
UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

SCHEDULE 13D
Under the Securities Exchange Act of 1934

(Amendment No. 2)*

Bicycle Therapeutics plc

(Name of Issuer)

Ordinary Shares, nominal value £0.01 per share

(Title of Class of Securities)

088786108**

(CUSIP number)

Alexandra A. Toohey
Chief Financial Officer
Baker Bros. Advisors LP
860 Washington Street, 3rd Floor
New York, NY 10014
(212) 339-5690

(Name, address and telephone number of person authorized to receive notices and communications)

December 13, 2024

(Date of event which requires filing of this statement)

If the filing person has previously filed a statement on Schedule 13G to report the acquisition that is the subject of this Schedule 13D, and is filing this schedule because of Rule 13d-1(e), 13d-1(f) or 13d-1(g), check the following box.

(Continued on the following pages)

Note: Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See Rule 13d-7 for other parties to whom copies are to be sent.

*The remainder of this cover page shall be filled out for a reporting person's initial filing on this form with respect to the subject class of securities, and for any subsequent amendment containing information which would alter disclosures provided in a prior cover page.

The information required on the remainder of this cover page shall not be deemed to be "filed" for the purpose of Section 18 of the Securities Exchange Act of 1934 ("Act") or otherwise subject to the liabilities of that section of the Act but shall be subject to all other provisions of the Act (however, see the Notes).

**This CUSIP applies to the American Depositary Shares, each representing one Ordinary Share.

1. NAMES OF REPORTING PERSONS Baker Bros. Advisors LP	
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (b) <input type="checkbox"/> (a) <input type="checkbox"/>
3.	SEC USE ONLY
4.	SOURCE OF FUNDS (See Instructions) OO
5.	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>
6.	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7. SOLE VOTING POWER 10,885,357 (1)
	8. SHARED VOTING POWER: 0
	9. SOLE DISPOSITIVE POWER: 10,885,357 (1)
	10. SHARED DISPOSITIVE POWER: 0
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 10,885,357 (1)
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 22.9% (1)(2)
14.	TYPE OF REPORTING PERSON (See Instructions) IA, PN

(1) Includes 10,885,357 Ordinary Shares ("Ordinary Shares") of Bicycle Therapeutics plc (the "Issuer") held in the form of 10,885,357 American Depositary Shares ("ADS"). Each ADS represents one Ordinary Share of the Issuer.

(2) Based on 47,553,922 Ordinary Shares of the Issuer outstanding as of October 28, 2024, as reported in the Issuer's Form 10-Q filed with the Securities and Exchange Commission ("SEC") on October 31, 2024.

1.	NAMES OF REPORTING PERSONS Baker Bros. Advisors (GP) LLC	
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP*	(b) <input type="checkbox"/> (a) <input type="checkbox"/>
3.	SEC USE ONLY	
4.	SOURCE OF FUNDS (See Instructions) OO	
5.	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>	
6.	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER 10,885,357 (1)
	8.	SHARED VOTING POWER: 0
	9.	SOLE DISPOSITIVE POWER: 10,885,357 (1)
	10.	SHARED DISPOSITIVE POWER: 0
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 10,885,357 (1)	
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>	
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 22.9% (1)(2)	
14.	TYPE OF REPORTING PERSON (See Instructions) HC, OO	

(1) Includes 10,885,357 Ordinary Shares held in the form of 10,885,357 ADS. Each ADS represents one Ordinary Share.

(2) Based on 47,553,922 Ordinary Shares of the Issuer outstanding as of October 28, 2024, as reported in the Issuer's Form 10-Q filed with the SEC on October 31, 2024.

1.	NAMES OF REPORTING PERSONS Julian C. Baker		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP*		(b) <input type="checkbox"/> (a) <input type="checkbox"/>
3.	SEC USE ONLY		
4.	SOURCE OF FUNDS (See Instructions) OO		
5.	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION United States		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 10,885,357 (1)	
	8.	SHARED VOTING POWER: 0	
	9.	SOLE DISPOSITIVE POWER: 10,885,357 (1)	
	10.	SHARED DISPOSITIVE POWER: 0	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 10,885,357 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 22.9% (1)(2)		
14.	TYPE OF REPORTING PERSON (See Instructions) IN, HC		

(1) Includes 10,885,357 Ordinary Shares held in the form of 10,885,357 ADS. Each ADS represents one Ordinary Share.

(2) Based on 47,553,922 Ordinary Shares of the Issuer outstanding as of October 28, 2024, as reported in the Issuer's Form 10-Q filed with the SEC on October 31, 2024.

