

UPSTREAM BIO, INC.

CORPORATE GOVERNANCE GUIDELINES

The Board of Directors (the “**Board**”) of Upstream Bio, Inc. (the “**Company**”) has adopted these corporate governance guidelines to assist and guide the Board in the exercise of its responsibilities. These guidelines should be interpreted in accordance with any requirements imposed by applicable federal or state law or regulation, the Nasdaq Stock Market LLC (“**Nasdaq**”) and the certificate of incorporation and bylaws of the Company. The Board may review and amend these guidelines from time to time.

I. DIRECTOR CRITERIA AND SELECTION

- A. **Responsibility and Process For Identifying and Selecting Directors:** The Board will be responsible for nominating members for election to the Board by the Company’s stockholders at the annual meeting of stockholders. The Board is also responsible for filling vacancies on the Board that may occur between annual meetings of stockholders. The Nominating and Corporate Governance Committee of the Board (the “**Nominating Committee**”) is responsible for identifying, reviewing, evaluating and recommending to the Board candidates to serve as directors of the Company in accordance with the Nominating Committee’s charter and the Company’s bylaws and consistent with the criteria listed below.
- B. **Director Criteria:** With advice and input from the Nominating Committee, the Board will determine the appropriate characteristics, skills and experience for the Board as a whole and for its individual members. In evaluating director nominee recommendations from the Nominating Committee or otherwise, the Board will consider the minimum general criteria set forth below and may add any specific additional criteria with respect to specific searches. There is no requirement that an acceptable candidate fully satisfy all of the criteria and the assessment of the degree to which a candidate does so is in the Board’s sole judgment and discretion. The Board believes that director candidates should have certain minimum qualifications, including being able to read and understand basic financial statements and having the highest personal integrity and ethics.

In considering candidates recommended by the Nominating Committee and otherwise, the Board intends to consider such factors as: (i) the candidate possessing relevant experience and expertise to enable him or her to be able to offer germane advice and guidance to management; (ii) proven achievement and competence in his or her field; (iii) the ability to exercise sound business judgment; (iv) the candidate having an understanding of the fiduciary responsibilities required of a director; (v) commitment to devoting time and energy to the affairs of the Company; (vi) the candidate having a diverse personal background, perspective and experience; and (vii) commitment to vigorously represent the long-term interests of the Company’s stockholders.

In addition, the Board reviews candidates for director nomination in the context of the current composition of the Board, any specific needs of committees of the Board, the operating requirements of the Company, the long-term interests of the Company’s

stockholders, the matters discussed in Paragraphs C through G below and applicable laws, regulations, exchange listing requirements and contractual obligations of the Company.

In the case of incumbent directors whose terms of office are set to expire, the Board reviews such directors' overall service to the Company 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. In the case of new director candidates, the Board also determines whether the nominee must be independent for purposes of satisfying applicable listing requirements.

- C. **Independence**: At least a majority of the members of the Board shall meet the independence requirements set forth in the Nasdaq Stock Market Rules.

The Board will periodically evaluate all relationships between the Company and each independent director for the purposes of determining whether a material relationship exists that might represent a potential conflict of interest or otherwise interfere with the director's ability to satisfy his or her responsibilities as an independent director.

- D. **Limit on Number of Other Boards**: Performing the duties and fulfilling the responsibilities of a Director requires a significant commitment of time and attention. The Board does not believe, however, that explicit limits on the number of other boards of directors on which a Director sits, or on other activities a Director pursues, are appropriate. The Board, however, recognizes that excessive time commitments can interfere with a Director's ability to perform and fulfill his or her duties and responsibilities effectively. The Nominating Committee will consider whether the performance of a Director has been or is likely to be adversely affected by excessive time commitments, including service on other boards of directors. Directors must notify the Chair of the Nominating Committee prior to accepting a seat on the board of directors of another business corporation so that the potential for conflicts or other factors compromising the Director's ability to perform or fulfill his duties and responsibilities may be fully assessed by the Board's leadership.

- E. **Term and Age Limits**: The Board does not believe that limits on the number of consecutive terms a Director may serve or on the Directors' ages are appropriate in light of the substantial benefits of a sustained focus on the Company's business, strategy and industry over a significant period of time. Each Director's performance will be assessed by the Nominating Committee in light of relevant factors.

- F. **Succession**: The Nominating Committee shall be responsible for developing succession plans for the Board.

- G. **Consideration of Diversity**: The Board believes that diversity (including diversity of professional experience, social and economic background, gender, race, ethnicity, age, sexual orientation and gender identity) in its membership is important to serving the long-term interests of stockholders.

- H. **Stockholder Recommendations and Nominations**: The Nominating Committee shall consider candidate recommendations from stockholders and evaluate such candidates in accordance with the provisions discussed herein. A stockholder desiring to nominate a person directly for election to the Board at an annual meeting of the stockholders must

meet the deadlines and other requirements in the Company's bylaws and all applicable laws and regulatory requirements.

II. DIRECTOR RESPONSIBILITIES AND COMPENSATION

- A. **Role of Directors:** The business and affairs of the Company are managed by or under the direction of the Board, acting on behalf of the stockholders. The Board has delegated to the officers of the Company the authority and responsibility for managing the Company's everyday affairs. The Board has an oversight role and is not expected to perform or duplicate the tasks of the Chief Executive Officer (the "CEO") or senior management.
- B. **Attendance at Meetings:** Each member of the Board is expected to make reasonable efforts to attend meetings of the Board, whether regular or special. If a Director does not attend at least 75% of the Board's regular or special meetings (together with the meetings of committees on which the Director serves), the Company will be required to disclose that fact in its annual proxy statement. In addition, attendance and participation at meetings is an important component of the Directors' duties and, as such, attendance rates will be taken into account by the Nominating Committee in assessing Directors for renomination as Directors.
- C. **Time Commitment; Advance Distribution and Review of Materials:** Directors are expected to spend the time needed and meet as frequently as the Board deems necessary or appropriate to discharge their responsibilities. Senior management is responsible for distributing in advance to Directors information important to the Board's understanding of the business to be conducted at a Board or Committee meeting. Directors should review these materials before the meeting.
- D. **Director Compensation:** The Compensation Committee will periodically review and recommend to the Board the form and amount of non-employee director compensation, except as otherwise determined by the Board. The Company's executive officers shall not receive additional compensation for their service as Directors.

