

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>BAKER BROS. ADVISORS LP</u> (Last) (First) (Middle) 860 WASHINGTON STREET, 3RD FLOOR (Street) NEW YORK NY 10014 (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) <input checked="" type="checkbox"/> Director <input checked="" type="checkbox"/> 10% Owner Officer (give title below) Other (specify below)
	3. Date of Earliest Transaction (Month/Day/Year) 05/29/2024	
	4. If Amendment, Date of Original Filed (Month/Day/Year)	
Rule 10b5-1(c) Transaction Indication <input type="checkbox"/> Check this box to indicate that a transaction was made pursuant to a contract, instruction or written plan that is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c). See Instruction 10.		

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 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
Non-Voting Ordinary Shares	(1)(2)(3)	05/29/2024		A		1,429,986		(1)(2)(3)	(1)(2)(3)	Ordinary Shares	1,429,986	\$21.42	1,793,439	I	See Footnotes ⁽⁴⁾⁽⁵⁾⁽⁶⁾
Non-Voting Ordinary Shares	(1)(2)(3)	05/29/2024		A		15,684,860		(1)(2)(3)	(1)(2)(3)	Ordinary Shares	15,684,860	\$21.42	20,027,289	I	See Footnotes ⁽⁵⁾⁽⁶⁾⁽⁷⁾

1. Name and Address of Reporting Person*
BAKER BROS. ADVISORS LP
 (Last) (First) (Middle)
 860 WASHINGTON STREET, 3RD FLOOR
 (Street)
 NEW YORK NY 10014
 (City) (State) (Zip)

1. Name and Address of Reporting Person*
667, L.P.
 (Last) (First) (Middle)
 860 WASHINGTON STREET, 3RD FLOOR
 (Street)
 NEW YORK NY 10014
 (City) (State) (Zip)

1. Name and Address of Reporting Person*
Baker Bros. Advisors (GP) LLC
 (Last) (First) (Middle)
 860 WASHINGTON STREET, 3RD FLOOR
 (Street)
 NEW YORK NY 10014
 (City) (State) (Zip)

1. Name and Address of Reporting Person*
Baker Brothers Life Sciences LP

(Last)	(First)	(Middle)
860 WASHINGTON STREET, 3RD FLOOR		
(Street)		
NEW YORK	NY	10014
(City)	(State)	(Zip)
1. Name and Address of Reporting Person*		
BAKER FELIX		
(Last)	(First)	(Middle)
860 WASHINGTON STREET, 3RD FLOOR		
(Street)		
NEW YORK	NY	10014
(City)	(State)	(Zip)
1. Name and Address of Reporting Person*		
BAKER JULIAN		
(Last)	(First)	(Middle)
860 WASHINGTON STREET, 3RD FLOOR		
(Street)		
NEW YORK	NY	10014
(City)	(State)	(Zip)

Explanation of Responses:

- 667, L.P. ("667") and Baker Brothers Life Sciences, L.P. ("Life Sciences" and, together with 667, the "Funds") purchased, respectively, 1,429,986 and 15,684,860 non-voting ordinary shares ("May 2024 Non-Voting Ordinary Shares") of Bicycle Therapeutics plc (the "Issuer") for \$21.42 per share pursuant to a private placement that closed on May 29, 2024 (the "Offering"). The May 2024 Non-Voting Ordinary Shares and the Pre-Offering Non-Voting Ordinary Shares (as defined below) (collectively, the "Non-Voting Ordinary Shares") have no expiration date and are convertible immediately at any time at the option of the holder on a 1-for-1 basis without consideration into ordinary shares of the Issuer ("Ordinary Shares") to the extent that immediately prior to or after giving effect to such conversion the holders thereof, together with their affiliates and any members of a Section 13(d) group with such holders, (continued in footnote 2)
- would beneficially own, for purposes of Rule 13d-3 under the Securities Act of 1934, as amended, no more than 9.99% of the outstanding Ordinary Shares (the "Beneficial Ownership Limitation") following such conversion. By written notice to the Issuer, the Funds may from time to time increase or decrease the Beneficial Ownership Limitation applicable to that Fund to any other percentage not in excess of 19.9%. Any such increase will not be effective until the 61st day after such notice is delivered to the Issuer. Baker Bros. Advisors LP (the "Adviser") on behalf of the Funds submitted written notice to the Issuer of an increase in the Beneficial Ownership Limitation from 9.99% to 19.9% on April 16, 2024 related to the 4,705,882 Non-Voting Ordinary Shares held prior to the Offering ("Pre-Offering Non-Voting Ordinary Shares"). This increase in the Beneficial Ownership Limitation on the Pre-Offering Non-Voting Ordinary Shares will take effect on June 16, 2024.
- The Adviser on behalf of the Funds submitted written notice to the Issuer on May 28, 2024 of an increase in the Beneficial Ownership Limitation from 9.99% to 19.9% on May 29, 2024 related to the May 2024 Non-Voting Ordinary Shares. This increase in the Beneficial Ownership Limitation on the May 2024 Non-Voting Ordinary Shares will take effect on July 29, 2024.
- After giving effect to the transactions reported herein and as a result of their ownership interest in (i) Baker Biotech Capital, L.P. and (ii) 667, Julian C. Baker and Felix J. Baker each may be deemed to have an indirect pecuniary interest in the securities reported in column 9 of Table II held directly by 667, a limited partnership of which the sole general partner is Baker Biotech Capital, L.P., a limited partnership of which the sole general partner is Baker Biotech Capital (GP), LLC, due to their interest in 667 and Baker Biotech Capital, L.P.'s right to receive an allocation of a portion of the profits from 667.
- The Adviser serves as the investment adviser to the Funds. In connection with the services provided by the Adviser, the Adviser receives an asset-based management fee that does not confer any pecuniary interest in the securities held directly by the Funds or for the benefit of Funds. Baker Bros. Advisors (GP) LLC (the "Adviser GP") is the Adviser's sole general partner. Julian C. Baker and Felix J. Baker are managing members of the Adviser GP. The Adviser has complete and unlimited discretion and authority with respect to the investment and voting power of the securities held directly by the Funds or for the benefit of the Funds. The general partners of the Funds relinquished to the Adviser all discretion and authority with respect to the investment and voting power of the securities held directly by the Funds or for the benefit of the Funds.
- Julian C. Baker, Felix J. Baker, the Adviser GP and the Adviser disclaim beneficial ownership of the securities held directly by the Funds or for the benefit of the Funds except to the extent of their pecuniary interest therein, and this report shall not be deemed an admission that any of Julian C. Baker, Felix J. Baker, the Adviser GP or the Adviser is a beneficial owner of such securities for purposes of Section 16 or any other purpose.
- After giving effect to the transaction reported herein and as a result of their ownership interest in (i) Baker Brothers Life Sciences Capital, L.P. and (ii) Life Sciences, Julian C. Baker and Felix J. Baker may be deemed to have an indirect pecuniary interest in the securities reported in column 9 of Table II directly held by Life Sciences, a limited partnership of which the sole general partner is Baker Brothers Life Sciences Capital, L.P., a limited partnership of which the sole general partner is Baker Brothers Life Sciences Capital (GP), LLC, due to their interest in Life Sciences and Baker Brothers Life Sciences Capital, L.P.'s right to receive an allocation of a portion of the profits from Life Sciences.

Remarks:

Felix J. Baker, a managing member of Baker Bros. Advisors (GP) LLC, the sole general partner of Baker Bros. Advisors LP, is a director of Bicycle Therapeutics plc (the "Issuer"). By virtue of their representation on the board of directors of the Issuer, for purposes of Section 16 of the Securities Exchange Act of 1934, as amended, the reporting persons other than Felix J. Baker are deemed directors by deputization of the Issuer.

[By: Baker Bros. Advisors LP,](#)
[Name: Scott L. Lessing, Title: 05/29/2024](#)
[President /s/ Scott L. Lessing](#)
[Baker Bros. Advisors LP, Mgmt.](#)
[Co. and Inv. Adviser to 667, L.P.,](#)
[pursuant to authority granted by](#)
[Baker Biotech Capital, L.P., GP to 05/29/2024](#)
[667, L.P. Name: Scott L. Lessing,](#)
[Title: President /s/ Scott L.](#)
[Lessing](#)
[By: Baker Bros. Advisors \(GP\),](#)
[LLC, Name: Scott L. Lessing, 05/29/2024](#)
[Title: President /s/ Scott L.](#)
[Lessing](#)
[Baker Bros. Advisors LP, Mgmt.](#)
[Co. and Inv. Adviser to BAKER](#)
[BROTHERS LIFE SCIENCES,](#)
[L.P., pursuant to](#)
[authority granted by Baker 05/29/2024](#)
[Brothers Life Sciences Capital,](#)
[L.P., GP to Baker Brothers Life](#)
[Sciences, L.P., Name: Scott L.](#)
[Lessing, Title: President /s/](#)
[/s/ Felix J. Baker 05/29/2024](#)
[/s/ Julian C. Baker 05/29/2024](#)

** 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.