

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM S-8

REGISTRATION STATEMENT UNDER THE SECURITIES ACT OF 1933

Bicycle Therapeutics plc

(Exact name of registrant as specified in its charter)

England and Wales
(State or other jurisdiction of
incorporation or organization)

Not applicable
(I.R.S. Employer
Identification No.)

B900, Babraham Research Campus
Cambridge CB22 3AT
United Kingdom
(Address of Principal Executive Offices)

Not applicable
(Zip Code)

Bicycle Therapeutics plc 2020 Equity Incentive Plan

Bicycle Therapeutics plc 2019 Employee Share Purchase Plan
(Full title of the plan)

Lee Kalowski
Chief Financial Officer
Bicycle Therapeutics Inc.
4 Hartwell Place
Lexington, Massachusetts 02421
(Name and address of agent for service)

(617)945-8155
(Telephone number, including area code, of agent for service)

Copy to:

Laura Berezin
Ryan Sansom
Jaime Chase
Cooley LLP
3175 Hanover Street
Palo Alto, California 94304-1130

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer Accelerated filer
Non-accelerated filer Smaller reporting company
Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

**REGISTRATION OF ADDITIONAL SHARES
PURSUANT TO GENERAL INSTRUCTION E**

Pursuant to General Instruction E of Form S-8, Bicycle Therapeutics plc (the “Registrant”) is filing this Registration Statement with the Securities and Exchange Commission (the “Commission”) to register an additional (a) 1,478,968 ordinary shares, nominal value £0.01 per share (the “Ordinary Shares”), of the Registrant under the Bicycle Therapeutics plc 2020 Equity Incentive Plan (the “2020 Plan”), pursuant to the provisions of the 2020 Plan providing for an automatic increase in the number of shares reserved and available for issuance under the 2020 Plan on January 1, 2022 and (b) 295,793 Ordinary Shares under the Bicycle Therapeutics plc 2019 Employee Share Purchase Plan (the “ESPP”), pursuant to the provisions of the ESPP providing for an automatic increase in the number of shares reserved and available for issuance under the ESPP on January 1, 2022. In accordance with the instructional note to Part I of Form S-8 as promulgated by the Commission, the information specified by Part I of the Form S-8 has been omitted from this Registration Statement.

PART II

INFORMATION REQUIRED IN THE REGISTRATION STATEMENT

Item 3. Incorporation of Documents by Reference.

The following documents filed by the Registrant with the Commission are incorporated herein by reference:

- (a) the contents of the Registrant’s Registration Statements on Form S-8 filed with the Commission on [May 23, 2019](#) (File No. 333-231718), [August 5, 2020](#) (File No. 333-240993), and [March 11, 2021](#) (File No. 333-254163);
- (b) [the Registrant’s Annual Report on Form 10-K \(File No. 001-38916\) for the fiscal year ended December 31, 2021, filed with the Commission on March 1, 2022 \(the “Annual Report”\);](#)
- (c) [the Registrant’s Current Report on Form 8-K \(File No. 001-38916\) filed with the Commission on January 5, 2022 \(except for information contained therein which is furnished rather than filed\); and](#)
- (d) [The description of the Registrant’s Ordinary Shares and American Depositary Shares contained in the Registrant’s Registration Statement on Form 8-A \(File No. 001-38916\), filed by the Registrant with the Commission under Section 12\(b\) of the Exchange Act on May 20, 2019, including any amendments or reports filed for the purpose of updating such description, including Exhibit 4.6 to the Annual Report.](#)

All reports and other documents filed by the Registrant after the date hereof pursuant to Sections 13(a), 13(c), 14 and 15(d) of the Exchange Act prior to the filing of a post-effective amendment which indicates that all securities offered hereby have been sold or which deregisters all securities then remaining unsold, shall be deemed to be incorporated by reference herein and to be part hereof from the date of filing of such reports and documents, except for documents or information deemed furnished and not filed in accordance with the rules of the Commission. Any statement contained in a document incorporated or deemed to be incorporated by reference herein shall be deemed to be modified or superseded for purposes of this Registration Statement to the extent that a statement contained herein or in any subsequently filed document that also is deemed to be incorporated by reference herein modifies or supersedes such statement. Any such statement so modified or superseded shall not be deemed, except as so modified or superseded, to constitute a part of this Registration Statement.

Item 8. Exhibits.

