FORM 4

## UNITED STATES SECURITIES AND EXCHANGE COMMISSION

| Washington, | D.C. | 20549 |
|-------------|------|-------|
|-------------|------|-------|

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

| OMB APPROVAL             |     |  |  |  |  |  |  |  |  |
|--------------------------|-----|--|--|--|--|--|--|--|--|
| OMB Number: 3235-0287    |     |  |  |  |  |  |  |  |  |
| Estimated average burden |     |  |  |  |  |  |  |  |  |
| hours per response:      | 0.5 |  |  |  |  |  |  |  |  |

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

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

| Name and Address of Reporting Person*  Keen Nicholas                             |  |            |          |        | 2. Issuer Name <b>and</b> Ticker or Trading Symbol BICYCLE THERAPEUTICS plc [ BCYC ] |        |                                  |                     |                                |   | (Che  | eck all applic<br>Directo                           | able)   | ng Person(s) to Is                     |  |  |  |
|--|--|------------|----------|--------|--|--------|----------------------------------|---------------------|--------------------------------|---|---|---|---|--|--|--|--|
| (Last) (First) (Middle) C/O BICYCLE THERAPEUTICS PLC                             |  |            |          |        | 3. Date of Earliest Transaction (Month/Day/Year) 01/04/2021                          |        |                                  |                     |                                |   | 7   | below)  |   |  | below)   | poon,  |  |
| B900, BABRAHAM RESEARCH CAMPUS   |  |            |          | 4      | If Amendment, Date of Original Filed (Month/Day/Year)                                |        |                                  |                     |                                |   | 6. Individual or Joint/Group Filing (Check Applicable |   |   |  |  |  |  |
| (Street)   | IDGE X   | 0          | CB22 3AT |        | T. I Americanical, Date of Original Fried (Montariday) Teal)                         |        |                                  |                     |                                | Line  |   |   |   |  |  |  |  |
| (City)   | (S   | tate)      | (Zip)    |        |  |        |                                  |                     |                                |   |   |   |   |  |  |  |  |
| Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned |  |            |          |        |  |        |                                  |                     |                                |   |   |   |   |  |  |  |  |
| 1. Title of Security (Instr. 3)  2. Transac Date (Month/Date)                    |  |            |          |        | Execution Date,  |        | Code (Instr. 5)                  |                     |                                | 4 and Securit   |   | es For<br>ially (D)<br>Following (I) (              |   | : Direct<br>r Indirect<br>str. 4)      | 7. Nature<br>of Indirect<br>Beneficial<br>Ownership<br>(Instr. 4)        |  |  |
|  |  |            |          |        |  |        | Code                             | Amou                | it (A)                         | (A) or (D) Price  |   | Transaction(s)<br>(Instr. 3 and 4)                  |   |  |  |  |  |
|  | Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) |            |          |        |  |        |                                  |                     |                                |   |   |   |   |  |  |  |  |
| 1. Title of<br>Derivative<br>Security<br>(Instr. 3)                              | erivative Conversion Date Execution Date, Courity or Exercise (Month/Day/Year) if any  |            |          | Code ( | ansaction of ode (Instr. Derivative  |        | Expiration Date (Month/Day/Year) |                     | of Secu<br>Underly<br>Derivati | 7. Title and Amou<br>of Securities<br>Underlying<br>Derivative Securi<br>(Instr. 3 and 4) |   | 8. Price of<br>Derivative<br>Security<br>(Instr. 5) | 9. Number<br>derivative<br>Securities<br>Beneficial<br>Owned<br>Following<br>Reported<br>Transactio<br>(Instr. 4) | ve<br>es<br>ally<br>ng<br>d<br>tion(s) | 10.<br>Ownership<br>Form:<br>Direct (D)<br>or Indirect<br>(I) (Instr. 4) | 11. Nature<br>of Indirect<br>Beneficial<br>Ownership<br>(Instr. 4) |  |
|  |  |            |          | Code   | v  | (A)    | (D)                              | Date<br>Exercisable | Expiratio<br>Date              | n Title   | or<br>Nui<br>of                                       | mber<br>ares  |   |  |  |  |  |
| Employee<br>Stock<br>Option<br>(right to<br>buy)                                 | \$17.95  | 01/04/2021 |          | A      |  | 70,500 |                                  | (1)                 | 01/04/203                      | 1 Commo<br>Stock  | 70  | ,500  | \$0.00  | 70,500                                 | )  | D  |  |

## **Explanation of Responses:**

1. This option shall vest one-fourth (1/4) of the total number of shares under option on January 4, 2022 and the remaining shares in 36 equal monthly installments thereafter.

## Remarks:

/s/ Lee Kalowski, Attorney-in-

**Fact** 

01/05/2021

\*\* 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.