

BICYCLE THERAPEUTICS PLC

AMENDED AND RESTATED CORPORATE GOVERNANCE GUIDELINES

The Board of Directors (the “*Board*”) of BICYCLE THERAPEUTICS PLC (the “*Company*”) has established the following guidelines (“*Guidelines*”) for the conduct and operation of the Board.

1. BOARD COMPOSITION AND SELECTION

1.1 Size of the Board

The Board shall establish the number of directors in accordance with the articles of association, as amended, restated or otherwise modified from time to time (the “*Articles*”), of the Company. The Nominating and Corporate Governance Committee (the “*Nominating Committee*”) periodically reviews the appropriate size of the Board, which may vary to accommodate the availability of suitable candidates and the Company’s needs. The Board is divided into three classes that serve staggered three-year terms and are as nearly as equal as possible.

1.2 Independence of Directors

The Board will be composed of not less than a majority of independent directors, subject to any exceptions permitted by the applicable listing standards and rules of The Nasdaq Stock Market, LLC (“*Nasdaq*”) and the Securities Exchange Act of 1934, as amended (the “*Exchange Act*”), together with the rules promulgated thereunder. In determining independence, the Board will consider the definition of independence set forth in such listing standards, rules and regulations, as well as other factors that will contribute to effective oversight and decision-making by the Board.

Board members are expected to disclose promptly to the Board and respond promptly and accurately to periodic questionnaires or other inquiries from the Company regarding any existing or proposed relationships with the Company, including compensation and stock ownership, which could affect the independence of the director. Board members shall also promptly inform the Board of any material changes in such information, to the extent not already known by the Board.

1.3 Management Directors

The Board anticipates that the Company’s Chief Executive Officer will serve on the Board. The Board also may appoint or nominate other members of the Company’s management whose experience and role at the Company are expected to assist the Board in fulfilling its responsibilities.

1.4 Selection of Chief Executive Officer and Chairperson of the Board

The Board will select the Company’s Chief Executive Officer and Chairperson of the Board (“*Chairperson*”) in the manner that it determines to be in the best interests of the Company’s shareholders. The Company does not believe there should be a fixed rule regarding the positions of Chief Executive Officer and Chairperson being held by different individuals, or whether the Chairperson should be an employee of the Company or should be elected from among the non-employee directors. The needs of the Company and the individuals available to assume these roles may require different outcomes at different times, and the Board believes that retaining flexibility in these decisions is in the best interests of the Company. The Nominating Committee will periodically review this matter and make recommendations to the Board.

1.5 Selection of Directors

The Board will be responsible for nominating members for election to the Board by the Company's shareholders at the annual general meeting of shareholders. The Board is also responsible for filling vacancies on the Board that may occur between annual general meetings of shareholders. The Nominating Committee is responsible for identifying, reviewing and evaluating and recommending to the Board candidates to serve as directors of the Company, in accordance with the Nominating Committee's charter and consistent with the criteria listed below. The invitation to join the Board should be extended by the Chairman.

1.6 Shareholder Recommendations of Director Nominees

The Nominating Committee will consider director candidates recommended or nominated by the Company's shareholders so long as such recommendations and nominations comply with the Articles and applicable laws, including the rules and regulations of the Securities and Exchange Commission. The Nominating Committee does not intend to alter the manner in which it evaluates a candidate for nomination to the Board based on whether or not the candidate was recommended by a Company shareholder.

Shareholders who wish to recommend individuals for consideration by the Nominating Committee to become nominees for election to the Board may do so by providing timely notice in writing to the Company's Secretary at Bicycle Therapeutic plc, Blocks A&B, Portway Building, Granta Park Great Abington, Cambridge CB21 6GS, United Kingdom. The shareholder must also provide the shareholder's name and address of record, a representation that the shareholder is a record holder of the Company's securities (or, if not a record holder, evidence of ownership in accordance with Rule 14a-8(b)(2) of the Exchange Act), the nominee's name, age, business and residential addresses, educational background, current principal occupation or employment, and principal occupation or employment for the preceding five full fiscal years, a description of the qualifications and background of the nominee which addresses the minimum qualifications and other criteria for Board membership approved by the Board; a description of all arrangements or understandings between the shareholder and the proposed director candidate, and consent of the nominee (i) to be named in the proxy statement relating to our annual meeting of shareholders and (ii) to serve as a director if elected at such annual meeting. Following verification of the shareholder status of the person submitting the recommendation, all properly submitted recommendations will be promptly brought to the attention of the Nominating Committee.