1.	NAMES OF REPORTING PERSONS Felix J. Baker		
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP*		(b) <input type="checkbox"/> (a) <input type="checkbox"/>
3.	SEC USE ONLY		
4.	SOURCE OF FUNDS (See Instructions) OO		
5.	CHECK BOX IF DISCLOSURE OF LEGAL PROCEEDINGS IS REQUIRED PURSUANT TO ITEM 2(d) or 2(e) <input type="checkbox"/>		
6.	CITIZENSHIP OR PLACE OF ORGANIZATION United States		
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	7.	SOLE VOTING POWER: 10,885,357 (1)	
	8.	SHARED VOTING POWER: 0	
	9.	SOLE DISPOSITIVE POWER: 10,885,357 (1)	
	10.	SHARED DISPOSITIVE POWER: 0	
11.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON: 10,885,357 (1)		
12.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (11) EXCLUDES CERTAIN SHARES (See Instructions) <input type="checkbox"/>		
13.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW (11) 22.9% (1)(2)		
14.	TYPE OF REPORTING PERSON (See Instructions) IN, HC		

(1) Includes 10,885,357 Ordinary Shares held in the form of 10,885,357 ADS. Each ADS represents one Ordinary Share.

(2) Based on 47,553,922 Ordinary Shares of the Issuer outstanding as of October 28, 2024, as reported in the Issuer's Form 10-Q filed with the SEC on October 31, 2024.

Amendment No. 2 to Schedule 13D

This Amendment No. 2 to Schedule 13D amends and supplements the previously filed Schedule 13D filed by Baker Bros. Advisors LP (the “Adviser”), Baker Bros. Advisors (GP) LLC (the “Adviser GP”), Julian C. Baker and Felix J. Baker (collectively, the “Reporting Persons”). Except as supplemented herein, such statements, as heretofore amended and supplemented, remain in full force and effect.

The Adviser GP is the sole general partner of the Adviser. Pursuant to management agreements, as amended, among the Adviser, Baker Brothers Life Sciences, L.P. (“Life Sciences”) and 667, L.P. (“667”, and together with Life Sciences, the “Funds”), and their respective general partners, the Funds’ respective general partners relinquished to the Adviser all discretion and authority with respect to the investment and voting power of the securities held by the Funds, and thus the Adviser has complete and unlimited discretion and authority with respect to the Funds’ investments and voting power over investments.

All capitalized terms contained herein but not otherwise defined shall have the meanings ascribed to such terms in the Schedule 13D, as amended. Information given in response to each item shall be deemed incorporated by reference in all other items, as applicable.

Item 3. Source and Amount of Funds or Other Consideration.

Item 3 of Schedule 13D is supplemented and amended, as the case may be, as follows:

The disclosure in Item 5(c) below is incorporated herein by reference.

The Reporting Persons may in the ordinary course of business hold securities in margin accounts maintained for the Funds with prime brokers, which extend margin credit as and when required, subject to applicable margin regulations, stock exchange rules and such firms’ credit policies. Positions in securities may be pledged as collateral security for the repayment of debit balances in such accounts.

Item 4. Purpose of the Transaction.

Item 4 of this Schedule 13D is supplemented and amended, as the case may be, as follows:

This Amendment No. 2 is being filed to report the purchase of American Depositary Shares (“ADS”) of Bicycle Therapeutics plc (the “Issuer”) reported in Item 5(c) that resulted in a more than 1 percent change in beneficial ownership. Each ADS represents one Ordinary Share of the Issuer. The disclosure regarding the purchases in Item 5(c) below is incorporated herein by reference.

Non-Voting Ordinary Shares are only convertible on a 1-for-1 basis into Ordinary Shares (“Non-Voting Ordinary Shares”) to the extent that after giving effect to such conversion the holders thereof, their affiliates and any persons who are members of a Section 13(d) group with the holders or their affiliates would beneficially own in the aggregate, for purposes of Rule 13d-3 under the Exchange Act, no more than 19.9% of the outstanding Ordinary Shares (“Beneficial Ownership Limitation”). 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. As a result of this restriction, the number of Ordinary Shares that may be issued upon conversion of the Non-Voting Ordinary Shares by the above holders may change depending upon changes in the outstanding Ordinary Shares. As a result of this restriction the Funds cannot presently convert any of the Non-Voting Ordinary Shares.

The Funds hold securities of the Issuer for investment purposes. The Reporting Persons or their affiliates may purchase additional securities or dispose of securities in varying amounts and at varying times depending upon the Reporting Persons’ continuing assessments of pertinent factors, including the availability of Ordinary Shares or ADS or other securities for purchase at particular price levels, the business prospects of the Issuer, other business investment opportunities, economic conditions, stock market conditions, money market conditions, the attitudes and actions of the Board and management of the Issuer, the availability and nature of opportunities to dispose of securities of the Issuer and other plans and requirements of the particular entities.

