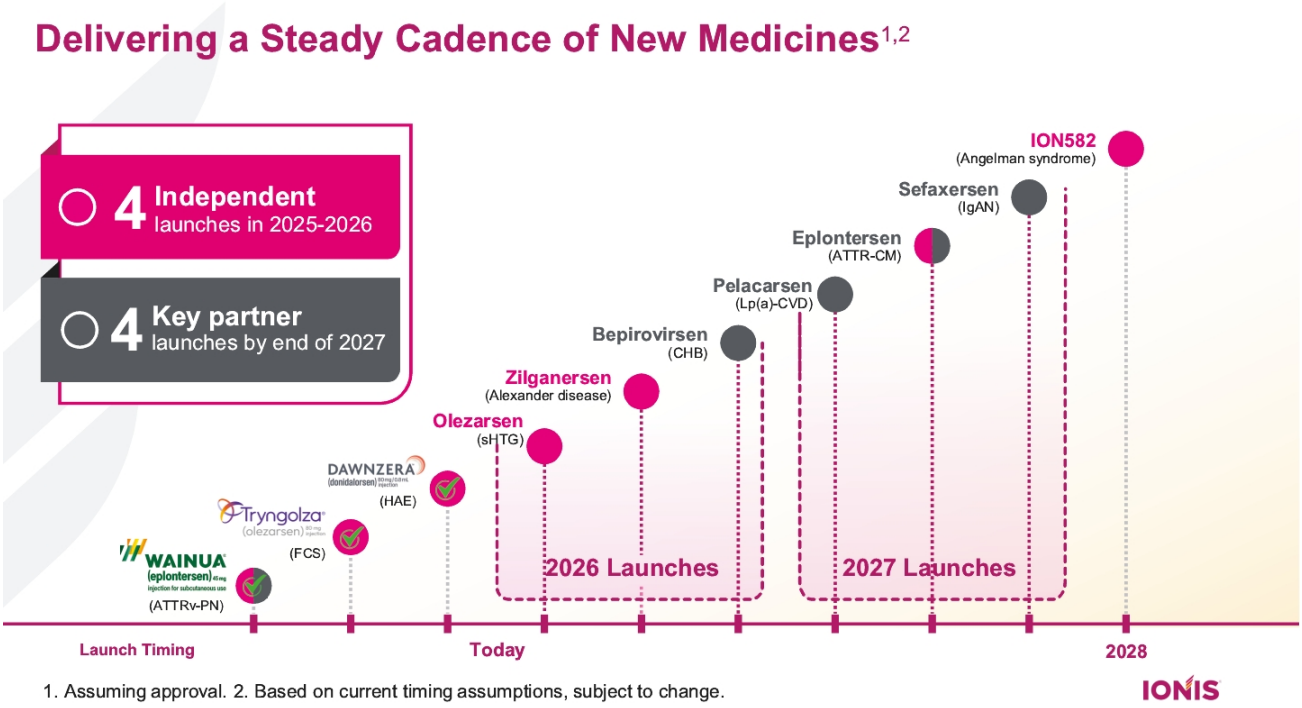
With a commitment to progress our RNA-targeting technology, we have expanded our technology platform to include siRNA, and we are forging ahead towards our goals to optimize delivery and expand our therapeutic opportunities.

**2025 was a defining year for Ionis, marked by the execution of our first two independent launches and multiple positive data readouts from our rich pipeline.**

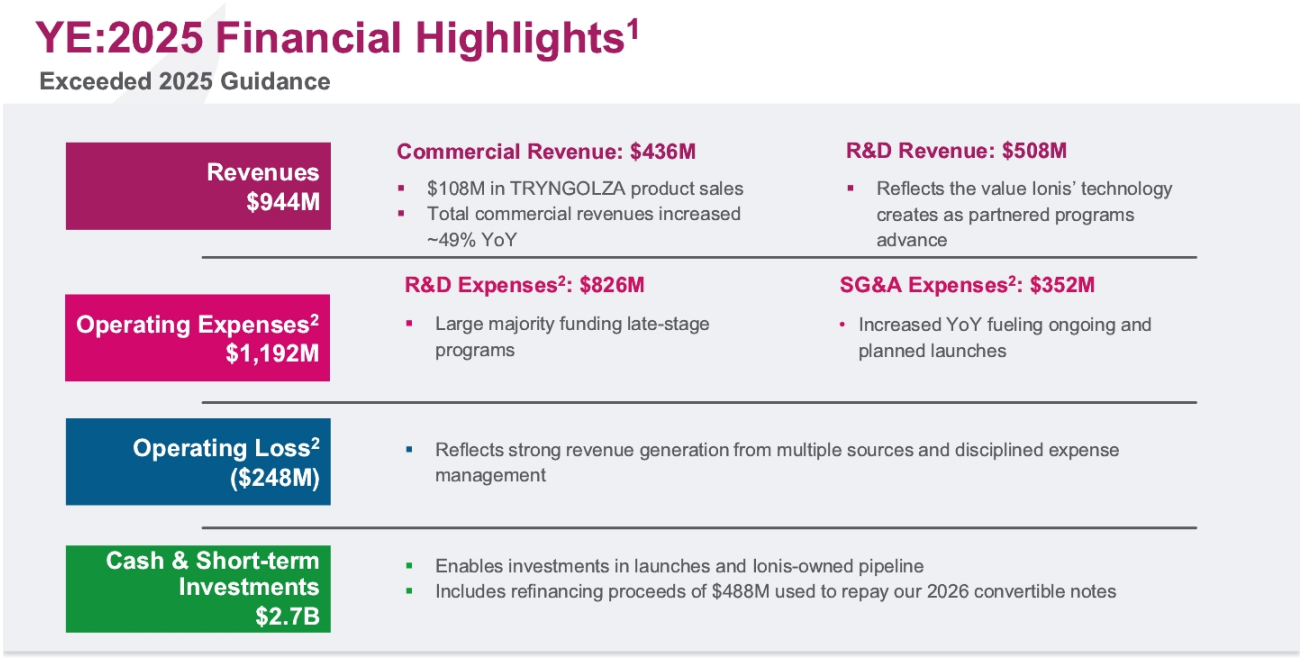
**Our ongoing and upcoming independent and partnered product launches position us well to help millions of patients with serious diseases. Coupled with our disciplined financial management, we are positioned well for continued growth and value creation in the years ahead.**

Further, we also have numerous partnered medicines that enable our innovative science to reach more patients, while allowing us to focus our efforts on advancing the medicines we plan to commercialize. These include SPINRAZA for spinal muscular atrophy ("***SMA***"), which Biogen is commercializing, QALSODY for certain adults with amyotrophic lateral sclerosis, which Biogen is also commercializing, and WAINUA for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis ("***ATTRv-PN***"), in adults, which we are co-commercializing in the U.S. with AstraZeneca. Our partnered pipeline has also recently delivered positive data readouts, including positive Phase 3 data for bepirovirsen in chronic hepatitis B and Phase 2 data for sapablursen in polycythemia vera.

Our key recent achievements, combined with our ongoing and planned independent and partnered product launches, position us well to help millions of patients with serious diseases.




*Our Financial Resources*. Our financial discipline has been an enduring quality of Ionis for many years. Our multiple sources of revenue and our capital structure enable our continued investment to support ongoing and planned launches and to advance our wholly owned medicines in development. In 2025, we earned revenues of $944 million and ended the year with a cash and short-term investment balance of $2.7 billion. Our strong progress in 2025, coupled with our disciplined financial management, position us well for continued growth and value creation in the years ahead. The Compensation Committee considered this performance context, including progress toward durable commercial execution and balance sheet strength, when evaluating overall year-end compensation outcomes and the rigor of forward-looking goals.

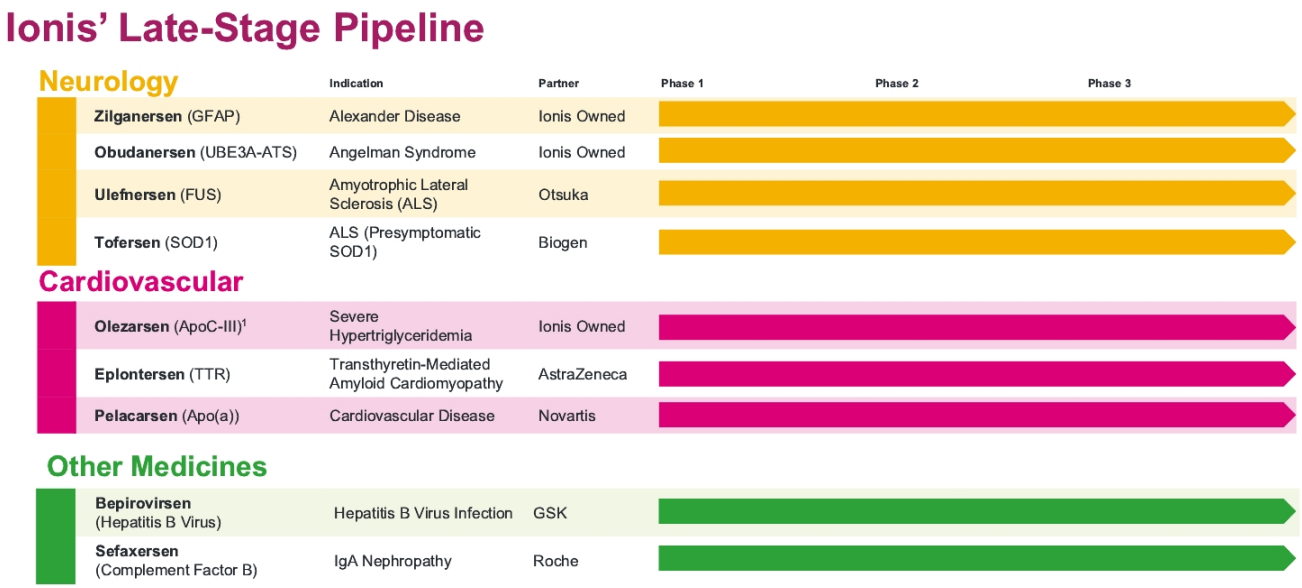



(1) For the year ended December 31, 2025.

(2) Non-GAAP financial measure that excludes non-cash compensation expense related to equity awards. We use "non-GAAP" in place of "pro-forma" when discussing our financial results that exclude non-cash compensation expense related to equity awards because we believe that non-GAAP financial results better represent the economics of our business and how we manage our business. For a detailed reconciliation of non-GAAP and GAAP measures, see Appendix C.

*Advancing Our Pipeline*

In addition to our marketed medicines, we have a rich innovative late- and mid-stage pipeline in neurology, cardiology and select areas of high patient need. We currently have ten medicines in Phase 3 development and multiple additional medicines in early and mid-stage development.




(1) Granted Sobi exclusive rights to commercialize olezarsen in countries outside of the U.S., Canada and China.

## Summary of Compensation Practices

Below we summarize some of our compensation practices, both the practices we implement because we believe they are consistent with our vision and building long-term stockholder value, and those we choose not to implement as we believe they are counter to our vision and building long-term stockholder value.

| | |
|---|---|
| ✓ General compensation principles | We design our compensation structure to drive the creation of long-term stockholder value and mitigate unnecessary or imprudent business risk taking. Specifically, we:<br>• Use a combination of compensation vehicles that provide a balanced mix of fixed and variable cash incentives, and long-term stock incentives;<br>• Require a 12-month minimum vesting period for equity awards;<br>• Set explicit and demanding objectives at the beginning of each year from which we measure performance for the year;<br>• Set a strict budget for equity awards and salary increases;<br>• Do *not* provide perquisites for any employees; and<br>• Do *not* provide "gross-up" payments, other than for relocation. |
| ✓ Align executive compensation with Company performance and design performance-based awards to drive creation of long-term stockholder value | We tie a significant portion of our executive officers' compensation to Company performance and design performance-based awards to drive the creation of long-term stockholder value. For example, we:<br>• Increased the proportion of PRSUs to be awarded to our executive officers beginning in 2026 as follows: from 33% to 40% of our CEO's total equity awards and from 20% to 40% of our other executive officers' total equity awards<br>• Allocated approximately 60% of our Chief Executive Officer's 2025 compensation in the form of performance-based compensation, which we consider to consist of cash bonuses, stock options and PRSUs;<br>• Revised our PRSU structure for grants made beginning in 2023 such that:<br>  ○ awards have a single vesting period at the end of three years; and<br>  ○ the relative TSR percentile rank for maximum payout of the awards increased from the 75th percentile to the 90th percentile.<br>• Place a maximum limit on cash bonuses and do not guarantee a cash bonus – cash bonuses can be, and have been, zero; and<br>• Empower our Compensation Committee with the ability to reduce the Company Performance Factor (used to determine cash bonuses) for our executive officers based on Company performance. |
| ✓ Stock ownership and holding guidelines | We maintain stock ownership and holding guidelines that require our executive officers and non-employee directors to meet certain ownership thresholds. We increased such ownership requirements for our non-employee directors in 2023. |
| ✓ Clawback policy | We use an executive "clawback" policy that applies to all Section 16 officers and is consistent with the clawback policy rules adopted by the SEC and Nasdaq in 2023. |
| ✓ Disallow hedging and pledging | We do not allow pledging, shorting, or hedging against our stock by directors or employees. |
| ✓ No option re-pricing or cash buyouts | We do not reprice or "cash-out" stock options without stockholder approval. |
| ✓ Engage an independent compensation consultant | The Compensation Committee has retained a compensation consultant whose relationship with the Company was confirmed to be independent for 2025.<br><br>The compensation consultant, among other things, assists us in selecting an appropriate peer group and annually reviews our compensation levels, policies, practices, and procedures for our employees and non-employee directors compared to our peer group. |
| ✓ Use a "double trigger" for change in control for our executive officers | We use a "double trigger" for cash payments and equity acceleration for change in control for our executive officers. |
| ✓ Hold a "say on pay" vote annually | Provides an effective way for us to obtain information on stockholder sentiment about our executive compensation program each year. |

*Compensation Overview and the Role of the Compensation Committee*

We have designed our executive compensation program to attract and retain executives who can help us meet our business objectives and to motivate our executive officers to enhance long-term stockholder value. The Compensation Committee, with input from an independent compensation consultant, manages and oversees our executive compensation program. At the end of each year, and as otherwise required, the Compensation Committee recommends that the Board approve the total compensation for our Chief Executive Officer and approves the total compensation for our other executive officers.

The Compensation Committee's responsibilities include:

- reviewing and approving overall compensation strategy;
- reviewing and approving corporate performance goals and objectives relevant to the compensation of our executive officers;
- evaluating and recommending to the Board the compensation plans and programs advisable for Ionis, as well as modifying or terminating existing plans and programs;
- establishing policies with respect to stock compensation arrangements;
- reviewing and recommending that the Board approve the total compensation for our Chief Executive Officer and reviewing and approving the total compensation for our other executive officers;
- reviewing and recommending that the Board approve the compensation arrangements for our non-employee directors;
- administering our stock-based awards and ESPP;
- evaluating risks associated with our compensation policies and practices and assessing whether these risks are reasonably likely to have a material adverse effect on us;
- selecting and retaining a qualified, independent compensation consultant;
- performing other functions as may be necessary or convenient in the efficient discharge of the foregoing; and
- reporting to the Board from time to time, or whenever it is called upon to do so.

*Independent Compensation Consultant*

The Compensation Committee has the authority and budget to hire an independent compensation consultant as it deems necessary. The Compensation Committee has retained Aon's Human Capital Solutions practice, a division of Aon plc (formerly known as Radford) ("***Aon***") as its independent compensation consultant. For 2025, Aon primarily provided the Compensation Committee advice in the following areas:

- assessing Board of Directors compensation;
- selecting the 2025 Peer Group used to assess executive officer and non-employee director compensation;
- reviewing the mix of stock options and RSUs for all employees, including for new hires and employees receiving promotions;
- assessing our bonus targets for non-executive employees;
- assessing executive officer compensation, including base salary, bonus and equity grants;
- performing the valuation calculations for our CEO's and executive officers' PRSU awards that vested and paid out in 2025; and
- performing the valuation calculations for equity awards granted in 2020-2025 to calculate compensation actually paid pursuant to Item 402(v) of Regulation S-K.

*Compensation Consultant Fees*

As described above, the Compensation Committee has engaged Aon to provide the committee with peer company and industry compensation data and advice regarding executive officers' compensation. In 2025, we paid Aon approximately $203,000 for Aon's consulting services directly related to Compensation Committee support.

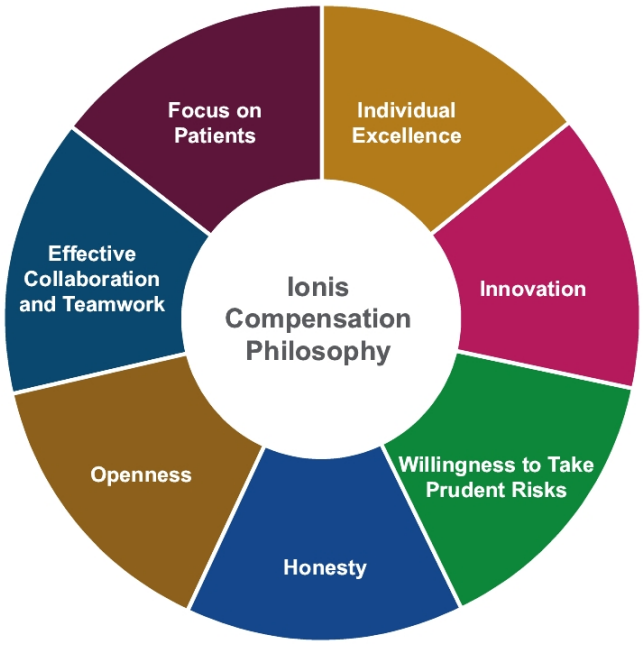
In addition, management of the Company engaged affiliates of Aon for other services in 2025 that were not related to Aon's Compensation Committee consulting services. Our Human Resources department obtained general benchmarking survey data, for which we paid approximately $49,000. Additionally, in 2025 our Finance department engaged Aon to provide equity valuation services, for which we

paid approximately $30,000, and an affiliate of Aon for insurance brokerage services, for which we paid approximately $726,000. Although the Compensation Committee was aware of the nature of these additional services, the committee does not review or approve such services. Management reviewed and approved the insurance premiums in the ordinary course of business in consultation with the Audit Committee of the Board.

Aon maintains certain policies and practices to protect the independence of the executive compensation consultants engaged by the Compensation Committee. In particular, Aon provides an annual update to the Compensation Committee on the financial relationship between Aon and the Company and provides written assurances that, within Aon, the compensation of the affiliate consultants who perform executive compensation services for the Compensation Committee is determined separately from Aon's other lines of business and from the other services it provides to the Company. These safeguards were designed to help ensure that the Compensation Committee's executive compensation consultants continue to fulfill their role in providing independent, objective advice.

*Compensation Philosophy*

Our compensation philosophy supports and rewards the characteristics and behaviors we believe will make us successful and create long-term stockholder value:



*Pay for Performance*. We incorporate several features into our compensation structure to mitigate the risk that our compensation policies and practices could encourage unnecessary or imprudent business risk taking. We use a combination of compensation vehicles that provide a balanced mix of fixed and variable cash incentives, and long-term stock incentives. Our Performance Management by Objective ("***MBO***") awards are not guaranteed (i.e., are 100% at risk) and include a multiplier, or performance factor, based on Ionis' and the employee's performance (respectively, the "***Company Performance Factor***" and the "***Individual Performance Factor***"). Therefore, if *either* Ionis or the employee performs poorly, the MBO award can be, and has been, zero. For 2025 performance, the Compensation Committee awarded a Company Performance Factor of 190% in recognition of the Company's strong performance, achieving almost all its goals for the year across all aspects of our business and, for a significant number of these goals, exceeding the target performance.

Based on stockholder feedback, beginning in 2020, we added PRSU awards to our Chief Executive Officer's compensation, and increased the proportion of such awards for our CEO's total equity awards beginning in 2022. Additionally, in 2022, we added PRSU awards to the compensation of our other executive officers. These PRSU awards provide our executive officers the opportunity to earn a defined number of shares of our common stock if we achieve pre-determined performance goals. For grants made in 2022 through 2025, at target level of achievement, the PRSU awards represent 33% of our CEO's total equity awards and 20% of each of the other executive officer's total equity awards. Beginning with grants made in 2026, at target level of achievement, the PRSU awards represent 40% of all our executive officers' total equity awards.

**Beginning with grants made in 2026, at target level of achievement, the PRSU awards represent 40% of all our executive officers' total equity awards.**

We structure PRSU awards to pay out based on relative TSR, which we believe is the best way to directly tie performance that positively impacts stockholders with the payout that the executive officers receive at the end of the performance period. PRSU grants have a single vesting period at the end of three years following the grant date. No number of PRSUs is guaranteed to vest and the actual number of PRSUs that will vest at the end of the performance period may be anywhere from zero to the maximum amount depending on the Company's relative TSR. If the Company's TSR is negative over the performance period, the payout will not exceed 100% of the target number even if the percentile rank exceeds the 50th percentile. Below are the PRSU payout thresholds (with linear interpolation for performance between percentile ranks):

**No number of PRSUs is guaranteed to vest. If the Company's TSR is negative over the performance period, the payout will not exceed 100% of the target number.**

| Relative TSR Percentile Rank | TSR Performance Multiplier |
|---|---|
| <25$^{th}$ percentile | 0% |
| 25$^{th}$ percentile (**Threshold**) | 50% |
| 50$^{th}$ percentile (**Target**) | 100% |
| 60$^{th}$ percentile | 125% |
| 75$^{th}$ percentile | 150% |
| 90$^{th}$ percentile (**Maximum**) | 200% |

The PRSUs granted to all our executive officers in 2023, including our NEOs, paid out to our NEOs in January 2026 as follows:

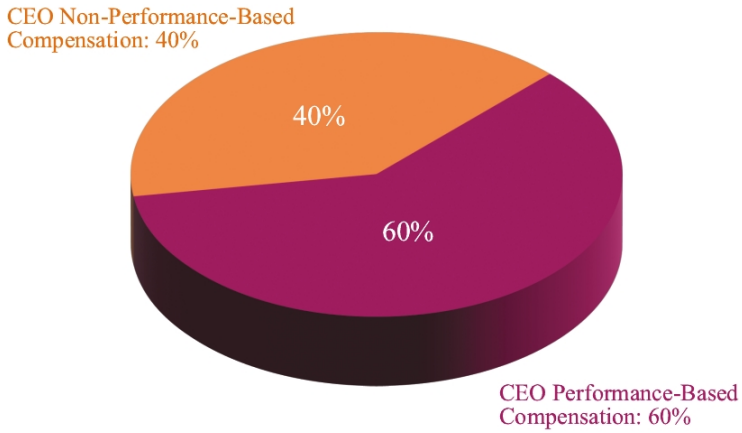
| Performance Period | Ionis' TSR | Relative TSR Percentile Ranking | Percent of Target Number | Total Shares Earned |
|---|---|---|---|---|
| 1of 1 | 99.64% | 80th | 167.27% | Dr. Monia: 122,214<br>Ms. Hougen: 13,562<br>Dr. Geary: 11,991<br>Mr. Birchler: 11,991<br>Dr. Swayze: 11,991<br>Mr. O'Neil: 11,991 |

## 2025 NEO Compensation: Performance-Based vs. Non-Performance-Based

We are committed to ensuring that a significant portion of our NEOs' compensation is tied to Company performance. The charts below illustrate the proportion of our CEO's and average NEOs' (excluding the CEO) 2025 total compensation that was allocated among performance-based compensation and non-performance-based compensation. We consider cash bonuses, stock options and PRSUs to be performance-based compensation, as the realization of the amount of such bonuses, and value of such options and PRSUs, are directly related to one or more measures of Company performance.

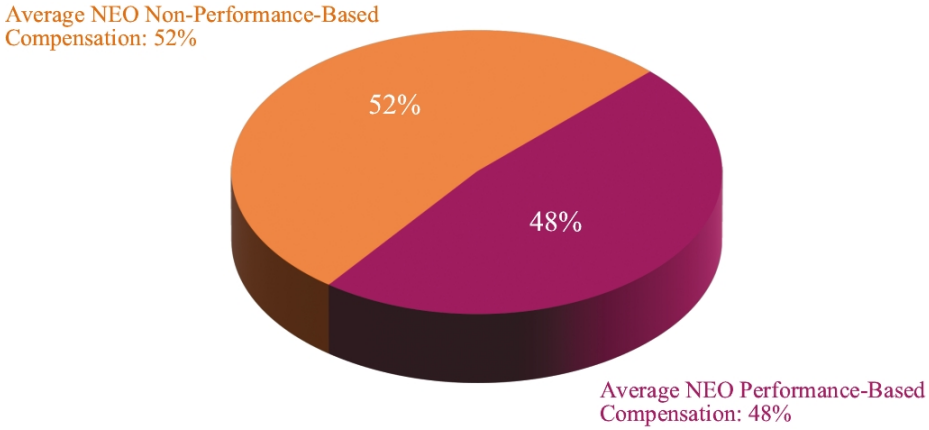
### *2025 CEO Compensation: Performance-Based vs. Non-Performance-Based*

The performance-based compensation reflected below includes the CEO's cash bonus for 2025 performance ($2,398,049), fair value of stock options granted in 2025 ($1,438,105), and fair value of PRSU awards granted in 2025 ($4,147,630). The non-performance-based compensation reflected below includes the CEO's 2025 base salary ($1,051,776) and fair value of time-vested RSU awards granted in 2025 ($4,297,208).



