

UPSTREAM BIO, INC.

AUDIT COMMITTEE CHARTER

I. General Statement of Purpose

The purposes of the Audit Committee of the Board of Directors (the “**Audit Committee**”) of Upstream Bio, Inc. (the “**Company**”) are to (A) assist the Board of Directors (the “**Board**”) in its oversight of (1) the integrity of the Company’s financial statements, (2) the Company’s compliance with legal and regulatory requirements, (3) the qualifications, independence and performance of the Company’s independent auditors engaged for the purpose of preparing or issuing an audit report or performing other audit, review or attest services for the Company (the “**Independent Auditors**”) and (4) the performance of the Company’s internal audit function; and (B) prepare the report required by the rules of the Securities and Exchange Commission (the “**SEC**”) to be included in the Company’s annual proxy statement.

II. Composition

The Audit Committee shall have at least three (3) members, each of whom is a member of the Board (a “**director**”) who: (1) is “independent” as defined in Rule 5605(a)(2) under the Listing Rules of The Nasdaq Stock Market LLC (as amended from time to time and in effect, the “**Nasdaq Rules**”); (2) meets the criteria for independence set forth in Rule 10A-3(b)(1) promulgated under Section 10A(m)(3) of the Securities Exchange Act of 1934, as amended (the “**Exchange Act**”), subject to the exemptions provided in Rule 10A-3(c) under the Exchange Act; and (3) has not participated in the preparation of the financial statements of the Company or a current subsidiary of the Company at any time during the past three years.

Notwithstanding the foregoing, one director who is not “independent” as defined in Rule 5605(a)(2) under the Nasdaq Rules but satisfies the criteria for independence set forth in Section 10A(m)(3) of the Exchange Act and the rules thereunder and is not a current officer or employee or a Family Member (as defined in the Exchange Act) of such officer or employee, may serve on the Audit Committee if the Board, under exceptional and limited circumstances, determines that membership on the Audit Committee by the director is required by the best interests of the Company and its stockholders, and the Board discloses, in the next annual proxy statement subsequent to such determination (or, if the Company does not file a proxy statement, in its Form 10-K or 20-F), the nature of the relationship and the reasons for that determination. A director serving on the Audit Committee under this exception may not serve on the Audit Committee for more than two years and may not chair the Audit Committee.

Each member of the Audit Committee shall be able to read and understand fundamental financial statements, including a company’s balance sheet, income statement and cash flow statement. At least one member of the Audit Committee shall have past employment experience in finance or accounting, requisite professional certification in accounting or comparable experience or background that results in the individual’s financial sophistication, including being or having been a chief executive officer, chief financial officer or other senior officer with

financial oversight responsibilities. One or more members of the Audit Committee must qualify as an “audit committee financial expert” as defined under the rules promulgated by the SEC.

The members of the Audit Committee shall be appointed by the Board and may be replaced or removed by the Board with or without cause. Resignation or removal of a Director from the Board, for whatever reason, shall automatically constitute resignation or removal, as applicable, from the Audit Committee. Vacancies, for whatever reason, may be filled only by the Board. The Board shall designate one member of the Audit Committee to be Chair (the “**Chair**”) of the committee.

III. Compensation

A member of the Audit Committee may not, other than as a member of the Audit Committee, the Board or any other committee established by the Board, receive directly or indirectly any consulting, advisory or other compensatory fee from the Company. A member of the Audit Committee may receive additional directors’ fees to compensate such member for the significant time and effort expended by such member to fulfill his or her duties as an Audit Committee member.

IV. Meetings

The Audit Committee shall meet as often as it deems appropriate, but not less frequently than quarterly. The Audit Committee can meet in person or by video or telephone conference or such other means by which all participants in the meeting can hear each other. A majority of the members of the Audit Committee shall constitute a quorum for purposes of holding a meeting, and the Audit Committee may act by vote of a majority of members present at a meeting. In lieu of a meeting, the Audit Committee may act by unanimous written consent in accordance with the Company’s bylaws. The Chair of the Audit Committee, in consultation with the other committee members, may determine the frequency and length of the committee meetings and may set meeting agendas consistent with this Audit Committee Charter (the “**Charter**”).

Periodically, the Audit Committee shall also meet separately with management, with internal auditors (or other personnel responsible for the internal audit function) and with the Independent Auditors.

V. Responsibilities and Authority

A. Matters Relating to Selection, Performance and Independence of Independent Auditors.

1. The Audit Committee shall be directly responsible for appointing, retaining, terminating and determining the compensation of the Company’s Independent Auditors. The Audit Committee may consult with management in fulfilling these duties but may not delegate these responsibilities to management.