Exhibit Number	Exhibit Description
3.1	Articles of Association (incorporated by reference to Exhibit 3.2 to Amendment No. 1 to the Company’s Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).
4.1	Form of Deposit Agreement (incorporated by reference to Exhibit 4.1 to Amendment No. 1 to the Company’s Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).
4.2	Form of American Depositary Receipt (included in Exhibit 4.1) (incorporated by reference to Exhibit 4.2 to Amendment No. 1 to the Company’s Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).

5.1	Opinion of Cooley_(UK)_LLP.
23.1	Consent of PricewaterhouseCoopers LLP.
23.3	Consent of Cooley_(UK)_LLP (included in Exhibit 5.1).
24.1	Power of Attorney_(included on the signature page to this Registration Statement).
99.1	Bicycle Therapeutics plc 2020 Equity Incentive Plan and forms of award thereunder (incorporated by reference to Exhibit 10.2 to the Registrant's Quarterly Report on Form 10-Q (File No. 001-38916) for the fiscal quarter ended June 30, 2020 filed with the Securities and Exchange Commission on August 5, 2020).
99.2	Bicycle Therapeutics plc 2019 Employee Share Purchase Plan (incorporated by reference to Exhibit 10.5 to the Registrant's Registration Statement on Form S-1 (File No. 333-231076), filed with the Securities and Exchange Commission on May 13, 2019).
107	Filing Fee Table

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-8 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Cambridge, United Kingdom, on March 1, 2022.

BICYCLE THERAPEUTICS PLC

By: /s/Kevin Lee
Kevin Lee, Ph.D., MBA
Chief Executive Officer

SIGNATURES AND POWER OF ATTORNEY

We, the undersigned officers and directors of Bicycle Therapeutics plc, hereby severally constitute and appoint Kevin Lee and Lee Kalowski, and each of them singly (with full power to each of them to act alone), our true and lawful attorneys-in-fact and agents, with full power of substitution and resubstitution in each of them for him or her and in his or her name, place and stead, and in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement on Form S-8 of Bicycle Therapeutics plc and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done in and about the premises, as full to all intents and purposes as he or she might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them or their or his or her substitute or substitutes may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed below by the following persons in the capacities on March 1, 2022.

<u>Name</u>	<u>Title</u>
<u>/s/Kevin Lee</u> Kevin Lee, Ph.D., MBA	Chief Executive Officer and Director (Principal Executive Officer)
<u>/s/Lee Kalowski</u> Lee Kalowski, MBA	Chief Financial Officer and President (Principal Financial and Accounting Officer)
<u>/s/Pierre Legault</u> Pierre Legault, MBA, CPA	Chairman of the Board and Director
<u>/s/Janice Bourque</u> Janice Bourque, MBA	Director
<u>/s/Jose-Carlos Gutiérrez-Ramos</u> Jose-Carlos Gutiérrez-Ramos, Ph.D.	Director
<u>/s/Veronica Jordan</u> Veronica Jordan, Ph.D.	Director
<u>/s/Richard Kender</u> Richard Kender	Director
<u>/s/Gregory Winter</u> Sir Gregory Winter, FRS	Director
<u>/s/Lee Kalowski</u> Lee Kalowski, MBA	Authorized Representative in the United States



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Bicycle Therapeutics plc
Building 900, Babraham Research Campus
Babraham, Cambridgeshire, CB22 3AT
United Kingdom

1 March 2022

Ladies and Gentlemen:

Re: Bicycle Therapeutics plc – Registration Statement on Form S-8 – Exhibit 5.1

1. INTRODUCTION

- 1.1 We have acted as English legal advisers to Bicycle Therapeutics plc, a public limited company incorporated in England and Wales (the “**Company**”), in relation to the preparation and filing of the registration statement on Form S-8 to which this opinion letter is attached as an exhibit (such registration statement, as amended, including the documents incorporated by reference therein, the “**Registration Statement**”) filed with the United States Securities and Exchange Commission (the “**SEC**”) pursuant to the United States Securities Act of 1933, as amended (the “**Securities Act**”) and the rules and regulations promulgated thereunder.
- 1.2 As set out in the Registration Statement, it is proposed that (i) up to 1,478,968 ordinary shares of the Company each having a nominal value of £0.01 (“**Ordinary Shares**”) will be allotted and issued upon the exercise or settlement of equity awards granted under the Bicycle Therapeutics plc 2020 Equity Incentive Plan, adopted by the Company’s board of directors (the “**Board**” or the “**Directors**”) on 23 April 2020 and approved by the Company’s shareholders on 29 June 2020 (the “**2020 Equity Incentive Plan**”) pursuant to the provisions of the 2020 Equity Incentive Plan providing for an automatic increase in the number of shares reserved and available for issuance under the 2020 Equity Incentive Plan on 1 January 2022 (the “**2020 Equity Incentive Plan Shares**”) and (ii) up to 295,793 Ordinary Shares will be allotted and issued upon the exercise or settlement of equity awards granted under the Bicycle Therapeutics plc 2019 Employee Share Purchase Plan, adopted by the Board on 9 May 2019 and approved by the Company’s shareholders on 13 May 2019 (the “**ESPP**” and, together with the 2020 Equity Incentive Plan, the “**Plans**”) pursuant to the provisions of the ESPP providing for an automatic increase in the number of shares reserved and available for issuance under the ESPP on 1 January 2022 (the “**ESPP Shares**” and together with the 2020 Equity Incentive Plan Shares, the “**Shares**”).
- 1.3 We are rendering this letter at the request of the Company in connection with the Registration Statement. We have taken instructions solely from the Company.
- 1.4 Except as otherwise defined in this letter, capitalised terms used have the respective meanings given to them in the Registration Statement (as defined above) and headings are for ease of reference only and shall not affect interpretation.
- 1.5 All references to legislation in this letter are to the legislation of England unless the contrary is indicated, and any reference to any provision of any legislation shall include any amendment, modification, re-enactment or extension thereof, as in force on the date of this letter.

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Cooley (UK) LLP is a limited liability partnership and is registered in England and Wales with registered number OC395270. Our registered office is at the address above. Cooley (UK) LLP is authorised and regulated by the Solicitors Regulation Authority (SRA number 617791). A list of the members of Cooley (UK) LLP and their professional qualifications is open to inspection at its registered office. The word 'partner,' used in relation to Cooley (UK) LLP, refers to a member of Cooley (UK) LLP or an employee or consultant of Cooley (UK) LLP (or any affiliated firm) of equivalent standing.

2. DOCUMENTS

For the purpose of issuing this letter, we have reviewed the following documents only:

- 2.1 a draft PDF copy of the Registration Statement to be filed with the SEC on 1 March 2022;
- 2.2 a PDF copy of the 2020 Equity Incentive Plan;
- 2.3 a PDF copy of the ESPP;
- 2.4 a PDF executed copy of the written resolutions of the Board adopted on 23 April 2020, in which it was resolved, *inter alia*, to adopt and approve the 2020 Equity Incentive Plan effective upon shareholder approval and to grant the compensation committee of the Board (the “**Compensation Committee**”) the authority to administer the 2020 Equity Incentive Plan (the “**Written Board Resolutions**”);
- 2.5 a PDF executed copy of the written resolutions of the Compensation Committee adopted on 29 June 2020, in which it was resolved, *inter alia*, to delegate certain authorities of the Compensation Committee to the Chief Executive Officer of the Company to grant certain equity awards (the “**Committee Written Resolutions**”);
- 2.6 a PDF executed copy of the minutes of a meeting of the Board held on 9 May 2019 (the “**Board Minutes**”) at which it was resolved, *inter alia*, to (i) adopt and approve the ESPP effective upon shareholder approval and (ii) grant the Compensation Committee the authority to administer the ESPP;
- 2.7 a PDF executed copy of the written resolutions passed by the shareholders of the Company on 13 May 2019, in which it was resolved, *inter alia*, to approve the ESPP (the “**Written Shareholder Resolutions**”);
- 2.8 a PDF executed copy of the minutes of the annual general meeting of the Company held on 29 June 2020 (the “**2020 AGM**”) at which the shareholders of the Company resolved, *inter alia*, to approve the 2020 Equity Incentive Plan;
- 2.9 a PDF executed copy of the resolutions passed by the shareholders of the Company at the annual general meeting of the Company held on 28 June 2021 (the “**2021 AGM**”) at which it was resolved, *inter alia*, to authorise the directors to (i) allot new shares in the capital of the Company or to grant rights to subscribe for or to convert any security into shares in the Company, up to a maximum aggregate nominal amount of £250,000 (the “**2021 AGM Allotment Authority**”); and (ii) allot equity securities pursuant to the 2021 AGM Allotment Authority as if the statutory pre-emption rights contained in section 561(1) of the Companies Act 2006 (the “**Companies Act**”) did not apply to such allotment (the “**2021 AGM Resolutions**”);
- 2.10 a PDF copy of the certificate of incorporation of the Company dated 27 October 2017 and a PDF copy of the certificate of incorporation on re-registration of the Company as a public company dated 22 May 2019; and
- 2.11 a PDF copy of the current articles of association of the Company adopted on 13 May 2019 (the “**Articles**”).