*2025 Average NEO Compensation: Performance-Based vs. Non-Performance-Based*

The performance-based compensation reflected below includes the NEOs' (excluding the CEO) average cash bonus for 2025 performance ($663,799), average fair value of stock options granted in 2025 ($396,775), and average fair value of PRSU awards granted in 2025 ($580,839). The non-performance-based compensation reflected below includes the NEOs' (excluding the CEO) average 2025 base salary ($626,556) and average fair value of time-vested RSU awards granted in 2025 ($1,185,597).




## Overview of Our Compensation Program

Drug discovery and development across a portfolio of many medicines is a long process that spans many years, where decisions we make today can have a positive or negative consequence five years, ten years, and even further into the future. In addition, as we continue to transition from primarily a research and development organization to independently commercializing our own medicines, our compensation program must support both the continued advancement of our innovative pipeline and the build-out and scaling of our commercial capabilities. This includes planning for and executing multiple product launches, expanding our commercial infrastructure, and supporting the investments necessary to independently bring our medicines to patients. As such, it is essential that we set goals that incentivize our employees to execute our long-term strategy, because we believe our long-term strategy should continue to reward our stockholders into the future.

For us to retain our technology leadership and effectively manage the technical complexity of our development pipeline, our most senior executives and the members of their teams must advance multiple drug strategies and collaborative partnerships in parallel and consistently over many years, versus emphasizing one or two at the expense of others that deserve attention. Managing this portfolio also requires the ability to execute multiple product launches in overlapping timeframes without compromising the continued advancement of earlier-stage programs. As a result, we use a mix of financial and operational objectives that reflect those achievements that we believe should drive near and longer term stockholder value. By taking this approach, we avoid the temptation to deviate from creating fundamental long-term value to meet a short-term metric.

**At the beginning of each year, we set aggressive corporate objectives, including objective measures, that our Board approves. On at least a quarterly basis, the Board evaluates our progress toward achieving these objectives.**

At the beginning of each year, we set aggressive corporate objectives, including objective measures, that our Board approves. We strive to structure our corporate objectives such that they are results driven rather than task driven to encourage the prudent spending of stockholder money. In other words, we want to structure our objectives to reward success based on judgment, rather than the making of "bad bets." On at least a quarterly basis, the Board evaluates our progress toward achieving these objectives. We define excellent performance as a year in which we have met most of our objectives.

*Importance of Tenure; Our Investment in Knowledge-Rich Employees*

It takes a significant period of time and a substantial investment to recruit and develop employees who possess the experience and talent necessary to lead at Ionis given our transformative technology, rich drug development pipeline and expanding portfolio of commercial medicines. Senior executives must have experience with all aspects of our business to be effective leaders. Given the uniqueness and complexity of our technology, it is critical to retain the knowledge and experience of outstanding long service employees. The experience and seniority of our employees is critical to our future success. For these reasons, it is our objective to attract and retain the best talent available and to invest in those individuals who deliver long-term productivity. The principles below outline our general approach to achieving this objective:

**Given the uniqueness and complexity of our technology, it is critical to retain the knowledge and experience of outstanding long service employees.**

- Long tenure among a dedicated and highly skilled workforce, combined with the highest performance standards, contributes to our leadership in the industry and serves the interests of stockholders.
- Our focus on retention is coupled with a strong belief that executive talent most often should be developed and promoted from within Ionis.
    - The long tenure of high-performing executive officers reflects this strategy. Our current executive officers have on average approximately 22 years and individually as much as over 36 years of tenure at Ionis.
- The Company has carefully evaluated and selected each of our executive officers through a rigorous performance assessment process over a long career. In their current assignments, they remain subject to a challenging annual performance assessment in which they must continue to meet the highest standards or be reassigned or separated from the Company.

In addition, as we have evolved into a fully integrated commercial-stage biotechnology company, we have hired numerous senior-level executives with deep experience across all aspects of commercialization to spearhead our commercial growth. Working alongside our long-tenured employees, these senior-level commercial executives will help us ensure we fully realize the potential of our innovative medicines reaching patients and their healthcare providers.

To recognize our employees, including our named executive officers, who deliver long-term productivity to the Company, Ionis has two cash-based awards: the "Career Achievement Award" in the amount of $50,000 to recognize our distinguished, long-tenured, senior-level contributors, including Board members, who made extraordinary contributions that helped determine the Company's future, and the "Commitment to Ionis Award" to thank employees for their commitment to the Company. The amount of the Commitment to Ionis Award correlates to the employee's length of service with the Company and is paid following the employee's milestone anniversary. The table below shows the Commitment to Ionis Award for each corresponding milestone anniversary. In 2025, none of our named executive officers received a Career Achievement Award, but Dr. Geary and Mr. Birchler each received a Commitment to Ionis Award to recognize 30 years of service, and Ms. Hougen received a Commitment to Ionis Award to recognize 25 years of service.

| Years of Service | Award |
|---|---|
| 1 | $1,000 |
| 5 | $5,000 |
| 10 | $10,000 |
| 15 | $15,000 |
| 20 | $20,000 |
| 25 | $25,000 |
| 30 | $30,000 |
| 35 | $35,000 |
| 40 | $40,000 |

*Elements of Executive Compensation*

Employees in our organization do not share either accountability or responsibility equally for strategic and tactical decisions. It is well ingrained in our culture that not everyone should share the same level of risk/reward for the consequences of these decisions. As a result, we have structured the various components of our compensation system to reflect accountability both for the successes and failures (both long-term and short-term) of Ionis and of our employees. We pay our executive officers for results and their use of judgment in executing the strategies they have established. Therefore, the more senior a person becomes within Ionis, the more the person's cash compensation will be "at risk." We compensate the more junior employees for accomplishing their work well and, therefore, a lower portion of their cash compensation is "at risk."

**The more senior role a person plays, the more that person's cash compensation will be "at risk."**

Our executive officers' total compensation consists of four elements:

(1) base salary;

(2) MBO award – performance-based, at-risk cash compensation, *no portion of which is guaranteed*;

(3) stock-based compensation, including PRSU awards, which are granted annually each January following the performance year for which such grants are awarded; and

(4) the same benefits, including 401(k) matching, that we provide to all employees.

The PRSU component is the only component of this compensation structure that does not apply to all employees.

We consider many factors in determining the amounts we grant to our executive officers for all the compensation elements listed above, with the exception of element 4. These factors include:

- Company-wide performance, including achievement of pre-established corporate objectives;
- the Compensation Committee's and Board's assessment of our CEO's and executive officers' individual performance;
- competitive compensation practices;
- general economic conditions, industry conditions and the Compensation Committee's and Board's collective business judgment;
- increased efficiencies and process improvements;
- effective collaboration and teamwork;
- individual expertise, skills and knowledge;
- the need to retain and motivate;
- the impact an individual's judgment has on our success or failure; and
- the advice of the Compensation Committee's independent compensation consultant.

We do not have specific weightings assigned to these factors, as the importance of each factor can vary among the executive officers and from year to year.

*Peer Group*

The Compensation Committee considers relevant market pay practices when setting executive compensation to ensure our ability to recruit and retain high performing talent. The Compensation Committee, in consultation with its independent compensation consultant, evaluated and selected a peer group of 20 life sciences companies for evaluating Ionis' 2025 compensation (the "***Peer Group***"). On an annual basis, the Compensation Committee compares the compensation opportunity for our executive officers to similarly situated executives at the 25$^{th}$, 50$^{th}$ and 75$^{th}$ percentiles of the Peer Group as a "market check" to ensure, in its judgment, that the executive officers' compensation remains appropriate. The Compensation Committee also reviews our compensation policies, practices, and procedures compared to the Peer Group to benchmark compensation for both our executive officers and non-employee directors. While the Compensation Committee uses these data to inform and shape decision-making, it does not strictly adhere to quantitative benchmarks. The Peer Group data is just one factor considered in the annual compensation approval process, in addition to the factors described above under "Elements of Executive Compensation."

The Peer Group, which the Compensation Committee reviews on an annual basis, consists of companies that generally:

- are similar to Ionis in terms of certain factors, including one or more of the following: size (*i.e.*, revenue, market capitalization), industry, stage of development and location;
- have named executive officer positions that are comparable to ours in terms of breadth, complexity, and scope of responsibilities; and
- compete with us for executive talent.

The Peer Group generally does not include companies headquartered outside the United States (because compensation and benefit practices are generally different outside the United States, the comparable compensation data for the named executive officers and non-employee directors is not available and cost of living is different) or companies in industries whose compensation programs are not comparable to our programs, such as non-life sciences companies.

In June 2025, the Compensation Committee reviewed the Peer Group using the criteria listed above and publicly available data as of May 2025. The Compensation Committee noted Ionis' 30-day average market capitalization was approximately $4.6 billion and trailing 12-month revenue was approximately $717 million. As part of this process, the Compensation Committee looked at companies in Ionis' industry with an emphasis on companies with 30-day average market capitalizations of between $1.5 billion and $15.5 billion and trailing 12-month revenue between $225 million and $2.25 billion. The Compensation Committee also looked at companies that identified Ionis as a peer, so called "reverse peers." Based on this evaluation, the Compensation Committee added Axsome Therapeutics, BioCryst Pharmaceuticals, and Corcept Therapeutics to the Peer Group because they fell within the target market capitalization and revenue ranges and are in Ionis' sector. The Compensation Committee retained BioMarin Pharmaceuticals, Exact Sciences Corporation, Incyte Corporation, Jazz Pharmaceuticals, Neurocrine Biosciences and United Therapeutics Corporation in the Peer Group despite their annual revenues being outside the selection criteria because these companies have been within the selection criteria we have used in recent years and retaining them as peers this year helps to preserve consistency in our benchmarking and because we compete with them for talent. The Compensation Committee removed Alnylam Pharmaceuticals from the Peer Group because it exceeded the target market capitalization and revenue ranges, and Ironwood Pharmaceuticals because it fell below the target market capitalization range.

The following table lists the companies in the 2025 Peer Group, along with Ionis' rankings among these companies, based on market capitalization and financial data reported by each company at the time the Compensation Committee selected the Peer Group in June 2025.

| Company (ticker) | Annual Revenues (in millions)[1] | Market Capitalization (in millions)[2] | Stage of Lead Drug |
|---|---|---|---|
| Acadia Pharmaceuticals (ACAD) | $957.8 | $2,454.9 | Market |
| Alkermes (ALKS) | $1,513.8 | $4,678.9 | Market |
| Amicus Therapeutics (FOLD) | $543.1 | $2,161.3 | Market |
| Apellis Pharmaceuticals (APLS) | $781.4 | $2,375.2 | Market |
| Axsome Therapeutics, Inc. (AXSM) | $385.7 | $5,102.3 | Market |
| BioCryst Pharmaceuticals, Inc. (BCRX) | $450.7 | $1,589.3 | Market |
| BioMarin Pharmaceuticals (BMRN) | $2,950.2 | $11,641.4 | Market |
| Blueprint Medicines Corp (BPMC) | $562.1 | $5,497.3 | Market |
| Corcept Therapeutics Inc. (CORT) | $675.0 | $7,410.4 | Market |
| Exact Sciences Corp (EXAS) | $2,828.1 | $8,271.3 | Market |
| Exelixis (EXEL) | $2,168.7 | $10,144.4 | Market |
| Halozyme Therapeutics (HALO) | $1,015.3 | $7,383.2 | Market |
| Incyte Corporation (INCY) | $4,413.2 | $11,448.9 | Market |
| Insmed (INSM) | $363.7 | $12,723.2 | Market |
| Jazz Pharmaceuticals (JAZZ) | $4,069.0 | $6,574.9 | Market |
| Neurocrine Biosciences (NBIX) | $2,355.3 | $9,928.9 | Market |
| PTC Therapeutics (PTCT) | $806.8 | $3,674.6 | Market |
| Sarepta Therapeutics (SRPT) | $1,902.0 | $5,550.5 | Market |
| Ultragenyx Pharmaceutical (RARE) | $560.2 | $3,356.0 | Market |
| United Therapeutics (UTHR) | $2,994.1 | $13,077.2 | Market |
| Ionis Pharmaceuticals, Inc. (IONS) | $717.3 | $4,585.0 | Market |
| Ionis' Percentile Rank | 34% | 31% | N/A |

(1) Trailing 12-month revenue as of May 2025.

(2) 30-day average market cap as of May 2025.

*Compensation Allocation/Pay Mix*

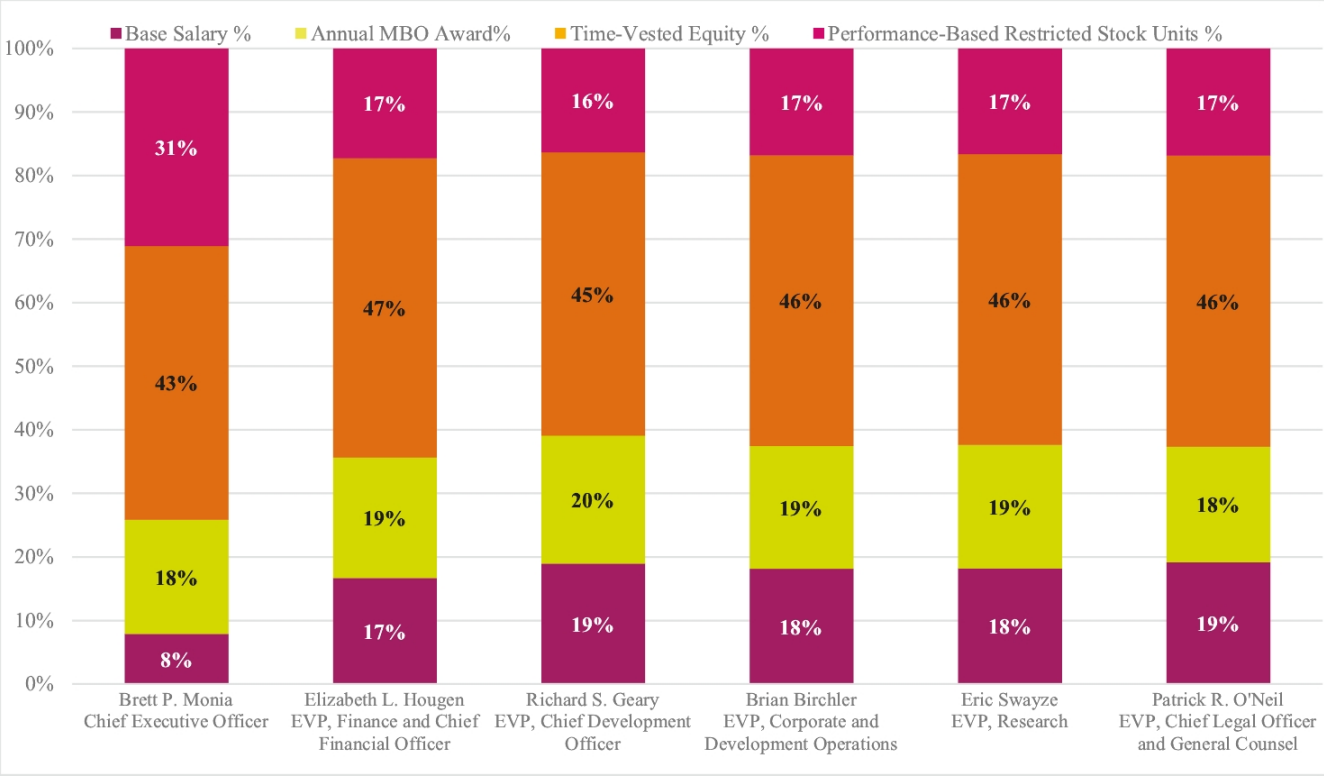
A key element of our compensation philosophy is to monitor and adjust our pay mix for our executive officers so the pay mix is less heavily weighted on fixed compensation (salary) and more heavily weighted on at-risk cash compensation and long-term equity incentive compensation. As part of the Compensation Committee's review of our total pay mix for executive officers, the Compensation Committee focuses on the following:

- *A significant portion of cash compensation is at risk*. The Compensation Committee structures cash compensation such that a significant proportion of our CEO's and other executive officers' cash compensation is at risk.
- *More of total compensation is long-term equity*. The Compensation Committee structures the total pay mix for our CEO and other executive officers such that more of their compensation is in the form of long-term equity compensation.
- *Less of total compensation is salary*. The Compensation Committee strives to structure the total pay mix for our CEO and other executive officers such that less of their compensation is in the form of salary.
- *Meaningful portions of annual equity awards are performance-based*. The Compensation Committee grants a significant proportion of performance-based equity awards to our CEO and executive officers and increased the proportion of PRSUs to be awarded to our executive officers beginning in 2026 as follows: from 33% to 40% of our CEO's total equity and from 20% to 40% of our other executive officer's total equity.

An annual review of our total pay mix helps Ionis compete for and retain talent in the competitive marketplace and maintain compensation equity and balance among positions with similar responsibilities. The target pay mix for our executive officers is a result of the compensation targets that emphasize long-term compensation versus short-term compensation. Actual salary levels, annual MBO awards and long-term incentive awards vary based on one or more of the following: an individual's responsibilities, tenure in a particular position, experience, individual performance, and Company performance.

*Pay Mix Chart*

The following chart illustrates the portions of actual total direct compensation for the named executive officers that are composed of base salary, annual MBO award and long-term equity ($ shown in thousands) for 2025:



| Name | Year | Base Salary | | Annual MBO Award | | Time-Based Equity | | Performance-Based Restricted Stock Units | |
|---|---|---|---|---|---|---|---|---|---|
| | | $ | % | $ | % | $ | % | $ | % |
| Brett P. Monia<br>Chief Executive Officer | 2025 | $1,051,776 | 8% | $2,398,049 | 18% | $5,735,313 | 43% | $4,147,630 | 31% |
| Elizabeth L. Hougen<br>EVP, Finance and Chief Financial Officer | 2025 | $729,750 | 17% | $831,915 | 19% | $2,061,073 | 47% | $756,555 | 17% |
| Richard S. Geary<br>EVP, Chief Development Officer | 2025 | $622,074 | 19% | $661,887 | 20% | $1,462,697 | 45% | $536,910 | 16% |
| Brian Birchler<br>EVP, Corporate and Development Operations | 2025 | $580,154 | 18% | $617,284 | 19% | $1,462,697 | 46% | $536,910 | 17% |
| Eric Swayze<br>EVP, Research | 2025 | $589,013 | 18% | $626,710 | 19% | $1,462,697 | 46% | $536,910 | 17% |
| Patrick R. O'Neil<br>EVP, Chief Legal Officer and General Counsel | 2025 | $611,791 | 19% | $581,201 | 18% | $1,462,697 | 46% | $536,910 | 17% |

## 2025 Compensation Decisions and Results

### *Base Salary*

We determine base compensation levels for all our employees primarily by market forces. Accordingly, the Compensation Committee and Board believe that it is important when making compensation decisions to be informed as to the current practices of comparable publicly held companies with which we compete for top talent. To this end, the Compensation Committee and Board review market and peer company data, which includes competitive information relating to the mix and levels of compensation for executives in the life sciences industry. We obtain this information for the Peer Group based on recent public filings with the SEC. In addition, we also review data from the Radford McLagan Compensation Database, which is a summary of compensation data submitted by over 1,700 life sciences companies. The Compensation Committee and Board use these data to inform and shape their decision-making but do not strictly adhere to quantitative benchmarks. In addition, we assess whether the scope of job responsibilities and internal equity warrant a given base salary.

**We determine base compensation levels for all our employees primarily by market forces. Accordingly, the Compensation Committee and Board believe that it is important when making compensation decisions to be informed as to the current practices of comparable publicly held companies with which we compete for top talent.**

Each year most of our employees are eligible to receive an appropriate merit salary increase. The Compensation Committee sets a Company-wide merit budget percentage based on Ionis' performance and external factors such as the average merit budget of comparable companies. The actual merit increase award for each employee, including our executive officers, will vary depending upon the respective employee's performance. For example, the Company-wide merit budget for increases effective in January 2025 was 4%, with a potential range of individual merit award increases of 0% to 10%. However, regardless of individual employee variances, we do not exceed the Company-wide approved merit budget.

The Compensation Committee evaluates each executive officer's performance to set, or for the CEO, recommend Board approval of, such executive officer's annual merit increase. As part of this process, the Compensation Committee reviews the written reports prepared by the CEO evaluating the performance of each individual executive officer. The Compensation Committee carefully considers these reports since our CEO is in the best position to evaluate our executive officers' day-to-day and overall performance. The Compensation Committee meets in executive session and evaluates the CEO's performance, primarily based upon the CEO's achievement of our key corporate objectives for the year. At the end of this process, the Compensation Committee recommends Board approval of the CEO's merit increase and approves the merit increases for the remaining executive officers. The Board then meets in executive session and approves our CEO's merit increase. Our CEO has no role in determining his own compensation.

The executive officers' new salaries for each year are generally calculated as follows:

- Current Base Salary (x) Merit Increase = Increase to Base Salary
- Current Base Salary (+) Increase to Base Salary (+) Market Adjustment (if applicable) = New Base Salary

*2025 Base Salary Calculations*

The table below reflects the 2025 base salary calculations effective beginning on December 22, 2024, for our named executive officers. The Compensation Committee, or in the case of our CEO, the Board, approved merit increases to the salaries of the named executive officers of approximately 4.33% on average, which was consistent with the corporate performance ranges and approved by the Compensation Committee. The Compensation Committee noted its desired target mix of compensation that is less weighted on salary.

When reviewing salaries in December 2024, the Compensation Committee noted that the salaries of our named executive officers were within the competitive range of the Peer Group. However, in recognition of the impact of his role, responsibilities, contributions and performance, the Compensation Committee approved an adjustment for Mr. Birchler as reflected in the table below.

| Name | 2024 Base Salary | Merit Increase for 2025 | Market Adjustment | 2025 Base Salary |
|---|---|---|---|---|
| Brett P. Monia | $1,008,898 | 4.25% | — | $1,051,776 |
| Elizabeth L. Hougen | $700,000 | 4.25% | — | $729,750 |
| Richard S. Geary | $593,865 | 4.75% | — | $622,074 |
| Brian Birchler | $531,003 | 4.25% | $25,500 | $580,154 |
| Eric Swayze | $565,000 | 4.25% | — | $589,013 |
| Patrick R. O'Neil | $586,850 | 4.25% | — | $611,791 |

*2026 Base Salary Calculations*

The table below reflects the 2026 base salary calculations effective beginning on December 21, 2025 for our named executive officers. The Compensation Committee, or in the case of our CEO, the Board, approved merit increases to the salaries of the named executive officers of approximately 4.39% on average, which was consistent with the corporate merit ranges and approved by the Compensation Committee. The Compensation Committee noted its desired target mix of compensation that is less weighted on salary.

When reviewing salaries in December 2025, the Compensation Committee noted that the salaries of our named executive officers were within the competitive range of the Peer Group.

| Name | 2025 Base Salary | Merit Increase for 2026 | 2026 Base Salary |
|---|---|---|---|
| Brett P. Monia | $1,051,776 | 4.6% | $1,100,158 |
| Elizabeth L. Hougen | $729,750 | 4.8% | $764,778 |
| Richard S. Geary | $622,074 | 4.6% | $650,689 |
| Brian Birchler | $580,154 | 4.6% | $606,841 |
| Eric Swayze | $589,013 | 4.6% | $616,108 |
| Patrick R. O'Neil | $611,791 | 3.75% | $634,733 |

*MBO Program – Performance-Based, At-Risk Cash Compensation*

The next component of an executive officer's compensation, and the compensation of the rest of our employees, is an annual performance-based cash payment through our MBO program. While an employee's base salary compensates the employee for continued service and performance, our MBO program rewards employees for reaching specific objectives and for the judgment they use in making decisions. We do not guarantee an MBO award as compensation. It is totally at risk. As such, an MBO award represents an opportunity for reward based upon the individual's level of accountability and depends on the relative success of both Ionis and the individual. Our approach for awarding MBO bonuses differs from salary increases because, unlike salary increases, market forces do not impact bonus amounts.

We calculate the actual amount of each executive officer's respective MBO award based on the following formula:

Base Salary (x) target MBO % (x) Company Performance Factor (x) Individual Performance Factor = MBO Award Amount

*MBO awards can be zero*. The multipliers in this formula ensure we award bonuses based on *both* Ionis' performance and individual performance. This means an employee might not receive an MBO award even if the employee performed well in a year in which the Company does not meet its corporate objectives. Similarly, if an employee performed poorly in a year in which the Company met its key corporate objectives, the employee might not receive an MBO award.

**MBO awards can be, and have in the past been, *zero*.**

**MBO awards have a maximum amount.**

For example, in 2021 the Compensation Committee awarded the Company's executive officers a Company Performance Factor of 95%, and all other employees a Company Performance Factor of 110%, due to a few key Company disappointments during the year. In a prior year, we did not pay MBO awards to executive officers due to the failures we faced at the time. Conversely, in successful years, we reward our executive officers consistent with Ionis' success.

*MBO awards have a maximum limit*. MBO awards are limited by a maximum Company Performance Factor, maximum Individual Performance Factor and target MBO percentage:

- We have a maximum Company Performance Factor of 200% and a maximum Individual Performance Factor of 160%. This range represents the boundary conditions for our Performance Factors and ensures we reward our employees consistent with Ionis' success.
- We base target MBO percentages on position levels within Ionis. The target MBO percentage for 2025 for Executive Vice Presidents was 40% and for the CEO was 75%.

