Charter of the Commercial Operations and Compliance Oversight Committee of the Board of Directors of Ionis Pharmaceuticals, Inc.

Purpose

The Board of Directors (the "***Board***") of Ionis Pharmaceuticals, Inc. (the "***Company***") has established a Commercial Operations and Compliance Oversight Committee (the "***Committee***") to assist the Board in overseeing the Company's: (i) commercial strategy and execution, to include sales and marketing metrics, pricing, strategic planning, global expansion, investment plans in support of such strategy and associated risks; and (ii) healthcare compliance, supply chain, regulatory, quality assurance, and data privacy functions.

The purpose of the Committee is to advise management at a strategic level regarding these aspects of the Company functions. The intention is to leverage the Committee members' past experiences, insights into industry trends, and knowledge of best practices to provide appropriate oversight, including informing, challenging, and partnering with Company executives on behalf of the Board to optimize results from key commercial and related functions of the Company. There will be a strong emphasis on collaborative problem-solving with appropriate subject matter experts to achieve strategic outcomes.

Membership

The Committee will have at least three non-employee Board members appointed by the Board after considering the recommendation of the Nominating, Governance and Review Committee who will collaborate with the Chief Executive Officer for guidance. Committee members will serve at the pleasure of the Board and for such term as the Board determines. The Board will designate one Committee member as the Committee's chair (the "***Chair***").

The Committee will hold regular meetings at least four times per year and at such other times as may be called by the Chair and report to the Board on a regular basis. The EVP, Chief Global Product Strategy Officer; SVP, Chief Compliance Officer and Quality Assurance Officer; and EVP, Chief Legal Officer and General Counsel will generally attend all regularly scheduled quarterly meetings of the Committee. The Chief Executive Officer of the Company will be an *ex officio*, non-voting member of the Committee.

The Committee may meet in executive session without management, unless the Committee Chair expressly requests one or more members of management attend.

The Committee may receive information from, and participate in informal meetings and briefings with, management as necessary and appropriate between formal meetings of the Committee. Such briefings and informal meetings may be organized through the Chair or individual Committee members, as appropriate.

The Committee may form and delegate to one or more subcommittees all or any portion of the Committee's authority, duties and responsibilities, and may establish such rules as it determines necessary or appropriate to conduct the Committee's business.

Duties and Responsibilities

A majority of the Committee members will constitute a quorum for the transaction of business.

The Committee will maintain minutes of all meetings. The Committee Chair is responsible for ensuring that important issues discussed at the Committee meetings are reported to the Board in a timely manner. The minutes will reflect that executive sessions have convened and the Committee Chair will use discretion as to the level of detail to be shared or escalated as appropriate.

The Committee will review and assess the adequacy of this charter annually and, if appropriate, recommend changes to the charter to the Board.

The Committee will:

1. Receive reports, as necessary and appropriate, from management on market research, payer dynamics and execution metrics that may affect the Company's strategy.

2. Review management assessment of current and evolving industry trends, and competitive assessments that may impact portfolio goal achievement.

3. Review the Company's commercial business plan, including revenue forecasts as well as the in-line product P&Ls.

4. Receive reports, as necessary and appropriate, from management on the Company's risk management strategy related to its commercial activities.

5. Oversee and review the Company's healthcare compliance program and the status of compliance with laws, regulations, and industry standards related to the development or commercialization of pharmaceutical products.

6. Periodically evaluate the Company's healthcare compliance and quality compliance programs to ensure that they are adequate in scope and reasonably designed, funded and implemented taking into consideration the size and complexity of the Company's operations.

7. Oversee the Company's data privacy program encompassing proper use, processing, and storage of personal information of patients, customers and employees.

8. Receive reports and, as necessary and appropriate, make recommendations to the Board as needed and deemed appropriate.

    a. Examples of in-scope topics may include reviews of pricing, payer positioning and discounting, competitive analysis, portfolio product prioritization and road map, product market research, go-to-market plans, and sales and marketing effectiveness, labeling and regulatory strategy.

    b. Review significant risk management and regulatory reports and findings, as applicable to the mandate of the Committee, including management's remediation plans and progress against such plans.

Resources and Authority; Coordination with Management and Other Board Committees

The Board will provide the Committee with adequate resources and authority to discharge its responsibilities and duties. In particular, the 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. In addition, the Committee will have appropriate funding, as determined by the Committee, in its capacity as a committee of the Board, for payment of independent counsel or other advisors it deems necessary to conduct its duties.

The Committee will coordinate with management and other committees of the Board (which coordination may be through the committee chairs) to help ensure that the committees have received the information necessary to permit them to fulfill their duties and responsibilities with respect to oversight of risk management and risk assessment guidelines and policies.

Nothing in this Charter will expand the duties or liabilities of any Company director or officer beyond any duties and liabilities otherwise imposed by law.