In accordance with the Articles, no person (other than a director retiring by rotation or otherwise) shall be elected or re-elected as a director at any general meeting unless: (a) he or she is recommended by the Board; or (b) at least seven but not more than 42 clear days before the date appointed for the annual general meeting the Company has received notice from a shareholder (other than the person proposed) entitled to vote at the meeting of their intention to propose a resolution for the election or re-election of that person, stating the particulars which would, if he or she were so elected or re-elected, be required to be included in the Company's register of directors and a notice executed by that person of his or her willingness to be elected, or re-elected, is lodged at the Company's registered office.

1.7 Board Membership Criteria

The Board will determine, upon the recommendation of the Nominating Committee, the appropriate characteristics, skills and experience for the Board as a whole and for its individual members. The Board considers director nominee recommendations from the Nominating Committee. The Board will consider the minimum general criteria set forth below, and may use specific additional criteria with respect

to specific searches, in selecting candidates and existing directors for service on the Board. An acceptable candidate may not fully satisfy all of the criteria, but is expected to satisfy nearly all of them. The Board believes that director candidates should have certain minimum qualifications, including: experience at a strategic or policymaking level in a business, government, non-profit or academic organization of high standing; proven achievement and competence in the nominee's field and the ability to exercise sound business judgment; high standards of personal and professional ethics and integrity; having sufficient time to devote to the affairs of our Company; and a demonstrated history of actively contributing at board meetings if the nominee serves or has previously served on other boards.

Candidates for director nomination are reviewed in the context of the current composition of the Board, the operating requirements of the Company, requirements of applicable law and the long-term interests of shareholders. In conducting this assessment, the Nominating Committee and the Board consider diversity, age, skills, and such other factors as it deems appropriate given the current needs of the Board and the Company, to maintain a balance of knowledge, experience and capability. The Board and the Nominating Committee actively seek to achieve a diversity of professional and personal backgrounds on the Board, including diversity with respect to demographics such as gender, race, ethnic and national background, geography, age and sexual orientation. In the case of incumbent directors whose terms of office are set to expire, the Nominating Committee and the Board review 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 Nasdaq listing requirements.

1.8 Changes in Board Member Criteria

The Board and the Company wish to maintain a Board composed of members who can productively contribute to the success of the Company. From time to time, the Board may change the criteria for Board membership to maximize the opportunity to achieve success. When this occurs, the Nominating Committee and Board will evaluate existing members according to the new criteria. The Board may ask a director who no longer meets the complete criteria for board membership to adjust his or her committee assignments or resign from the Board.

1.9 Term Limits

The Board does not believe it should limit the number of terms for which an individual may serve as a director. Directors who have served on the Board for an extended period of time are able to provide continuity and valuable insight into the Company, the Company's operations and prospects based on their experience with, and understanding of, the Company's history, policies and objectives. The Board believes that, as an alternative to term limits, the director nomination process described in these Guidelines can ensure that the Board continues to evolve and adopt new ideas and viewpoints.

1.10 Limits on Board Memberships

The Board does not believe that its members should be prohibited from serving on boards or committees of other companies, and the Board has not adopted any guidelines limiting such activities. Directors should advise the Chairperson and the Chairperson of the Nominating Committee in advance of accepting an invitation to serve on the board or board committee of another company. The Board and the Nominating Committee will take into account the nature and time involved in a directors' service on other boards in evaluating the suitability of directors. Service on boards and board committees of other companies should be consistent with the Company's conflict-of-interest policies.

1.11 Retirement Age

The Board does not believe that a fixed retirement age for directors is appropriate.

1.12 Directors Who Change Their Job Responsibility

A director who retires from his or her present employment or who materially changes his or her position should promptly notify the Board and the Nominating Committee. The Board does not believe any director who retires from his or her present employment, or who materially changes his or her position, should necessarily leave the Board. However, there should be an opportunity for the Board, through the Nominating Committee, to review the continued appropriateness of Board membership under these circumstances.

2. ROLE OF THE BOARD OF DIRECTORS

The Company's shareholders select the Board to provide oversight of, and strategic guidance to, senior management. Key areas of oversight and guidance of each Board member involve risk assessment and mitigation, financial plans and reporting and executive leadership development and compensation. A director's responsibility is to have a long-term commitment to the interests of the Company, to fulfill his or her fiduciary duties of care and loyalty and otherwise to exercise his or her business judgment in the best interests of the Company and the Company's shareholders. Service on the Board requires significant time and attention on the part of directors. More specifically, the Board has responsibilities to (i) review, approve and monitor fundamental financial and business strategies and major corporate actions, (ii) assess major risks facing the Company and consider ways to address those risks, (iii) select and oversee management and determine its composition and (iv) oversee the establishment and maintenance of processes and conditions to maintain the integrity of the Company. Directors must participate in Board meetings, review relevant materials, and prepare for meetings and discussions with management. The Company expects directors to maintain an attitude of constructive involvement and oversight; to ask relevant, incisive and probing questions and to require honest and accurate answers. Directors must act with integrity, and the Company expects them to demonstrate a commitment to the Company, the Company's values and the Company's business and to long-term shareholder value.