An individual's target MBO percentage does not change unless the individual changes position level or the Compensation Committee sets a new target for that level. The table below summarizes the minimum and maximum MBO award for 2025 as a percentage of salary:

| Name | Minimum MBO Percentage of Salary | Maximum MBO Percentage of Salary |
|---|---|---|
| Brett P. Monia | 0% | 240% |
| Elizabeth L. Hougen | 0% | 128% |
| Richard S. Geary | 0% | 128% |
| Brian Birchler | 0% | 128% |
| Eric Swayze | 0% | 128% |
| Patrick R. O'Neil | 0% | 128% |

The Compensation Committee sets the Company Performance Factor based on the following process:

- At the end of each year, the Compensation Committee meets to evaluate Ionis' overall performance for the year. As described below in the chart called "Evaluation of 2025 Key Corporate Objectives," the Compensation Committee measures Ionis' performance based upon the achievement of goals set at the beginning of the year with objective measures and agreed upon by our Board and executive officers.
- In addition, the Compensation Committee considers our one-, three- and five-year TSRs, and based on these returns has discretion to reduce the Company Performance Factor and Individual Performance Factors for all of our executive officers, including our CEO.

**Based on our one-, three- and five year TSRs, the Compensation Committee has discretion to *reduce* the Company Performance Factor and Individual Performance Factors for our executive officers.**

- The Compensation Committee then reviews the Company Performance Factor history from the prior ten years to form a comparison for our current year's successes and/or failures.
- Finally, based on the individual's performance, the Compensation Committee recommends Board approval of the CEO's Individual Performance Factor and approves the Individual Performance Factors for our other executive officers.

Once the Compensation Committee has determined the elements of the formula above, we use that formula to calculate each executive officer's MBO award.

*Evaluation of 2025 Key Corporate Objectives*. In December 2025, the Compensation Committee completed its evaluation of the Company's performance against the 2025 Key Corporate Objectives. The Compensation Committee evaluates performance based on the achievement of goals (*including objective measures*) that the Board and management set at the beginning of each year. The Compensation Committee does not apply weightings to the corporate goals when conducting such evaluation of the Company's achievement. The table below provides a detailed evaluation of each key objective and the related achievements for 2025. The Compensation Committee set the Company Performance Factor for the 2025 MBO award at 190% in recognition of a year full of many significant accomplishments across all aspects of our business, including the following:

- Earned $944 million in revenue, exceeded our 2025 guidance and ended the year with $2.7 billion in cash and short-term investments.

- Successfully launched TRYNGOLZA in the US and EU for the treatment of FCS in adults as an adjunct to diet.
- Launched DAWNZERA for the treatment of HAE in patients 12 years of age and older.
- Achieved highly positive results in the ESSENCE, CORE and CORE2 studies of olezarsen and submitted an sNDA to the FDA.
- Advanced our go-to-market plans for our next near-term commercial opportunities: olezarsen for sHTG, our first launch in a broad patient population, and zilganersen for AxD, our first launch from our neurology pipeline.
- Advanced one wholly-owned program to Phase 3 development.
- Achieved three positive mid-stage pipeline readouts.
- Advanced four new drugs to IND-enabling toxicology studies.
- Approved eight new development targets.
- Significantly outperformed the Nasdaq Biotechnology Index ("***NBI***"), with our stock performance at 134% versus the NBI median of 27%.

| **Evaluation of 2025 Key Corporate Objectives** | | |
|---|---|---|
| | **Objective & Pre-Approved Objective Measures** | **Evaluation** |
| **1.** | **Meet financial goals** | **Ionis *exceeded* this objective** |
| | • Meet budget and achieve specified overall revenue target and end of year cash goal | • Exceeded budget across all key financial metrics, the specified overall revenue target and end of year cash goal |
| | • Meet financial guidance | • Significantly exceeded our financial guidance, raising it three times during the year |
| | • Execute on key action items to support Strategic Financial Plan | • Executed on key action items to support Strategic Financial Plan, including effective management of revenue and expenses to maintain desired cash balance and completion of a debt refinance on highly favorable terms |
| | • Achieve specified revenue goal for WAINUA and support OUS launches for ATTRv-PN | • Exceeded specified revenue goal; WAINUA approved in 15 additional countries in 2025 |
| **2.** | **Ensure success for olezarsen program** | **Ionis *exceeded* this objective** |
| | • Achieve specified annual revenue budget target | • Exceeded specified annual revenue budget target |
| | • Obtain on-time approval in the EU for FCS with a competitive label | • Obtained on-time approval and launched in the EU for FCS with a competitive label |
| | • Establish OUS commercialization plan and successfully execute such plan for FCS. Establish commercialization plan including strategy for on-time implementation for sHTG | • Established and successfully executed on OUS commercial strategy with Sobi partnership and launched in the EU for FCS. Established commercialization plan for sHTG. |
| | • Achieve positive and competitive Phase 3 outcomes in ESSENCE, CORE and CORE2 studies and sNDA submission | • Achieved highly positive results in ESSENCE, CORE and CORE2 studies and submitted the sNDA to the FDA |
| **3.** | **Ensure success for donidalorsen program** | **Ionis *substantially met* this objective** |
| | • Obtain on-time FDA approval and launch in the U.S. | • Achieved on-time FDA approval in August 2025 and launched in the U.S. |
| | • Achieve specified annual net revenue budget | • Did not achieve budget goal; however, the U.S. launch is progressing well |
| | • In collaboration with Otsuka, obtain positive CHMP opinion and keep on track for H1 2026 approval | • Received a positive CHMP opinion in November 2025 and EU approval in January 2026 |

| Evaluation of 2025 Key Corporate Objectives | | |
|---|---|---|
| | **Objective & Pre-Approved Objective Measures** | **Evaluation** |
| **4.** | **Ensure success for obudanersen program** | **Ionis *substantially met* this objective** |
| | • Initiate Phase 3 REVEAL study on time<br>• Initiate Phase 3 supportive studies on time<br>• Achieve specified enrollment goal in Phase 3 REVEAL study and keep on track for enrollment completion by a specified timeframe<br>• Obtain positive results in the Phase 1-2 long-term extension study | • Initiated Phase 3 REVEAL study on time<br>• Initiated Phase 3 supportive studies on time<br>• Made significant progress towards achieving specified enrollment goal and kept on track to complete enrollment by a specified timeframe<br>• Achieved with 18-month data |
| **5.** | **Achieve additional late-stage key pipeline goals** | **Ionis *met* this objective** |
| | • Eplontersen Cardio TTRansform study on track to support readout in H2 2026<br>• Achieve positive outcome to support 2026 New Drug Application ("***NDA***") submission for zilganersen Phase 3 AxD program<br>• Achieve positive outcome to support NDA submission for Phase 3 pelacarsen program (assuming on-time readout by Novartis)<br>• Keep additional specified Phase 3 programs on track for scheduled readouts | • Cardio TTRansform study on track for a H2 2026 readout<br>• Achieved highly positive outcome and submitted the NDA to the FDA in January 2026<br>• Novartis delayed readout and regulatory submission to 2026<br>• Kept all specified Phase 3 programs on track for scheduled readouts |
| **6.** | **Achieve additional pipeline goals** | **Ionis *exceeded* this objective** |
| | • Achieve at least three positive mid-stage pipeline readouts<br>• Achieved enrollment goals for mid-stage wholly-owned programs on time<br>• Initiate at least three new IND-enabling toxicology studies including specified Ionis-owned ligands | • Achieved three positive mid-stage pipeline readouts<br>• Achieve enrollment goals for mid-stage wholly-owned programs on time<br>• Initiated four new IND-enabling toxicology studies including specified Ionis-owned ligands |
| **7.** | **Further strengthen expansion and diversification of Ionis technology** | **Ionis *substantially met* this objective** |
| | • Achieve competitive target engagement and duration for at least one of two specified clinical development programs<br>• Approve blood brain barrier ("***BBB***")-crossing development candidate for preclinical development<br>• Achieved competitive target reduction in non-human primate CNS with systemic delivery of non-antibody ligand<br>• Approve a gene editing development candidate for a specified target and preliminary development plan | • Achieved competitive target engagement and duration for one of two specified clinical development programs<br>• Advanced BBB-crossing development candidate into preclinical development<br>• Achieve competitive target reduction in non-human primate CNS with systemic delivery of non-antibody ligand<br>• Made progress toward selection of a gene editing development candidate for a specified target |

| Evaluation of 2025 Key Corporate Objectives | | |
|---|---|---|
| | **Objective & Pre-Approved Objective Measures** | **Evaluation** |
| **8.** | **Achieve strategic business development goals** | **Ionis *met* this objective** |
| | • Complete transaction(s) that support OUS commercialization of olezarsen in major geographic locations | • Achieved with Sobi transaction |
| | • Complete transactions to advance two development-stage programs not selected as Ionis wholly-owned | • Completed the sapablursen transaction with Ono Pharmaceutical Co., Ltd. on terms that significantly surpassed revenue expectations for this goal, resulting in Ionis raising its revenue guidance for 2025 |
| **9.** | **Deliver on key corporate goals to ensure growth success** | **Ionis *met* this objective** |
| | • Successfully deploy release 1 of the Enterprise Resource Planning ("***ERP***") system on budget | • Achieved on-time and on-budget deployment |
| | • Keep release 2 of the ERP system on target and on budget for January 1, 2026 deployment | • Achieved on-time and on-budget deployment |
| | • Establish, gain Board approval of, and initiate implementation of manufacturing plan | • Manufacturing plan established, approved and implementation initiated |
| | • Keep construction of new building at Carlsbad campus on track for H1 2026 occupancy | • New building at Carlsbad campus on track for H1 2026 occupancy |
| | • Deliver against Corporate Responsibility goals to increase internal and external impact | • Executed various corporate responsibility action plans, published 2025 corporate responsibility report and created social impact strategy |
| | • Sustain employee engagement scores above industry benchmarks and maintain voluntary turnover rates below industry average | • Sustained employee engagement scores above industry benchmarks and maintained voluntary turnover rates below industry average |
| **10.** | **Stock price outperform Nasdaq Biotechnology Index** | **Ionis *exceeded* this objective** |
| | • Stock price increase greater than or equal to 110% of the median NBI | • Significantly exceeded, with IONS at 134% versus the NBI median of 27% as of December 4, 2025, which was the pre-determined measurement date based on timing of Board materials preparation |
| **Unplanned key corporate achievements** | | |
| • Received positive decision from Biogen to initiate Phase 3 development for salanersen | | |
| • Approved eight new development candidates | | |
| • Received Breakthrough Therapy Designation for olezarsen (sHTG) | | |
| • Received Breakthrough Therapy Designation for zilganersen (AxD) | | |
| • Ranked #2 top employer in 2025 by Science Magazine | | |

Once the Compensation Committee establishes the Company Performance Factor, the committee next reviews each executive officer's individual performance and contribution towards the key corporate objectives and other accomplishments set forth above and for our CEO, recommends Board approval of CEO compensation, and for all other executive officers, approves MBO awards accordingly. The following table illustrates the MBO awards approved for 2025 performance:

| Name | 2025 Base Salary | Target MBO % | Company Performance Factor | Individual Performance Factor | Resulting MBO Award | Results Considered When Setting Individual Performance Factor[(1)] |
|---|---|---|---|---|---|---|
| Brett P. Monia | $1,051,776 | 75% | 190% | 160%[(2)] | $2,398,049 | 1-10 |
| Elizabeth L. Hougen | $729,750 | 40% | 190% | 150% | $831,915 | 1-3 & 8-10 |
| Richard S. Geary | $622,074 | 40% | 190% | 140% | $661,887 | 1-6 & 9-10 |
| Brian Birchler | $580,154 | 40% | 190% | 140% | $617,284 | 1-6 & 9-10 |
| Eric Swayze | $589,013 | 40% | 190% | 140% | $626,710 | 1, 6, 7 & 9-10 |
| Patrick R. O'Neil | $611,791 | 40% | 190% | 125% | $581,201 | 1, 4-6 & 8-10 |

(1) The numbers correspond to the enumerated key objectives in the table entitled "Evaluation of 2025 Key Corporate Objectives" on pages 61 through 63. The Compensation Committee reviews the individual's contribution towards the key corporate objectives and other accomplishments set forth above when determining or recommending the Individual Performance Factors.

(2) Since our CEO is ultimately responsible for the Company's performance, his Individual Performance Factor is usually the same as the Company Performance Factor, up to an Individual Performance Factor maximum of 160%. Nonetheless, the Compensation Committee retains discretion to apply a lower Individual Performance Factor, including an Individual Performance Factor of 0%.

*Stock Compensation*

We use stock options and RSUs to give *all* employees, including Ionis' executive officers, an economic interest in the long-term appreciation of our common stock. We believe awarding a combination of stock options and RSUs provides several benefits. Stock options provide a way to align employee interests with those of upper management and the stockholders because as our stock price increases, so too does the employee's compensation. We have been granting RSUs as part of the annual merit equity awards for more than a decade because they are a strong retention vehicle for employees as the RSUs vest in annual installments over four years. The RSUs also have value upon vesting, but at the same time, require fewer shares than stock option awards.

We grant existing employees new stock options and RSUs annually to provide a continuing incentive in Ionis' long-term success. Each year, the Compensation Committee sets a budget of option equivalents for our executive officers and a budget of option equivalents for all other employees. From these budgets, we set a target number of option equivalents for each employee level in the Company. The actual award for each employee can be higher or lower than the target for their level depending on individual performance, but the total awards cannot exceed the budget set by the Compensation Committee. In 2025, we allocated 25% of option equivalents to stock options and 75% to RSUs for our non-executive officers. For our executive officers' 2025 awards, we allocated 33% (for our CEO) or 20% (for all of our other executive officers) of their total equity awards in the form of PRSUs, with the remaining option equivalents allocated 25% to stock options and 75% to RSUs. Beginning with grants made in 2026, for all our executive officers, including the CEO, we allocate total equity as 30% stock options, 30% RSUs and 40% PRSUs.

**We use stock options and RSUs to give all employees, including Ionis' executive officers, an economic interest in the long-term appreciation of our common stock.**

*Performance-Based Stock Awards*

We use PRSU awards to provide our executive officers the opportunity to earn a defined number of shares of our common stock if we achieve pre-determined performance goals. At target level of achievement, the PRSU awards granted before 2026 represent 33% of our CEO's total equity awards and 20% of each of our other executive officer's total equity awards. Beginning with grants made in 2026, we increased the proportion of PRSUs to be awarded to our executive officers, including our CEO, to 40% of their total equity awards. The PRSU awards pay out based on our relative stock price performance compared to a peer group. Measuring our stock performance relative to peers mitigates the impact of macroeconomic factors, both positive and negative, that affect the industry and stock price performance and that are beyond the control of management. Measuring our performance in this way also provides rewards that are more directly aligned with performance through different economic cycles. We believe these PRSU awards provide a challenging incentive to the executive officers to deliver stockholder value.

**Measuring our stock performance relative to peers mitigates the impact of macroeconomic factors, both positive and negative, that affect the industry and stock price performance and that are beyond the control of management. Measuring our performance in this way also provides rewards that are more directly aligned with performance through different economic cycles.**

PRSU grants have a single vesting period at the end of three years following the grant date. No number of PRSUs is guaranteed to vest and the actual number of PRSUs that will vest at the end of the performance period may be anywhere from zero to the maximum amount depending on the Company's relative TSR. If the Company's TSR is negative over the performance period, the payout will not exceed 100% of the target number even if the percentile rank exceeds the 50th percentile. Below are the PRSU payout thresholds:

| Relative TSR Percentile Rank | TSR Performance Multiplier |
|---|---|
| <25$^{th}$ percentile | 0% |
| 25$^{th}$ percentile (**Threshold**) | 50% |
| 50$^{th}$ percentile (**Target**) | 100% |
| 60$^{th}$ percentile | 125% |
| 75$^{th}$ percentile | 150% |
| 90$^{th}$ percentile (**Maximum**) | 200% |

For 2024 performance, in January 2025, Dr. Monia received 86,263 time-vested stock options, 129,395 time-vested RSUs and 169,950 PRSUs (target payout of 84,975, multiplied by 200% to account for potential upside). For 2025 performance, in January 2026, Dr. Monia received 85,410 time-vested stock options, 42,705 time-vested RSUs and 113,880 PRSUs (target payout of 56,940 multiplied by 200% to account for potential upside).

*Vesting of Stock Awards*

Vesting schedules reward long-term performance and incentivize long-term stock appreciation and increased stockholder returns. For each stock option and RSU granted (except PRSUs), the Compensation Committee sets a vesting schedule over four years, with no vesting during the first year. Therefore, the stock options and RSUs granted to our executive officers directly align the interests of our executive officers with the interests of our stockholders and Ionis' long-term success. The actual economic value of stock option awards depends directly on the performance of our stock price over the period during which the awards vest and the period during which the stock options may be exercised. In other words, our executive officers will only realize economic value when our stock price, and consequently stockholder value, increases, which aligns pay with performance and fosters accountability for Ionis' long-term success. Conversely, the stock options are not worth anything if our stock price does not increase above the exercise price. For example, over the last three years, a total of 566,270 stock options expired underwater for our executive officers.

Similarly, in the same way our stockholder returns increase and decrease based on our stock's performance, the value to our employees of the RSUs increases and decreases based on our stock's performance. In addition, RSUs promote retention, reinforce an ownership culture, and provide value even during periods of stock price or market underperformance.

With the exception of PRSUs awarded to our executive officers, we do not tie vesting to the achievement of specific events, such as annual metrics, because we do not want to encourage our employees to deviate from our company objectives, which we believe optimizes sustained stockholder value; nor do we want our employees to take unnecessary risks just to meet a short-term metric.

**Each year the Compensation Committee approves a stock option, RSU and PRSU budget for annual employee merit awards. We do not grant options, RSUs or PRSUs in excess of this budget without Compensation Committee approval.**

The stock option vesting schedule is typically over a four-year period at the rate of 25% at the end of the first year and then at the rate of 2.08% per month for 36 months thereafter during the optionee's employment. The RSU vesting schedule is typically over a four-year period at the rate of 25% per year. In addition, as further described below, our executive officers must hold shares received upon vesting of their RSUs until they meet certain ownership thresholds or no longer serve the Company. These practices align our employee compensation with our stockholders' interests because if stockholder value declines over time, so too will the value of the equity compensation provided to all employees.

*Our stock compensation budget minimizes dilution*. Each year the Compensation Committee approves a budget that sets the number of stock options, RSUs and PRSUs we can grant our employees for annual merit awards. We do not grant stock options, RSUs or PRSUs that exceed this budget without the Compensation Committee's approval. Over the past three years, the average merit award stock budget set by the Compensation Committee has been approximately 2.36% of our outstanding common stock on an issued and outstanding basis. This stock compensation budget, and therefore our equity compensation burn rate, is below the Peer Group average of 3.4% from 2022 through 2024. We believe this stock budget is an important tool to balance our compensation objectives with stockholder interests. For 2025 performance, the Compensation Committee set a merit stock award budget that resulted in approximately 1.4 million stock options, approximately 1.8 million RSUs and a target number of approximately 190,000 PRSUs awarded to our employees (as applicable), including the executive officers. Together these shares represent approximately 2.06% of our outstanding common stock on an issued and outstanding basis for that year. This budget, as well as each employee's position level and performance in the previous year, ultimately determines the size of the individual annual stock grants.

**Over the past 3 years, the average merit award stock budget set by the Compensation Committee has been approximately 2.36% of our outstanding common stock on an issued and outstanding basis.**

## Corporate Governance

### *Stock Ownership Guidelines and Holding Periods*

*Our executive officers and members of our Board of Directors must meet a stock ownership guideline and all employees must hold shares purchased under our ESPP for at least six months*.

Our Compensation Committee and our Board set stock ownership and holding guidelines for our executive officers and members of the Board. These guidelines require our executive officers and non-employee Board members to accumulate shares of our stock up to specified amounts. Shares sold or surrendered to pay for withholding taxes associated with the RSU and PRSU awards are exempt from these holding requirements.

The number of shares subject to the guidelines is generally determined at the beginning of each calendar quarter, using the product of (i) the number of shares held by the individual on the first business day of such quarter and (ii) the average closing price of the Company's common stock over the 30 trading days immediately preceding the start of such quarter.

In 2022 we increased the ownership guidelines for our executive officers and in 2023 we increased the ownership guidelines for our non-employee Board members such that the current ownership guidelines are as follows:

| Executive Officer/Director | Stock Ownership Guideline (as a multiple of base salary/annual cash retainer) |
|---|---|
| CEO | 6 times Base Salary |
| All other executive officers | 2 times Base Salary |
| Non-employee directors | 5 times Base Annual Cash Retainer |

As of March 31, 2026, all our non-employee directors except for Ms. Diaz, and all our executive officers except Mr. Jenne and Dr. Kordasiewicz met these guidelines. Due to Mr. Jenne's and Dr. Kordasiewicz's recent appointments, and stock price volatility, these individuals narrowly missed the ownership guidelines.

In addition, our ESPP has a six-month minimum holding period for shares purchased under the ESPP.

*Clawback Policy*

*We have a recoupment/"clawback" policy*. For many years we have maintained an executive compensation clawback policy that provides the Company with authority to recover certain performance-based cash and equity incentive compensation from any current or former "officer" of the Company, as such term is defined under Rule 16a-1(f) of the Securities Exchange Act of 1934, as amended (the "***Securities Act***"), and as determined by the Company.

In October 2023, we amended such policy to comply with Rule 10D-1 of the Securities Act and Nasdaq's listing standards. Our amended clawback policy requires the Company to recoup the full amount of certain incentive compensation, as described below, reasonably promptly from officers if the Company is required to prepare an accounting restatement due to the material noncompliance of the Company with any financial reporting requirement under the securities laws.

The incentive compensation subject to this amended clawback policy is compensation that is granted, earned or vested based wholly or in part upon the attainment of a measure that is determined and presented in accordance with the accounting principles used in preparing the Company's financial statements, and any measures derived wholly or in part from such measures, received by an officer during the three completed fiscal years immediately preceding the date of the accounting restatement that exceeds the amount of compensation such officer would have received had such amount been determined based on the accounting restatement, computed without regard to any taxes paid.

Under our amended clawback policy, recoupment is required regardless of whether the officer engaged in any misconduct and regardless of fault, and the Company's obligation to recoup the applicable compensation is not dependent on whether or when any restated financial statements are filed. The Company is not required to recoup compensation if the Compensation Committee of the Board determines recoupment would be impractical, as further set forth under the terms of the amended policy.

*Anti-Hedging Policy and Anti-Pledging Policy*

*We explicitly prohibit employees from "shorting" and hedging against our stock and from pledging our stock*. To help avoid situations in which our employees may benefit from transactions that harm our stockholders, or that remove economic risk from their holdings of our securities, our policies specifically prohibit all employees, including our executive officers, from taking a "short" position in our stock and otherwise hedging their position in our stock against a future drop in our stock price including short sales and derivatives such as put or call options, swaps, forwards, and futures, or other inherently speculative transactions with respect to Ionis' securities at any time. In addition, we also prohibit all directors and employees, including our named executive officers, from pledging our stock as collateral.

*Rule 10b5-1 Trading Policy*

*10b5-1 plan required for executive officers and vice presidents*. We have a Rule 10b5-1 trading policy that allows our executive officers, vice presidents and other employees to establish plans that permit prearranged future sales of the employee's stock, which plans may be established when the individual is not in possession of material non-public information. We do not allow our executive officers or vice presidents to buy or sell our stock outside of a Rule 10b5-1 trading plan except for purchases of our stock under our ESPP (but not subsequent sales of the stock) and transactions that are automatically effected by Ionis' stock plan administrator in connection with the vesting and release of RSUs and PRSUs.

In early 2023, we modified our Rule 10b5-1 trading policy to comply with the SEC's final rules released in December 2022 that imposed new conditions on the availability of the Rule 10b5-1 affirmative defense to insider trading and require enhanced disclosures regarding the adoption, modification and termination of Rule 10b5-1 plans and other trading arrangements.

*Perquisites*

We are committed to using stockholder money responsibly, to building stockholder value and ensuring our processes are transparent. As a result, Ionis' policies do not provide for perquisites for any employees, including our executive officers.

*Retirement & Other Benefits*

We maintain a highly competitive benefits package that we offer to all regular employees, including our executive officers. These benefits include medical, dental and vision insurance, employee assistance program, basic life insurance, short-term disability/sick pay, long-term disability, vacation, holidays, a 401(k) plan with employer match, Accidental Death & Dismemberment ("***AD&D***") insurance, and for U.S. employees, an ESPP.

*Retention and Change of Control Agreements*

As part of our normal course of business, we engage in discussions with other biotechnology and pharmaceutical companies about possible collaborations, licensing and/or other ways in which the companies may work together to further our respective long-term objectives. In addition, many larger established pharmaceutical companies consider companies at similar stages of development to ours as potential acquisition targets. Occasionally, a transaction in the biotech/biopharmaceutical industry may start as a licensing transaction, but ultimately result in an acquisition. In certain scenarios, the potential for merger or being acquired may be in the best interests of our stockholders. As further described on page 79, we adopted a Severance Benefit Plan to provide certain economic benefits to our employees at or above the level of Vice President if their employment is terminated in certain circumstances, including because of a transaction that results in a change in control of the Company.

