

SPERO THERAPEUTICS, INC.

CORPORATE GOVERNANCE GUIDELINES

The Board of Directors (the “Board”) of Spero Therapeutics, Inc. (the “Company”) has adopted the following Corporate Governance Guidelines (the “Guidelines”) to assist the Board in the exercise of its duties and responsibilities and to serve the best interests of the Company and its stockholders. The Guidelines should be applied in a manner consistent with all applicable laws and stock exchange rules and the Company’s charter and bylaws, each as amended and in effect from time to time. The Guidelines are intended to serve as a flexible framework for the conduct of the Board’s business and not as a set of legally binding obligations. The Board may modify or make exceptions to the Guidelines from time to time in its discretion and consistent with its duties and responsibilities to the Company and its stockholders.

A. Director Responsibilities

1. Oversee Management of the Company. The principal responsibility of the directors is to oversee the management of the Company and, in so doing, serve the best interests of the Company and its stockholders. This responsibility includes:
 - Reviewing and approving fundamental operating, financial and other corporate plans, strategies and objectives;
 - Evaluating the performance of the Company and its senior executives and taking appropriate action, including removal, when warranted;
 - Evaluating the Company’s compensation programs on a regular basis and determining the compensation of its senior executives;
 - Reviewing and approving senior executive succession plans;
 - Evaluating whether corporate resources are used only for appropriate business purposes;
 - Establishing a corporate environment that promotes timely and effective disclosure (including robust and appropriate controls, procedures and incentives), fiscal accountability, high ethical standards and compliance with all applicable laws and regulations;
 - Reviewing the Company’s policies and practices with respect to risk assessment and risk management;
 - Reviewing and approving material transactions and commitments not entered into in the ordinary course of business;

- Developing a corporate governance structure that allows and encourages the Board to fulfill its responsibilities;
 - Providing advice and assistance to the Company's senior executives; and
 - Evaluating the overall effectiveness of the Board and its committees.
2. Exercise Business Judgment. In discharging their fiduciary duties, directors are expected to exercise their business judgment to act in what they reasonably believe to be the best interests of the Company and its stockholders.
3. Understand the Company and its Business. Directors have an obligation to become and remain informed about the Company and its business, including the following:
- The principal operational and financial objectives, strategies and plans of the Company;
 - The results of operations and financial condition of the Company and of significant subsidiaries and business segments, if any;
 - The relative standing of the business segments within the Company and as compared to competitors;
 - The factors that determine the Company's success; and
 - The risks and problems that affect the Company's business and prospects.
4. Establish Effective Systems. Directors are responsible for determining that effective systems are in place for the periodic and timely reporting to the Board on important matters concerning the Company, including the following:
- Current business and financial performance, the degree of achievement of approved objectives and the need to address forward-planning issues;
 - Future business prospects and forecasts, including actions, facilities, personnel and financial resources required to achieve forecasted results;
 - Financial statements, with appropriate segment or divisional breakdowns;
 - Compliance programs to assure the Company's compliance with law and corporate policies;
 - Material litigation and governmental and regulatory matters; and
 - Monitoring and, where appropriate, responding to communications from stockholders.

Directors should also periodically review the integrity of the Company's internal control and management information systems.

5. Board, Stockholder and Committee Meetings. Directors are responsible for attending Board meetings, meetings of committees on which they serve and the annual meeting of stockholders, and devoting the time needed, and meeting as frequently as necessary, to discharge their responsibilities properly.
6. Reliance on Management and Advisors; Indemnification. The directors are entitled to rely on the Company's senior executives and its outside advisors, auditors and legal counsel, except to the extent that any such person's integrity, honesty or competence is in doubt. The directors are also entitled to Company-provided indemnification, statutory exculpation and directors' and officers' liability insurance.

B. Director Qualification Standards

1. Independence. Except as may otherwise be permitted by the rules of the NASDAQ Stock Market ("NASDAQ"), a majority of the members of the Board shall be independent directors. To be considered independent: (1) a director must be independent as determined under NASDAQ Rule 5605(a)(2) and (2) in the Board's judgment, the director must not have a relationship with the Company that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director.
2. Size of the Board. The Board will periodically consider whether the size of the Board is appropriate given the Company's present circumstances and any changes in the Company's business.
3. Other Directorships. The Board does not believe that its members should be prohibited from serving on boards of other organizations, and the Board has not adopted any guidelines limiting such activities. However, the Nominating and Corporate Governance Committee shall take into account the nature of and time involved in a director's service on other boards in evaluating the suitability of individual directors and making its recommendations to the Board. Service on boards and/or committees of other organizations shall comply with the Company's conflict of interest policies.
4. Tenure. The Board does not believe it should establish term limits. Term limits could result in the loss of directors who have been able to develop, over a period of time, increasing insight into the Company and its operations and an institutional memory that benefits the entire membership of the Board as well as management. As an alternative to term limits, the Nominating and Corporate Governance Committee shall review each director's continuation on the Board at least once every three years. This will allow each director the opportunity to conveniently confirm his or her desire to continue as a member of the Board and

allow the Company to conveniently replace directors who are no longer interested or effective.