III. BOARD STRUCTURE AND PROCEDURES

- A. **Size of Board:** The Board reserves the right at any time to increase or decrease its size, subject to any provisions in the Company's certificate of incorporation and bylaws, depending on the Board's assessment of its needs and other factors. The size of the Board may vary based upon the size of the business and the availability of qualified candidates. Board size should facilitate active interaction and participation by all Board members. The Board will review from time to time the appropriateness of its size.
- B. **Board Leadership:** The Board shall fill the positions of Chair and CEO based upon its view of what is in the best interests of the Company. The Chair and CEO may, but need not be, the same person.
- C. **Committees:** The Board intends at all times to have an Audit Committee, a Compensation Committee and a Nominating Committee. Each of these committees will have a written charter that sets forth its responsibilities and qualifications for committee membership. The Board may from time to time establish additional committees as it

deems appropriate. Membership on the Audit, Compensation and Nominating Committees is limited to independent directors meeting the independence requirements of the Nasdaq Stock Market Rules, the Sarbanes-Oxley Act of 2002 and any other applicable rules or regulations of the Securities and Exchange Commission and the Internal Revenue Service. The Board retains discretion to form new committees or disband current committees depending upon the circumstances.

- D. **Executive Sessions**: The non-management Directors will meet at regularly scheduled executive sessions without management participation, and at least once each year the non-management Directors alone will meet in executive session. If the Chair is a non-management director and an independent director, then the Chair will preside at these meetings. If the Chair is not an independent director, then the Director who presides at these meetings will be chosen by those present at a meeting. In either case, the Director who presides at these meetings, and his or her name, or the process by which he or she is selected, will be disclosed, if required by SEC rules, in the annual proxy statement or, if the Company does not file an annual proxy statement, in the Company's annual report on Form 10-K filed with the SEC. To permit interested parties to make their concerns known to the non-management Directors, the Company will also disclose a method by which they can communicate directly and confidentially with the presiding Director or with the non-management Directors as a group.
- E. **Director Access to Management and Independent Advisers**: In performing its responsibilities, the Board, and each committee, shall be entitled to rely on the advice and information it receives from management and the experts, advisers and professionals whom the Board, or a committee, may consult. The Board and each committee shall have the authority to request that any officer or employee of the Company, the Company's outside legal counsel, the Company's independent auditor or any other professional retained by the Company to provide advice to the Company, attend a meeting of the Board or a committee, or meet with any members of or advisers to the Board. The Board or any committee shall also have the authority to engage legal, accounting or other advisers to provide advice and information it deems appropriate to carry out its responsibilities.
- F. **Directors With a Change in Professional Status**: The Board does not believe Directors who retire or change their principal occupation or business association should necessarily leave the Board. However, promptly following any such event, the Director should notify the Nominating Committee, so that it can review and advise the Board regarding the continued appropriateness of the Director's Board membership.
- G. **Director Orientation and Continuing Education**: The Board believes that each Director should be aware of corporate governance issues, legal duties and obligations and best practices involved in serving on a public company board of directors. Directors are encouraged to enhance their awareness by joining other boards of directors, reading relevant publications, attending director education programs and pursuing other educational opportunities. The Company will conduct an orientation program for each new Director. The orientation will be designed to familiarize the new Director with the Company's business and strategic plans, key policies and practices, principal officers and management structure, auditing and compliance processes and its code of business conduct and ethics. The Nominating Committee will be responsible for periodically

providing, or arranging for the provision of, materials or briefing sessions for continuing Directors on topics that will assist them in discharging their duties.

- H. **Management Succession**: The Nominating Committee shall be responsible for developing a CEO succession plan for consideration by the Board and reporting on the plan to the Board.

IV. OTHER CORPORATE GOVERNANCE MATTERS

- A. **Annual Performance Evaluations of the Board and Committees**: The Board will conduct a self-evaluation at least annually for the purpose of determining whether it and its committees are functioning effectively, and the Audit Committee, Nominating Committee and Compensation Committee will conduct a self-evaluation at least annually for the purpose of determining whether it is functioning effectively, and report the results thereof to the Nominating Committee, or in the case of the Nominating Committee's self-evaluation results, to the Board. The Nominating Committee will oversee the evaluation process.
- B. **Communications with Outside Interested Parties**: The Board believes that management should be responsible for communications with the press, media and other outside parties on behalf of the Company, although individual Board members may, at the request of management or the Board, communicate with outside parties on behalf of the Company.
- C. **No Limitation on Other Rights**: These guidelines are not intended to modify, eliminate or in any other manner limit the indemnification, exculpation and similar rights available to the Directors of the Company under applicable law and/or the Company's certificate of incorporation and/or its bylaws.
- D. **Modifications to Guidelines**: Although these guidelines have been approved by the Board, they may evolve over time as customary practice and legal requirements change. In particular, guidelines that reflect legal, regulatory or exchange requirements as they currently exist will be deemed to be modified as and to the extent those requirements change. In addition, the guidelines may be amended by the Board at any time as it deems appropriate.

Adopted on August 19, 2024 and effective upon the effectiveness of the S-1 registration statement.