*Tax and Accounting Considerations*

Under Section 162(m), compensation paid to each of the Company's "covered employees" that exceeds $1 million per taxable year is generally non-deductible unless the compensation qualifies for certain grandfathered exceptions (including the "performance-based compensation" exception) for certain compensation paid to such covered employees.

Although the Compensation Committee will continue to consider tax implications as one factor in determining executive compensation, the Compensation Committee also looks at other factors in making its decisions and retains the flexibility to provide compensation for the Company's named executive officers in a manner consistent with the goals of the Company's executive compensation program and the best interests of the Company and its stockholders, which may include providing for compensation that is not deductible by the Company due to the deduction limit under Section 162(m). The Compensation Committee also retains the flexibility to modify compensation that was initially intended to be exempt from the deduction limit under Section 162(m) if it determines that such modifications are consistent with the Company's business needs.

Under ASC 718, the Company is required to estimate and record an expense for each award of equity compensation over the vesting period of the award. We record share-based compensation expense on an ongoing basis according to ASC 718.

## Compensation of Executive Officers

The following table shows for the fiscal years ended December 31, 2025, 2024, and 2023, compensation awarded to or paid to, or earned by, our named executive officers.

**Summary Compensation Table**

| Name and Principal Position | Year | Salary ($) | Bonus[1] ($) | Stock Awards[2] | | Option Awards[5] ($) | All Other Compensation ($) | Total ($) |
|---|---|---|---|---|---|---|---|---|
| | | | | RSUs[3] | PRSUs[4] | | | |
| Brett P. Monia Chief Executive Officer | 2025 | $1,051,776 | $2,398,049 | $4,297,208 | $4,147,630 | $1,438,105 | $18,009[6] | $13,350,777 |
| | 2024 | $1,008,898 | $1,024,662 | $4,681,270 | $5,627,878 | $3,004,746 | $52,889[7] | $15,400,343 |
| | 2023 | $960,855 | $1,405,250 | $3,546,849 | $4,310,045 | $2,259,883 | $17,141 | $12,500,023 |
| Elizabeth L. Hougen EVP, Finance and Chief Financial Officer | 2025 | $729,750 | $831,915 | $1,544,265 | $756,555 | $516,808 | $43,009[8] | $4,422,302 |
| | 2024 | $700,000 | $437,500 | $1,734,696 | $1,058,535 | $1,113,441 | $17,889 | $5,062,061 |
| | 2023 | $612,243 | $514,284 | $775,481 | $478,291 | $494,087 | $17,141 | $2,891,527 |
| Richard S. Geary EVP, Chief Development Officer | 2025 | $622,074 | $661,887 | $1,095,930 | $536,910 | $366,767 | $47,831[9] | $3,331,400 |
| | 2024 | $593,865 | $400,859 | $1,092,216 | $666,485 | $701,057 | $17,666 | $3,472,148 |
| | 2023 | $569,655 | $427,241 | $685,699 | $422,899 | $436,882 | $16,917 | $2,559,293 |
| Brian Birchler EVP, Corporate and Development Operations | 2025 | $580,154 | $617,284 | $1,095,930 | $536,910 | $366,767 | $48,009[10] | $3,245,054 |
| | 2024 | $531,003 | $331,877 | $1,092,216 | $666,485 | $701,057 | $17,889 | $3,340,527 |
| | 2023 | $510,580 | $367,618 | $685,699 | $422,899 | $436,882 | $17,141 | $2,440,819 |
| Eric Swayze, EVP, Research | 2025 | $589,013 | $626,710 | $1,095,930 | $536,910 | $366,767 | $18,009[6] | $3,233,339 |
| | 2024 | $565,000 | $353,125 | $1,092,216 | $666,485 | $701,057 | $47,889[11] | $3,425,772 |
| | 2023 | $513,828 | $431,616 | $685,699 | $422,899 | $436,882 | $67,141[12] | $2,558,065 |
| Patrick R. O'Neil EVP, Chief Legal Officer and General Counsel | 2025 | $611,791 | $581,201 | $1,095,930 | $536,910 | $366,767 | $18,009[6] | $3,210,608 |
| | 2024 | $586,850 | $366,781 | $1,092,216 | $666,485 | $701,057 | $17,889 | $3,431,278 |
| | 2023 | $562,926 | $422,194 | $685,699 | $422,899 | $436,882 | $17,141 | $2,547,741 |

(1) We present bonuses in the years they were earned, not in the year paid. Bonuses represent cash compensation for achievements as a result of our MBO program and are not necessarily paid in the year they are earned; for example, in January 2026 we paid bonuses for 2025 performance. As a result of the discretionary nature of our MBO program, we have concluded the entire amount of cash compensation resulting from that program is properly disclosed under the "Bonus" column to this Summary Compensation Table. For more information, please see the section titled "*MBO Program – Performance-Based, At-Risk Cash Compensation*."

(2) We present stock awards in the years they were awarded, not in the year earned. For example, in January 2026 we granted stock awards for 2025 performance.

(3) Amounts represent the aggregate expense recognized for financial statement reporting purposes in accordance with ASC 718 for RSU and option awards granted to our named executive officers. The fair value of RSUs is based on the market price of our common stock on the date of grant. For more information, please see Note 8, *Stockholders' Equity*, of the consolidated financial statements in our Annual Report on Form 10-K for the year ended December 31, 2025 regarding assumptions underlying valuation of equity awards.

(4) Amounts represent the values of the PRSUs at target level of achievement. The fair value of PRSUs is based on the then-probable outcome of the performance conditions underlying such awards and calculated using a Monte Carlo simulation because the performance target is based on our relative TSR, which represents a market condition. For more information, please see Note 8, *Stockholders' Equity,* of the consolidated financial statements in our Annual Report on Form 10-K for the year ended December 31, 2025 regarding assumptions underlying valuation of equity awards. At maximum level of achievement, the values of the PRSUs awarded in 2025 are as follows: Dr. Monia: $8,295,260; Ms. Hougen: $1,513,110; Dr. Geary: $1,073,820; Mr. Birchler: $1,073,820; Dr. Swayze: $1,073,820; and Mr. O'Neil: $1,073,820.

(5) Amounts represent the aggregate expense recognized for financial statement reporting purposes in accordance with ASC 718 for stock and option awards granted to our named executive officers. ASC 718 expense for the option awards is based on the fair value of the awards on the date of grant using an option-pricing model. For more information, please see Note 8, *Stockholders' Equity*, of the consolidated financial statements in our Annual Report on Form 10-K for the year ended December 31, 2025 regarding assumptions underlying valuation of equity awards.

(6) Includes AD&D ($109), basic life ($400), 401(k) matching contributions ($17,500) which are available to all employees.

(7) Includes a Commitment to Ionis Award to recognize his 35 years of service to the Company ($35,000).

(8) Includes AD&D ($109), basic life ($400), 401(k) matching contributions ($17,500) which are available to all employees. In addition, Ms. Hougen received a Commitment to Ionis Award to recognize her 25 years of service to the Company ($25,000).

(9) Includes AD&D ($71), basic life ($261), and 401(k) matching contributions ($17,5000) which are available to all employees. In addition, Dr. Geary received a Commitment to Ionis Award to recognize his 30 years of service to the Company ($30,000).

(10) Includes AD&D ($109), basic life ($400), 401(k) matching contributions ($17,500) which are available to all employees. In addition, Mr. Birchler received a Commitment to Ionis Award to recognize his 30 years of service to the Company ($30,000).

(11) Includes a Commitment to Ionis Award to recognize his 30 years of service to the Company ($30,000).

(12) Includes a Career Achievement Award ($50,000).

## Grants of Plan-Based Awards

The following table shows for the fiscal year ended December 31, 2025, certain information regarding grants of plan-based awards to our named executive officers:

**Grants of Plan-Based Awards in Fiscal 2025**

| Name | Grant Date | Estimated Future Payments Under Equity Incentive Plan Awards | | | All Other Stock Awards: Number of Shares of Stock or Units (#) | All Other Option Awards: Number of Securities Underlying Options (#) | Exercise or Base Price of Option Awards ($/Sh) | Grant Date Fair Value of Stock and Option Awards[1] ($) |
|---|---|---|---|---|---|---|---|---|
| | | Threshold (#) | Target (#) | Maximim (#) | | | | |
| Brett P. Monia | 1/2/2025 | — | — | — | — | 86,263 | $34.69 | $1,438,105 |
| | 1/15/2025 | — | — | — | 129,395 | — | — | $4,297,208 |
| | 1/15/2025 | 42,488 | 84,975 | 169,950 | — | — | — | $4,147,630 |
| Elizabeth L. Hougen | 1/2/2025 | — | — | — | — | 31,000 | $34.69 | $516,808 |
| | 1/15/2025 | — | — | — | 46,500 | — | — | $1,544,265 |
| | 1/15/2025 | 7,750 | 15,500 | 31,000 | — | — | — | $756,555 |
| Richard S. Geary | 1/2/2025 | — | — | — | — | 22,000 | $34.69 | $366,767 |
| | 1/15/2025 | — | — | — | 33,000 | — | — | $1,095,930 |
| | 1/15/2025 | 5,500 | 11,000 | 22,000 | — | — | — | $536,910 |
| Brian Birchler | 1/2/2025 | — | — | — | — | 22,000 | $34.69 | $366,767 |
| | 1/15/2025 | — | — | — | 33,000 | — | — | $1,095,930 |
| | 1/15/2025 | 5,500 | 11,000 | 22,000 | — | — | — | $536,910 |
| Eric Swayze | 1/2/2025 | — | — | — | — | 22,000 | $34.69 | $366,767 |
| | 1/15/2025 | — | — | — | 33,000 | — | — | $1,095,930 |
| | 1/15/2025 | 5,500 | 11,000 | 22,000 | — | — | — | $536,910 |
| Patrick R. O'Neil | 1/2/2025 | — | — | — | — | 22,000 | $34.69 | $366,767 |
| | 1/15/2025 | — | — | — | 33,000 | — | — | $1,095,930 |
| | 1/15/2025 | 5,500 | 11,000 | 22,000 | — | — | — | $536,910 |

(1) Amounts represent the aggregate expense recognized for financial statement reporting purposes in accordance with ASC 718 for RSU, PRSU and option awards granted to our named executive officers. ASC 718 expense for the option awards is based on the fair value of the awards on the date of grant using an option-pricing model. The fair value of RSUs is based on the market price of our common stock on the date of grant. The fair value of PRSUs is based on the then-probable outcome of the performance

conditions underlying such awards and calculated using a Monte Carlo simulation because the performance target is based on our relative TSR, which represents a market condition. For more information, please see Note 8, *Stockholders' Equity,* of the consolidated financial statements in our Annual Report on Form 10-K for the year ended December 31, 2025 regarding assumptions underlying valuation of equity awards.

## Narrative to Summary Compensation Table and Grants of Plan-Based Awards Table

The Compensation Committee granted merit non-statutory stock options to the executive officers on January 2, 2025, for their 2024 performance. Stock options were granted out of our 2011 Plan for all named executive officers. The options have a term of ten years and vest at the rate of 25% for the first year and then at the rate of 2.08% per month for 36 months thereafter during the optionee's employment.

The Compensation Committee granted RSUs to the executive officers on January 15, 2025 for their 2024 performance. RSUs were granted out of our 2011 Plan for all named executive officers. The RSUs vest at the rate of 25% per year over four years with a vesting commencement date of January 15, 2025.

In 2025, Dr. Monia received 33% of his total equity awards in the form of PRSUs, and all other named executive officers received 20% of their total equity awards in the form of PRSUs. These PRSU awards vest at the end of the three-year performance period following the date of grant based on the Company's TSR as compared to a peer group of companies as measured at the end of the performance period. No number of PRSUs is guaranteed to vest and the actual number of PRSUs that will vest at the end of the performance period may be anywhere from zero to 200% of the target number depending on the Company's relative TSR. Performance below the threshold level results in a payout of 0 shares, performance at the threshold level (25$^{th}$ percentile) results in a payout of 50% of target shares, performance at the target level (50$^{th}$ percentile) results in a payout of 100% of target shares, and performance at the maximum level (90$^{th}$ percentile and above) results in a payout of 200% of target shares. We use linear interpolation to calculate payout percentages for performance between the percentile ranks.

## Pay Versus Performance

### *Pay Versus Performance Table*

As required by Section 953(a) of the Dodd-Frank Wall Street Reform and Consumer Protection Act, and Item 402(v) of Regulation S-K ("***Item 402(v)***"), we are providing the following information about the relationship between executive compensation actually paid and certain financial performance of the Company. The amounts set forth below under the headings "Compensation Actually Paid to PEO" and "Average Compensation Actually Paid to non-PEO NEOs" have been calculated in a manner consistent with Item 402(v). Use of the term "compensation actually paid" is required by the SEC's rules and as a result of the calculation methodology required by the SEC, such amounts differ from compensation actually received by the individuals and the compensation decisions described in the CD&A section of this Proxy Statement. For further information concerning the Company's pay-for-performance philosophy and how the Company seeks to align executive compensation with the Company's performance, refer to the CD&A section of this Proxy Statement.

| Year | Summary Compensation Table Total for PEO[1] | Compensation Actually Paid to PEO[2] | Average Summary Compensation Table Total for Non-PEO NEOs[3] | Average Compensation Actually Paid to Non-PEO NEOs[4] | Value of Initial Fixed $100 Investment Based On: | | Net Income (Loss)[7] | Company-Selected Measure[8] |
|---|---|---|---|---|---|---|---|---|
| | | | | | Total Shareholder Return[5] | Peer Group Total Shareholder Return[6] | | |
| 2025 | $13,350,777 | $42,609,834 | $3,488,541 | $5,594,309 | $139.92 | $124.75 | ($381,387,000) | 90th percentile |
| 2024 | $15,400,343 | ($ 2,697,612) | $4,066,897 | $1,803,424 | $ 57.87 | $118.20 | ($453,897,000) | 34th percentile |
| 2023 | $12,500,023 | $14,224,215 | $2,699,299 | $3,119,211 | $ 83.74 | $118.87 | ($366,286,000) | 89th percentile |
| 2022 | $ 7,264,496 | $ 9,536,336 | $2,803,964 | $2,735,368 | $ 62.52 | $113.65 | ($269,722,000) | 81st percentile |
| 2021 | $13,305,673 | ($ 2,596,842) | $3,834,223 | $ 713,811 | $ 50.37 | $126.45 | ($ 28,597,000) | 41st percentile |

(1) The dollar amounts reported are the amounts of total compensation reported for Dr. Monia (our Chief Executive Officer) for each corresponding year in the "Total" column of the Summary Compensation Table on page 69 of this Proxy Statement.

(2) The dollar amounts represent the amount of compensation actually paid to Dr. Monia, as computed in accordance with Item 402(v). The dollar amounts do not reflect the actual amount of compensation earned by or paid to Dr. Monia during the applicable year. In accordance with the requirements of Item 402(v), the following adjustments were made to Dr. Monia's total compensation for each year to determine the compensation actually paid:

| Year | Reported Summary Compensation Table Total for PEO | Deduct: Reported Value of Equity Awards[(a)] | Add: Equity Award Adjustments[(b)] | Compensation Actually Paid to PEO |
|---|---|---|---|---|
| 2025 | $13,350,777 | ($9,882,943) | $39,142,000 | $42,609,834 |

(a) The grant date fair value of equity awards represents the total of the amounts reported in the "Stock Awards" and "Option Awards" columns in the Summary Compensation Table for the applicable year.

(b) The equity award adjustments for each applicable year include the addition (or subtraction, as applicable) of the following: (i) the year-end fair value of any equity awards granted in the applicable year that are outstanding and unvested as of the end of the year; (ii) the amount of change as of the end of the applicable year (from the end of the prior fiscal year) in fair value of any awards granted in prior years that are outstanding and unvested as of the end of the applicable year; (iii) for awards that are granted and vest in the same applicable year, the fair value as of the vesting date; (iv) for awards granted in prior years that vest in the applicable year, the amount equal to the change as of the vesting date (from the end of the prior fiscal year) in fair value; (v) for awards granted in prior years that are determined to fail to meet the applicable vesting conditions during the applicable year, a deduction for the amount equal to the fair value at the end of the prior fiscal year; and (vi) the dollar value of any dividends or other earnings paid on stock or option awards in the applicable year prior to the vesting date that are not otherwise reflected in the fair value of such award or included in any other component of total compensation for the applicable year. The valuation assumptions used to calculate fair values did not materially differ from those disclosed at the time of grant. The amounts deducted or added in calculating the equity award adjustments are as follows:

| Year | Year End Fair Value of Equity Awards | Change in Fair Value of Outstanding and Unvested Equity Awards | Change in Fair Value of Equity Awards Granted in Prior Years that Vested in the Year | Fair Value at the End of the Prior Year of Equity Awards that Failed to Meet Vesting Conditions in the Year | Total Equity Award Adjustments |
|---|---|---|---|---|---|
| 2025 | $27,164,376 | $4,112,268 | $7,865,356 | $— | $39,142,000 |

(3) The dollar amounts reported represent the average of the amounts reported for the Company's NEOs as a group (excluding Dr. Monia) in the "Total" column of the Summary Compensation Table of the Proxy Statement for each applicable year. The names of each of the NEOs (excluding Dr. Monia) included for purposes of calculating the average amounts in each applicable year are as follows:

i. For 2025, Elizabeth L. Hougen (EVP & CFO), Richard S. Geary (EVP, Chief Development Officer), Brian Birchler (EVP, Corporate and Development Operations), Eric Swayze (EVP, Research), and Patrick R. O'Neil (EVP, Chief Legal Officer and General Counsel).

ii. For 2024, Elizabeth L. Hougen (EVP & CFO), Kyle Jenne (EVP, Chief Global Product Strategy Officer), Richard S. Geary (EVP, Chief Development Officer), and Patrick R. O'Neil (EVP, Chief Legal Officer and General Counsel).

iii. For 2023, Elizabeth L. Hougen (EVP & CFO), Onaiza Cadoret-Manier (EVP, Chief Global Product Strategy and Operations Officer), Richard S. Geary (EVP, Chief Development Officer), and Eric Swayze (EVP, Research).

iv. For 2022, Elizabeth L. Hougen (EVP & CFO), Joseph T. Baroldi (EVP, Chief Business Officer), Onaiza Cadoret-Manier (EVP, Chief Global Product Strategy and Operations Officer) and Richard S. Geary (EVP, Chief Development Officer).

v. For 2021, Elizabeth L. Hougen (EVP & CFO), Patrick R. O'Neil (EVP, Chief Legal Officer and General Counsel), Onaiza Cadoret-Manier (EVP, Chief Global Product Strategy and Operations Officer) and Eric Swayze (EVP, Research).

(4) The dollar amounts reported represent the average amount of compensation actually paid to the NEOs as a group (excluding Dr. Monia), as computed in accordance with Item 402(v). The dollar amounts do not reflect the actual average amount of compensation earned by or paid to the NEOs as a group (excluding Dr. Monia) during the applicable year. In accordance with the requirements of Item 402(v), the following adjustments were made to average total compensation for the NEOs as a group (excluding Dr. Monia) for each year to determine the compensation actually paid, using the same methodology described above in Note 2:

| Year | Average Reported Summary Compensation Table Total for Non-PEO NEOs | Deduct: Average Reported Value of Equity Awards | Add: Average Award Adjustments[(a)] | Average Compensation Actually Paid to Non-PEO NEOs |
|---|---|---|---|---|
| 2025 | $3,488,541 | ($2,163,211) | $4,268,979 | $5,594,309 |

(a) The amounts deducted or added in calculating the total average equity award adjustments are as follows:

| Year | Year End Fair Value of Equity Awards | Change in Fair Value of Outstanding and Unvested Equity Awards | Change in Fair Value of Equity Awards Granted in Prior Years that Vested in the Year | Total Equity Award Adjustments |
|---|---|---|---|---|
| 2025 | $6,266,152 | ($2,156,114) | $158,942 | $4,268,979 |

(5) Cumulative TSR is calculated by dividing the sum of the cumulative amount of dividends for the measurement period, assuming dividend reinvestment, and the difference between the Company's stock price at the end and the beginning of the measurement period by the Company's stock price at the beginning of the measurement period.

(6) Represents the weighted peer group TSR, weighted according to the respective companies' stock market capitalization at the beginning of each period for which a return is indicated. The peer group used for this purpose is the Nasdaq Biotechnology Index.

(7) The dollar amounts reported represent the amount of net income (loss) reflected in the Company's audited financial statements for the applicable year.

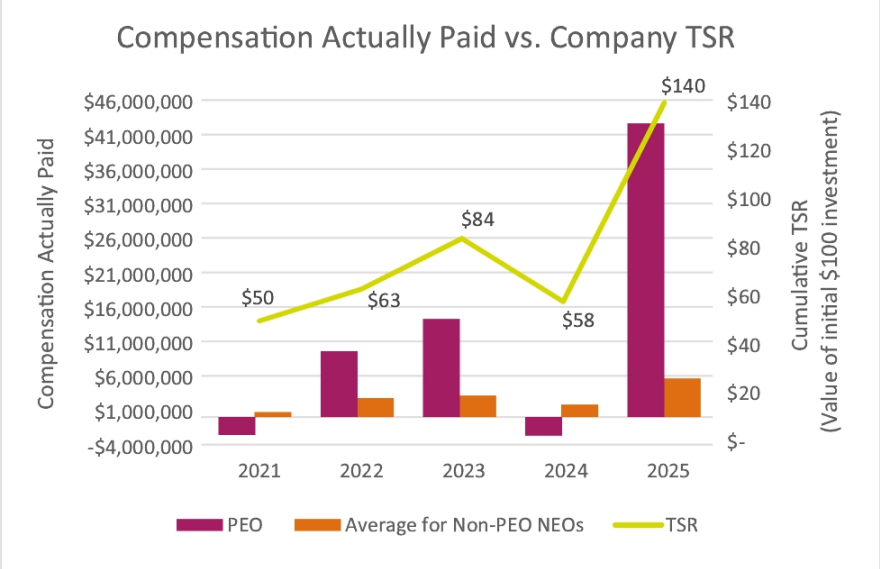
(8) One-year relative TSR shown is the percentile rank of the Company's TSR as compared to the TSRs of all members of the Nasdaq Biotechnology Index, ranked in descending order, for the one-year period commencing on January 15th of the applicable year and ending January 15th of the following year, which time period is consistent with the one-year measurement period used in the PRSUs awarded in 2021-2025.

*Analysis of the Information Presented in the Pay Versus Performance Table*

While the Company utilizes several performance measures as it seeks to align executive compensation with Company performance, all of those Company measures are not presented in the Pay Versus Performance Table ("***PVP Table***"). Moreover, the Company generally seeks to incentivize long-term performance, and therefore does not specifically align the Company's performance measures with compensation that is actually paid (as computed in accordance with Item 402(v)) for a particular year. In accordance with Item 402(v), the Company is providing the descriptions and graphs below regarding the relationships between certain information presented in the PVP Table.

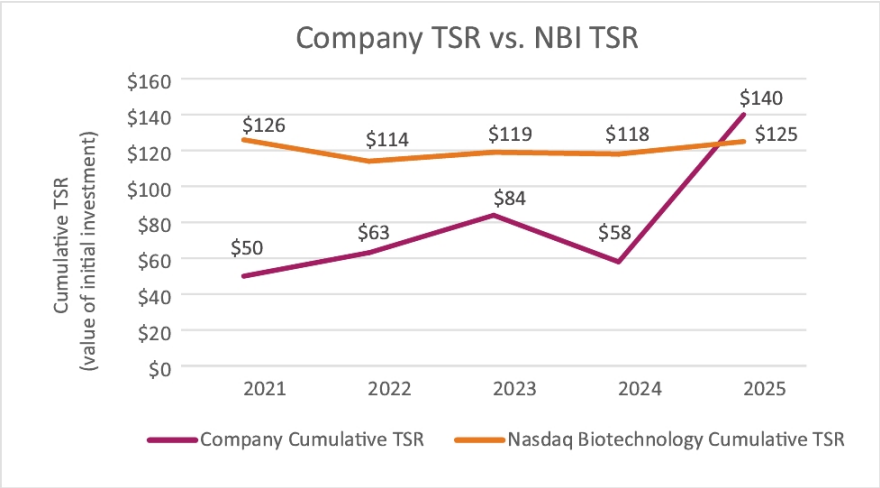
*Compensation Actually Paid and Cumulative TSR*

The graph below shows the amount of compensation actually paid to Dr. Monia and the average amount of compensation actually paid to the Company's NEOs as a group (excluding Dr. Monia) against the Company's cumulative TSR over the five years presented in the table.