5. Board Leadership Structure. The Nominating and Corporate Governance Committee shall periodically assess the Board's leadership structure, including whether the offices of Chairman of the Board and Chief Executive Officer should be separate, whether the Company should have an independent "Lead Director" in the event that the Chairman of the Board is not an independent director, and why the Board's leadership structure is appropriate given the specific characteristics or circumstances of the Company. In the event that the Chairman of the Board is not an independent director, the Nominating and Corporate Governance Committee may designate an independent director to serve as "Lead Director," who shall be approved by a majority of the independent directors.

The Lead Director, if one is appointed, shall:

- Chair any meeting of the independent directors in executive session;
 - Meet with any director who is not adequately performing his or her duties as a member of the Board or any committee;
 - Facilitate communications between other members of the Board and the Chairman of the Board and/or the Chief Executive Officer; however, each director is free to communicate directly with the Chairman of the Board and with the Chief Executive Officer;
 - Monitor, with the assistance of the Company's legal advisors, communications from stockholders and other interested parties and provide copies or summaries to the other directors as he or she considers appropriate;
 - Work with the Chairman of the Board in the preparation of the agenda for each Board meeting and in determining the need for special meetings of the Board; and
 - Otherwise consult with the Chairman of the Board and/or the Chief Executive Officer on matters relating to corporate governance and Board performance.
6. Selection of New Director Candidates. Except where the Company is legally required by contract, bylaw or otherwise to provide third parties with the right to nominate directors, the Nominating and Corporate Governance Committee shall be responsible for (i) identifying individuals qualified to become Board members, consistent with criteria approved by the Board, and (ii) recommending to the Board the persons to be nominated for election as directors at any meeting of stockholders and the persons to be elected by the Board to fill any vacancies on the Board. Director nominees shall be considered for recommendation by the

Nominating and Corporate Governance Committee in accordance with these Guidelines, the policies and principles in its charter and the criteria set forth in Attachment A to these Guidelines. It is expected that the Nominating and Corporate Governance Committee will have direct input from the Chairman of the Board if not then serving on the Nominating and Corporate Governance Committee, the Chief Executive Officer and, if one is appointed, the Lead Director if not then serving on the Nominating and Corporate Governance Committee. The Nominating and Corporate Governance Committee shall consider candidates proposed by stockholders.

7. Extending the Invitation to a New Director Candidate to Join the Board. The invitation to join the Board should be extended either by the Chairman of the Board, on behalf of the Board, or the Chairman of the Nominating and Corporate Governance Committee, on behalf of such Committee. Unauthorized approaches to prospective directors can be premature, embarrassing and harmful.
8. Former Chief Executive Officer's Board Membership. The Board believes that the continuation of a former Chief Executive Officer of the Company on the Board is a matter to be decided in each individual instance by the Board, upon recommendation of the Nominating and Corporate Governance Committee. Accordingly, when the Chief Executive Officer ceases to serve in that position, he or she will be expected to resign from the Board if so requested by the Board, upon recommendation of the Nominating and Corporate Governance Committee.

C. Board Meetings

1. Selection of Agenda Items. The Chairman of the Board shall approve the agenda for each Board meeting. Each Board member is free to suggest the inclusion of agenda items and is free to raise at any Board meeting subjects that are not on the agenda for that meeting.
2. Frequency and Length of Meetings. The Chairman of the Board, in consultation with the members of the Board, shall determine the frequency and length of the Board meetings. Special meetings may be called from time to time as determined by the needs of the business.
3. Advance Distribution of Materials. Information and data that are important to the Board's understanding of the business to be conducted at a Board or committee meeting should generally be distributed in writing to the directors before the meeting, and directors should review these materials in advance of the meeting. The Board acknowledges that certain items to be discussed at a Board or committee meeting may be of an extremely confidential or time-sensitive nature and that the distribution of materials on these matters prior to meetings may not be appropriate or practicable. Presentations made at Board meetings should do more than summarize previously distributed Board meeting materials.