2. The Audit Committee shall be directly responsible for overseeing the work of the Independent Auditors (including resolving disagreements between management and the Independent Auditors regarding financial reporting).
3. The Audit Committee shall instruct the Independent Auditors that the Independent Auditors shall report directly to the Audit Committee.
4. The Audit Committee shall pre-approve all auditing services and the terms of those services (which may include providing comfort letters in connection with securities underwritings) and non-audit services to be provided to the Company by the Independent Auditors (other than non-audit services if the “de minimis” provisions of Section 10A(i)(1)(B) of the Exchange Act are satisfied and non-audit services prohibited under Section 10A(g) of the Exchange Act or the applicable rules of the SEC or the Public Company Accounting Oversight Board (the “PCAOB”). The Audit Committee may delegate authority to pre-approve audit and non-audit services to its Chair, who shall report all pre-approval decisions to the Audit Committee at its next scheduled meeting.
5. The Audit Committee may review and approve the scope and staffing of the Independent Auditors’ annual audit plan(s).
6. The Audit Committee shall (1) request that the Independent Auditors provide it with the written disclosures and the letter required by PCAOB Rule 3526 (“**Rule 3526**”), (2) require that the Independent Auditors submit to the Audit Committee at least annually a formal written statement describing all relationships between the Independent Auditors or any of its affiliates and the Company or persons in financial reporting oversight roles at the Company that might reasonably be thought to bear on the independence of the Independent Auditors, (3) discuss with the Independent Auditors the potential effects of any disclosed relationships or services on the objectivity and independence of the Independent Auditors, (4) require that the Independent Auditors provide to the Audit Committee written affirmation that the Independent Auditor is, as of the date of the affirmation, independent in compliance with PCAOB Rule 3520 and (5) based on such disclosures, statement, discussion and affirmation, take or recommend that the Board take appropriate action in response to the Independent Auditors’ report to satisfy itself of the Independent Auditors’ independence. In addition, before approving the initial engagement of any Independent Auditor, the Audit Committee shall receive, review and discuss with the audit firm all information required by, and otherwise take all actions necessary for compliance with the requirements of, Rule 3526. References to rules of the PCAOB shall refer to any substantially equivalent rules adopted to replace the rules referred to above, in each case as subsequently amended, modified or supplemented.
7. The Audit Committee may consider whether the provision of the services covered in Items 9(e)(2) and 9(e)(3) of Schedule 14A of the Exchange Act (or

any successor provision) is compatible with maintaining the Independent Auditors' independence.

8. The Audit Committee shall evaluate the Independent Auditors' qualifications, performance and independence, and shall present its conclusions to the full Board. As part of its evaluation, at least annually, the Audit Committee shall:
 - obtain and review a report or reports from the Independent Auditors describing (1) its internal quality control procedures, (2) any material issues raised by its most recent internal quality control review or peer review or by any inquiry or investigation by government or professional authorities, within the preceding five years, regarding one or more independent audits it has conducted, and any steps it has taken to address any issues that were identified and (3) to assess its independence and all relationships between it and the Company;
 - review and evaluate the performance of the Independent Auditors and the lead partner (and the Audit Committee may review and evaluate the performance of other members of the Independent Auditors' audit staff); and
 - assure the regular rotation of the audit partners (including, without limitation, the lead and concurring partners) as required under the Exchange Act and Regulation S-X.

In this regard, the Audit Committee also shall (1) seek the opinion of management and the internal auditors of the Independent Auditors' performance and (2) consider whether, to assure continuing auditor independence, the audit firm engaged by the Company to serve as Independent Auditors should be regularly changed.

9. The Audit Committee may establish, or recommend to the Board, policies with respect to the potential hiring by the Company of current or former employees of the Independent Auditors.

B. Audited Financial Statements and Annual Audit

1. The Audit Committee shall review the overall audit plan (both internal and external) with the Independent Auditors and the members of management responsible for preparing the Company's financial statements, including the Company's Chief Financial Officer and/or principal accounting officer or principal financial officer (the Chief Financial Officer and such other officer or officers are referred to collectively as the "**Senior Accounting Executive**").
2. The Audit Committee shall review and discuss with management (including the Company's Senior Accounting Executive) and with the Independent

Auditors the Company's annual audited financial statements, including (a) all critical accounting policies and practices used or to be used by the Company, (b) the Company's disclosures under "Management's Discussion and Analysis of Financial Condition and Results of Operations" before the filing of the Company's Annual Report on Form 10-K and (c) any significant financial reporting issues that have arisen in connection with the preparation of the audited financial statements. The Audit Committee shall also review and discuss with the independent auditor the nature of each identified critical audit matter, the auditor's basis for identifying a matter as a critical audit matter and how each such identified matter will be described in the auditor's report.