3. SEARCHES

In addition to examining the documents referred to in paragraph 2 (*Documents*), we have carried out the following searches only:

- 3.1 an online search at Companies House in England and Wales (“**Companies House**”) with respect to the Company, carried out at 9:47 a.m. (London time) on 1 March 2022 (the “**Online Search**”); and
 - 3.2 a telephone enquiry at the Companies Court in London of the Central Registry of Winding-up Petitions in England and Wales with respect to the Company, carried out at 10:07 a.m. (London time) on 1 March 2022 (the “**Telephone Enquiry**” and, together with the Online Search, the “**Searches**”).
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4. OPINION

Subject to the assumptions set out in paragraph 5 (*Assumptions*), the scope of the opinion set out in paragraph 6 (*Scope of Opinion*) and the reservations set out in paragraph 7 (*Reservations*), and subject further to the following:

- 4.1 the Registration Statement, as finally amended, having become effective under the Securities Act;
- 4.2 the delegations of authority to the Compensation Committee and the Company's Chief Executive Officer, as applicable, having been validly effected (among other things, in accordance with articles 98 and 97 of the Company's Articles, the 2020 Equity Incentive Plan, the ESPP and applicable laws);
- 4.3 the Directors, the Compensation Committee or the Company's Chief Executive Officer having validly granted the awards in respect of the Shares under the 2020 Equity Incentive Plan and the ESPP, as applicable;
- 4.4 the Directors or the Compensation Committee having validly resolved to allot and issue the Shares, or grant rights to subscribe for the Shares, at duly convened and quorate meetings of the Board or the Compensation Committee, or by way of duly passed written resolutions of the Board or the Compensation Committee in compliance with all applicable laws and regulations and with such resolutions being in full force and effect and not having been rescinded or amended;
- 4.5 the receipt in full of payment for the Shares in an amount of "cash consideration" (as defined in section 583(3) of the Companies Act) of not less than the aggregate nominal value for such Shares, assuming in each case that the individual grants or awards under the 2020 Equity Incentive Plan and the ESPP are duly authorised by all necessary corporate action and duly granted or awarded and exercised in accordance with the requirements of applicable law, the Company's Articles, the 2020 Equity Incentive Plan and the ESPP (and the agreements and awards duly adopted thereunder and in accordance therewith); and
- 4.6 valid entries having been made in relation to the allotment and issue of the Shares in the books and registers of the Company,

it is our opinion that, as at today's date, the Shares, if and when allotted and issued, registered in the name of the recipient in the register of members of the Company and delivered in accordance with the terms and conditions referred to in the 2020 Equity Incentive Plan and/or the ESPP, as applicable, and as described in the Registration Statement, will be duly and validly authorised and issued, fully paid or credited as fully paid (subject to the receipt of valid consideration by the Company for the issue thereof) and will not be subject to any call for payment of further capital.

5. ASSUMPTIONS

In giving the opinion in this letter, we have assumed (without making enquiry or investigation) that:

