

Charter of the Audit Committee of the Board of Directors of Ionis Pharmaceuticals, Inc.

The general purpose of the Audit Committee is to assist the Board of Directors in the exercise of its fiduciary responsibility to provide oversight of the Company's financial statements and the financial reporting processes, internal accounting and financial controls, the annual independent audit of the Company's financial statements, and other aspects of the financial management of the Company.

The Audit Committee will be appointed by the Board of Directors and will be comprised of at least three directors, each of whom are independent of management and the Company. Members of the committee will be considered independent as long as they do not accept any consulting, advisory, or other compensatory fee from the Company (except in connection with their service as a director) and are not an affiliated person of the Company or its subsidiaries and meet Nasdaq independence requirements. All committee members must be financially literate, and at least one member must be a "financial expert" as defined by SEC regulations.

The powers and duties of the Audit Committee include the following:

1. The Audit Committee will oversee the annual and quarterly financial reporting processes.
2. The Audit Committee will select the independent auditor for the Company. The selection shall be proposed by management, confirmed by the Audit Committee and submitted to the stockholders on an advisory basis. The Audit Committee will have a clear understanding with management and the independent auditors that the independent auditors are ultimately accountable to the Board and the Audit Committee, as representatives of the Company's stockholders. The Audit Committee shall have the ultimate authority and responsibility to appoint, compensate, retain, and oversee the work of, and where appropriate, replace the independent auditors.
3. The Audit Committee will pre-approve all audit and non-audit services provided by the independent auditors and will not engage the independent auditors to perform the non-audit services prohibited by law or regulation.
4. The Audit Committee will discuss with the auditors their independence from management and the Company and the matters included in the written disclosures required by the Independence Standards Board.
5. The Audit Committee will meet with management, the independent auditors, and the internal auditors (when the Company has such a function) prior to their audits to review and discuss the planned scope and objectives of the audits.
6. The Audit Committee will meet with the independent auditors and the internal auditors, with and without management present, after their audits to review and discuss the results of their examinations and appropriate analyses of the financial statements.
7. The Audit Committee will review management's assertion on its assessment of the effectiveness of internal controls as of the end of the most recent fiscal year and the independent

auditors' report on management's assertion as well as recommendations for improving internal accounting controls.

8. The Audit Committee will review and discuss the reports of the independent auditors, with and without management present, as to the state of the Company's financial reporting systems and procedures, the adequacy of internal accounting and financial controls, the integrity and competency of the financial and accounting staff, and other aspects of the financial management of the Company. The Audit Committee will have the authority to ultimately resolve any disagreements between management and the independent auditors regarding financial reporting.

9. The Audit Committee will review and discuss earnings press releases, as well as financial information and earnings guidance provided to the public.

10. The Audit Committee will review the interim financial statements with management and the independent auditors prior to the filing of the Company's Quarterly Reports on Form 10-Q. The Audit Committee will also discuss the results of the quarterly reviews and any other matters required to be communicated to the Audit Committee by the independent auditors under generally accepted auditing standards. The Chair of the Audit Committee may represent the entire committee for the purposes of this review.

11. The Audit Committee will review with management and the independent auditors the financial statements to be included in the Company's Annual Report on Form 10-K (or the annual report to stockholders if distributed prior to the filing of Form 10-K), including their judgment about the quality, not just acceptability, of accounting principles, the reasonableness of significant judgments, and the clarity of the disclosures in the financial statements. Also, the Audit Committee will discuss the results of the annual audit and any other matters required to be communicated to the Audit Committee by the independent auditors under generally accepted auditing standards.

12. The Audit Committee will review and, if appropriate, approve, transactions that would qualify as a related party transaction under the Securities Act of 1933.

13. The Audit Committee will establish procedures for the receipt, retention, and treatment of complaints received by the Company regarding accounting, internal accounting controls, or auditing matters, and the confidential, anonymous submission by employees of the Company of concerns regarding questionable accounting or auditing matters.

14. The Audit Committee will maintain free and open communication between the Audit Committee, directors who are not members of the Audit Committee, the Company's management, the internal auditors, and the independent auditors.

15. The Audit Committee shall have adequate resources and authority to discharge its responsibilities and duties including the following:

- a. The Audit Committee will have full authority at its own discretion to institute investigations of any matter brought to its attention, with full access to all books, records, facilities and personnel of the Company, and the authority to engage

independent counsel and other advisors it deems necessary to conduct its duties.

- b. The Audit Committee will have the authority to review all aspects of the Company's financial operations on a planned basis.
- c. The Audit Committee will have the authority to review the Company's policies and procedures and the actual implementation of such policies and procedures with respect to officers' expenses and perquisites.

16. The Audit Committee will have appropriate funding, as determined by the Audit Committee, in its capacity as a committee of the Board of Directors, for payment of:

- a. Compensation to any registered public accounting firm engaged for the purpose of preparing or issuing an audit report or performing other audit, review or attest services for the Company;
- b. Compensation to any advisors employed by the Audit Committee under Section 15 of this charter;
- c. Ordinary administrative expenses of the Audit Committee that are necessary or appropriate in carrying out its duties.

17. The Audit Committee will report annually to the Board of Directors, outlining the Audit Committee's activities for the past year and its plans for the coming year. In addition, the Audit Committee shall report to the Board of Directors any significant matters as they occur during the year.