3. DIRECTOR ORIENTATION AND EDUCATION

The Nominating Committee will implement an orientation process for directors. This orientation will include familiarizing 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, and its internal and independent auditors. In addition, the orientation program will include a visit to the Company to meet with senior management, including the General Counsel regarding his or her legal duties as a director, and tours of Company facilities to understand better the Company's business and culture. All other directors are also invited to attend the orientation program. In addition, each director is expected to maintain the necessary level of expertise to perform his or her responsibilities as a director. The Company may, from time to time, offer continuing education programs to assist the directors in maintaining such level of expertise.

Each director is encouraged 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 appropriately address issues that arise. Board members are encouraged to attend seminars, conferences and other continuing education programs designed especially for directors of public companies, including but not limited to, accredited director education programs. The Company shall pay all reasonable expenses related to continuing director education.

4. DIRECTOR COMPENSATION

The Compensation Committee of the Board (the “*Compensation Committee*”) shall review and recommend to the Board for approval the form and amount of director compensation for Board and committee service for non-employee directors in accordance with the principles set forth in its charter and applicable legal and regulatory guidelines. The amount of compensation for non-management directors and committee members should be consistent with market practices of similarly situated companies and should encourage increased ownership of the Company’s equity securities through the payment of a portion of director compensation in Company ordinary shares or options to purchase the Company’s shares. In determining compensation, the Compensation Committee and the Board will consider the impact on the director’s independence and objectivity. Directors who are officers or employees shall not receive any additional compensation for serving on the Board. To assist in setting compensation, the Compensation Committee or the Board may request compensation information from the Company or from independent consultants.

5. BOARD MEETINGS

5.1 Number of Meetings

The Board expects to have at least four regular meetings each year.

5.2 Attendance

The Company expects Board members to attend all meetings of the Board and committees on which they serve, including attendance by means of videoconference. Directors must notify the Chairperson of the Board of circumstances preventing attendance at a meeting. Directors are encouraged, but not required, to attend the Company’s annual general meeting of shareholders, either in person or telephonically.

5.3 Preparation and Commitment

The Company will provide directors with appropriate preparatory materials in advance of a meeting. Board members are expected to devote sufficient time and attention to prepare for, attend and participate in Board meetings and meetings of committees on which they serve, including advance review of meeting materials that may be circulated prior to each meeting. Each director should ensure that other existing and planned future commitments do not materially interfere with the member’s service as director.

5.4 Agenda

The Chairperson will establish a schedule of subjects to be discussed during the year (to the extent this can be foreseen) and an agenda for each Board meeting. Each Board member is encouraged to suggest the inclusion of items on the agenda at any time, and each Board member is free to raise subjects that are not on the agenda.

5.5 Executive Session

The independent, non-employee directors of the Board will meet periodically in executive session without management and any non-independent directors, but no less than two (2) times per year or such greater number as required by Nasdaq listing standards. Executive session discussions may include such topics as the independent directors determine. The directors generally shall not take formal action at these sessions, but may make recommendations for consideration by the full Board.

5.6 Committee Reports

At each regular Board meeting, each committee that held a meeting subsequent to the last Board meeting and prior to the current Board meeting will present a brief summary of its committee meeting to the Board, including the principal subjects discussed and the conclusions and actions of the committee. In general, the chairperson of the appropriate committee will present such report. Minutes of committee meetings shall be available to any director.

6. BOARD COMMITTEES

6.1 Number of Committees; Independence of Members

The committee structure of the Board will consist of at least the following standing committees: (a) an Audit Committee, (b) a Compensation Committee, and (c) a Nominating and Corporate Governance Committee. The Board may form, merge or dissolve committees as it deems appropriate from time to time, in accordance with applicable law. The Audit Committee, the Compensation Committee and the Nominating Committee shall be composed entirely of independent directors except to the extent allowed under applicable Nasdaq listing standards and Exchange Act rules.