- 5.1 all signatures, stamps and seals on all documents are genuine. All original documents are complete, authentic and up-to-date, and all documents submitted to us as a copy (whether by email or otherwise) are complete and accurate and conform to the original documents of which they are copies and that no amendments (whether oral, in writing or by conduct of the parties) have been made to any of the documents since they were examined by us;
 - 5.2 where a document has been examined by us in draft or specimen form, it will be or has been duly executed in the form of that draft or specimen;
 - 5.3 the Articles referred to in paragraph 2.11 of this letter remain in full force and effect, and no alteration has been made or will be made to the Articles, in each case prior to the relevant date of the granting of rights to subscribe for the Shares and/or the allotment and issue of the Shares (each such date, an "**Allotment Date**");
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- 5.4 at the time of each allotment and issue of any Shares the Company shall have received in full “cash consideration” (as such term is defined in section 583(3) of the Companies Act) equal to the subscription price payable for such Shares and shall have entered the holder or holders thereof in the register of members of the Company showing that all such Shares shall have been fully paid up as to their nominal value and any premium thereon as at each Allotment Date;
 - 5.5 each of the Plans has been validly adopted and remains in full force and effect, and no alteration has been made or will be made to the Plans prior to any Allotment Date;
 - 5.6 in relation to any allotment and issue of any Shares by the Company pursuant to the Plans, the recipient shall have become entitled to such Shares under the terms of the relevant Plan and such Shares, or rights over Shares, where applicable, will be fully vested each in accordance with the terms of the relevant Plan and such recipient has or will have complied with all other requirements of the relevant Plan in connection with the allotment and issue of such Shares;
 - 5.7 all awards have been made under the terms of the 2020 Equity Incentive Plan or the ESPP, as applicable, that the terms of all awards have not materially deviated from the terms set out in the 2020 Equity Incentive Plan or the ESPP, as applicable, and that any Shares will be allotted and issued in accordance with the terms set out in the 2020 Equity Incentive Plan or the ESPP, as applicable, in accordance with the Articles and applicable laws;
 - 5.8 the 2020 Equity Incentive Plan (other than the 2020 Non-Employee Sub-Plan) and the ESPP each qualify as an “employees’ share scheme” as defined in section 1166 of the Companies Act;
 - 5.9 immediately prior to each Allotment Date, the Directors shall have sufficient authority and powers conferred upon them to allot and issue such Shares and grant such rights (as applicable) under section 551 of the Companies Act (unless such allotment and issue or grant is exempt under section 549(2) of the Companies Act) and under section 570 or section 571 of the Companies Act as if section 561 of the Companies Act did not apply to such allotment and issue or grant (unless such allotment and issue or grant is exempt from section 561 of the Companies Act pursuant to section 566 of the Companies Act) pursuant to the 2021 AGM Resolutions, or if the relevant authorities and powers under the 2021 AGM Resolutions have expired or been fully utilised the Company in general meeting having duly and validly resolved to grant such authorities and powers to the Directors, and the Directors shall not allot or issue (or purport to allot or issue) Shares and shall not grant rights (or purport to grant rights) to acquire Shares in excess of such powers or in breach of any other limitation on their power to allot and issue Shares or grant rights to acquire Shares;
 - 5.10 no Shares shall be allotted or issued, or are or shall be committed to be allotted or issued, at a discount to their nominal value (whether in dollars or equivalent in any other currency);
 - 5.11 all documents, forms and notices which should have been delivered to Companies House in respect of the Company have been so delivered;
 - 5.12 the information revealed by the Searches is true, accurate, complete and up-to-date in all respects, and there is no information which should have been disclosed by the Searches that has not been disclosed for any reason and there has been no alteration in the status or condition of the Company since the date and time that the Searches were made and that the results of the Searches will remain complete and accurate as at each Allotment Date;
 - 5.13 in relation to the allotment and issue of the Shares, the Directors have acted and will act in the manner required by section 172 of the Companies Act and the Shares will be allotted and issued in good faith and on bona fide commercial terms and on arms’ length terms and for the purpose of carrying on the business of the Company and that there are reasonable grounds for believing that the allotment and issue of the Shares will promote the success of the Company for the benefit of its members as a whole;
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- 5.14 there has not been and will not be any bad faith, breach of trust, fraud, coercion, duress or undue influence on the part of any of the Directors in relation to any allotment and issue of Shares;
- 5.15 the resolutions set out in the Written Board Resolutions and the Committee Written Resolutions referred to in paragraph 2 (*Documents*) were validly passed as written resolutions in accordance with the Articles, that all eligible Directors of the Company (being all the Directors of the Company who would have been entitled to vote on the matter had it been proposed as a resolution at a Directors' meeting or a meeting of the Compensation Committee, as applicable, but excluding any director whose vote is not to be counted in respect of a particular matter) have signed one or more copies of the Written Board Resolutions and/or the Committee Written Resolutions, as applicable, that all relevant provisions of the Companies Act and the Articles were complied with and the Articles were duly observed (including, if applicable, those relating to the declaration of Directors' interests or the power of interested Directors to vote) and such resolutions were duly adopted, and have not been revoked or varied and remain in full force and effect and will remain so as at each Allotment Date;
