

INITIAL STATEMENT OF BENEFICIAL OWNERSHIP OF SECURITIES

OMB APPROVAL	
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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. Date of Event Requiring Statement (Month/Day/Year) 04/18/2024	3. Issuer Name and Ticker or Trading Symbol <u>BICYCLE THERAPEUTICS plc</u> [<u>BCYC</u>]	
		4. 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)	5. If Amendment, Date of Original Filed (Month/Day/Year) 6. Individual or Joint/Group Filing (Check Applicable Line) <input type="checkbox"/> Form filed by One Reporting Person <input checked="" type="checkbox"/> Form filed by More than One Reporting Person

Table I - Non-Derivative Securities Beneficially Owned

1. Title of Security (Instr. 4)	2. Amount of Securities Beneficially Owned (Instr. 4)	3. Ownership Form: Direct (D) or Indirect (I) (Instr. 5)	4. Nature of Indirect Beneficial Ownership (Instr. 5)
American Depositary Shares	579,856	I	See Footnotes ⁽¹⁾⁽²⁾⁽³⁾⁽⁴⁾
American Depositary Shares	6,437,320	I	See Footnotes ⁽¹⁾⁽³⁾⁽⁴⁾⁽⁵⁾

Table II - Derivative Securities Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

1. Title of Derivative Security (Instr. 4)	2. Date Exercisable and Expiration Date (Month/Day/Year)		3. Title and Amount of Securities Underlying Derivative Security (Instr. 4)		4. Conversion or Exercise Price of Derivative Security	5. Ownership Form: Direct (D) or Indirect (I) (Instr. 5)	6. Nature of Indirect Beneficial Ownership (Instr. 5)
	Date Exercisable	Expiration Date	Title	Amount or Number of Shares			
Non-Voting Ordinary Shares ⁽⁶⁾	(6)(7)	(6)	Ordinary Shares	363,453	(6)	I	See Footnotes ⁽²⁾⁽³⁾⁽⁴⁾
Non-Voting Ordinary Shares ⁽⁶⁾	(6)(7)	(6)	Ordinary Shares	4,342,429	(6)	I	See Footnotes ⁽³⁾⁽⁴⁾⁽⁵⁾

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:

- American Depositary Shares ("ADS") of Bicycle Therapeutics plc (the "Issuer") each represent 1 Ordinary Share ("Ordinary Shares") of the Issuer.
- As a result of their ownership interest in (i) Baker Biotech Capital, L.P. and (ii) 667, L.P. ("667"), Julian C. Baker and Felix J. Baker each may be deemed to have an indirect pecuniary interest in the securities reported in column 2 of Table I and column 3 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.
- Baker Bros. Advisors LP (the "Adviser") serves as the investment adviser to 667 and Baker Brothers Life Sciences, L.P. ("Life Sciences" and together with 667, 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. 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. 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.
- 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.
- 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 each may be deemed to have an indirect pecuniary interest in the securities reported in column 2 of Table I and column 3 of Table II held directly 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.
- These securities consist of non-voting ordinary shares of the Issuer ("Non-Voting Ordinary Shares") convertible at any time at the option of the holder on a 1-for-1 basis without consideration into 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, 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. The Non-Voting Ordinary Shares have no expiration date.

7. 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. The Funds notified the Issuer of an increase in the Beneficial Ownership Limitation from 9.99% to 19.9% on April 16, 2024. This increase in the Beneficial Ownership Limitation will be effective on June 16, 2024.

Remarks:

Felix J. Baker, a managing member of Baker Bros. Advisors (GP) LLC, was appointed as director on April 18, 2024 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: President /s/ 04/18/2024

Scott L. Lessing
Baker Bros. Advisors LP,
Mgmt. Co. and Inv.
Adviser to 667, L.P.,
pursuant to authority
granted by Baker Biotech 04/18/2024
Capital, L.P., GP to 667,

L.P. Name: Scott L.
Lessing, Title: President /s/
Scott L. Lessing

By: Baker Bros. Advisors
(GP) LLC, Name: Scott L. 04/18/2024
Lessing, 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. 04/18/2024
Baker 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 04/18/2024

/s/ Julian C. Baker 04/18/2024

** 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 5 (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.

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