

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* <b>BAKER BROS. ADVISORS LP</b>			2. Issuer Name and Ticker or Trading Symbol <b>BICYCLE THERAPEUTICS plc [ BCYC ]</b>			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)		
(Last)	(First)	(Middle)	3. Date of Earliest Transaction (Month/Day/Year) <b>04/18/2024</b>			6. Individual or Joint/Group Filing (Check Applicable Line) Form filed by One Reporting Person <input checked="" type="checkbox"/> Form filed by More than One Reporting Person		
860 WASHINGTON STREET, 3RD FLOOR			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.		
(Street)	NEW YORK NY 10014							
(City)	(State)	(Zip)						

**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			
American Depositary Shares	04/18/2024		A		12,000 <sup>(1)</sup>	A	\$0	591,856	I	See Footnotes <sup>(1)(2)(3)(4)(5)(6)(7)(8)</sup>
American Depositary Shares	04/18/2024		A		12,000 <sup>(1)</sup>	A	\$0	6,449,320	I	See Footnotes <sup>(1)(3)(4)(5)(6)(7)(8)(9)</sup>

**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
Share Option (Right to Buy)	\$21.82	04/18/2024		A		24,000 <sup>(10)</sup>		(10)	04/18/2034	American Depositary Shares	24,000	\$0	24,000	I	See Footnotes <sup>(2)(3)(4)(5)(6)(7)(8)(10)</sup>
Share Option (Right to Buy)	\$21.82	04/18/2024		A		24,000 <sup>(10)</sup>		(10)	04/18/2034	American Depositary Shares	24,000	\$0	24,000	I	See Footnotes <sup>(3)(4)(5)(6)(7)(8)(9)(10)</sup>

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 <sup>*</sup>		
<a href="#">Baker Brothers Life Sciences LP</a>		
(Last)	(First)	(Middle)
860 WASHINGTON STREET, 3RD FLOOR		
(Street)		
NEW YORK	NY	10014
(City) (State) (Zip)		
1. Name and Address of Reporting Person <sup>*</sup>		
<a href="#">BAKER FELIX</a>		
(Last)	(First)	(Middle)
860 WASHINGTON STREET, 3RD FLOOR		
(Street)		
NEW YORK	NY	10014
(City) (State) (Zip)		
1. Name and Address of Reporting Person <sup>*</sup>		
<a href="#">BAKER JULIAN</a>		
(Last)	(First)	(Middle)
860 WASHINGTON STREET, 3RD FLOOR		
(Street)		
NEW YORK	NY	10014
(City) (State) (Zip)		

**Explanation of Responses:**

- Includes 12,000 restricted stock units (each an "RSU") payable solely in American Depositary Shares ("ADS") of Bicycle Therapeutics plc (the "Issuer") granted by the Issuer to Felix J. Baker, a managing member of Baker Bros. Advisors (GP) LLC (the "Adviser GP") on April 18, 2024, pursuant to the Issuer's 2020 Equity Incentive Plan (the "2020 Plan"). The RSUs vest in three equal annual installments beginning on April 18, 2025, subject to Felix J. Baker's continuous service on the board of directors of the Issuer (the "Board") through the vesting date. Felix J. Baker serves on the Board as a representative of 667, L.P. ("667") and Baker Brothers Life Sciences, L.P. ("Life Sciences", and together with 667, the "Funds"). Each RSU represents a contingent right to receive one Ordinary Share.
- 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 5 of Table I and in column 9 of Table II held directly by or held for the benefit of 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 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. 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 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.
- Pursuant to the policies of the Adviser, Felix J. Baker does not have any right to any of the Issuer's securities issued as part of his service on the Board and the Funds are entitled to an indirect proportionate pecuniary interest in the securities. The Funds each own an indirect proportionate pecuniary interest in the ADS received upon vesting of RSUs and non-qualified share options convertible solely into ADS of the Issuer ("Share Options") received as a result of his service on the Board. Solely as a result of their ownership interest in (i) the general partners of the Funds and (ii) the Funds, Felix J. Baker and Julian C. Baker may be deemed to have an indirect pecuniary interest in the ADS upon vesting of RSUs, Share Options, and ADS received upon the exercise of Share Options (i.e. no direct pecuniary interest).
- The acquisitions of the RSUs and Share Options reported on this form represent a single grant to Felix J. Baker of 12,000 RSUs on Table I and 24,000 Share Options on Table II. These grants, totaling 12,000 RSUs and 24,000 Share Options for Felix J. Baker, are reported for each of the Funds as each has an indirect pecuniary interest in such securities.
- Pursuant to agreements between Felix J. Baker and the Adviser and the policies of the Adviser, the Adviser has voting and dispositive power over the Share Options, RSUs and any ADS received as a result of the exercise of Share Options or vesting of RSUs.
- ADS each represent 1 Ordinary Share.
- 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 5 of Table I and in column 9 of Table II directly held by or held for the benefit of 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.
- Includes 24,000 Share Options granted by the Issuer to Felix J. Baker, in his capacity as a director of the Issuer pursuant to the 2020 Plan. The Share Options have a strike price of \$21.82 and vest in three equal annual installments beginning on April 18, 2025, provided, however, that all vesting of Share Options granted to a director shall cease if that director resigns from the Board or otherwise ceases to serve as a director, unless the Board determines otherwise.

**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 deputation of the Issuer.

[By: Baker Bros. Advisors LP.](#)  
[Name: Scott L. Lessing, Title: 04/22/2024](#)  
[President /s/ Scott L. Lessing](#)  
[Baker Bros. Advisors LP, Mgmt.](#)  
[Co. and Inv. Adviser to 667, L.P.,](#)  
[pursuant to authority granted by 04/22/2024](#)  
[Baker Biotech 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. Lessing. 04/22/2024](#)  
[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 Brothers 04/22/2024](#)  
[Life Sciences Capital, L.P., GP to](#)  
[Baker Brothers Life Sciences, L.P.,](#)  
[Name: Scott L. Lessing,](#)  
[Title: President /s/](#)  
[/s/ Felix J. Baker 04/22/2024](#)  
[/s/ Julian C. Baker 04/22/2024](#)  
 \*\* Signature of Reporting Person Date

\* 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.**