- 5.16 the Board Minutes referred to in paragraph 2 (*Documents*) provided to us in connection with the giving of this opinion, are a true record of the proceedings described therein, and that the meeting recorded in such minutes was and each meeting of the Directors or the Compensation Committee referred to in paragraph 4.4 of this letter were and/or will be duly conducted as described therein, duly constituted and convened and all constitutional, statutory and other formalities were and/or will be duly observed (including, if applicable, those relating to the declaration of Directors' interests or the power of interested Directors to vote), a quorum was and/or will be present throughout, the requisite majority of Directors voted and/or will vote in favour of approving the resolutions and the resolutions passed at that meeting of the Board or Compensation Committee, as applicable, were and/or will be duly adopted, have not been and will not be revoked or varied and remain in full force and effect and will remain so as at each Allotment Date;
- 5.17 the Written Shareholder Resolutions were duly passed as written resolutions on 13 May 2019, the requisite majority of eligible shareholders signed one or more copies of the written resolutions, all provisions of the Companies Act and the Articles were duly observed and such resolutions were duly passed and have not been revoked or varied and remain in full force and effect and will remain so as at each Allotment Date, and all filings required to be made with Companies House in connection therewith have been made within the relevant time limits;
- 5.18 the 2020 AGM was duly convened and held on 29 June 2020 at which all constitutional, statutory and other formalities were duly observed, a quorum of shareholders was present throughout and the shareholder resolutions at the 2020 AGM were duly passed and have not been revoked or varied and remain in full force and effect and will remain so as at each Allotment Date, and that all filings required to be made with Companies House in connection therewith have been made within the relevant time limits;
- 5.19 the 2021 AGM was duly convened and held on 28 June 2021 at which all constitutional, statutory and other formalities were duly observed, a quorum of shareholders was present throughout and the shareholder resolutions at the 2021 AGM were duly passed and have not been revoked or varied and remain in full force and effect and will remain so as at each Allotment Date, and that all filings required to be made with Companies House in connection therewith have been made within the relevant time limits;
- 5.20 the resolutions of the shareholders of the Company referred to in paragraph 5.9 will be duly passed as resolutions of the Company, all constitutional, statutory and other formalities will be observed and such resolutions will not have expired and will not be revoked or varied prior to each Allotment Date and will remain in full force and effect as at each Allotment Date;
- 5.21 the Company has complied and will comply with all applicable anti-terrorism, anti-money laundering, sanctions and human rights laws and regulations and that each grant of rights to acquire Shares under the 2020 Equity Incentive Plan or the ESPP, as applicable, and that each allotment and issue of Shares pursuant to the 2020 Equity Incentive Plan or the ESPP, as applicable, will be consistent with all such laws and regulations;
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- 5.22 no Shares or rights to subscribe for Shares have been or shall be offered to the public in the United Kingdom in breach of the Financial Services and Markets Act 2000 (“**FSMA**”), the EU Prospectus Regulation (Regulation (EU) 2017/1129) as it forms part of domestic law in the United Kingdom by virtue of the European Union (Withdrawal) Act 2018 or of any other United Kingdom laws or regulations concerning offers of securities to the public, and no communication has been or shall be made in relation to the Shares in breach of section 21 (*Restrictions on financial promotion*) of FSMA or any other United Kingdom laws or regulations relating to offers or invitations to subscribe for, or to acquire rights to subscribe for or otherwise acquire, shares or other securities;
- 5.23 in issuing and allotting and granting rights to acquire Shares and administering the 2020 Equity Incentive Plan and the ESPP, the Company is not carrying on a regulated activity (within the meaning of section 19 (*The general prohibition*) of FSMA); and
- 5.24 the Company has not taken any corporate or other action nor have any steps been taken or legal proceedings been started against the Company for the liquidation, winding-up, dissolution or reorganisation of, or for the appointment of a liquidator, receiver, trustee, administrator, administrative receiver or similar officer of, any such party (including the Company) or all or any of its or their assets (or any analogous proceedings in any jurisdiction) and no such steps or proceedings will have been taken as at each Allotment Date, and the Company is not unable to pay its debts as they fall due within the meaning of section 123 of the Insolvency Act 1986, as amended (the “**Insolvency Act**”) and will not become unable to pay its debts within the meaning of that section as a result of any of the transactions contemplated herein, is not insolvent and has not been dissolved (although the Searches gave no indication that any winding-up, dissolution or administration order or appointment of a receiver, administrator, administrative receiver or similar officer has been made with respect to the Company) and such actions and steps will not have been taken as at any Allotment Date.