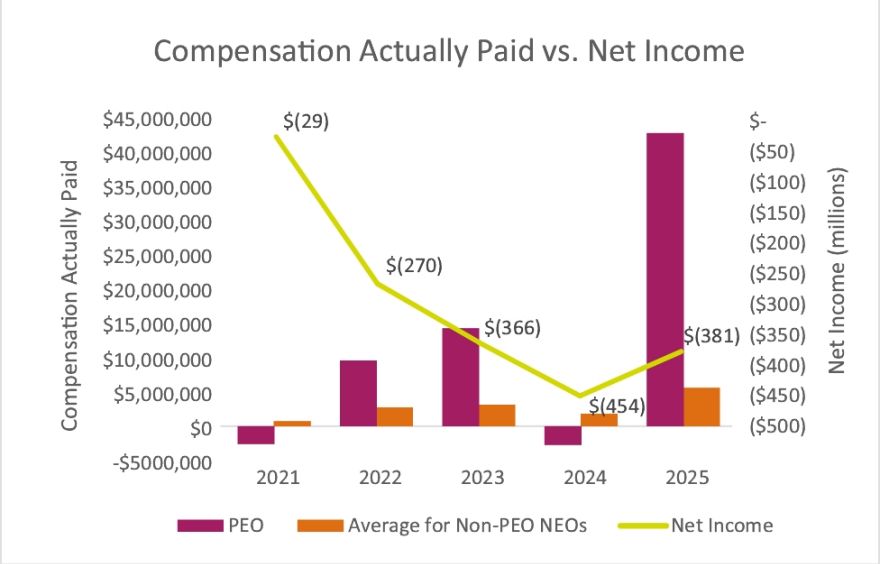
*Cumulative TSR of the Company and Cumulative TSR of the NBI*

The graph below shows the Company's cumulative TSR over the five-year period against the cumulative TSR of the peer group presented for this purpose, the Nasdaq Biotechnology Index.



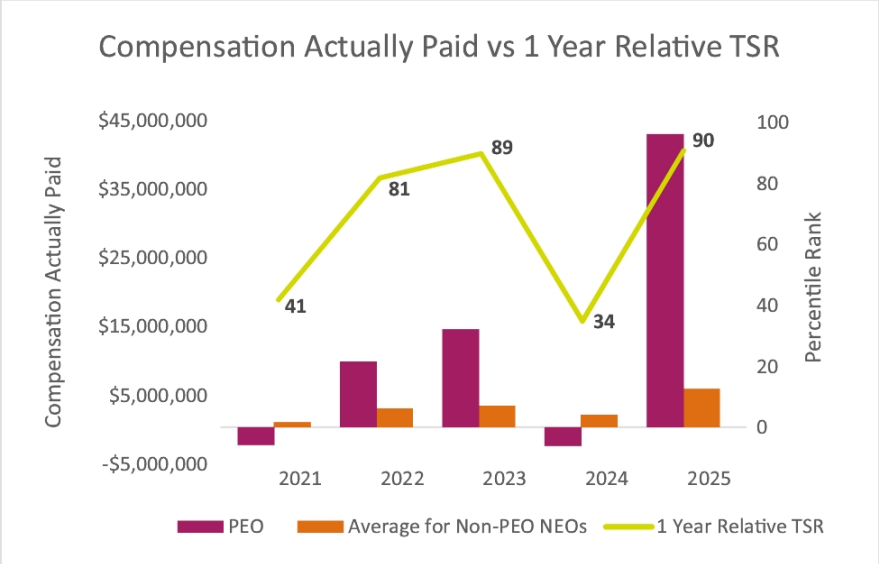

*Compensation Actually Paid and Net Income*

The graph below shows the amount of compensation actually paid to Dr. Monia and the average amount of compensation actually paid to the Company's NEOs as a group (excluding Dr. Monia) and the Company's net income over the five years presented in the table. As noted above, the Company does not use compensation actually paid to set executive compensation.



*Compensation Actually Paid and One-Year Relative Total Shareholder Return (our Company-Selected Measure)*

The graph below shows the amount of compensation actually paid to Dr. Monia and the average amount of compensation actually paid to the Company's NEOs as a group (excluding Dr. Monia) and the Company's one-year relative total shareholder return shown as a percentile rank of the Company's TSR as compared to the TSRs of all members of the Nasdaq Biotechnology Index for each of the five years presented in the table.



*Financial Performance Measures*

As described in greater detail in the CD&A, we design our executive compensation program to drive the creation of long-term stockholder value and mitigate unnecessary or imprudent business risk taking. To that end, we seek to structure our executive compensation program to align executive compensation with Company performance. The most important financial performance measures used by the Company in fiscal year 2025 to link executive compensation actually paid to the Company's named executive officers to the Company's performance are listed in the table to the right.

| Most Important Financial Performance Measures |
|---|
| Revenue |
| One-Year Relative TSR Versus the NBI |
| Whether We Met Our Non-GAAP Net Operating Loss Guidance |

*All information provided above under the "Item 402(v) Pay Versus Performance" heading will not be deemed to be incorporated by reference into any filing of the Company under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended, whether made before or after the date hereof and irrespective of any general incorporation language in any such filing, except to the extent the Company specifically incorporates such information by reference.*

## Outstanding Equity Awards at Fiscal Year-End – Executive Officers

The following table shows for the fiscal year ended December 31, 2025, certain information regarding outstanding equity awards at fiscal year-end for our named executive officers.

Other than the equity awards described in the table below, there were no equity incentive plan awards outstanding for our named executive officers at December 31, 2025.

**Outstanding Equity Awards as of December 31, 2025**

| | Option Awards | | | | | Stock Awards | | | |
|---|---|---|---|---|---|---|---|---|---|
| Name | Grant Date | Number of Securities Underlying Unexercised Options (#) Exercisable[1] | Number of Securities Underlying Unexercised Options (#) Unexercisable | Option Exercise Price ($) | Option Expiration Date | Number of Shares or Units of Stock that Have Not Vested[2] | Market Value of Shares or Units of Stock that Have Not Vested[3] | Equity incentive plan awards: number of unearned shares, units or other rights that have not vested (#)[4] | Equity incentive plan awards: market or payout value of unearned shares, units or other rights that have not vested ($) [5] |
| Brett P. Monia | 1/2/2020 | 107,632 | — | $60.89 | 1/1/2027 | — | — | — | — |
| | 1/2/2020 | 40,822 | — | $60.89 | 1/1/2027 | — | — | — | — |
| | 1/4/2021 | 149,872 | — | $56.78 | 1/3/2028 | — | — | — | — |
| | 1/3/2022 | 38,058 | 2,115 | $32.60 | 1/2/2032 | — | — | — | — |
| | 1/3/2023 | 44,502 | 32,141 | $37.58 | 1/2/2033 | — | — | — | — |
| | 1/2/2024 | 55,861 | 60,719 | $52.87 | 1/1/2034 | — | — | — | — |
| | 1/2/2025 | — | 86,263 | $34.69 | 1/1/2035 | — | — | — | — |
| | 1/15/2022 | — | — | — | — | 12,686 | $1,003,589 | — | — |
| | 1/15/2023 | — | — | — | — | 44,502 | $3,520,553 | — | — |
| | 1/15/2024 | — | — | — | — | 65,576 | $5,187,717 | — | — |
| | 1/15/2025 | — | — | — | — | 129,395 | $10,236,438 | — | — |
| | 1/15/2023 | — | — | — | — | 122,214[6] | $9,668,350 | — | — |
| | 1/15/2024 | — | — | — | — | — | — | 35,887 | $2,839,021 |
| | 1/15/2025 | — | — | — | — | — | — | 42,487 | $3,361,147 |

| | Option Awards | | | | | Stock Awards | | | |
|---|---|---|---|---|---|---|---|---|---|
| Name | Grant Date | Number of Securities Underlying Unexercised Options (#) Exercisable[1] | Number of Securities Underlying Unexercised Options (#) Unexercisable | Option Exercise Price ($) | Option Expiration Date | Number of Shares or Units of Stock that Have Not Vested[2] | Market Value of Shares or Units of Stock that Have Not Vested[3] | Equity incentive plan awards: number of unearned shares, units or other rights that have not vested (#)[4] | Equity incentive plan awards: market or payout value of unearned shares, units or other rights that have not vested ($) [5] |
| Elizabeth L. Hougen | 1/2/2020 | 60,299 | — | $60.89 | 1/1/2027 | — | — | — | — |
| | 1/4/2021 | 61,041 | — | $56.78 | 1/3/2028 | — | — | — | — |
| | 1/3/2022 | 32,428 | 690 | $32.60 | 1/2/2032 | — | — | — | — |
| | 1/3/2023 | 18,919 | 7,027 | $37.58 | 1/2/2033 | — | — | — | — |
| | 1/2/2024 | 20,700 | 22,500 | $52.87 | 1/1/2034 | — | — | — | — |
| | 1/2/2025 | — | 31,000 | $34.69 | 1/1/2035 | — | — | — | — |
| | 1/15/2022 | — | — | — | — | 4,139 | $327,436 | — | — |
| | 1/15/2023 | — | — | — | — | 9,730 | $769,740 | — | — |
| | 1/15/2024 | — | — | — | — | 24,300 | $1,922,373 | — | — |
| | 1/15/2025 | — | — | — | — | 46,500 | $3,678,615 | — | — |
| | 1/15/2023 | — | — | — | — | 13,562[6] | $1,072,890 | — | — |
| | 1/15/2024 | — | — | — | — | — | — | 6,750 | $533,993 |
| | 1/15/2025 | — | — | — | — | — | — | 7,750 | $613,103 |
| Richard S. Geary | 1/3/2022 | 29,930 | 637 | $32.60 | 1/2/2032 | — | — | — | — |
| | 1/3/2023 | 16,729 | 6,213 | $37.58 | 1/2/2033 | — | — | — | — |
| | 1/2/2024 | 13,033 | 14,167 | $52.87 | 1/1/2034 | — | — | — | — |
| | 1/2/2025 | — | 22,000 | $34.69 | 1/1/2035 | — | — | — | — |
| | 1/15/2022 | — | — | — | — | 3,821 | $302,279 | — | — |
| | 1/15/2023 | — | — | — | — | 8,603 | $680,583 | — | — |
| | 1/15/2024 | — | — | — | — | 15,300 | $1,210,383 | — | — |
| | 1/15/2025 | — | — | — | — | 33,000 | $2,610,630 | — | — |
| | 1/15/2023 | — | — | — | — | 11,991[6] | $948,608 | — | — |
| | 1/15/2024 | — | — | — | — | — | — | 4,250 | $336,218 |
| | 1/15/2025 | — | — | — | — | — | — | 5,500 | $435,105 |
| Brian Birchler | 1/2/2020 | 26,063 | — | $60.89 | 1/1/2027 | — | — | — | — |
| | 1/4/2021 | 22,000 | — | $56.78 | 1/3/2028 | — | — | — | — |
| | 1/3/2022 | 19,093 | 407 | $32.60 | 1/2/2032 | — | — | — | — |
| | 3/20/2022 | 14,062 | 938 | $35.25 | 3/19/2032 | — | — | — | — |
| | 1/3/2023 | 16,729 | 6,213 | $37.58 | 1/2/2033 | — | — | — | — |
| | 1/2/2024 | 13,033 | 14,167 | $52.87 | 1/1/2034 | — | — | — | — |
| | 1/2/2025 | — | 22,000 | $34.69 | 1/1/2035 | — | — | — | — |
| | 1/15/2022 | — | — | — | — | 2,437 | $192,791 | — | — |
| | 4/15/2022 | — | — | — | — | 1,875 | $148,331 | — | — |
| | 1/15/2023 | — | — | — | — | 8,603 | $680,583 | — | — |
| | 1/15/2024 | — | — | — | — | 15,300 | $1,210,383 | — | — |
| | 1/15/2025 | — | — | — | — | 33,000 | $2,610,630 | — | — |
| | 1/15/2023 | — | — | — | — | 11,991[6] | $948,608 | — | — |
| | 1/15/2024 | — | — | — | — | — | — | 4,250 | $336,218 |
| | 1/15/2025 | — | — | — | — | — | — | 5,500 | $435,105 |

| | Option Awards | | | | | Stock Awards | | | |
|---|---|---|---|---|---|---|---|---|---|
| Name | Grant Date | Number of Securities Underlying Unexercised Options (#) Exercisable[1] | Number of Securities Underlying Unexercised Options (#) Unexercisable | Option Exercise Price ($) | Option Expiration Date | Number of Shares or Units of Stock that Have Not Vested[2] | Market Value of Shares or Units of Stock that Have Not Vested[3] | Equity incentive plan awards: number of unearned shares, units or other rights that have not vested (#)[4] | Equity incentive plan awards: market or payout value of unearned shares, units or other rights that have not vested ($) [5] |
| Eric Swayze | 1/2/2020 | 21,528 | — | $60.89 | 1/1/2027 | — | — | — | — |
| | 1/2/2020 | 6,000 | — | $60.89 | 1/1/2027 | — | — | — | — |
| | 1/4/2021 | 53,945 | — | $56.78 | 1/3/2028 | — | — | — | — |
| | 1/3/2022 | 29,098 | 620 | $32.60 | 1/2/2032 | — | — | — | — |
| | 1/3/2023 | 16,729 | 6,213 | $37.58 | 1/2/2033 | — | — | — | — |
| | 1/2/2024 | 13,033 | 14,167 | $52.87 | 1/1/2034 | — | — | — | — |
| | 1/2/2025 | — | 22,000 | $34.69 | 1/1/2035 | — | — | — | — |
| | 1/15/2022 | — | — | — | — | 3,714 | $293,815 | — | — |
| | 1/15/2023 | — | — | — | — | 8,603 | $680,583 | — | — |
| | 1/15/2024 | — | — | — | — | 15,300 | $1,210,383 | — | — |
| | 1/15/2025 | — | — | — | — | 33,000 | $2,610,630 | — | — |
| | 1/15/2023 | — | — | — | — | 11,991[6] | $948,608 | — | — |
| | 1/15/2024 | — | — | — | — | — | — | 4,250 | $336,218 |
| | 1/15/2025 | — | — | — | — | — | — | 5,500 | $435,105 |
| Patrick R. O'Neil | 1/3/2022 | 3,830 | 637 | $32.60 | 1/2/2032 | — | — | — | — |
| | 1/3/2023 | 2,729 | 6,213 | $37.58 | 1/2/2033 | — | — | — | — |
| | 1/2/2024 | 2,833 | 14,167 | $52.87 | 1/1/2034 | — | — | — | — |
| | 1/2/2025 | — | 22,000 | $34.69 | 1/1/2035 | — | — | — | — |
| | 1/15/2022 | — | — | — | — | 3,821 | $302,279 | — | — |
| | 1/15/2023 | — | — | — | — | 8,603 | $680,583 | — | — |
| | 1/15/2024 | — | — | — | — | 15,300 | $1,210,383 | — | — |
| | 1/15/2025 | — | — | — | — | 33,000 | $2,610,630 | — | — |
| | 1/15/2023 | — | — | — | — | 11,991[6] | $948,608 | — | — |
| | 1/15/2024 | — | — | — | — | — | — | 4,250 | $336,218 |
| | 1/15/2025 | — | — | — | — | — | — | 5,500 | $435,105 |

(1) The options granted to our employees were granted out of our 2011 Plan and vest at the rate of 25% for the first year and then at the rate of 2.08% per month for 36 months thereafter during the optionee's employment. Options granted to our employees before January 1, 2022 have a term of seven years and options granted to our employees beginning January 1, 2022 have a term of ten years.

(2) The RSUs granted to our employees were granted out of our 2011 Plan. The RSUs vest at the rate of 25% per year over four years.

(3) Market value of stock awards was determined by multiplying the number of unvested shares by $79.11, which was the closing market price of our common stock on the Nasdaq Global Select Market on December 31, 2025, the last trading day of fiscal 2025.

(4) Represents the threshold payout of shares under the PRSU awards granted to our named executive officers out of our 2011 Plan.

(5) Market value of PRSUs was determined by multiplying the threshold payout of shares by $79.11, which was the closing market price of our common stock on the Nasdaq Global Select Market on December 31, 2025, the last trading day of fiscal 2025.

(6) Represents the PRSU awards granted in 2023 that had a performance period ending on December 31, 2025. In January 2026, the Compensation Committee certified achievement of such PRSU awards at 167.27% of target.

## Option Exercises and Stock Vested – Executive Officers

The following table shows for the fiscal year ended December 31, 2025, certain information regarding option exercises and stock awards vesting during the last fiscal year with respect to our named executive officers:

| | Option Awards | | Stock Awards | |
|---|---|---|---|---|
| Name | Number of Shares Acquired on Exercise (#) | Value Realized on Exercise ($)[1] | Number of Shares Acquired on Vesting (#) | Value Realized on Vesting ($)[2] |
| Brett P. Monia | 206,246 | $12,436,031 | 98,820 | $3,284,603 |
| Elizabeth L. Hougen | 49,800 | $3,249,734 | 28,025 | $931,165 |
| Richard S. Geary | 163,468 | $11,726,750 | 22,721 | $754,985 |
| Brian Birchler | 23,900 | $1,723,987 | 16,158 | $527,551 |
| Eric Swayze | 27,114 | $1,793,744 | 22,825 | $758,427 |
| Patrick R. O'Neil | 212,764 | $13,586,873 | 23,510 | $781,187 |

(1) The value realized on exercise was calculated using the closing price of our common stock on the Nasdaq Global Select Market at exercise less the applicable option exercise price.

(2) The value realized on vesting of RSUs and PRSUs was calculated using the closing price of a share of our common stock on the Nasdaq Global Select Market on the vesting date multiplied by the number of shares vested.

## Post-Employment Compensation

### *Pension Benefits and Nonqualified Deferred Compensation*

Our executive officers are eligible to participate in our 401(k) contributory defined contribution plan. In 2025, we contributed to each participant a matching contribution equal to 100% of the first 5% of the participant's compensation they contributed to the plan. In 2025, the maximum matching contribution was $17,500. The Compensation Committee can also grant discretionary contributions under our 401(k) plan. We do not provide any nonqualified defined contribution or other deferred compensation plans.

### *Employment Agreements*

Our executive officers do not have employment contracts with us; however, they are entitled to participate in our Severance Benefit Plan, as described below.

## Potential Payments Upon Termination or Change in Control

### *Severance and Change in Control Arrangements*

On October 18, 2018, the Company implemented a Severance Benefit Plan, which was amended and restated on March 17, 2022 (the "***Plan***"). The Plan provides for change in control and severance benefits to the Company's executive officers, including but not limited to the Chief Executive Officer and the Chief Financial Officer, and vice presidents (each, a "***Covered Employee***").

The Plan provides that if a Covered Employee is terminated without "cause" (as defined in the Plan) or resigns for "good reason" (as defined in the Plan), except in connection with a "change in control" of the Company (as defined in the Plan), the Covered Employee will generally be entitled to receive (i) a lump sum payment of the Covered Employee's then-current monthly base salary, (ii) accelerated vesting of stock options and time-based restricted stock units previously granted to the Covered Employee by the Compensation Committee and outstanding as of the termination date that otherwise would have vested during the periods noted below, and (iii) continued medical group health and dental plan coverage, in each case for the following durations:

- Chief Executive Officer: 18 months;
- Executive Vice Presidents: 12 months;
- Senior Vice Presidents: 9 months; and
- Vice Presidents: 6 months.

In addition, for the Chief Executive Officer only, payment of the then-current target bonus, prorated for time served during such calendar year.

The Plan also provides that if a Covered Employee's termination or resignation occurs during the period that begins three months before and ends twelve months following a change in control (as defined in the Plan), the Covered Employee will generally be entitled to receive (i) a lump sum payment of the Covered Employee's then-current monthly base salary, (ii) payment of the then-current target bonus, (iii) accelerated vesting of all stock options and time-based restricted stock units previously granted to the Covered Employee by the Compensation Committee and outstanding as of the termination date, and (iv) continued medical group health and dental plan coverage, in each of (i), (ii) and (iv) for the following durations:

- Chief Executive Officer: 24 months;
- Executive Vice Presidents: 18 months;
- Senior Vice Presidents: 12 months; and
- Vice Presidents: 9 months.

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 Code. The Plan does not include any tax gross-up or other tax indemnity related to payments made to Covered Employees under the Plan; however, payments, benefits or distributions to or for the benefit of the Covered Employee under the Plan may be reduced if doing so would result in a more favorable after-tax position for the Covered Employee.

*Conditions*

As a condition to receiving benefits under the Plan, the Covered Employee is required to execute and not revoke a release in favor of the Company, which release will contain a standard release from liability, non-solicitation and non-disparagement provisions, and a reaffirmation of the Covered Employee's confidentiality obligations to the Company.

*Estimate of Benefits under Severance Benefit Plan*

The following table estimates the lump sum payments and health benefits that would be required to be paid to our named executive officers under the Plan as of December 31, 2025. This table estimates the lump sum payments based upon either a termination without cause, a resignation with good reason or a termination in connection with a change in control, assuming such event occurred on December 31, 2025. The estimates in this table are forward-looking statements. Please see the special note regarding forward-looking statements on page 91 of this Proxy Statement.

| Name | Total – Change in Control Event | Total – Non-Change in Control Event |
|---|---|---|
| Brett P. Monia | $3,912,115 | $2,521,528 |
| Elizabeth L. Hougen | $1,652,206 | $795,559 |
| Richard S. Geary | $1,410,801 | $680,258 |
| Brian Birchler | $1,340,403 | $650,865 |
| Eric Swayze | $1,339,999 | $646,889 |
| Patrick R. O'Neil | $1,379,111 | $665,514 |

In addition, in the case of a termination or resignation with good reason in connection with a change in control (as defined in the Plan), stock options and time-based restricted stock units previously granted by the Compensation Committee and outstanding as of the termination date will accelerate as described above.

## Director Compensation

For the fiscal year ending December 31, 2025, we paid our non-employee directors a base cash retainer of $60,000 with additional role-based compensation as noted below:

| Role | 2025 Cash Compensation |
|---|---|
| Board Member (Base) | $60,000 |
| Non-Executive Chairman of the Board | $40,000 |
| Independent Lead Director | $40,000 |
| Committee Chairs (Additional) | |
| Audit | $25,000 |
| Compliance | $20,000 |
| Compensation | $20,000 |
| Finance | $20,000 |
| Nominating, Governance and Review | $20,000 |
| Medical and Science | $20,000 |
| Committee Member (Additional) | |
| Audit | $12,500 |
| Compliance | $10,000 |
| Compensation | $10,000 |
| Finance | $10,000 |
| Nominating, Governance and Review | $10,000 |
| Medical and Science | $10,000 |

If the Board creates new committees, we anticipate that the non-employee members of such new committees will receive additional compensation for their role on those committees. We do not pay Board members additional compensation for attending Board meetings, but we do reimburse them for the expenses they incur to attend the meetings.

In 2025 each non-employee director also received automatic stock award grants under our Non-Employee Directors' Stock Option Plan. On July 1, 2025, under the Non-Employee Directors' Stock Option Plan, each of our non-employee directors serving at that time received an option to purchase 11,518 shares of our common stock, at an exercise price of $39.94 per share, the fair market value of the common stock on the date of the grant, based on the closing sales price reported on the Nasdaq Global Select Market, and an RSU award of 5,220 shares. The options and RSUs vest on either (1) the annual anniversary of the date of grant, or (2) the next regularly scheduled annual meeting of stockholders, whichever occurs earlier.

In March 2021, the Compensation Committee and Board adopted a policy governing compensation the Company pays to its non-employee directors, which policy the Compensation Committee and Board have amended on several occasions (the "***Director Compensation Policy***"). In addition to stating the cash compensation amounts set forth above and the equity grants each non-employee director will receive upon joining the Board and annually thereafter pursuant to the Non-Employee Directors' Stock Option Plan, the Director Compensation Policy also includes an annual equity cap, which, until March 2026, was $450,000 for annual awards to incumbent non-employee directors and $675,000 for initial awards to newly appointed non-employee directors, in each case based on the aggregate grant date fair value (as determined in accordance with FASB Topic ASC 718 or its successor). The grant date fair value of annual awards to be automatically granted in July 2025 would have exceeded $450,000; thus, for 2025, each non-employee director received a reduced annual award of 11,518 stock options and 5,220 RSUs such that the awards did not exceed the $450,000 cap.

The Compensation Committee reviews pay levels for non-employee directors every year, with assistance from Aon, which prepares a comprehensive assessment of Ionis' non-employee director compensation program. That assessment includes benchmarking against the same peer group used for executive compensation purposes, an update on recent trends in director compensation, and a review of related corporate governance best practices. The Compensation Committee reviews these assessments prior to making recommendations to the Board regarding non-employee director compensation. In March 2025, the Compensation Committee reviewed Aon's assessment in which Aon did not recommend any changes to our non-employee director compensation program for 2025. Following review and discussion of such report the Compensation Committee did not recommend any changes to the Board regarding our non-employee director compensation program for 2025. In March 2026, the Compensation Committee reviewed Aon's assessment of market data with respect to non-employee director equity grants. Following review and discussion of such assessment, the Compensation Committee recommended, and the Board

approved, beginning with grants made in 2026, reducing the cap of our annual equity awards to incumbent non-employee directors from $450,000 to $400,000, and reducing the cap for initial awards to newly appointed non-employee directors from $675,000 to $600,000. We will continue to assess our non-employee director compensation program annually with the assistance of Aon.

In December 2022, the Company adopted a deferral program for annual RSUs granted to non-employee directors beginning in January 2023 and going forward. Such deferral program allows non-employee directors to defer receipt of shares that may vest under future RSU grants until (1) separation from service to Ionis, or (2) the earlier to occur of five years following the vesting date of the RSUs and separation from service to Ionis, subject in all cases to earlier delivery of deferred RSUs upon a change in control of the Company.