6.2 Committee Functions and Charters

All standing committees will operate pursuant to a written charter, which sets forth the responsibilities of the committee and procedures that the committee will follow. Unless otherwise directed by the Board, the Board will develop and approve a written charter delineating each standing committee's responsibilities. The charters of all standing committees will be subject to periodic review and assessment by each committee and each committee shall recommend any proposed charter changes to the Board.

6.3 Board Committee Membership

The Nominating Committee oversees the Board's committee structure and operations. The Nominating Committee, after due consideration of the interests, independence and experience of the individual directors and the independence and experience requirements set forth in the listing standards of any stock exchange on which any of the Company's securities are listed, the rules and regulations of the Securities and Exchange Commission and applicable law, shall make recommendations to the entire Board regarding the appointment of directors to serve as members of each committee and committee Chairperson.

6.4 Committee Meetings and Agenda

The committee Chairperson, in consultation with committee members, will determine the frequency and length of the meetings of the committee, consistent with any requirements set forth in the committee's charter. The Chairperson of each committee, in consultation with the appropriate members of the committee and management, will develop the committee's agenda.

7. BOARD ACCESS TO MANAGEMENT; USE OF OUTSIDE ADVISORS

Board members have complete and open access to the Company's management. The Company expects the Company's Board members to use their judgment to ensure that this contact is not distracting to the operations of the Company or to management's duties and responsibilities and that such contact, to the extent reasonably practical or appropriate, will be coordinated with the Chief Executive Officer. Board members should copy the Chief Executive Officer on written communications to management whenever appropriate.

The Board and each committee shall have the power to hire at the expense of the Company, independent legal, financial or other advisors as they may deem necessary, without consulting or obtaining the approval of any officer of the Company in advance.

8. CONFIDENTIALITY

Board members have an obligation to protect and keep confidential all our non-public information unless the Company has authorized public disclosure or unless otherwise required by applicable law. Confidential information includes all non-public information entrusted to or obtained by a director by reason of his or her position on the Board. This includes information regarding our strategy, business, finances, and operations, and will include minutes, reports, and materials of the Board and its committees and other documents identified as confidential by the Company.

Board members may not use such confidential information for personal benefit or to benefit other persons or entities other than the Company. Unless authorized by the Company or applicable law, directors will refrain from disclosing confidential information to anyone outside the Company, especially anyone affiliated with any entity or person that employs the director or has sponsored the director's election to the Board. These obligations continue even after service on the Board has ended. Any questions or concerns about potential disclosures should be directed to the Company's Compliance Officer, who then may communicate with the Chief Executive Officer or the Nominating Committee regarding potential disclosures.

9. CHIEF EXECUTIVE OFFICER EVALUATION

The Compensation Committee of the Board shall conduct an annual review of the Chief Executive Officer's performance. The Board will evaluate performance based on criteria approved by the Compensation Committee or recommended by the Compensation Committee and approved by the Board. The Compensation Committee will use the evaluation in the course of its deliberations when considering the compensation of the Chief Executive Officer.

10. SUCCESSION PLANNING

The Nominating Committee should develop and periodically review with the Chief Executive Officer the plans for succession for the Company's executive officers, as it sees fit, and Chairperson and make recommendations to the Board with respect to the selection of appropriate individuals to succeed to such positions. The Chief Executive Officer should at all times make available his or her recommendations and evaluations of potential successors, along with a review of any development plans recommended for such individuals.

11. BOARD ASSESSMENT

The Nominating Committee will periodically review, discuss and assess the performance of the Board, including Board committees, seeking input from the full Board and others as deemed appropriate. The Nominating Committee may also consider and assess the independence of directors. The Nominating Committee should provide the results of these evaluations to the Board for further discussion as appropriate.

12. SHAREHOLDER COMMUNICATIONS WITH THE BOARD

Shareholders of the Company wishing to communicate with the Board or an individual director may send a written communication to the Board or such director c/o Bicycle Therapeutics plc, Blocks A&B, Portway Building, Granta Park Great Abington, Cambridge CB21 6GS, Attn: Secretary. The Secretary will

review each communication. The Secretary will forward such communication to the Board or to any individual director to whom the communication is addressed unless the communication contains advertisements or solicitations or is unduly hostile, threatening or similarly inappropriate, in which case the Secretary shall discard the communication or inform the proper authorities, as may be appropriate.

13. REVIEW OF GUIDELINES

The Nominating Committee will review and assess the adequacy of these Guidelines at least annually and recommend any proposed changes to the Board for approval. These Guidelines, as may be amended from time to time, shall be posted on the Company's website.

Adopted by the Board of Directors: September 22, 2022

Effective: September 22, 2022