6. SCOPE OF OPINION

- 6.1 The opinion given in this letter is limited to English law as it would be applied by English courts on the date of this letter.
- 6.2 We express no opinion in this letter on the laws of any other jurisdiction. We have not investigated the laws of any country other than England and we assume that no foreign law affects the opinion stated in paragraph 4 (*Opinion*).
- 6.3 We express no opinion as to any agreement, instrument or other document other than as specified in this letter. For the purposes of giving the opinion in paragraph 4 (*Opinion*), we have only examined and relied on those documents set out in paragraph 2 (*Documents*) and made those searches and enquiries set out in paragraph 3 (*Searches*), respectively. We have made no further enquiries concerning the Company or any other matter in connection with the giving of the opinion in paragraph 4 (*Opinion*).
- 6.4 No opinion is expressed with respect to taxation in the United Kingdom or otherwise in this letter.
- 6.5 We have not been responsible for investigating or verifying the accuracy of the facts or the reasonableness of any statement of opinion or intention, contained in or relevant to any document referred to in this letter, or that no material facts have been omitted therefrom.
- 6.6 The opinion given in this letter is given on the basis of each of the assumptions set out in paragraph 5 (*Assumptions*) and is subject to each of the reservations set out in paragraph 7 (*Reservations*) to this letter. The opinion given in this letter is strictly limited to the matters stated in paragraph 4 (*Opinion*) and does not extend, and should not be read as extending, by implication or otherwise, to any other matters.
- 6.7 This letter only applies to those facts and circumstances which exist as at today’s date and we assume no obligation or responsibility to update or supplement this letter to reflect any facts or circumstances which may subsequently come to our attention, any changes in laws which may occur after today, or to inform the addressee of any change in circumstances happening after the date of this letter which would alter the opinion given in this letter.
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- 6.8 We have not been responsible for investigation or verification of statements of fact (including statements as to foreign law) or to the reasonableness of any statements of opinion in the Registration Statement, or that no material facts have been omitted therefrom.
- 6.9 This letter is given by Cooley (UK) LLP and no partner or employee assumes any personal responsibility for it nor shall owe any duty of care in respect of it.
- 6.10 This letter, the opinion given in it, and any non-contractual obligations arising out of or in connection with this letter and/or the opinion given in it, are governed by and shall be construed in accordance with English law as at the date of this letter.

7. RESERVATIONS

7.1 The Online Search described at paragraph 3.1 (*Searches*) is not capable of revealing conclusively whether or not:

- (a) a winding-up order has been made or a resolution passed for the winding-up of a company;
- (b) an administration order has been made; or
- (c) a receiver, administrative receiver, administrator or liquidator has been appointed,

since notice of these matters may not be filed with the Registrar of Companies in England and Wales immediately and, when filed, may not be entered on the public database or recorded on the public microfiches of the relevant company immediately.

In addition, such a company search is not capable of revealing, prior to the making of the relevant order, whether or not a winding-up petition or a petition for an administration order has been presented.

- 7.2 The Telephone Enquiry described at paragraph 3.2 (*Searches*) relates only to a compulsory winding-up and is not capable of revealing conclusively whether or not a winding-up petition in respect of a compulsory winding-up has been presented, since details of the petition may not have been entered on the records of the Central Registry of Winding-up Petitions in England and Wales immediately or, in the case of a petition presented to a County Court in England and Wales, may not have been notified to the Central Registry of Winding-up Petitions in England and Wales and entered on such records at all, and the response to an enquiry only relates to the period of approximately four years prior to the date when the enquiry was made. We have not made enquiries of any District Registry or County Court in England and Wales.
- 7.3 The opinion set out in this letter is subject to: (i) any limitations arising from applicable laws relating to insolvency, bankruptcy, administration, reorganisation, liquidation, moratoria, schemes or analogous circumstances; and (ii) an English court exercising its discretion under section 426 of the Insolvency Act (*co-operation between courts exercising jurisdiction in relation to insolvency*) to assist the courts having the corresponding jurisdiction in any part of the United Kingdom or any relevant country or territory.
- 7.4 We express no opinion as to matters of fact.
- 7.5 We have made no enquiries of any individual connected with the Company.
- 7.6 We express no opinion on the compliance of the 2020 Equity Incentive Plan or the ESPP, or the compliance of any award made under the 2020 Equity Incentive Plan or the ESPP, with the rules or regulations of the Nasdaq Global Select Market or the rules or regulations of any other securities exchange that are applicable to the Company.
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7.7 A certificate, documentation, notification, opinion or the like might be held by the English courts not to be conclusive if it can be shown to have an unreasonable or arbitrary basis or in the event of a manifest error.

7.8 We express no opinion in relation to the legality, enforceability or validity of the 2020 Equity Incentive Plan or the ESPP or any award agreement entered into pursuant to the 2020 Equity Incentive Plan or the ESPP. In particular, but without prejudice to the generality of the foregoing, we have assumed that the Shares to be allotted under the 2020 Equity Incentive Plan or the ESPP, as applicable, or any such award agreement will be paid up in full (as to their nominal value and any premium) in cash (within the meaning of section 583(1) of the Companies Act) and we express no opinion as to whether any consideration other than "cash consideration" (as such term is defined in section 583(3) of the Companies Act) which might be paid, or purport to be paid, for the Shares would result in such Shares being validly issued, fully paid and not subject to any call for payment of further capital.