4. Executive Sessions. The independent directors shall meet in executive session at least twice a year to discuss, among other matters, the performance of the Chief Executive Officer. The independent directors will meet in executive session at other times at the request of any independent director. Absent unusual circumstances, these sessions shall be held in conjunction with regular Board meetings. The director who presides at these meetings shall be the Lead Director if there is one, and if not, shall be chosen by the independent directors, and his or her name shall be disclosed in the Company's proxy statement for its annual meeting of stockholders.
5. Attendance of Non-Directors at Board Meetings. The Board encourages the senior executives of the Company to, from time to time, bring Company personnel into Board meetings who (i) can provide additional insight into the items being discussed because of personal involvement in these areas or (ii) should be given exposure to the Board.

D. Board Committees

1. Key Committees. The Board shall have at all times an Audit Committee, a Compensation Committee and a Nominating and Corporate Governance Committee. Each such committee shall have a charter that has been approved by the Board. The Board may, from time to time, establish or maintain additional committees as necessary or appropriate.
2. Assignment and Rotation of Committee Members. The Nominating and Corporate Governance Committee shall be responsible for recommending to the Board the directors to be appointed to each committee of the Board. Except as otherwise permitted by the applicable rules of the Securities and Exchange Commission and NASDAQ, each member of the Audit Committee, the Compensation Committee and the Nominating and Corporate Governance Committee shall be an "independent director" as defined by such rules.
3. Committee Charters. In accordance with applicable NASDAQ rules, the charters of the Audit Committee, the Compensation Committee and the Nominating and Corporate Governance Committee shall set forth the purposes, goals and responsibilities of the committees as well as qualifications for committee membership, procedures for committee member appointment and removal, committee structure and operations and committee reporting to the Board. The Board shall, from time to time as it deems appropriate, review and reassess the adequacy of each charter and make appropriate changes.
4. Selection of Agenda Items. The chairman of each committee, in consultation with the committee members, shall develop the committee's agenda. At the beginning of the year each committee shall establish a schedule of subjects to be discussed during the year (to the extent practicable). The schedule for each committee meeting shall be furnished to all directors.

5. Frequency and Length of Committee Meetings. The chairman of each committee, in consultation with the committee members, shall determine the frequency and length of the committee meetings consistent with any requirements set forth in the committee's charter. Special meetings may be called from time to time as determined by the needs of the business and the responsibilities of the committees.

E. Director Access to Management and Independent Advisors

1. Access to Officers and Employees. Directors have full and free access to officers and employees of the Company. Any meetings or contacts that a director wishes to initiate may be arranged through the Chief Executive Officer or the Secretary or directly by the director. The directors shall use their judgment to ensure that any such contact is not disruptive to the business operations of the Company and shall, to the extent appropriate, copy the Chief Executive Officer on any written communications between a director and an officer or employee of the Company.
2. Access to Independent Advisors. The Board and each committee have the power to hire and consult with independent legal, financial or other advisors for the benefit of the Board or such committee, as they may deem necessary, without consulting or obtaining the approval of any officer of the Company in advance. In the discretion of the Board or applicable committee, such independent advisors may (but need not) be the regular advisors to the Company. The Board or any such committee is empowered, without further action by the Company, to cause the Company to pay the compensation of such advisors as established by the Board or any such committee.

F. Director Compensation

1. Role of Board and Compensation Committee. The form and amount of director compensation shall be determined by the Board in accordance with the policies and principles set forth below. The Compensation Committee shall periodically review and make recommendations to the Board with respect to the compensation of the Company's directors. The Compensation Committee shall consider that questions as to directors' independence may be raised if director compensation and perquisites exceed customary levels, if the Company makes substantial charitable contributions to organizations with which a director is affiliated or if the Company enters into consulting contracts or business arrangements with (or provides other indirect forms of compensation to) a director or an organization with which the director is affiliated.
2. Form of Compensation. The Board believes that directors should be incentivized to focus on long-term stockholder value. Including equity as part of director compensation helps align the interest of directors with those of the Company's stockholders.

3. Amount of Consideration. The Company seeks to attract exceptional talent to its Board. Therefore, the Company's policy is to compensate directors competitively relative to comparable companies. The Company's management shall, from time to time, present a comparison report to the Board, comparing the Company's director compensation with that of comparable companies. The Board believes that it is appropriate for the Chairman of the Board and the chairmen and members of the committees to receive additional compensation for their services in those positions.
4. Employee Directors. Directors who are also employees of the Company shall receive no additional compensation for Board or committee service.

