

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* <u>Milnes Alistair</u> (Last) (First) (Middle) <u>C/O BICYCLE THERAPEUTICS PLC</u> <u>BLOCKS A & B, PORTWAY BUILDING</u> (Street) <u>CAMBRIDGE X0 CB21 6GS</u> (City) (State) (Zip)	2. Issuer Name and Ticker or Trading Symbol <u>BICYCLE THERAPEUTICS plc [BCYC]</u>	5. Relationship of Reporting Person(s) to Issuer (Check all applicable) Director <input type="checkbox"/> 10% Owner <input type="checkbox"/> Officer (give title below) <input checked="" type="checkbox"/> Other (specify below) <input type="checkbox"/> <u>Chief Operating Officer</u>
	3. Date of Earliest Transaction (Month/Day/Year) <u>01/03/2023</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			
Ordinary Shares	01/03/2023		A		17,500 ⁽¹⁾	A	\$0.00 ⁽²⁾	39,980	D	
Ordinary Shares	01/03/2023		S ⁽³⁾		1,801	D	\$29.06 ⁽⁴⁾	38,179	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					
Employee Stock Option (right to buy)	\$29.6	01/03/2023		A		35,000		⁽⁵⁾	01/03/2023	Ordinary Shares	35,000		D	

Explanation of Responses:

- Represents a restricted stock unit ("RSU") award. One-fourth (1/4) of the total number of RSUs shall vest on January 3, 2024 and the remaining RSUs shall vest in 12 equal quarterly installments thereafter.
- Each RSU represents a contingent right to receive one ordinary share.
- Represents the number of shares required to be sold to cover the statutory tax withholding obligations in connection with the vesting and settlement of the RSUs. This sale is mandated by the Reporting Person's award agreement that requires the satisfaction of minimum statutory tax withholding obligations to be funded by a "sell to cover" transaction and does not represent a discretionary sale by the Reporting Person.
- The price reported in Column 4 is a weighted average price. These shares were sold in multiple transactions at prices ranging from \$29.00 to \$29.545 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 one-fourth (1/4) of the total number of shares underlying the option on January 3, 2024 and the remaining shares in 36 equal monthly installments thereafter.

Remarks:

/s/ Lee Kalowski, Attorney-in-Fact 01/05/2023

** 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.