The following table shows for the fiscal year ended December 31, 2025 certain information with respect to the compensation of our non-employee directors:

**Director Compensation for Fiscal 2025**

| Name | Cash Compensation Earned or Paid ($) | Stock Awards ($)[1] | Option Awards ($)[1] | All Other Compensation ($) | Total ($) |
|---|---|---|---|---|---|
| Spencer R. Berthelsen | $100,000 | $208,487 | $240,293 | — | $548,780 |
| Allene Diaz | $82,500 | $208,487[3] | $240,293 | — | $531,280 |
| Michael Hayden | $80,000 | $208,487[2] | $240,293 | — | $528,780 |
| Joan Herman | $92,500 | $208,487 | $240,293 | — | $541,280 |
| Joseph Klein, III | $95,000 | $208,487[2] | $240,293 | — | $543,780 |
| Joseph Loscalzo | $120,000 | $208,487[2] | $240,293 | — | $568,780 |
| B. Lynne Parshall | $90,000 | $208,487 | $240,293 | — | $538,780 |
| Joseph H. Wender | $150,000 | $208,487 | $240,293 | — | $598,780 |
| Michael Yang | $70,000 | $208,487[3] | $240,293 | — | $518,780 |

(1) Amounts represent the aggregate expense recognized for financial statement reporting purposes in accordance with ASC 718 for stock and option awards granted to the directors. ASC 718 expense for the option awards is based on the fair value of the awards on the date of grant using an option-pricing model. The fair value of RSUs is based on the market price of our common stock on the date of grant. For more information, please see Note 8, *Stockholders' Equity,* of the consolidated financial statements in our Annual Report on Form 10-K for the year ended December 31, 2025 regarding assumptions underlying valuation of equity awards.

(2) Director has elected to defer the release of these shares until 30 days following separation from service to the Company.

(3) Director has elected to defer the release of these shares until the earliest of the fifth anniversary of the vesting date or 30 days following separation from service to the Company.

## Outstanding Equity Awards at Fiscal Year-End – Directors

The following table shows for the fiscal year ended December 31, 2025, certain information regarding outstanding awards at fiscal year-end of all our non-employee directors:

**Outstanding Equity Awards as of December 31, 2025**

| | | Option Awards | | | | Stock Awards | |
|---|---|---|---|---|---|---|---|
| Name | Grant Date | Number of Securities Underlying Unexercised Options (#) Exercisable[1] | Number of Securities Underlying Unexercised Options (#) Unexercisable | Option Exercise Price ($) | Option Expiration Date | Number of Shares or Units of Stock that Have Not Vested[2][3] | Market Value of Shares or Units of Stock that Have Not Vested[4] |
| Spencer R. Berthelsen | 7/1/2016 | 16,000 | — | $24.42 | 6/30/2026 | 5,220 | $412,954 |
| | 7/3/2017 | 16,000 | — | $52.22 | 7/2/2027 | | |
| | 7/2/2018 | 16,000 | — | $42.88 | 7/1/2028 | | |
| | 7/1/2019 | 16,000 | — | $64.80 | 6/30/2029 | | |
| | 7/1/2020 | 12,000 | — | $60.20 | 6/30/2030 | | |
| | 7/1/2021 | 12,000 | — | $40.05 | 6/30/2031 | | |
| | 7/1/2022 | 12,000 | — | $38.06 | 6/30/2032 | | |
| | 7/3/2023 | 10,321 | — | $41.08 | 7/2/2033 | | |
| | 7/1/2024 | 10,111 | — | $47.11 | 6/30/2034 | | |
| | 7/1/2025 | — | 11,518 | $39.94 | 6/30/2035 | | |
| Allene M. Diaz | 7/1/2021 | 18,000 | — | $40.05 | 6/30/2031 | 5,220[5] | $412,954 |
| | 7/1/2022 | 12,000 | — | $38.06 | 6/30/2032 | | |
| | 7/3/2023 | 10,321 | — | $41.08 | 7/2/2033 | | |
| | 7/1/2024 | 10,111 | — | $47.11 | 6/30/2034 | | |
| | 7/1/2025 | — | 11,518 | $39.94 | 6/30/2035 | | |
| Michael R. Hayden | 9/20/2018 | 32,000 | — | $50.80 | 9/19/2028 | 9,897[6] | $782,952 |
| | 7/1/2019 | 16,000 | — | $64.80 | 6/30/2029 | | |
| | 7/1/2020 | 12,000 | — | $60.20 | 6/30/2030 | | |
| | 7/1/2021 | 12,000 | — | $40.05 | 6/30/2031 | | |
| | 7/1/2022 | 12,000 | — | $38.06 | 6/30/2032 | | |
| | 7/3/2023 | 10,321 | — | $41.08 | 7/2/2033 | | |
| | 7/1/2024 | 10,111 | — | $47.11 | 6/30/2034 | | |
| | 7/1/2025 | — | 11,518 | $39.94 | 6/30/2035 | | |
| Joan E. Herman | 7/1/2019 | 16,000 | — | $64.80 | 6/30/2029 | 5,220 | $412,954 |
| | 7/1/2020 | 12,000 | — | $60.20 | 6/30/2030 | | |
| | 7/1/2022 | 12,000 | — | $38.06 | 6/30/2032 | | |
| | 7/3/2023 | 10,321 | — | $41.08 | 7/2/2033 | | |
| | 7/1/2024 | 10,111 | — | $47.11 | 6/30/2034 | | |
| | 7/1/2025 | — | 11,518 | $39.94 | 6/30/2035 | | |
| Joseph Klein, III | 7/2/2018 | 4,000 | — | $42.88 | 7/1/2028 | 13,976[7] | $1,105,641 |
| | 7/1/2019 | 16,000 | — | $64.80 | 6/30/2029 | | |
| | 7/1/2021 | 12,000 | — | $40.05 | 6/30/2031 | | |
| | 7/1/2022 | 12,000 | — | $38.06 | 6/30/2032 | | |
| | 7/3/2023 | 10,321 | — | $41.08 | 7/2/2033 | | |
| | 7/1/2024 | 10,111 | — | $47.11 | 6/30/2034 | | |
| | 7/1/2025 | — | 11,518 | $39.94 | 6/30/2035 | | |

| | | Option Awards | | | | Stock Awards | |
|---|---|---|---|---|---|---|---|
| Name | Grant Date | Number of Securities Underlying Unexercised Options (#) Exercisable[1] | Number of Securities Underlying Unexercised Options (#) Unexercisable | Option Exercise Price ($) | Option Expiration Date | Number of Shares or Units of Stock that Have Not Vested[2][3] | Market Value of Shares or Units of Stock that Have Not Vested[4] |
| Joseph Loscalzo | 7/2/2018 | 16,000 | — | $42.88 | 7/1/2028 | 5,220[5] | $412,954 |
| | 7/1/2019 | 16,000 | — | $64.80 | 6/30/2029 | | |
| | 7/1/2020 | 12,000 | — | $60.20 | 6/30/2030 | | |
| | 7/1/2021 | 12,000 | — | $40.05 | 6/30/2031 | | |
| | 7/1/2022 | 12,000 | — | $38.06 | 6/30/2032 | | |
| | 7/3/2023 | 10,321 | — | $41.08 | 7/2/2033 | | |
| | 7/1/2024 | 10,111 | — | $47.11 | 6/30/2034 | | |
| | 7/1/2025 | — | 11,518 | $39.94 | 6/30/2035 | | |
| B. Lynne Parshall | 7/2/2018 | 16,000 | — | $42.88 | 7/1/2028 | 5,220 | $412,954 |
| | 7/1/2019 | 16,000 | — | $64.80 | 6/30/2029 | | |
| | 7/1/2020 | 12,000 | — | $60.20 | 6/30/2030 | | |
| | 7/1/2021 | 12,000 | — | $40.05 | 6/30/2031 | | |
| | 7/1/2022 | 12,000 | — | $38.06 | 6/30/2032 | | |
| | 7/3/2023 | 10,321 | — | $41.08 | 7/2/2033 | | |
| | 7/1/2024 | 10,111 | — | $47.11 | 6/30/2034 | | |
| | 7/1/2025 | — | 11,518 | $39.94 | 6/30/2035 | | |
| Joseph H. Wender | 7/3/2017 | 16,000 | — | $52.22 | 7/2/2027 | 5,220 | $412,954 |
| | 7/2/2018 | 16,000 | — | $42.88 | 7/1/2028 | | |
| | 7/1/2019 | 16,000 | — | $64.80 | 6/30/2029 | | |
| | 7/1/2020 | 12,000 | — | $60.20 | 6/30/2030 | | |
| | 7/1/2021 | 12,000 | — | $40.05 | 6/30/2031 | | |
| | 7/1/2022 | 12,000 | — | $38.06 | 6/30/2032 | | |
| | 7/3/2023 | 10,321 | — | $41.08 | 7/2/2033 | | |
| | 7/1/2024 | 10,111 | — | $47.11 | 6/30/2034 | | |
| | 7/1/2025 | — | 11,518 | $39.94 | 6/30/2035 | | |
| Michael J. Yang | 12/14/2023 | 8,238 | 4,118 | $49.82 | 12/14/2033 | 9,080[8] | $718,319 |
| | 7/1/2024 | 10,111 | — | $47.11 | 6/30/2035 | | |
| | 7/1/2025 | — | 11,518 | $39.94 | 6/30/2034 | | |

(1) The options have a term of ten years and were granted out of the Non-Employee Directors' Stock Option Plan. Initial options granted upon commencement of Board service from June 4, 2020 through June 1, 2023 vest 100% on the first anniversary of the date of grant, and those granted after June 1, 2023 vest 33.3% per year for each of the three years following the anniversary of the grant date. Annual options vest 100% on either (a) the annual anniversary of the date of grant, or (b) the next regularly scheduled annual meeting of stockholders, whichever occurs earlier.

(2) The RSUs were granted out of our Non-Employee Directors' Stock Option Plan. Initial RSUs granted upon commencement of Board service from June 4, 2020 through June 1, 2023 vest 100% on the first anniversary of the date of grant, and those granted after June 1, 2023 vest 33.3% per year for each of the three years following the anniversary of the grant date. Annual RSUs vest 100% on either (a) the annual anniversary of the date of grant, or (b) the next regularly scheduled annual meeting of stockholders, whichever occurs earlier.

(3) All of our non-employee directors are subject to our Stock Holding and Ownership Guidelines for RSU Shares, which requires each non-employee director to accumulate and maintain shares of common stock equal to five times such non-employee director's base annual cash retainer for service as a director (but not for service on a Board committee or as a chair or lead independent director), or until the director's termination of service.

(4) Market value of stock awards was determined by multiplying the number of unvested shares by $79.11, which was the closing market price of our common stock on the Nasdaq Global Select Market on December 31, 2025, the last trading day of fiscal year 2025.

(5) Director has elected to defer the release of the shares until the earliest of the fifth anniversary of the vesting date or 30 days following separation from service to the Company.

(6) Director has elected to defer release of 4,677 of these shares until 30 days following separation from service to the Company.

(7) Director has elected to defer release of these shares until 30 days following separation from service to the Company.

(8) Director has elected to defer release of 5,220 of these shares until the earliest of the fifth anniversary of the vesting date or 30 days following separation from service to the Company.

## Option Exercises and Stock Vested - Directors

The following table shows for the fiscal year ended December 31, 2025, certain information regarding option exercises and stock awards vested during the last fiscal year with respect to our non-employee directors:

**Option Exercises and Stock Vested in Fiscal 2025**

| Name | Option Awards | | Stock Awards | |
|---|---|---|---|---|
| | Number of Shares Acquired on Exercise (#) | Value Realized on Exercise ($)[1] | Number of Shares Acquired on Vesting (#) | Value Realized on Vesting ($)[2] |
| Spencer R. Berthelsen | — | — | 4,079 | $171,318 |
| Allene M. Diaz | — | — | 4,079 | $171,318 |
| Michael R. Hayden | — | — | 4,079 | $171,318 |
| Joan E. Herman | 44,000 | $2,525,400 | 4,079 | $171,318 |
| Joseph Klein, III | 40,000 | $2,072,480 | —[3] | —[3] |
| Joseph Loscalzo | 32,000 | $1,226,240 | 4,079 | $171,318 |
| B. Lynne Parshall | — | — | 4,079 | $171,318 |
| Joseph H. Wender | 16,000 | $390,720 | 4,079 | $171,318 |
| Michael J. Yang | — | — | 6,010 | $235,447 |

(1) The value realized on exercise was calculated using the closing price of our common stock on the Nasdaq Global Select Market at exercise less the applicable option exercise price.

(2) The value realized on vesting of RSUs was calculated using the closing price of a share of our common stock on the Nasdaq Global Select Market on the vesting date multiplied by the number of shares vested.

(3) Mr. Klein elected to defer release of these shares until 30 days following separation from service to the Company.

## Certain Relationships and Related Transactions

We have provided some of the information below because you may find it useful when evaluating the proposals contained in this Proxy Statement. When we include a transaction in this section, we do not necessarily mean that the transaction qualifies as a related party transaction under the securities laws.

Mariana Baroldi is an Executive Director in our Corporate Operations department and the wife of Joseph T. Baroldi, EVP and Chief Business Officer. We reviewed Ms. Baroldi's compensation and determined it is within the range that we target for other employees at the same level at Ionis. Ms. Baroldi's total compensation for fiscal year 2025 was $632,709, consisting of salary, bonuses, equity awards, and all other compensation.

One of our directors, Joseph Wender, is a Senior Consultant to Goldman Sachs & Co. ("***Goldman***"), a firm we engage from time to time for investment banking services. We paid Goldman an aggregate amount of approximately $448,000 in 2025, which is substantially less than 5% of Goldman's gross revenues for its 2025 fiscal year.

One of our directors, Joseph Loscalzo, is a Hersey Distinguished Professor of the Theory and Practice of Medicine, the Samuel A. Levine Professor of Medicine at Harvard Medical School and Physician-in-Chief Emeritus at Brigham and Women's Hospital, which we engage from time to time for clinical research support services. We paid Brigham and Women's Hospital an aggregate amount of approximately $3.1 million in 2025, which is substantially less than 5% of Mass General Brigham's gross revenues for its 2025 fiscal year. Mass General Brigham is the integrated health care system of which Brigham and Women's Hospital is a part.

In late 2019, the n-Lorem Foundation, a non-profit organization, was formed to provide advanced, experimental RNA-targeted medicines free of charge for life to patients living with ultra-rare diseases. The n-Lorem Foundation was established with an initial investment by our former Executive Chairman of the Board and Chief Executive Officer, Dr. Stanley Crooke, and his wife, Dr. Rosanne Crooke. Prior to 2022, the Company made cash donations to n-Lorem. Ms. Parshall, one of the Company's non-employee directors, also serves as a director for the n-Lorem Foundation. Additionally, Dr. Geary, who served as our EVP, Chief Development Officer until December 2025, serves as a director for the n-Lorem Foundation. None of our executive officers or directors is compensated for service to the n-Lorem Foundation.

We have entered into indemnity agreements with each of our executive officers and directors and certain non-executive officers which provide, among other things, that we will indemnify such officer or director, under the circumstances and to the extent provided for therein, for expenses, damages, judgments, fines and settlements they may be required to pay in actions or proceedings which they are or may be made a party by reason of their position as a director, officer or other agent of Ionis, and otherwise to the fullest extent permitted under Delaware law and our bylaws. Our bylaws provide that we will indemnify our directors and executive officers to the fullest extent not prohibited by Delaware law or any other applicable law, except that we will generally not be required to indemnify a director or executive officer in connection with any proceeding initiated by such director or executive officer.

### *Policies and Procedures Regarding Related Party Transactions*

A committee of the Board composed entirely of independent directors approves transactions with related persons, as defined under SEC regulations. The Compensation Committee approves all compensation we pay to employees who may qualify as related persons, and the Nominating, Governance and Review Committee approves all other related party transactions, as specified in its charter.

For transactions that do not qualify as related party transactions, but may otherwise present a conflict of interest, our Code of Ethics and Business Conduct requires the Nominating, Governance and Review Committee (for our executive officers and directors) or the Chief Executive Officer or Chief Legal Officer (for non-executive officers and non-directors) to determine whether a conflict of interest exists.

Our written policies and procedures specifically prohibit personal loans to our executive officers and any employee with a title of Vice President or higher.

## Policies and Practices Related to the Grant of Certain Equity Awards Close in Time to the Release of Material Nonpublic information

From time to time, the Company grants stock options to its employees, including the named executive officers. Each year, all current employees receive a stock option grant on the first business day of the year in recognition of their performance in the preceding year. In addition, all new hires receive a stock option grant on their date of hire. Employees who are promoted receive a stock option grant on the date of such employee's promotion.

Non-employee directors receive automatic grants of initial and annual stock option awards at the time of a director's initial appointment or election to the board and on July 1 of each year, respectively, pursuant to the Non-Employee Directors' Stock Option Plan. In addition to regular, predetermined grants of stock options to employees as discussed above, non-employee directors receive option grants on the regular, predetermined grant dates pursuant to the Non-Employee Directors' Stock Option Plan. The grants to employees and non-employee directors occur regardless of whether there is any material nonpublic information ("***MNPI***") about the Company on such dates, and such grant dates are not specifically timed in relation to the Company's disclosure of MNPI. The Company does not otherwise maintain any written policies on the timing of awards of stock options, stock appreciation rights, or similar instruments with option-like features. Furthermore, the Company has not timed the release of MNPI for the purpose of affecting the value of executive compensation.

For calendar year 2025, there were no items to disclose pursuant to Item 402(x)(2) of Regulation S-K.

## CEO Pay Ratio

Under SEC rules, we disclose below the annual total compensation of our median employee, and the ratio of the annual total compensation of our CEO compared to the annual total compensation of our median employee ("***CEO Pay Ratio***"). We identified our median employee for 2024 using the following methodology:

- We included all employees of Ionis who were employed by us on December 31, 2024.

- We identified our median employee from this employee population based on the W-2 income for 2024. We did not annualize any of these amounts.

We used the same median employee identified for 2024 to calculate our CEO Pay Ratio for 2025 because there was no significant change to our employee population or employee compensation arrangements in 2025.

Using this approach, we calculated the annual total compensation of this employee for 2025 in accordance with the requirements of the Summary Compensation Table.

For 2025, the median annual total compensation of our employees (other than our CEO) was $304,680 and the annual total compensation of our CEO, as reported in the Summary Compensation Table included in this Proxy Statement, was $13,350,777. Based on this information, the ratio of the annual total compensation of our CEO to the median of the annual total compensation of all employees was approximately 44 to 1.

The CEO Pay Ratio above represents our reasonable estimate calculated in a manner consistent with SEC rules and applicable guidance. SEC rules and guidance provide significant flexibility in how companies identify the median employee, and each company may use a different methodology and make different assumptions particular to that company. As a result, and as explained by the SEC when it adopted these rules, in considering the pay ratio disclosure, stockholders should keep in mind that the rule was not designed to facilitate comparisons of pay ratios among different companies, even companies within the same industry, but rather to allow stockholders to better understand and assess each particular company's compensation practices and pay ratio disclosures.

Currently, neither the Compensation Committee nor our management uses the CEO Pay Ratio described above to make compensation decisions.

## COMPENSATION COMMITTEE REPORT*

The Compensation Committee has:

- reviewed and discussed the Compensation Discussion and Analysis included in this Proxy Statement with management; and
- based on this review and discussion, the Compensation Committee recommended to the Board of Directors that the Compensation Discussion and Analysis be included in our Proxy Statement relating to the 2026 Annual Meeting of Stockholders.

*The Compensation Committee*
Spencer R. Berthelsen, *Chair*
Joan E. Herman
Joseph H. Wender

* This Section is not "soliciting material," is not deemed filed with the SEC and is not to be incorporated by reference in any filing of Ionis under the Securities Act or the Exchange Act.

## AUDIT COMMITTEE REPORT*

The Audit Committee is made up entirely of independent directors and operates under a written charter that has been adopted by the Board of Directors and is reviewed annually. During fiscal year 2025, the Audit Committee fulfilled its duties and responsibilities as outlined in the charter. At its meetings, the Audit Committee meets as a group with members of the Company's financial management, the independent auditors, and the internal auditors. In addition, the Audit Committee regularly holds separate, private, executive sessions with executive officers, the independent auditors, and the internal audit team to discuss applicable audit matters and provide oversight.

The Audit Committee oversees our financial reporting process on behalf of the Board of Directors. Management has the primary responsibility for the financial statements and the financial reporting process, including the systems of internal controls. In fulfilling its oversight responsibilities, the Audit Committee reviewed the audited consolidated financial statements and the related schedules in our Annual Report on Form 10-K for the fiscal year ended December 31, 2025 with management, including a discussion of the quality, not just the acceptability, of the accounting principles, the reasonableness of significant judgments, and the clarity of disclosures in the financial statements.

The Audit Committee reviewed with our independent registered public accounting firm, which is responsible for expressing an opinion on the conformity of our audited consolidated financial statements with U.S. generally accepted accounting principles, their judgments as to the quality, not just the acceptability, of our accounting principles and any other matters that are required to be discussed with the Audit Committee under Public Company Accounting Oversight Board (United States) ("***PCAOB***") standards. In addition, the Audit Committee has discussed with the independent auditors, the auditors' independence from management and Ionis, including the matters in the written disclosures required by PCAOB Rule 3526. The Audit Committee received from Ernst & Young LLP written disclosure and the letter regarding its independence as required by applicable requirements of the PCAOB regarding Ernst & Young LLP's communications with the Audit Committee concerning independence. The Audit Committee also discussed with our independent auditors the matters required by Auditing Standard No. 1301, *Communications with Audit Committees*, issued by the PCAOB.

The Audit Committee also reviewed and discussed, together with management and the independent auditors, the audited consolidated financial statements for the fiscal year ended December 31, 2025, and the results of management's assessment of the effectiveness of the Company's internal control over financial reporting and the independent auditor's audit of internal control over financial reporting.

The Audit Committee discussed with our independent auditors the overall scope and plans for their audit. The Audit Committee met with the independent auditors, with and without management present, to discuss the results of their examinations, their evaluations of our internal controls, including internal control over financial reporting, and the overall quality of our financial reporting.

In reliance on the reviews and discussions referred to above, the Audit Committee recommended to the Board of Directors, and the Board has approved, that the audited financial statements be included in our Annual Report on Form 10-K for the fiscal year ended December 31, 2025 for filing with the SEC. The Audit Committee and the Board have also approved, subject to stockholder ratification, the selection of Ernst & Young LLP as our independent auditors for 2026.

*The Audit Committee*
Joseph Klein, III, *Chair*
Allene M. Diaz
Joan E. Herman

* This Section is not "soliciting material," is not deemed filed with the SEC and is not to be incorporated by reference in any filing of Ionis under the Securities Act or the Exchange Act.

## HOUSEHOLDING OF PROXY MATERIALS

The SEC has adopted rules that permit companies and intermediaries (e.g., brokers) to satisfy the delivery requirements for Notice Regarding the Availability of Proxy Materials with respect to two or more stockholders sharing the same address by delivering a single Notice Regarding the Availability of Proxy Materials addressed to those stockholders. This process, which is commonly referred to as "householding," potentially means extra convenience for stockholders and cost savings for companies.

This year, a number of brokers with account holders who are our stockholders will be "householding" our proxy materials. A single Notice Regarding the Availability of Proxy Materials will be delivered to multiple stockholders sharing an address unless contrary instructions have been received from the affected stockholders. Once you have been notified by your broker that they will be "householding" communications to your address, "householding" will continue until you are notified otherwise or until you revoke your consent. If, at any time, you no longer wish to participate in "householding" and would prefer to receive a separate Notice Regarding the Availability of Proxy Materials, please notify your broker and direct your written request to Ionis Pharmaceuticals, Inc., Attn: Corporate Secretary, 2855 Gazelle Court, Carlsbad, California 92010, or contact our Stock Plan Administrator at (760) 931-9200, and we will promptly provide you a separate Notice Regarding the Availability of Proxy Materials. Stockholders who currently receive multiple copies of the Proxy Statement or Notice Regarding the Availability of Proxy Materials at their address and would like to request "householding" of their communications should contact their broker.

### Other Matters

The Board of Directors knows of no other matters that will be presented for consideration at the Annual Meeting. If any other issues are properly brought before the meeting, we will ask our proxy holders to vote on the matters using their best judgment.

**For further information about Ionis Pharmaceuticals, Inc., please request a free copy of our Annual Report on Form 10-K for the year ended December 31, 2025 that we filed with the SEC. Please send written requests to:**

**Patrick R. O'Neil, Corporate Secretary**
**Ionis Pharmaceuticals, Inc.**
**2855 Gazelle Court**
**Carlsbad, CA 92010**

**You may also visit our website at www.ionis.com[10] to view our 2025 Annual Report on Form 10-K. The Annual Report on Form 10-K is not incorporated into this Proxy Statement and is not considered soliciting material.**

By Order of the Board of Directors,

*Patrick R. O'Neil*
Corporate Secretary

April 23, 2026

[10] Any information that is included on or linked to our website is not part of this Proxy Statement or any registration statement or report that incorporates this Proxy Statement by reference.

## Special Note Regarding Forward-Looking Statements

This Proxy Statement and the information incorporated herein by reference includes forward-looking statements regarding our business and the therapeutic and commercial potential of our commercial medicines, additional medicines in development, technologies and our expectations regarding development and regulatory milestones. Any statement describing our goals, expectations, financial or other projections, intentions or beliefs, is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties and particularly those inherent in the process of discovering, developing and commercializing medicines that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such medicines. Our forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in Item 1A "Risk Factors" of our Annual Report on Form 10-K for the year ended December 31, 2025, which is on file with the SEC. Although our forward-looking statements reflect the good faith judgment of our management, these statements are based only on facts and factors currently known by us. Except as required by law, we undertake no obligation to update any forward-looking statements for any reason. As a result, you are cautioned not to rely on these forward-looking statements.

