

| OMB APPROVAL                                 |           |
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**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

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

|   |   |   |
|---|---|---|
| 1. Name and Address of Reporting Person*<br><u>Lee Kevin</u><br><br>(Last) (First) (Middle)<br><u>C/O BICYCLE THERAPEUTICS PLC</u><br><u>B900, BABRAHAM RESEARCH CAMPUS</u><br><br>(Street)<br><u>CAMBRIDGE X0 CB22 3AT</u><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 (Check all applicable)<br><input checked="" type="checkbox"/> Director 10% Owner<br><input checked="" type="checkbox"/> Officer (give title below) Other (specify below)<br><u>Chief Executive Officer</u> |
|   | 3. Date of Earliest Transaction (Month/Day/Year)<br><u>07/23/2021</u>                   |   |
|   | 4. If Amendment, Date of Original Filed (Month/Day/Year)                                | 6. Individual or Joint/Group Filing (Check Applicable Line)<br><input checked="" type="checkbox"/> Form filed by One Reporting Person<br><input type="checkbox"/> Form filed by More than One Reporting Person  |

**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                  |   |  |   |
| Ordinary Shares                 | 07/23/2021                           |  | M                              |   | 4,782   | A          | \$14                   | 249,867   | D  |   |
| Ordinary Shares                 | 07/23/2021                           |  | s <sup>(1)</sup>               |   | 4,782   | D          | \$36.02 <sup>(2)</sup> | 245,085   | D  |   |
| Ordinary Shares                 | 07/26/2021                           |  | M                              |   | 100   | A          | \$14                   | 245,185   | D  |   |
| Ordinary Shares                 | 07/26/2021                           |  | s <sup>(1)</sup>               |   | 100   | D          | \$36                   | 245,085   | D  |   |

**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 |
| Stock Option (right to buy)                | \$14   | 07/23/2021                           |  | M                              |   |  | 4,782 | (3)  | 06/28/2029      | Ordinary Shares   | 4,782                                      | \$0.00   | 341,470   | D  |       |
| Stock Option (right to buy)                | \$14   | 07/26/2021                           |  | M                              |   |  | 100   | (3)  | 06/28/2029      | Ordinary Shares   | 100  | \$0.00   | 341,370   | D  |       |

**Explanation of Responses:**

- Shares sold pursuant to a Rule 10b5-1 trading plan.
- The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$36.00 to \$36.21 inclusive. The Reporting Person undertakes to provide to the Issuer, any security holder of the Issuer, or the staff of the Securities and Exchange Commission, upon request, full information regarding the number of shares sold at each separate price within the range set forth in this footnote.
- This option shall vest in 36 equal monthly installments at the end of each calendar month following the date of the grant.

**Remarks:**

/s/ Lee Kalowski, Attorney-in-Fact 07/27/2021

\*\* 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.