3. The Audit Committee must review:
 - (i) any analyses prepared by management, the internal auditors, if any, and/or the Independent Auditors setting forth significant financial reporting issues and judgments made in connection with the preparation of the financial statements, including analyses of the effects of alternative GAAP methods on the financial statements. The Audit Committee may consider the ramifications of the use of such alternative disclosures and treatments on the financial statements and the treatment preferred by the Independent Auditors. The Audit Committee may also consider other material written communications between the Independent Auditors and management, such as any management letter or schedule of unadjusted differences;
 - (ii) major issues as to the adequacy of the Company's internal controls and any special audit steps taken in light of material control deficiencies and the adequacy of disclosures about changes in internal control over financial reporting;
 - (iii) major issues regarding accounting principles and procedures and financial statement presentations, including any significant changes in the Company's selection or application of accounting principles; and
 - (iv) the effects of regulatory and accounting initiatives, as well as off-balance sheet transactions and structures, on the Company's financial statements.
4. The Audit Committee shall review and discuss with the Independent Auditors (outside of the presence of management) how the Independent Auditors plan to handle their responsibilities under the Private Securities Litigation Reform Act of 1995, and request assurance from the Independent Auditors that Section 10A(b) of the Exchange Act has not been implicated.
5. The Audit Committee shall review and discuss with the Independent Auditors any audit problems or difficulties and management's response thereto. This review shall include (1) any difficulties encountered by the Independent Auditors in the course of performing its audit work, including any restrictions

on the scope of its activities or its access to information, (2) any significant disagreements with management and (3) a discussion of the responsibilities, budget and staffing of the Company's internal audit function.

6. This review also may include:
 - (i) any accounting adjustments that were noted or proposed by the Independent Auditors but were "passed" (as immaterial or otherwise);
 - (ii) any communications between the audit team and the audit firm's national office regarding auditing or accounting issues presented by the engagement; and
 - (iii) any management or internal control letter issued, or proposed to be issued, by the Independent Auditors.
7. The Audit Committee shall discuss with the Independent Auditors those matters brought to the attention of the Audit Committee by the Independent Auditors pursuant to PCAOB AS 1301 Communications with Audit Committees (as may be amended, "AS 1301").
8. The Audit Committee also shall review and discuss with the Independent Auditors the report required to be delivered by such auditors pursuant to Section 10A(k) of the Exchange Act.
9. If brought to the attention of the Audit Committee, the Audit Committee shall discuss with the principal executive officer, principal financial officer and principal accounting officer of the Company (1) all significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting that are reasonably likely to adversely affect the Company's ability to record, process, summarize and report financial information required to be disclosed by the Company in the reports that it files or submits under the Exchange Act, within the time periods specified in the SEC's rules and forms and (2) any fraud involving management or other employees who have a significant role in the Company's internal control over financial reporting.
10. Based on the Audit Committee's review and discussions (1) with management of the audited financial statements, (2) with the Independent Auditors of the matters required to be discussed by AS 1301 and (3) with the Independent Auditors concerning the Independent Auditors' independence, the Audit Committee shall make a recommendation to the Board as to whether the Company's audited financial statements should be included in the Company's Annual Report on Form 10-K for the last fiscal year.

11. The Audit Committee shall prepare the Audit Committee report required by Item 407(d)(3) of Regulation S-K of the Exchange Act (or any successor provision) to be included in the Company's annual proxy statement.

C. Internal Auditors

1. At least annually, the Audit Committee shall evaluate the performance, responsibilities, budget and staffing of the Company's internal audit function and review the internal audit plan. Such evaluation may include a review of the responsibilities, budget and staffing of the Company's internal audit function with the Independent Auditor, as well as his or her independence and any relationships or services that might impact the objectivity and independence of the Internal Auditor.
2. In connection with the Audit Committee's evaluation of the Company's internal audit function, the Audit Committee may evaluate the performance of the senior officer or officers responsible for the internal audit function.

D. Unaudited Quarterly Financial Statements

1. The Audit Committee shall discuss with management and the Independent Auditors, before the filing of the Company's Quarterly Reports on Form 10-Q, (1) the Company's quarterly financial statements and the Company's related disclosures under "Management's Discussion and Analysis of Financial Condition and Results of Operations," (2) such issues as may be brought to the Audit Committee's attention by the Independent Auditors pursuant to PCAOB AS 4105 and (3) any significant financial reporting issues that have arisen in connection with the preparation of such financial statements.

E. Earnings Press Releases

1. The Audit Committee shall discuss the Company's quarterly earnings press releases, as well as financial information and earnings guidance provided to analysts and rating agencies, including, in general, the types of information to be disclosed and the types of presentations to be made (paying particular attention to the use of "pro forma" or "adjusted" non-GAAP information).

F. Risk Assessment and Management

1. The Audit Committee shall discuss the guidelines and policies that govern the process by which the Company's exposure to financial, accounting and financial statement risk is assessed and managed by management.