In this Proxy Statement, unless the context requires otherwise, "Ionis," "Company," "we," "our," and "us" refers to Ionis Pharmaceuticals, Inc. and its subsidiaries.

"Ionis," the Ionis logo, and other trademarks or service marks of Ionis Pharmaceuticals, Inc. appearing in this Proxy Statement are the property of Ionis Pharmaceuticals, Inc. This Proxy Statement contains additional trade names, trademarks, and service marks of others, which are the property of their respective owners. Solely for convenience, trademarks and trade names referred to in this Proxy Statement may appear without the ® or ™ symbols.

**Appendix A**

**AMENDED AND RESTATED IONIS PHARMACEUTICALS, INC.**
**2011 EQUITY INCENTIVE PLAN**

**ADOPTED BY THE BOARD OF DIRECTORS: MARCH 23, 2011**
**APPROVED BY THE STOCKHOLDERS: JUNE 16, 2011**
**TERMINATION DATE: JUNE 15, 2031**

**AMENDED**: June 25, 2013 (Amendment approved by Board on February 12, 2013 and by the Stockholders on June 25, 2013)

**AMENDED**: June 30, 2015 (Amendment approved by Board on March 20, 2015 and by the Stockholders on June 30, 2015)

**AMENDED**: May 24, 2017 (Amendment approved by Board on March 3, 2017 and by the Stockholders on May 24, 2017)

**AMENDED AND RESTATED**: June 6, 2019 (Amendment and Restatement approved by Board on March 22, 2019 and by the Stockholders on June 6, 2019)

**AMENDED**: June 2, 2021 (Amendment approved by Board on March 26, 2021 and by the Stockholders on June 2, 2021)

**AMENDED**: June 2, 2023 (Amendment approved by Board on March 14, 2023 and by the Stockholders on June 2, 2023)

**AMENDED**: June 6, 2024 (Amendment approved by Board on March 14, 2024 and by the Stockholders on June 6, 2024)

**AMENDED**: June 5, 2025 (Amendment approved by Board on March 6, 2025 and by the Stockholders on June 5, 2025)

Amendment approved by the Board on March 4, 2026

**1. GENERAL.** Effective upon approval by the Company's stockholders, section 3(a) of the Plan is amended and restated in its entirety as set forth in such section of the Plan below.

**(a) Eligible Award Recipients.** The persons eligible to receive Awards are Employees, Directors and Consultants.

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

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

**2. ADMINISTRATION.**

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

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

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

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

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

**(iv)** Subject to the limitations set forth in Sections 5(f) and 8(j), to accelerate the time at which an Award may first be exercised or the time during which an Award or any part thereof will vest in accordance with the Plan, notwithstanding the provisions in the Award stating the time at which it may first be exercised or the time during which it will vest.

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

**(vi)** To amend the Plan in any respect the Board deems necessary or advisable. However, except as provided in Section 9(a) relating to Capitalization Adjustments, to the extent required by applicable law or listing requirements, stockholder approval shall be required for any amendment of the Plan that either (A) materially increases the number of shares of Common Stock available for issuance under the Plan, (B) materially expands the class of individuals eligible to receive Awards under the Plan, (C) materially increases the benefits accruing to Participants under the Plan or materially reduces the price at which shares of Common Stock may be issued or purchased under the Plan, (D) materially extends the term of the Plan, or (E) expands the types of Awards available for issuance under the Plan. Except as provided above, rights under any Award granted before amendment of the Plan shall not be impaired by any amendment of the Plan unless (1) the Company requests the consent of the affected Participant, and (2) such Participant consents in writing.

**(vii)** To submit any amendment to the Plan for stockholder approval, including, but not limited to, amendments to the Plan intended to satisfy the requirements of Rule 16b-3.

**(viii)** To approve forms of Award Agreements for use under the Plan and to amend the terms of any one or more Awards, including, but not limited to, (subject to the limitations on repricing and non-acceleration as provided in Section 2(f), 5(f), and 8(j)) amendments to provide terms more favorable to the Participant than previously provided in the Award Agreement, subject to any specified limits in the Plan that are not subject to Board discretion; *provided however*, that a Participant's rights under any Award shall not be impaired by any such amendment unless (A) the Company requests the consent of the affected Participant, and (B) such Participant consents in writing. Notwithstanding the foregoing, subject to the limitations of applicable law, if any, the Board may amend the terms of any one or more Awards without the affected Participant's consent if necessary to bring the Award into compliance with Section 409A of the Code.

**(ix)** Generally, to exercise such powers and to perform such acts as the Board deems necessary or expedient to promote the best interests of the Company and that are not in conflict with the provisions of the Plan or Awards.

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

**(c) Delegation to Committee.**

**(i) General.** The Board may delegate some or all of the administration of the Plan to a Committee or Committees. If administration of the Plan is delegated to a Committee, the Committee shall have, in connection with the administration of the Plan, the powers theretofore possessed by the Board that have been delegated to the Committee, including the power to delegate to a subcommittee of the Committee any of the administrative powers the Committee is authorized to exercise (and references in this Plan to the Board shall thereafter be to the Committee or subcommittee), subject, however, to such resolutions, not inconsistent with the provisions of the Plan, as may be adopted from time to time by the Board. The Committee may, at any time, abolish the subcommittee and/or revest in the Committee any powers delegated to the subcommittee. The Board may retain the authority to concurrently administer the Plan with the Committee and may, at any time, revest in the Board some or all of the powers previously delegated.

**(ii) Rule 16b-3 Compliance.** The Committee may consist solely of two or more Non-Employee Directors, in accordance with Rule 16b-3 who are independent under applicable Nasdaq rules.

**(d) Delegation to an Executive Officer.** The Board may delegate to one or more Executive Officers of the Company the authority to do one or both of the following: (i) designate Employees who are not Executive Officers of the Company or any of its Subsidiaries to be recipients of Options and Stock Appreciation Rights (and, to the extent permitted by applicable law, other Stock Awards) and the terms thereof, and (ii) determine the number of shares of Common Stock to be subject to such Stock Awards granted to such Employees; *provided,*

*however*, that the Board resolutions regarding such delegation shall specify the total number of shares of Common Stock that may be subject to the Stock Awards granted by such Executive Officer and that such Executive Officer may not grant a Stock Award to himself or herself or to other Executive Officers. Notwithstanding the foregoing, the Board may not delegate authority to an Executive Officer to determine the Fair Market Value pursuant to Section 13(v) below.

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

**(f) Prohibition on Reduction of Exercise Prices, Cancellation and Re-Grant of Stock Awards**. Neither the Board nor any Committee (or subcommittee) shall have the authority to: (i) reduce the exercise price of any outstanding Options or Stock Appreciation Rights under the Plan, or (ii) cancel any outstanding Options or Stock Appreciation Rights that have an exercise price or strike price greater than the current Fair Market Value of the Common Stock in exchange for cash or other Stock Awards under the Plan, unless the stockholders of the Company have approved such an action within 12 months prior to such an event.

**(g) Dividends and Dividend Equivalents.** Dividends or dividend equivalents may be paid or credited, as applicable, with respect to any shares of Common Stock subject to a Stock Award (other than an Option or SAR), as determined by the Board and contained in the applicable Stock Award Agreement; *provided, however*, that (i) no dividends or dividend equivalents may be paid with respect to any such shares before the date such shares have vested under the terms of such Stock Award Agreement, (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 such Stock 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 the Company on the date, if any, such shares are forfeited to or repurchased by the Company due to a failure to meet any vesting conditions under the terms of such Stock Award Agreement.

**3. SHARES SUBJECT TO THE PLAN.**

**(a) Share Reserve.** Subject to Section 9(a) relating to Capitalization Adjustments, the aggregate number of shares of Common Stock that may be issued pursuant to Stock Awards from and after the Effective Date shall not exceed 52,000,000 shares (the "***Share Reserve***"). For clarity, the Share Reserve in this Section 3(a) is a limitation on the number of shares of the Common Stock that may be issued pursuant to the Plan and does not limit the granting of Stock Awards except as provided in Section 7(a). Shares may be issued in connection with a merger or acquisition as permitted by, as applicable, NASDAQ Listing Rule 5635(c) or, if applicable, NYSE Listed Company Manual Section 303A.08, AMEX Company Guide Section 711 or other applicable rule, and such issuance shall not reduce the number of shares available for issuance under the Plan. Furthermore, if a Stock Award or any portion thereof (i) expires or otherwise terminates without all of the shares covered by such Stock Award having been issued or (ii) is settled in cash (*i.e.*, the Participant receives cash rather than stock), such expiration, termination or settlement shall not reduce (or otherwise offset) the number of shares of Common Stock that may be available for issuance under the Plan. Subject to Section 3(b), the number of shares of Common Stock available for issuance under the Plan will be reduced by: (A) one share for each share of Common Stock issued pursuant to an Option or SAR with respect to which the exercise or strike price is at least 100% of the Fair Market Value of the Common Stock subject to the Option or SAR on the date of grant; and (B) one and seven tenths (1.7) shares for each share of Common Stock issued pursuant to a Full Value Award.

**(b) Reversion of Shares to the Share Reserve.** If (A) any shares of Common Stock subject to a Stock Award are not issued because such Stock Award or any portion thereof expires or otherwise terminates without all of the shares covered by such Stock Award having been issued or is settled in cash (*i.e.*, the Participant receives cash rather than stock), or (B) any shares of Common Stock issued pursuant to a Stock Award are forfeited back to the Company because of the failure to meet a contingency or condition required to vest such shares in the Participant, such shares will again become available for issuance under the Plan (collectively, the "***2011 Plan Returning Shares***"). For clarity, any shares underlying a Stock Award that are reacquired by the Company either pursuant to Section 8(f) or as consideration for the exercise of a Stock Award shall *not* again become available for issuance under the Plan. For each 2011 Plan Returning Share subject to a Full Value Award granted prior to June 2, 2021, the number of shares of Common Stock available for issuance under the Plan will increase by one share, and for each 2011 Plan Returning Share subject to a Full Value Award granted on or after June 2, 2021, the number of shares of Common Stock available for issuance under the Plan will increase by one and seven tenths (1.7) shares.

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

**4. ELIGIBILITY.**

**(a) Eligibility for Specific Stock Awards**. Stock Awards may be granted to Employees, Directors and Consultants; *provided, however*, Options and SARs may not be granted to Employees, Directors and Consultants who are providing Continuous Service only to any

"parent" of the Company, as such term is defined in Rule 405 promulgated under the Securities Act, unless the stock underlying such Stock Awards is treated as "service recipient stock" under Section 409A of the Code because the Stock Awards are granted pursuant to a corporate transaction (such as a spin off transaction) or unless such Stock Awards comply with the distribution requirements of Section 409A of the Code.

## 5. PROVISIONS RELATING TO OPTIONS AND STOCK APPRECIATION RIGHTS.

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

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

**(b) Exercise Price.** The exercise price (or strike price) of each Option or SAR shall be not less than 100% of the Fair Market Value of the Common Stock subject to the Option or SAR on the date the Option or SAR is granted. Notwithstanding the foregoing, an Option or SAR may be granted with an exercise price (or strike price) lower than 100% of the Fair Market Value of the Common Stock subject to the Option or SAR if such Option or SAR is granted pursuant to an assumption of or substitution for another option or stock appreciation right pursuant to a Corporate Transaction and in a manner consistent with the provisions of Sections 409A and, if applicable, 424(a) of the Code. Each SAR will be denominated in shares of Common Stock equivalents.

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

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

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

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

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

**(d) Exercise and Payment of a SAR.** To exercise any outstanding Stock Appreciation Right, the Participant must provide written notice of exercise to the Company in compliance with the provisions of the Stock Appreciation Right Agreement evidencing such Stock Appreciation Right. The appreciation distribution payable on the exercise of a Stock Appreciation Right will be not greater than an amount equal to the excess of (A) the aggregate Fair Market Value (on the date of the exercise of the Stock Appreciation Right) of a number of shares of Common Stock equal to the number of Common Stock equivalents in which the Participant is vested under such Stock Appreciation Right, and with respect to which the Participant is exercising the Stock Appreciation Right on such date, over (B) the strike price that will be determined by the Board at the time of grant of the Stock Appreciation Right. The appreciation distribution in respect to a Stock Appreciation Right may be paid in Common Stock, in cash, in any combination of the two or in any other form of consideration, as determined by the Board and contained in the Stock Appreciation Right Agreement evidencing such Stock Appreciation Right.

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

**(i) Restrictions on Transfer.** An Option or SAR shall not be transferable except by will or by the laws of descent and distribution and shall be exercisable during the lifetime of the Participant only by the Participant; *provided, however*, that the Board may, in its sole discretion, permit transfer of the Option or SAR in a manner that is not prohibited by applicable tax and securities laws upon the Participant's request. Except as explicitly provided herein, neither an Option nor a SAR may be transferred for consideration.

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

**(iii) Beneficiary Designation.** Notwithstanding the foregoing, the Participant may, by delivering written notice to the Company, in a form provided by or otherwise satisfactory to the Company and any broker designated by the Company to effect Option exercises, designate a third party who, in the event of the death of the Participant, shall thereafter be entitled to exercise the Option or SAR and receive the Common Stock or other consideration resulting from such exercise. In the absence of such a designation, the executor or administrator of the Participant's estate shall be entitled to exercise the Option or SAR and receive the Common Stock or other consideration resulting from such exercise.

**(f) Vesting Generally.** Subject to Section 8(j), the total number of shares of Common Stock subject to an Option or SAR may vest and therefore become exercisable in periodic installments that may or may not be equal. The Option or SAR may be subject to such other terms and conditions on the time or times when it may or may not be exercised (which may be based on the satisfaction of Performance Goals or other criteria) as the Board may deem appropriate.

**(g) Termination of Continuous Service.** Except as otherwise provided in the applicable Award Agreement or other agreement between the Participant and the Company (validly executed by an authorized Executive Officer of the Company), if a Participant's Continuous Service terminates (other than upon the Participant's death or Disability), the Participant may exercise his or her Option or SAR (to the extent that the Participant was entitled to exercise such Award as of the date of termination of Continuous Service) but only within such period of time ending on the earlier of (i) the date three months following the termination of the Participant's Continuous Service (or such longer or shorter period specified in the applicable Award Agreement), or (ii) the expiration of the term of the Option or SAR as set forth in the Award Agreement. If, after termination of Continuous Service, the Participant does not exercise his or her Option or SAR within the time specified herein or in the Award Agreement (as applicable), the Option or SAR shall terminate.

**(h) Extension of Termination Date.** If the exercise of an Option or SAR following the termination of the Participant's Continuous Service (other than upon the Participant's death or Disability) would be prohibited at any time solely because the issuance of shares of Common Stock would violate the registration requirements under the Securities Act, then the Option or SAR shall terminate on the earlier of (i) the expiration of a total period of three months (that need not be consecutive) after the termination of the Participant's Continuous Service during which the exercise of the Option or SAR would not be in violation of such registration requirements, or (ii) the expiration of the term of the Option or SAR as set forth in the applicable Award Agreement. In addition, unless otherwise provided in a Participant's Award Agreement, if the immediate sale of any Common Stock received upon exercise of an Option or SAR following the termination of the Participant's Continuous Service would violate the Company's insider trading policy, then the Option or SAR shall terminate on the earlier of (i) the expiration of a period equal to the applicable post-termination exercise period after the termination of the Participant's Continuous Service during which the sale of Common Stock received upon exercise of the Option or SAR would not be in violation of the Company's insider trading policy, or (ii) the expiration of the term of the Option or SAR as set forth in the applicable Award Agreement.

**(i) Disability of Participant.** Except as otherwise provided in the applicable Award Agreement or other agreement between the Participant and the Company (validly executed by an authorized Executive Officer of the Company), if a Participant's Continuous Service terminates as a result of the Participant's Disability, the Participant may exercise his or her Option or SAR (to the extent that the Participant was entitled to exercise such Option or SAR as of the date of termination of Continuous Service), but only within such period of time ending on the earlier of (i) the date 12 months following such termination of Continuous Service (or such longer or shorter period specified in the Award Agreement), or (ii) the expiration of the term of the Option or SAR as set forth in the Award Agreement. If, after termination of Continuous Service, the Participant does not exercise his or her Option or SAR within the time specified herein or in the Award Agreement (as applicable), the Option or SAR (as applicable) shall terminate.

**(j) Death of Participant.** Except as otherwise provided in the applicable Award Agreement or other agreement between the Participant and the Company (validly executed by an authorized Executive Officer of the Company), if (i) a Participant's Continuous Service terminates as a result of the Participant's death, or (ii) the Participant dies within the period (if any) specified in the Award Agreement for exercisability after the termination of the Participant's Continuous Service (for a reason other than death), then the Option or SAR may be exercised (to the extent the Participant was entitled to exercise such Option or SAR as of the date of death) by the Participant's estate, by a person who acquired the right to exercise the Option or SAR by bequest or inheritance or by a person designated to exercise the Option or

SAR upon the Participant's death, but only within the period ending on the earlier of (i) the date 18 months following the date of death (or such longer or shorter period specified in the Award Agreement), or (ii) the expiration of the term of such Option or SAR as set forth in the Award Agreement. If, after the Participant's death, the Option or SAR is not exercised within the time specified herein or in the Award Agreement (as applicable), the Option or SAR shall terminate.

**(k) Non-Exempt Employees**. Without limiting the provisions set forth in Section 5(f), no Option or SAR, whether or not vested, granted to an Employee who is a non-exempt employee for purposes of the Fair Labor Standards Act of 1938, as amended, shall be first exercisable for any shares of Common Stock until at least six months following the date of grant of the Option or SAR. Notwithstanding the foregoing, consistent with the provisions of the Worker Economic Opportunity Act, (i) in the event of the Participant's death or Disability, (ii) upon a Corporate Transaction in which such Option or SAR is not assumed, continued, or substituted, (iii) upon a Change in Control, or (iv) upon the Participant's retirement (as such term may be defined in the Participant's Award Agreement or in another applicable agreement or in accordance with the Company's then current employment policies and guidelines), any such vested Options and SARs may be exercised earlier than six months following the date of grant. The foregoing provision is intended to operate so that any income derived by a non-exempt employee in connection with the exercise or vesting of an Option or SAR will be exempt from his or her regular rate of pay.

## 6. PROVISIONS OF STOCK AWARDS OTHER THAN OPTIONS AND SARS.

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

**(i) Consideration.** A Restricted Stock Award may be awarded in consideration for (A) cash, check, bank draft or money order payable to the Company, (B) past services to the Company or an Affiliate, or (C) any other form of legal consideration (including future services) that may be acceptable to the Board, in its sole discretion, and permissible under applicable law.

**(ii) Vesting.** Shares of Common Stock awarded under the Restricted Stock Award Agreement may be subject to forfeiture to the Company in accordance with a vesting schedule to be determined by the Board.

**(iii) Termination of Participant's Continuous Service.** If a Participant's Continuous Service terminates, the Company may receive through a forfeiture condition or a repurchase right any or all of the shares of Common Stock held by the Participant that have not vested as of the date of termination of Continuous Service under the terms of the Restricted Stock Award Agreement.

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

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

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

**(ii) Vesting.** Subject to the limitations set forth in Section 8(j), at the time of the grant of a Restricted Stock Unit Award, the Board may impose such restrictions on or conditions to the vesting of the Restricted Stock Unit Award as it, in its sole discretion, deems appropriate.

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

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

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

**(c) Performance Awards**.

**(i) Performance Stock Awards**. A Performance Stock Award is a Stock Award that may vest or may be exercised contingent upon the attainment during a Performance Period of certain Performance Goals. A Performance Stock Award may, but need not, require the completion of a specified period of Continuous Service. The length of any Performance Period, the Performance Goals to be achieved during the Performance Period, and the measure of whether and to what degree such Performance Goals have been attained shall be conclusively determined by the Committee, in its sole discretion. The Board may provide for or, subject to such terms and conditions as the Board may specify, may permit a Participant to elect for, the payment of any Performance Stock Award to be deferred to a specified date or event. In addition, to the extent permitted by applicable law and the applicable Award Agreement, the Board may determine that cash may be used in payment of Performance Stock Awards.

**(ii) Performance Cash Awards**. A Performance Cash Award is a cash award that may be paid contingent upon the attainment during a Performance Period of certain Performance Goals. A Performance Cash Award may also require the completion of a specified period of Continuous Service. At the time of grant of a Performance Cash Award, the length of any Performance Period, the Performance Goals to be achieved during the Performance Period, and the measure of whether and to what degree such Performance Goals have been attained shall be conclusively determined by the Committee, in its sole discretion. The Board may provide for or, subject to such terms and conditions as the Board may specify, may permit a Participant to elect for, the payment of any Performance Cash Award to be deferred to a specified date or event. The Committee may specify the form of payment of Performance Cash Awards, which may be cash or other property, or may provide for a Participant to have the option for his or her Performance Cash Award, or such portion thereof as the Board may specify, to be paid in whole or in part in cash or other property.

**(iii) Board Discretion**. The Board retains the discretion to reduce or eliminate the compensation or economic benefit due upon attainment of Performance Goals and to define the manner of calculating the Performance Criteria it selects to use for a Performance Period.

## 7. COVENANTS OF THE COMPANY.

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

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

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

## 8. MISCELLANEOUS.

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

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

**(c) Stockholder Rights.** No Participant shall be deemed to be the holder of, or to have any of the rights of a holder with respect to, any shares of Common Stock subject to such Stock Award unless and until (i) such Participant has satisfied all requirements for exercise of the Stock Award pursuant to its terms, if applicable, and (ii) the issuance of the Common Stock subject to such Stock Award has been entered into the books and records of the Company.

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

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

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

**(g) Electronic Delivery**. Any reference herein to a "written" agreement or document shall include any agreement or document delivered electronically or posted on the Company's intranet (or other shared electronic medium controlled by the Company to which the Participant has access).

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

**(i) Compliance with Section 409A.** To the extent that the Board determines that any Award granted hereunder is subject to Section 409A of the Code, the Award Agreement evidencing such Award shall incorporate the terms and conditions necessary to avoid the consequences specified in Section 409A(a)(1) of the Code. To the extent applicable, the Plan and Award Agreements shall be interpreted in accordance with Section 409A of the Code. Notwithstanding anything to the contrary in this Plan (and unless the Award Agreement specifically provides otherwise), if the shares of Common Stock are publicly traded and a Participant holding an Award that constitutes "deferred compensation" under Section 409A of the Code is a "specified employee" for purposes of Section 409A of the Code, no distribution or payment of any amount shall be made upon a "separation from service" before a date that is six months following the date of such Participant's "separation from service" (as defined in Section 409A of the Code without regard to alternative definitions thereunder) or, if earlier, the date of the Participant's death.

**(j) Minimum Vesting.** Except as provided in Section 9, no Stock Award will vest until at least twelve (12) months following the date of grant of such Stock Award (excluding, for this purpose, any (A) Stock Award granted in assumption, substitution or exchange for previously granted awards of a company acquired by the Company or an Affiliate, and (B) Stock Awards to Non-Employee Directors that vest on the earlier of the one year anniversary of the date of grant or the next annual meeting of shareholders (provided that such vesting period may not be less than 50 weeks after grant); *provided, however*, that up to five percent (5%) of the Share Reserve (as defined in Section 3(a)) may be subject to Stock Awards that do not meet such vesting requirements; and *provided further* that for the avoidance of doubt, that the foregoing restriction does not apply to accelerated exercisability or vesting in accordance with Section 9(c) or 9(d) herein.

**(k) Compliance with Insider-Trading Policy**. The Company may limit or restrict a Participant's ability to exercise options or sell stock pursuant to the Company's then-applicable insider-trading policy (or similar policy adopted by the Company).

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

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

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

**(c) Corporate Transaction.** The provisions of this Section 9(c) will apply to Stock Awards in the event of a Corporate Transaction unless otherwise provided in the instrument evidencing the Stock Award or any other written agreement between the Company or any Affiliate and the Participant or in any director compensation policy of the Company or unless otherwise expressly provided by the Board at the time of grant of a Stock Award.

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

**(ii) Stock Awards Held by Current Participants**. In the event of a Corporate Transaction in which the surviving corporation or acquiring corporation (or its parent company) does not assume or continue such outstanding Stock Awards or substitute similar stock awards for such outstanding Stock Awards, then with respect to Stock Awards that have not been assumed, continued or substituted and that are held by Participants whose Continuous Service has not terminated prior to the effective time of the Corporate Transaction (referred to as the "Current Participants"), the vesting of any time-based Stock Awards (and, with respect to Options and Stock Appreciation Rights, the time when such Stock Awards may be exercised) will be accelerated in full (and the vesting of any performance-based Stock Awards shall be deemed satisfied at the greater of actual performance or target level) to a date prior to the effective time of such Corporate Transaction (contingent upon the effectiveness of the Corporate Transaction) as the Board will

determine (or, if the Board does not determine such a date, to the date that is five days prior to the effective time of the Corporate Transaction), and such Stock Awards will terminate if not exercised (if applicable) at or prior to the effective time of the Corporate Transaction, and any reacquisition or repurchase rights held by the Company with respect to such Stock Awards will lapse (contingent upon the effectiveness of the Corporate Transaction).

