

| OMB APPROVAL                                 |           |
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Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

**STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP**

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

|   |   |   |
|---|---|---|
| 1. Name and Address of Reporting Person *<br><u>Keen Nicholas</u><br><br>(Last) (First) (Middle)<br>C/O BICYCLE THERAPEUTICS PLC<br>B900, BABRAHAM RESEARCH CAMPUS<br><br>(Street)<br>CAMBRIDGE X0 CB22 3AT<br><br>(City) (State) (Zip) | 2. Issuer Name and Ticker or Trading Symbol<br><u>BICYCLE THERAPEUTICS plc [ BCYC ]</u> | 5. Relationship of Reporting Person(s) to Issuer<br>(Check all applicable)<br><br>Director 10% Owner<br><input checked="" type="checkbox"/> Officer (give title below) Other (specify below)<br><u>Chief Scientific Officer</u> |
|   | 3. Date of Earliest Transaction (Month/Day/Year)<br><u>01/02/2020</u>                   |   |
| 4. If Amendment, Date of Original Filed (Month/Day/Year)  |   |   |

**Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned**

| 1. Title of Security (Instr. 3) | 2. Transaction Date (Month/Day/Year) | 2A. Deemed Execution Date, if any (Month/Day/Year) | 3. Transaction Code (Instr. 8) |   | 4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5) |            |       | 5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4) | 6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 7. Nature of Indirect Beneficial Ownership (Instr. 4) |
|---------------------------------|--------------------------------------|--|--------------------------------|---|---|------------|-------|---|--|---|
|                                 |                                      |  | Code                           | V | Amount  | (A) or (D) | Price |   |  |   |

**Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)**

| 1. Title of Derivative Security (Instr. 3) | 2. Conversion or Exercise Price of Derivative Security | 3. Transaction Date (Month/Day/Year) | 3A. Deemed Execution Date, if any (Month/Day/Year) | 4. Transaction Code (Instr. 8) |   | 5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5) |     | 6. Date Exercisable and Expiration Date (Month/Day/Year) |                 | 7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4) | 8. Price of Derivative Security (Instr. 5) | 9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4) | 10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4) | 11. Nature of Indirect Beneficial Ownership (Instr. 4) |       |
|--|--|--------------------------------------|--|--------------------------------|---|--|-----|--|-----------------|---|--|--|---|--|-------|
|  |  |                                      |  | Code                           | V | (A)  | (D) | Date Exercisable   | Expiration Date |   |  |  |   |  | Title |
| Employee Stock Option (right to buy)       | \$9.82   | 01/02/2020                           |  | A                              |   | 60,000   |     | (I)  | 01/02/2030      | Ordinary Shares   | 60,000                                     | \$0.00   | 60,000  | D  |       |

**Explanation of Responses:**

1. This option shall vest one-fourth (1/4) of the total number of shares under option on January 2, 2021 and the remaining shares in 36 equal monthly installments at the end of each calendar month thereafter.

**Remarks:**

Exhibit List - Exhibit 24 - Power of Attorney

/s/ Lee Kalowski, Attorney-in-Fact 01/06/2020

\*\* Signature of Reporting Person Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

\* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

\*\* Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.

POWER OF ATTORNEY

(For Executing Form ID and Forms 3, 4 and 5)

Know all by these presents, that the undersigned hereby constitutes and appoints each of Lee Kalowski and Kevin Lee of Bicycle Therapeutics plc (the "Company") and Laura Berezin, Ryan S. Sansom, Brigitte Eichner and Jason Minio of Cooley LLP, signing individually, the undersigned's true and lawful attorneys-in fact and agents to:

(1) Prepare, execute in the undersigned's name and on the undersigned's behalf, and submit to the Securities and Exchange Commission (the "SEC"), a Form ID and Forms 3, 4 and 5 (including amendments thereto and joint filing agreements in connection therewith) in accordance with Section 16 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and the rules thereunder, in the undersigned's capacity as an officer, director or beneficial owner of more than 10% of a registered class of securities of the Company;

(2) Do and perform any and all acts for and on behalf of the undersigned that may be necessary or desirable to prepare and execute any such Form ID and Forms 3, 4 or 5 (including amendments thereto and joint filing agreements in connection therewith) and file such forms with the SEC and any stock exchange, self-regulatory association or any similar authority; and

(3) Take any other action of any type whatsoever in connection with the foregoing that, in the opinion of such attorney-in-fact, may be of benefit to, in the best interest of, or legally required of the undersigned, it being understood that the documents executed by the attorney-in-fact on behalf of the undersigned pursuant to this Power of Attorney shall be in such form and shall contain such terms and conditions as the attorney-in-fact may approve in the attorney-in-fact's discretion.

The undersigned hereby grants to each such attorney in fact full power and authority to do and perform any and every act and thing whatsoever requisite, necessary, or proper to be done in the exercise of any of the rights and powers herein granted, as fully to all intents and purposes as the undersigned might or could do if personally present, with full power of substitution or revocation, hereby ratifying and confirming all that such attorney in fact, or such attorney in fact's substitute or substitutes, shall lawfully do or cause to be done by virtue of this power of attorney and the rights and powers herein granted. The undersigned acknowledges that the foregoing attorneys-in-fact, and their substitutes, in serving in such capacity at the request of the undersigned, are not assuming (nor is the Company assuming) any of the undersigned's responsibilities to comply with Section 16 of the Exchange Act.

This Power of Attorney shall remain in full force and effect until the earliest to occur of (a) the undersigned is no longer required to file Forms 3, 4 and 5 with respect to the undersigned's holdings of and transactions in securities issued by the Company, (b) revocation by the undersigned in a signed writing delivered to the Company and the foregoing attorneys-in fact or (c) as to any attorney-in-fact individually, until such attorney-in-fact is no longer employed by the Company or employed by or a partner at Cooley LLP or another law firm representing the Company, as applicable.

IN WITNESS WHEREOF, the undersigned has caused this Power of Attorney to be executed as of the date written below.

Date: 1/6/2020  
/s/ Nicholas Keen  
Nicholas Keen