2. The Audit Committee shall periodically review the Company's enterprise risk management framework and major risk exposures, including the Company's enterprise risk processes.
3. In connection with the Audit Committee's discussion of the Company's financial, accounting and financial risk assessment and management guidelines and policies, it may consider the Company's major risk exposures, including financial, operational, privacy, security, cybersecurity, competition, legal, regulatory, hedging and accounting risk exposures and the steps that the Company's management has taken to monitor and control such exposures. With respect to oversight of management of cybersecurity risks, the Audit Committee shall obtain and review reports on data management and security initiatives and significant existing and emerging cybersecurity risks, including material cybersecurity incidents, the impact on the Company and its stakeholders of any significant cybersecurity incident and any disclosure obligations arising from any such incidents.

G. Procedures for Addressing Complaints and Concerns

1. The Audit Committee shall establish procedures for (1) the receipt, retention and treatment of complaints received by the Company regarding accounting, internal accounting controls or auditing matters and (2) the confidential, anonymous submission by employees of the Company of concerns regarding questionable accounting or auditing matters.
2. The Audit Committee may review and reassess the adequacy of these procedures periodically and adopt any changes to such procedures that it deems necessary or appropriate.

H. Regular Reports to the Board

1. The Audit Committee shall regularly report to and review with the Board any issues that arise with respect to the quality or integrity of the Company's financial statements, the Company's compliance with legal or regulatory requirements, the performance and independence of the Independent Auditors, the performance of the internal audit function, the Company's risk exposures and management, and any other matters that it deems appropriate or is requested to review for the benefit of the Board.

I. Review of Charter

1. The Audit Committee shall periodically review and reassess the adequacy of this Charter and recommend to the Board any amendments or modifications it deems appropriate.

J. Annual Performance Evaluation of the Audit Committee

1. At least annually, the Audit Committee shall evaluate its own performance and report the results of such evaluation to the Nominating and Corporate Governance Committee.

VI. Additional Authority

The Audit Committee is authorized, on behalf of the Board, to do any of the following as it deems necessary or appropriate:

A. Engagement of Advisers

1. The Audit Committee may engage, on whatever terms it approves, legal counsel and other advisers to assist it in performing its responsibilities.

B. Legal and Regulatory Compliance

1. The Audit Committee may discuss with management and the Independent Auditors, and review with the Board, the legal and regulatory requirements applicable to the Company and its subsidiaries and the Company's compliance with such requirements. After these discussions, the Audit Committee may, if it determines it to be appropriate, make recommendations to the Board with respect to the Company's policies and procedures for complying with legal and regulatory requirements.
2. The Audit Committee may discuss with management legal matters (including pending or threatened litigation) that may have a material effect on the Company's financial statements or its policies and procedures for complying with legal and regulatory requirements.
3. The Audit Committee has the authority to determine whether the Company is required to prepare a Financial Restatement. No officer of the Company shall have the authority to determine that a Financial Restatement is required without approval of the Audit Committee or the Board. A "Financial Restatement" means a restatement of previously issued financial statements of the Company due to the material noncompliance of the Company with any financial reporting requirement under the securities laws, including any required restatement to correct an error in previously-issued financial statements that is material to the previously-issued financial statements or that would result in a material misstatement if the error were corrected in the current period or left uncorrected in the then-current period.

C. Related Person Transactions

1. The Audit Committee shall review the Company's policies and procedures for reviewing and approving or ratifying "related person transactions" (defined as transactions required to be disclosed pursuant to Item 404 of Regulation S-K of the Exchange Act) and recommend any changes to the Board. In accordance with applicable Nasdaq Rules, the Audit Committee shall review all "related person transactions" on an ongoing basis, and all such transactions must be approved by the Audit Committee.

D. General

1. The Audit Committee may establish and delegate authority to carry out its responsibilities to one or more subcommittees consisting of one or more of its members.
2. The Audit Committee may perform such other functions as the Board may request.
3. In performing its oversight function, the Audit Committee shall be entitled to rely on advice and information it receives from management, the Independent Auditors or other experts, advisers and professionals whom it may consult.
4. The Audit Committee is authorized to request that any officer or employee of the Company, the Company's outside legal counsel, the Company's Independent Auditors or any other professional retained by the Company to meet with the Audit Committee or its members or advisers.
5. The Audit Committee is authorized to incur ordinary administrative expenses in performing its duties.

Notwithstanding the responsibilities and powers of the Audit Committee set forth in this Charter, the Audit Committee does not have the responsibility of planning or conducting audits of the Company's financial statements or determining whether the Company's financial statements are complete, accurate and in accordance with GAAP. In addition, the Audit Committee does not have the responsibility to conduct investigations or to ensure compliance with laws and regulations.

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