**(iii) Stock Awards Held by Persons other than Current Participants**. In the event of a Corporate Transaction in which the surviving corporation or acquiring corporation (or its parent company) does not assume or continue such outstanding Stock Awards or substitute similar stock awards for such outstanding Stock Awards, then with respect to Stock Awards that have not been assumed, continued or substituted and that are held by persons other than Current Participants, such Stock Awards will terminate if not exercised (if applicable) prior to the effective time of the Corporate Transaction; provided, however, that any reacquisition or repurchase rights held by the Company with respect to such Stock Awards will not terminate and may continue to be exercised notwithstanding the Corporate Transaction.

**(iv) Payment for Stock Awards in Lieu of Exercise**. Notwithstanding the foregoing, in the event a Stock Award will terminate if not exercised prior to the effective time of a Corporate Transaction, the Board may provide, in its sole discretion, that the holder of such Stock Award may not exercise such Stock Award but instead will receive a payment, in such form as may be determined by the Board, equal in value to the excess, if any, of (A) the value of the property the Participant would have received upon the exercise of the Stock Award immediately prior to the effective time of the Corporate Transaction after application of the vesting acceleration described in (iii) above), over (B) any exercise price payable by such holder in connection with such exercise. For clarity, this payment may be zero if the value of the property is equal to or less than the exercise price. Payments under this provision may be delayed to the same extent that payment of consideration to the holders of the Company's Common Stock in connection with the Corporate Transaction is delayed as a result of escrows, earn outs, holdbacks or any other contingencies.

**(d) Change in Control.** A Stock Award will not be subject to additional acceleration of vesting and exercisability in connection with a Change in Control, except upon certain termination events that are in connection with a Change in Control as provided in the Stock Award Agreement for such Stock Award or as otherwise may be provided in any other written agreement between the Company or any Affiliate and the Participant. In such a case, the Stock Award Agreement or other written agreement may provide that vesting (and, if applicable, exercisability) of time-based awards will be accelerated in full and performance-based Stock Awards will be deemed to have been satisfied at the greater of actual performance or target level.

## 10. TERMINATION OR SUSPENSION OF THE PLAN.

**(a) Plan Term.** The Board may suspend or terminate the Plan at any time. Unless terminated sooner by the Board, the Plan shall automatically terminate on June 15, 2031. No Awards may be granted under the Plan while the Plan is suspended or after it is terminated.

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

## 11. EFFECTIVE DATE OF PLAN.

This Plan shall become effective on the date of the annual meeting of stockholders of the Company held in 2011 provided this Plan is approved by the Company's stockholders at such meeting (the *"Effective Date"*).

## 12. CHOICE OF LAW.

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

## 13. DEFINITIONS. AS USED IN THE PLAN, THE FOLLOWING DEFINITIONS SHALL APPLY TO THE CAPITALIZED TERMS INDICATED BELOW:

**(a)** "***Affiliate***" means, at the time of determination, any "parent" or "subsidiary" of the Company as such terms are defined in Rule 405 promulgated under the Securities Act. The Board shall have the authority to determine the time or times at which "parent" or "subsidiary" status is determined within the foregoing definition, and such determination shall be final, binding and conclusive on all persons.

**(b)** "***Award***" means a Stock Award or a Performance Cash Award.

**(c)** "***Award Agreement***" means a written agreement between the Company and a Participant evidencing the terms and conditions of an Award.

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

**(e)** "***Capitalization Adjustment***" means any change that is made in, or other events that occur with respect to, the Common Stock subject to the Plan or subject to any Stock Award after the Effective Date without the receipt of consideration by the Company through merger, consolidation, reorganization, recapitalization, reincorporation, stock dividend, dividend in property other than cash, large nonrecurring cash dividend, stock split, liquidating dividend, combination of shares, exchange of shares, change in corporate structure or any similar equity restructuring transaction, as that term is used in Statement of Financial Accounting Standards No. 123 (revised). Notwithstanding the foregoing, the conversion of any convertible securities of the Company shall not be treated as a Capitalization Adjustment.

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

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

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

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

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

**(v)** individuals who, on the date the Plan is adopted by the Board, are members of the Board (the "***Incumbent Board***") cease for any reason to constitute at least a majority of the members of the Board; *provided, however*, that if the appointment or election (or nomination for election) of any new Board member was approved or recommended by a majority vote of the members of the Incumbent Board then still in office, such new member shall, for purposes of this Plan, be considered as a member of the Incumbent Board.

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

**(g)** "***Code***" means the Internal Revenue Code of 1986, as amended, including any applicable regulations and guidance thereunder.

**(h)** "***Committee***" means a committee of one or more Directors to whom authority has been delegated by the Board in accordance with Section 2(c).

**(i)** "***Common Stock***" means the common stock of the Company.

**(j)** "***Company***" means Ionis Pharmaceuticals, Inc., a Delaware corporation.

**(k)** "***Consultant***" means any person, including an advisor, who is (i) engaged by the Company or an Affiliate to render consulting or advisory services and is compensated for such services, or (ii) serving as a member of the board of directors of an Affiliate and is compensated for such services. However, service solely as a Director, or payment of a fee for such service, shall not cause a Director to be considered a "Consultant" for purposes of the Plan. Notwithstanding the foregoing, a person is treated as a Consultant under this Plan only if a Form S-8 Registration Statement under the Securities Act is available to register either the offer or the sale of the Company's securities to such person.

**(l)** "***Continuous Service***" means that the Participant's service with the Company or an Affiliate, whether as an Employee, Director or Consultant, is not interrupted or terminated. A change in the capacity in which the Participant renders service to the Company or an Affiliate as an Employee, Consultant or Director or a change in the entity for which the Participant renders such service, provided that there is no interruption or termination of the Participant's service with the Company or an Affiliate, shall not terminate a Participant's Continuous Service; *provided, however,* if the Entity for which a Participant is rendering services ceases to qualify as an Affiliate, as determined by the Board, in its sole discretion, such Participant's Continuous Service shall be considered to have terminated on the date such Entity ceases to qualify as an Affiliate. To the extent permitted by law, the Board or the chief executive officer of the Company, in that party's sole discretion, may determine whether Continuous Service shall be considered interrupted in the case of (i) any leave of absence approved by the Board or Chief Executive Officer, including sick leave, military leave or any other personal leave, or (ii) transfers between the Company, an Affiliate, or their successors. Notwithstanding the foregoing, a leave of absence shall be treated as Continuous Service for purposes of vesting in a Stock Award only to such extent as may be provided in the Company's leave of absence policy, in the written terms of any leave of absence agreement or policy applicable to the Participant, or as otherwise required by law.

**(m)** "***Corporate Transaction***" means the consummation, in a single transaction or in a series of related transactions, of any one or more of the following events:

**(i)** a sale or other disposition of all or substantially all, as determined by the Board, in its sole discretion, of the consolidated assets of the Company and its Subsidiaries;

**(ii)** a sale or other disposition of at least 90% of the outstanding securities of the Company;

**(iii)** a merger, consolidation or similar transaction following which the Company is not the surviving corporation; or

**(iv)** a merger, consolidation or similar transaction following which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger, consolidation or similar transaction are converted or exchanged by virtue of the merger, consolidation or similar transaction into other property, whether in the form of securities, cash or otherwise.

**(n)** "***Director***" means a member of the Board.

**(o)** "***Disability***" means, with respect to a Participant, the inability of such Participant to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than 12 months, as provided in Sections 22(e)(3) and 409A(a)(2)(c)(i) of the Code, and shall be determined by the Board on the basis of such medical evidence as the Board deems warranted under the circumstances.

**(p)** "***Effective Date***" has the meaning set forth in Section 11 of the Plan.

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

**(r)** "***Entity***" means a corporation, partnership, limited liability company or other entity.

**(s)** "***Exchange Act***" means the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder.

**(t)** "***Exchange Act Person***" means any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act), except that "Exchange Act Person" shall not include (i) the Company or any Subsidiary of the Company, (ii) any employee benefit plan of the Company or any Subsidiary of the Company or any trustee or other fiduciary holding securities under an employee benefit plan of the Company or any Subsidiary of the Company, (iii) an underwriter temporarily holding securities pursuant to a registered public offering of such securities, (iv) an Entity Owned, directly or indirectly, by the stockholders of the Company in substantially the same

proportions as their Ownership of stock of the Company; or (v) any natural person, Entity or "group" (within the meaning of Section 13(d) or 14(d) of the Exchange Act) that, as of the Effective Date, is the Owner, directly or indirectly, of securities of the Company representing more than 50% of the combined voting power of the Company's then outstanding securities.

**(u)** "***Executive Officer***" means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act.

**(v)** "***Fair Market Value***" means, as of any date, the value of the Common Stock determined as follows:

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

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

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

**(w)** "***Full Value Award***" means a Stock Award that is not an Option or SAR with respect to which the exercise or strike price is at least 100% of the Fair Market Value of the Common Stock subject to the Option or SAR on the date of grant.

**(x)** "***Non-Employee Director***" means a Director who either (i) is not a current employee or officer of the Company or an Affiliate, does not receive compensation, either directly or indirectly, from the Company or an Affiliate for services rendered as a consultant or in any capacity other than as a Director (except for an amount as to which disclosure would not be required under Item 404(a) of Regulation S-K promulgated pursuant to the Securities Act ("***Regulation S-K***")), does not possess an interest in any other transaction for which disclosure would be required under Item 404(a) of Regulation S-K, and is not engaged in a business relationship for which disclosure would be required pursuant to Item 404(b) of Regulation S-K; or (ii) is otherwise considered a "non-employee director" for purposes of Rule 16b-3.

**(y)** "***Option***" means a stock option granted pursuant to Section 5 of the Plan to purchase shares of Common Stock granted pursuant to the Plan.

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

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

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

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

**(dd)** "***Performance Cash Award***" means an award of cash granted pursuant to the terms and conditions of Section 6(c)(ii).

**(ee)** "***Performance Criteria***" means the one or more criteria that the Board shall select for purposes of establishing the Performance Goals for a Performance Period. The Performance Criteria that shall be used to establish such Performance Goals may be based on any one of, or combination of, the following as determined by the Board: (i) earnings (including earnings per share and net earnings); (ii) earnings before interest, taxes and depreciation; (iii) earnings before interest, taxes, depreciation and amortization; (iv) total stockholder return; (v) return on equity or average stockholder's equity; (vi) return on assets, investment, or capital employed; (vii) stock price; (viii) margin (including gross margin); (ix) income (before or after taxes); (x) operating income; (xi) operating income after taxes; (xii) pre-tax profit; (xiii) operating cash flow; (xiv) sales or revenue targets; (xv) increases in revenue or product revenue; (xvi) expenses and cost reduction goals; (xvii) improvement in or attainment of working capital levels; (xiii) economic value added (or an equivalent metric); (xix) market share; (xx) cash flow; (xxi) cash flow per share; (xxii) share price performance; (xxiii) debt reduction; (xxiv) implementation or completion of projects or processes (including, but not limited to development and regulatory milestones); (xxv) customer satisfaction; (xxvi) stockholders' equity; (xxvii) capital expenditures; (xxiii) debt levels; (xxix) operating profit or net operating profit; (xxx) workforce diversity; (xxxi) growth of net income or operating income; (xxxii) billings; and (xxxiii) any other measure or measures of performance selected by the Board.

**(ff)** "***Performance Goals***" means, for a Performance Period, the one or more goals established by the Board for the Performance Period based upon the Performance Criteria. Performance Goals may be based on a Company-wide basis, with respect to one or more business units, divisions, Affiliates, or business segments, and in either absolute terms or relative to the performance of one or more comparable companies or the performance of one or more relevant indices. Unless specified otherwise by the Board (i) in the Award Agreement at the time the Award is granted or (ii) in such other document setting forth the Performance Goals at the time the Performance Goals are established, the Board shall appropriately make adjustments in the method of calculating the attainment of Performance Goals for a Performance Period as follows: (1) to exclude restructuring and/or other nonrecurring charges; (2) to exclude exchange rate effects, as applicable, for non-U.S. dollar denominated Performance Goals; (3) to exclude the effects of changes to generally accepted accounting principles; (4) to exclude the effects of any statutory adjustments to corporate tax rates; (5) to exclude the effects of items that are "unusual" in nature or occur "infrequently" as determined under generally accepted accounting principles; and (6) to exclude accounting expenses relating to share-based compensation.

**(gg)** "***Performance Period***" means the period of time selected by the Board over which the attainment of one or more Performance Goals will be measured for the purpose of determining a Participant's right to and the payment of a Stock Award or a Performance Cash Award. Performance Periods may be of varying and overlapping duration, at the sole discretion of the Board.

**(hh)** "***Performance Stock Award***" means a Stock Award granted under the terms and conditions of Section 6(c)(i).

**(ii)** "***Plan***" means this Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan.

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

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

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

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

**(nn)** "***Rule 16b-3***" means Rule 16b-3 promulgated under the Exchange Act or any successor to Rule 16b-3, as in effect from time to time.

**(oo)** "***Securities Act***" means the Securities Act of 1933, as amended.

**(pp)** "***Stock Appreciation Right***" or "***SAR***" means a right to receive the appreciation on Common Stock that is granted pursuant to the terms and conditions of Section 5.

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

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

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

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

**Appendix B**

**IONIS PHARMACEUTICALS, INC.**

**2000 EMPLOYEE STOCK PURCHASE PLAN**

Approved by the Board of Directors on January 6, 2000
Approved by Stockholders on June 8, 2000
Amended on September 23, 2003
Amended and Restated by the Board of Directors on February 27, 2009
Amended and Restated by the Stockholders on June 2, 2009
Amended and Restated by the Board of Directors on March 22, 2019

Amendment approved by the Board of Directors on March 4, 2026

## 1. PURPOSE.

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

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

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

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

## 2. ADMINISTRATION.

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

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

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

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

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

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

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

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

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

## 3. SHARES SUBJECT TO THE PLAN.

**(a)** The Company's board of directors and stockholders have previously approved reserving a number of shares for purchase under this plan (the "Reserved Shares"). Effective after the A&R Effective Date, and subject to the provisions of Section 12 relating to the adjustments upon changes in stock, 1,499,699 shares will be available for future sale under the Plan, which number includes 749,699 shares originally reserved as of the A&R Effective Date, plus 750,000 shares added to the Plan in 2026. If any right granted under the Plan shall for any reason terminate without having been exercised, the Common Stock not purchased under such right shall again become available for the Plan.

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

## 4. GRANT OF RIGHTS; OFFERING.

The Board or the Committee may from time to time grant or provide for the grant of rights to purchase Common Stock of the Company under the Plan to eligible employees (an "Offering") on a date or dates (the "Offering Date(s)") selected by the Board or the Committee. Each Offering shall be in such form and shall contain such terms and conditions as the Board or the Committee shall deem appropriate, which shall comply with the requirements of Section 423(b)(5) of the Code that all employees granted rights to purchase stock under the Plan shall have the same rights and privileges. The terms and conditions of an Offering shall be incorporated by reference into the Plan and treated as part of the Plan. The provisions of separate Offerings need not be identical, but each Offering shall include (through incorporation of the provisions of this Plan by reference in the document comprising the Offering or otherwise) the period during which the Offering shall be effective, which period shall not exceed six (6) months beginning with the Offering Date (except the first offering following the A&R Effective Date may be nine (9) months, and the substance of the provisions contained in Sections 5 through 8, inclusive.

## 5. ELIGIBILITY.

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

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

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

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

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

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

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

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

## 6. RIGHTS; PURCHASE PRICE.

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

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

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

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

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

## 7. PARTICIPATION; WITHDRAWAL; TERMINATION.

**(a)** An eligible employee may become a participant in the Plan pursuant to an Offering by delivering a participation agreement to the Company within the time specified in the Offering, in such form as the Company provides. Each such agreement shall authorize payroll deductions of up to the maximum percentage specified by the Board or the Committee of such employee's Earnings during the Offering. "Earnings" is defined as the total compensation paid to an employee including all salary, wages (including amounts thereof elected to be deferred by the employee, that would otherwise have been paid, under any arrangement established by the Company that is intended to comply with Section 125, Section 40l(k), Section 402(h) or Section 403(b) of the Code or that provides non-qualified deferred compensation), which shall include overtime pay, commissions, bonuses and other remuneration paid directly to the employee, but shall exclude profit sharing, the cost of employee benefits paid for by the Company or an Affiliate, education or tuition reimbursements, imputed income arising under any group insurance or benefit program, traveling expenses, business and moving expense reimbursements, income received in connection with stock awards, contributions made by the Company or an Affiliate under any employee benefit plan, and similar items of compensation, as determined by the Board or the Committee. The payroll deductions made for each participant shall be credited to an account for such participant under the Plan and shall be deposited with the general funds of the Company. A participant may reduce (including to zero) or increase such payroll deductions, and an eligible employee may begin such payroll deductions, after the beginning of any Offering only as provided for in the Offering. A participant may make additional payments into his or her account only if specifically provided for in the Offering and only if the participant has not had the maximum permitted amount withheld during the Offering.

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

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

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

## 8. EXERCISE; MINIMUM HOLDING PERIOD.

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

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

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

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

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

## 9. COVENANTS OF THE COMPANY.

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

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

## 10. USE OF PROCEEDS FROM STOCK.

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

## 11. RIGHTS AS A STOCKHOLDER.

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

## 12. ADJUSTMENTS UPON CHANGES IN STOCK.

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

**(b)** In the event of: (1) a dissolution, liquidation or sale of all or substantially all of the assets of the Company, (2) a merger or consolidation in which the Company is not the surviving corporation, or (3) a reverse merger in which the Company is the surviving corporation but the shares of Common Stock outstanding immediately preceding the merger are converted by virtue of the merger into other property, whether in the form of securities, cash or otherwise or (4) any other capital reorganization in which more than fifty percent (50%) of the secunt1es of the Company entitled to vote are sold or otherwise exchanged, then any surviving corporation may assume outstanding rights or substitute similar rights for those under the Plan. In the event that no surviving corporation assumes such outstanding rights or substitutes similar rights therefor, participants' accumulated payroll deductions will be used to purchase Common Stock immediately prior to the transaction described above and the participants' rights under the ongoing Offering terminated immediately following such purchase.

## 13. AMENDMENT OF THE PLAN.

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

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

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

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

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

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

**14. DESIGNATION OF BENEFICIARY.**

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

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

**15. TERMINATION OR SUSPENSION OF THE PLAN.**

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

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

**16. EFFECTIVE DATE OF PLAN.**

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

## Appendix C

Reconciliation of GAAP to Non-GAAP Basis

As illustrated in the table below, non-GAAP operating expenses, non-GAAP loss from operations, and non-GAAP net loss were adjusted from GAAP to exclude compensation expense related to equity awards and the related tax effects. Compensation expense related to equity awards are non-cash. These measures are provided as supplementary information and are not a substitute for financial measures calculated in accordance with GAAP. Ionis reports these non-GAAP results to better enable financial statement users to assess and compare its historical performance and project its future operating results and cash flows. Further, the presentation of Ionis' non-GAAP results is consistent with how Ionis' management internally evaluates the performance of its operations.

**IONIS PHARMACEUTICALS, INC.**
**Reconciliation of GAAP to Non-GAAP Basis:**
**Condensed Consolidated Operating Expenses, Loss From Operations, and Net Loss**
**(In Millions)**

| | Three months ended December 31, | | Year ended December 31, | |
|---|---|---|---|---|
| | 2025 | 2024 | 2025 | 2024 |
| | (unaudited) | | | |
| **As reported research, development and patent expenses according to GAAP** | $280 | $245 | $ 916 | $ 902 |
| Excluding compensation expense related to equity awards | (29) | (25) | (90) | (92) |
| **Non-GAAP research, development and patent expenses** | $251 | $220 | $ 826 | $ 810 |
| **As reported selling, general and administrative expenses according to GAAP** | $130 | $ 88 | $ 394 | $ 267 |
| Excluding compensation expense related to equity awards | (13) | (11) | (42) | (37) |
| **Non-GAAP selling, general and administrative expenses** | $117 | $ 77 | $ 352 | $ 230 |
| **As reported operating expenses according to GAAP** | $418 | $337 | $1,326 | $1,180 |
| Excluding compensation expense related to equity awards | (43) | (36) | (134) | (130) |
| **Non-GAAP operating expenses** | $375 | $301 | $1,192 | $1,050 |
| **As reported loss from operations according to GAAP** | ($215) | ($110) | ($ 382) | ($ 475) |
| Excluding compensation expense related to equity awards | (43) | (36) | (134) | (130) |
| **Non-GAAP loss from operations** | ($172) | ($ 74) | ($ 248) | ($ 345) |
| **As reported net loss according to GAAP** | ($229) | ($104) | ($ 381) | ($ 454) |
| Excluding compensation expense related to equity awards and related tax effects | (43) | (36) | (134) | (130) |
| **Non-GAAP net loss** | ($186) | ($ 68) | ($ 247) | ($ 324) |

*IONIS PHARMACEUTICALS, INC.*
*2855 GAZELLE COURT*
*CARLSBAD, CALIFORNIA 92010*
*ATTN: CORPORATE SECRETARY*

**SCAN TO VIEW MATERIALS & VOTE**

**VOTE BY INTERNET - www.proxyvote.com or scan the QR Barcode above**
Use the Internet to transmit your voting instructions and for electronic delivery of information. Vote by 11:59 P.M. ET on 06/03/2026. Have your proxy card in hand when you access the web site and follow the instructions to obtain your records and to create an electronic voting instruction form.

*During The Meeting* - Go to **www.virtualshareholdermeeting.com/IONS2026**
You may attend the meeting via the Internet and vote during the meeting. Have the information that is printed in the box marked by the arrow available and follow the instructions.

**VOTE BY PHONE - 1-800-690-6903**
Use any touch-tone telephone to transmit your voting instructions. Vote by 11:59 P.M. ET on 06/03/2026. Have your proxy card in hand when you call and then follow the instructions.

**VOTE BY MAIL**
Mark, sign and date your proxy card and return it in the postage-paid envelope we have provided or return it to Vote Processing, c/o Broadridge, 51 Mercedes Way, Edgewood, NY 11717.

TO VOTE, MARK BLOCKS BELOW IN BLUE OR BLACK INK AS FOLLOWS:

KEEP THIS PORTION FOR YOUR RECORDS

**THIS PROXY CARD IS VALID ONLY WHEN SIGNED AND DATED.**

DETACH AND RETURN THIS PORTION ONLY

**The Board of Directors recommends you vote FOR the following:**

1. Election of Directors

| Nominees | For | Against | Abstain |
|---|---|---|---|
| 1a. Spencer R. Berthelsen | ☐ | ☐ | ☐ |
| 1b. Joan E. Herman | ☐ | ☐ | ☐ |

**The Board of Directors recommends you vote FOR proposals 2, 3, 4 and 5.**

| | For | Against | Abstain |
|---|---|---|---|
| 2. To make an advisory vote on executive compensation. | ☐ | ☐ | ☐ |
| 3. To approve an amendment of the Amended and Restated Ionis Pharmaceuticals, Inc. 2011 Equity Incentive Plan to increase the aggregate number of shares of common stock authorized for issuance under such plan by 9,500,000 shares to an aggregate of 52,000,000 shares. | ☐ | ☐ | ☐ |
| 4. To approve an amendment of the Amended and Restated 2000 Employee Stock Purchase Plan to increase the number of shares of common stock authorized for purchase under such plan by 750,000 shares and remove the termination date of the plan. | ☐ | ☐ | ☐ |
| 5. To ratify the Audit Committee's selection of Ernst & Young LLP as independent auditors for the 2026 fiscal year. | ☐ | ☐ | ☐ |

**NOTE**: In their discretion, the proxyholders are authorized to vote upon such other business as may properly come before the meeting or any continuation, adjournment or postponement thereof (with discretionary authority under proposal 1 to vote for a substitute nominee if any nominee is unable to serve or for good cause will not serve).

Please sign exactly as your name(s) appear(s) hereon. When signing as attorney, executor, administrator, or other fiduciary, please give full title as such. Joint owners should each sign personally. All holders must sign. If a corporation or partnership, please sign in full corporate or partnership name by authorized officer.

Signature [PLEASE SIGN WITHIN BOX] Date

Signature (Joint Owners) Date

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**Important Notice Regarding the Availability of Proxy Materials for the Annual Meeting:**
The Notice and Proxy Statement and Annual Report are available at www.proxyvote.com

**IONIS PHARMACEUTICALS, INC.**
**Annual Meeting of Stockholders**
**June 4, 2026 2:00 PM Pacific Time**
**This proxy is solicited by the Board of Directors of**
**Ionis Pharmaceuticals, Inc.**

The undersigned hereby appoints Brett Monia and Elizabeth L. Hougen, and each of them, with power to act without the other and with power of substitution, as proxies and attorneys-in-fact and hereby authorizes them to represent and vote, as provided on the reverse side, all the shares of Ionis Pharmaceuticals, Inc. Common Stock which the undersigned is entitled to vote and, in their discretion, to vote upon such other business as may properly come before the Annual Meeting of Stockholders of the Company to be held June 4, 2026 at www.virtualshareholdermeeting.com/IONS2026 or any continuation, adjournment or postponement thereof with all powers which the undersigned would possess if present at the meeting.

**This proxy, when properly executed, will be voted in the manner directed herein by the undersigned. If no such direction is made but the card is signed, this proxy will be voted FOR the election of the nominees under Proposal 1, FOR Proposal 2, FOR Proposal 3, FOR Proposal 4, and FOR Proposal 5 and in the discretion of the proxies with respect to such other business as may properly come before the meeting or any continuation, adjournment or postponement thereof, including discretionary authority under Proposal 1 to vote for a substitute nominee if any nominee is unable to serve or for good cause will not serve.**

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**Continued and to be signed on reverse side**