IONIS PHARMACEUTICALS, INC.
Stock Holding and Ownership Guidelines for RSU Shares

Purpose

The purpose of these Stock Holding and Ownership Guidelines for RSU Shares (the "***Guidelines***") of Ionis Pharmaceuticals, Inc. (the "***Company***") is to align the interests of the Covered Individuals (as defined below) with the interests of the Company's stockholders and to further promote the Company's commitment to sound corporate governance.

Covered Individuals

The individuals subject to the Guidelines (the "***Covered Individuals***") are the Company's Chief Executive Officer (the "***CEO***") and the other executive officers of the Company who are subject to the reporting requirements of Section 16 of the Securities Exchange Act of 1934, as amended (each, an "***Executive Officer***") and the non-employee members of the Company's Board of Directors (the "***Non-Employee Board Members***").

Guidelines

The Guidelines require a Covered Individual to hold the shares in the Company's common stock issued pursuant to restricted stock unit awards until (i) such Covered Individual has accumulated and maintains a substantial interest in the Company's common stock in an amount set forth below, or (ii) the date of his or her termination of service; *provided, however* that these guidelines will not restrict the sale or surrender of shares of common stock to cover withholding taxes and processing fees applicable to such restricted stock unit awards.

- The Guideline for the CEO is 6x the CEO's base salary.
- The Guideline for each other Executive Officer is 2x the Executive Officer's base salary.
- The Guideline for each Non-Employee Board Member is 5x the director's annual cash retainer for service as a Board Member, without including retainers for service on Board Committees.

The number of shares subject to the Guidelines will be determined (i) on the first business day of each calendar quarter, and (ii) on the first business day following each annual release of performance based restricted stock unit awards to the Company's Executive Officers, using the product of (a) the number of shares credited as held by the individual on the applicable determination date under (i) or (ii) above and (b) the average closing price of the Company's common stock over the 30 trading days immediately preceding the start of such quarter.

The Guidelines are revised whenever the base salary or retainer changes or if the individual's service status changes.

Compliance with the Guidelines

Shares that count toward satisfaction of these Guidelines include:

- shares owned outright by the Covered Individual (whether or not purchased on the open market);
- shares retained after the exercise of a stock option or issuance under another type of equity award granted under the Company's equity incentive plans;
- shares retained after purchase under the Employee Stock Purchase Plan; and
- shares held in trust for the benefit of the Covered Individual and his or her immediate family members.

All trading of the Company's common stock by the Covered Individuals must be made in strict adherence with the Company's insider trading policies and applicable securities laws.

Recourse

If a Covered Individual fails to hold the shares issued pursuant to their restricted stock unit awards unless they have satisfied and continue to maintain the Guidelines, the Board may take any one or more of the following actions:

- Prohibit the Covered Individual from selling any shares acquired through the vesting or the exercise of stock awards (including stock options and restricted stock unit awards), other than the minimum number of shares needed to pay applicable withholding taxes, processing fees and exercise prices, until the Guidelines are met and maintained, including, but not limited to the issuance of a stop transfer order to the Company's transfer agent, or a suspension of the Covered Individual's Rule 10b5-1 Sellers Plans; and
- Pay future compensation, including base salary, incentive compensation, and/or retainers in shares of the Company's common stock up to the value of the shares sold in violation of the Guidelines.

Exceptions

There may be instances where these Guidelines would place a severe hardship on a Covered Individual, although it is expected that these instances will be rare. The Company's Board of Directors will make the final decision as to developing an alternative stock ownership guideline for a Covered Individual that reflects the intention of these Guidelines and his or her personal circumstances.