8. DISCLOSURE AND RELIANCE

8.1 This letter is addressed to you solely for your benefit in connection with the Registration Statement. We consent to the filing of this letter as an exhibit to the Registration Statement. In giving such consent, we do not thereby admit that we are in the category of persons whose consent is required under section 7 of the Securities Act or the rules and regulations promulgated thereunder.

8.2 This letter may not be relied upon by you for any other purpose, or furnished to, assigned to, quoted to, or relied upon by any other person, firm or other entity for any purpose, other than for the purpose set out in above in paragraph 8.1, without our prior written consent, which may be granted or withheld at our sole discretion.

Yours faithfully

/s/ Cooley (UK) LLP

Cooley (UK) LLP



CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We hereby consent to the incorporation by reference in this Registration Statement on Form S-8 of Bicycle Therapeutics plc of our report dated March 1, 2022 relating to the financial statements, and the effectiveness of internal control over financial reporting, which appears in Bicycle Therapeutics plc's Annual Report on Form 10-K for the year ended December 31, 2021.

/s/ PricewaterhouseCoopers LLP
Cambridge, United Kingdom
March 1, 2022

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Calculation of Filing Fee Tables

Form S-8
(Form Type)

Bicycle Therapeutics plc
(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

Security Type	Security Class Title	Fee Calculation Rule	Amount Registered	Proposed Maximum Offering Price Per Unit	Maximum Aggregate Offering Price	Fee Rate	Amount of Registration Fee
Equity	Ordinary shares, nominal value £0.01 per share ⁽¹⁾	Rule 457(c) and Rule 457(h)	1,478,968 ⁽²⁾	\$ 44.43 ⁽³⁾	\$ 65,710,548.24 ⁽³⁾	\$92.70 per \$1,000,000	\$ 6,091.37
Equity	Ordinary shares, nominal value £0.01 per share ⁽¹⁾	Rule 457(c) and Rule 457(h)	295,793 ⁽⁴⁾	\$ 37.77 ⁽⁵⁾	\$ 11,172,101.61 ⁽⁵⁾	\$92.70 per \$1,000,000	\$ 1,035.65
Total Offering Amounts					\$ 76,882,649.85		\$ 7,127.02
Total Fee Offsets							—
Net Fee Due							\$ 7,127.02

- (1) These shares may be represented by the American Depositary Shares (“ADSs”) of Bicycle Therapeutics plc (the “Registrant”). Each ADS represents one Ordinary Share. ADSs issuable upon deposit of the Ordinary Shares registered hereby were registered pursuant to a separate Registration Statement on Form F-6 (File No. 333-231422).
- (2) Represents ordinary shares, nominal value £0.01 per share (the “Ordinary Shares”), of the Registrant that became available for issuance under the Bicycle Therapeutics plc 2020 Equity Incentive Plan (the “2020 Plan”), effective as of January 1, 2022, pursuant to the evergreen increase provision of the 2020 Plan. Pursuant to Rule 416 under the Securities Act of 1933, as amended (the “Securities Act”), this Registration Statement shall also cover any additional Ordinary Shares of the Registrant which become issuable under the 2020 Plan by reason of any stock dividend, stock split, recapitalization or any other similar transaction effected without the receipt of consideration which results in an increase in the number of the Registrant’s outstanding Ordinary Shares.
- (3) Estimated solely for the purpose of determining the registration fee pursuant to Rules 457(c) and (h) under the Securities Act, based upon the average of the high and low prices of the Registrant’s ADSs as quoted on the Nasdaq Global Select Market on February 24, 2022.
- (4) Represents Ordinary Shares that became available for issuance under the Bicycle Therapeutics plc 2019 Employee Share Purchase Plan (the “ESPP”), effective as of January 1, 2022, pursuant to the evergreen increase provision of the ESPP. Pursuant to Rule 416 under the Securities Act, this Registration Statement shall also cover any additional Ordinary Shares of the Registrant which become issuable under ESPP by reason of any stock dividend, stock split, recapitalization or any other similar transaction effected without the receipt of consideration which results in an increase in the number of the Registrant’s outstanding Ordinary Shares

- (5) Estimated solely for the purpose of calculating the registration fee pursuant to Rules 457(c) and 457(h) under the Securities Act. The proposed maximum offering price per share and proposed maximum aggregate offering price are based on 85% of the average of the high and low sale prices of the Registrant's ADSs as reported on the Nasdaq Global Select Market on February 24, 2022. Pursuant to the ESPP, the purchase price of the Ordinary Shares reserved for issuance thereunder will be 85% of the fair market value of an Ordinary Share on the first trading day of the offering period or on the exercise date, whichever is lower.
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