G. Director Orientation and Continuing Education

1. Director Orientation. The Board and the Company's management shall conduct a mandatory orientation program for new directors. The orientation program shall include presentations by management to familiarize new directors with the Company's strategic plans, its significant financial, accounting and risk management issues, its compliance programs, its code of business conduct and ethics, its principal officers, its auditors and its advisors. In addition, the orientation program shall include a review of the Company's expectations of its directors in terms of time and effort, a review of the directors' fiduciary duties and visits to Company headquarters and, to the extent practical, certain of the Company's significant facilities. All other directors are also invited to attend the orientation program.
2. Continuing Education. Each director is expected to be involved in continuing director education on an ongoing basis to enable him or her to better perform his or her duties and to recognize and deal appropriately with issues that arise. The Company shall pay all reasonable expenses related to continuing director education.

H. Management Evaluation and Succession

1. Selection of Chief Executive Officer. The Board selects the Company's Chief Executive Officer in the manner that it determines to be in the best interests of the Company's stockholders.
2. Evaluation of Senior Executives. The Compensation Committee shall be responsible for overseeing the evaluation of the Company's senior executives, including the Company's Chief Executive Officer. In conjunction with the Audit Committee, in the case of the evaluation of the senior financial executives, the Compensation Committee shall determine the nature and frequency of the evaluation and the persons subject to the evaluation, supervise the conduct of the evaluation and prepare assessments of the performance of the Company's senior executives, to be discussed with the Board periodically. The Board shall review

the assessments to ensure that the senior executives are providing the best leadership for the Company over both the long- and short-term.

3. Succession of Senior Executives. The Nominating and Corporate Governance Committee shall be responsible for overseeing an annual evaluation of succession planning for senior executives, including the Company's Chief Executive Officer.

I. Annual Performance Evaluation of the Board

The Nominating and Corporate Governance Committee shall oversee an annual self-evaluation of the Board to determine whether it and its committees are functioning effectively. The Nominating and Corporate Governance Committee shall determine the nature of the evaluation, supervise the conduct of the evaluation and prepare an assessment of the Board's performance, to be discussed with the Board. The purpose of this process is to improve the effectiveness of the Board and its committees and not to target individual Board members.

J. Board Interaction with Stockholders, Institutional Investors, the Press, Customers, Etc.

The Board believes that the Chief Executive Officer and his or her designees speak for the Company. Individual Board members may, from time to time, meet or otherwise communicate with various constituencies that are involved with the Company. It is, however, expected that the Chairman of the Board would do so with the knowledge of the Company's senior executives and that the other Board members would do so with the knowledge of and, absent unusual circumstances or as contemplated by the committee charters, only at the request of the Company's senior executives.

The Board will give appropriate attention to written communications that are submitted by stockholders and other interested parties, and will respond if and as appropriate. Absent unusual circumstances or as contemplated by the committee charters, the Chairman of the Board (if an independent director), or the Lead Director (if one is appointed), or otherwise the Chairman of the Nominating and Corporate Governance Committee shall, subject to advice and assistance from the Company's legal advisors, (1) be primarily responsible for monitoring communications from shareholders and other interested parties, and (2) provide copies or summaries of such communications to the other directors as he or she considers appropriate.

K. Periodic Review of the Corporate Governance Guidelines

The Nominating and Corporate Governance Committee shall, from time to time as it deems appropriate, review and reassess the adequacy of these Guidelines and recommend any proposed changes to the Board for approval.

Attachment A

SPERO THERAPEUTICS, INC.

CRITERIA FOR NOMINATION AS A DIRECTOR

General Criteria

1. Nominees should have a reputation for integrity, honesty and adherence to high ethical standards.
2. Nominees should have demonstrated business acumen, experience and ability to exercise sound judgments in matters that relate to the current and long-term objectives of the Company and should be willing and able to contribute positively to the decision-making process of the Company.
3. Nominees should have a commitment to understand the Company and its industry and to regularly attend and participate in meetings of the Board and its committees.
4. Nominees should have the interest and ability to understand the sometimes conflicting interests of the various constituencies of the Company, which include stockholders, employees, customers, governmental units, creditors and the general public, and to act in the interests of all stockholders.
5. Nominees should not have, nor appear to have, a conflict of interest that would impair the nominee's ability to represent the interests of all the Company's stockholders and to fulfill the responsibilities of a director.
6. Nominees shall not be discriminated against on the basis of race, religion, national origin, sex, sexual orientation, disability or any other basis proscribed by law. The value of diversity on the Board should be considered.

Application of Criteria to Existing Directors

The renomination of existing directors should not be viewed as automatic, but should be based on continuing qualification under the criteria set forth above. In addition, the Nominating and Corporate Governance Committee shall consider the existing directors' performance on the Board and any committee, which shall include consideration of the extent to which the directors undertook continuing director education.

Criteria for Composition of the Board

The backgrounds and qualifications of the directors considered as a group should provide a significant breadth of experience, knowledge and abilities that shall assist the Board in fulfilling its responsibilities.