

| OMB APPROVAL                                 |           |
|--|-----------|
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**STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP**

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

|   |   |  |
|---|---|--|
| 1. Name and Address of Reporting Person*<br><u>Novartis Bioventures Ltd</u><br><br>(Last) (First) (Middle)<br><u>C/O NOVARTIS INTERNATIONAL AG</u><br><u>WSJ-200.220</u><br><br>(Street)<br><u>CH-4002 BASEL V8 000000000</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><br>Director <input checked="" type="checkbox"/> 10% Owner<br><br>Officer (give title below) Other (specify below)                      |
|   | 3. Date of Earliest Transaction (Month/Day/Year)<br><u>05/28/2019</u>                   |  |
|   | 4. If Amendment, Date of Original Filed (Month/Day/Year)                                | 6. Individual or Joint/Group Filing (Check Applicable Line)<br><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                 | 05/28/2019                           |  | C                              |   | 893,195   | A          | (1)   | 893,195   | D  |   |
| Ordinary Shares                 | 05/28/2019                           |  | X                              |   | 71,450  | A          | (1)   | 964,645   | D  |   |
| Ordinary Shares                 | 05/28/2019                           |  | C                              |   | 636,366   | A          | (1)   | 1,601,011   | D  |   |
| Ordinary Shares                 | 05/28/2019                           |  | P                              |   | 168,630   | A          | \$14  | 1,769,641   | 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   | Amount or Number of Shares |  |  |   |  |
| Series A Preferred Shares                         | (1)  | 05/28/2019                           |  | C                              |   | 893,195  | (1) | (1)  | (1)             | Ordinary Shares   | 893,195                    | (1)  | 0  | D   |  |
| Series A Preferred Shares Warrants <sup>(2)</sup> | (1)  | 05/28/2019                           |  | X                              |   | 71,450   | (1) | (1)  | (1)             | Ordinary Shares <sup>(1)</sup>  | 71,450                     | (1)  | 0  | D   |  |
| Series B1 Preferred Shares                        | (1)  | 05/28/2019                           |  | C                              |   | 636,366  | (1) | (1)  | (1)             | Ordinary Shares   | 636,366                    | (1)  | 0  | D   |  |

1. Name and Address of Reporting Person\*  
Novartis Bioventures Ltd  
 (Last) (First) (Middle)  
C/O NOVARTIS INTERNATIONAL AG  
WSJ-200.220  
 (Street)  
CH-4002 BASEL V8 000000000  
 (City) (State) (Zip)

1. Name and Address of Reporting Person\*  
NOVARTIS AG  
 (Last) (First) (Middle)  
LICHTSTRASSE 35  
 (Street)

(City) (State) (Zip)

**Explanation of Responses:**

1. Each Series A and B1 Preferred Share automatically converted into Ordinary Shares on a one-for-1.429 basis upon the closing of the Issuer's initial public offering and had no expiration date.
2. Upon conversion of all of the Series B1 Preferred Shares into Ordinary Shares in connection with the Issuer's initial public offering, the Warrants became exercisable for Ordinary Shares. The Warrants had an exercise price of a nominal value per share and were exercised immediately prior to completion of the Issuer's initial public offering.

|   |                   |
|---|-------------------|
| <u>Novartis Bioventures Ltd. /s/<br/>Bart Dzikowski, Secretary of<br/>the Board</u> | <u>05/30/2019</u> |
| <u>/s/ Stephan Sandmeier,<br/>Authorized Signatory</u>                              | <u>05/30/2019</u> |
| <u>Novartis AG /s/ Bart<br/>Dzikowski, Attorney-in-Fact</u>                         | <u>05/30/2019</u> |
| <u>/s/ Stephan Sandmeier,<br/>Attorney-in-Fact</u>                                  | <u>05/30/2019</u> |
| ** 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.**