The Reporting Persons may discuss items of mutual interest with the Issuer’s management, other members of the Board and other investors, which could include items in subparagraphs (a) through (j) of Item 4 Schedule 13D.

Depending upon their assessments of the above factors, the Reporting Persons or their affiliates may change their present intentions as stated above and they may assess whether to make suggestions to the management of the Issuer regarding financing, and whether to acquire additional securities of the Issuer, including Ordinary Shares or ADS (by means of open market purchases, privately negotiated purchases, exercise of some or all of the Share Options, conversion of Non-Voting Ordinary Shares, or otherwise) or to dispose of some or all of the securities of the Issuer, including Ordinary Shares or ADS, under their control. Except as otherwise disclosed herein, at the present time, the Reporting Persons do not have any plans or proposals with respect to any extraordinary corporate transaction involving the Issuer including, without limitation, those matters described in subparagraphs (a) through (j) of Item 4 of Schedule 13D.

Item 5. Interest in Securities of the Issuer.

The disclosure in Item 4 is incorporated by reference herein.

(a) and (b) Items 7 through 11 and 13 of each of the cover pages of this Amendment No. 2 are incorporated herein by reference. Set forth below is the aggregate number of Ordinary Shares held in the form of ADS directly held by each of the Funds, which may be deemed to be indirectly beneficially owned by the Reporting Persons, as well as Ordinary Shares that may be acquired upon conversion of Non-Voting Ordinary Shares, subject to the limitations on conversion described above.

Holder	American Depositary Shares	Non-Voting Ordinary Shares
667, L.P.	902,083	1,597,341
Baker Brothers Life Sciences, L.P.	9,983,274	17,840,603
Total	10,885,357	19,437,944

Felix J. Baker, an independent director and a Class I director, serves as a member of the Nominating and Corporate Governance Committee and the Scientific Committee until the Issuer’s 2026 annual general meeting of shareholders and until his successor has been duly elected and qualified or until his earlier death, resignation or removal.

Felix J. Baker holds 24,000 options to purchase ADS at an exercise price of \$21.82 per share which vest in three equal annual installments over a three-year period commencing on April 18, 2025, subject to continued service throughout the applicable vesting dates and expire on April 18, 2034 (“Share Options”), none of which will vest within sixty days following the date of this filing. Felix J. Baker also holds 12,000 restricted stock units (each, an “RSU”) which vest into ADS in three equal annual installments over a three-year period commencing on April 18, 2025, subject to continued service throughout the applicable vesting dates. The policies of the Funds and the Adviser do not permit managing members of the Adviser GP to receive compensation for serving as a director of the Issuer, and the Funds are instead entitled to the pecuniary interest in any compensation received for Felix J. Baker’s service on the Board.

The Adviser has voting and investment power over the Share Options, Ordinary Shares underlying such Share Options, Ordinary Shares received from the exercise of Share Options, RSUs and Ordinary Shares received from the vesting of RSUs by Felix J. Baker received as directors' compensation. The Adviser GP, and Felix J. Baker and Julian C. Baker as managing members of the Adviser GP, may be deemed to have the power to vote or direct the vote of and the power to dispose or direct the disposition of the Share Options, Ordinary Shares received from the exercise of Share Options, Ordinary Shares underlying such Share Options, RSUs and Ordinary Shares received from the vesting of RSUs held by Felix J. Baker received as director's compensation.

(c) The following transactions in ADS were effected by the Funds during the sixty days preceding the filing of this statement. All transactions were effected in the over-the-counter market directly with a broker-dealer. Except as disclosed herein, none of the Reporting Persons or their affiliates has effected any other transactions in securities of the Issuer during the past 60 days.

Name	Date	Number of Shares	Transaction	Price/Share	Footnote
667, L.P.	12/13/2024	2,809	Purchase	13.4979	1
Baker Brothers Life Sciences, L.P.	12/13/2024	30,241	Purchase	13.4979	1
667, L.P.	12/13/2024	5,573	Purchase	13.6288	2
Baker Brothers Life Sciences, L.P.	12/13/2024	59,995	Purchase	13.6288	2
667, L.P.	12/13/2024	22,722	Purchase	13.7242	3
Baker Brothers Life Sciences, L.P.	12/13/2024	244,587	Purchase	13.7242	3
667, L.P.	12/13/2024	52,656	Purchase	13.8040	4
Baker Brothers Life Sciences, L.P.	12/13/2024	566,814	Purchase	13.8040	4
667, L.P.	12/16/2024	42,369	Purchase	15.3418	5
Baker Brothers Life Sciences, L.P.	12/16/2024	457,631	Purchase	15.3418	5

(1) The reported price is a weighted average price. These shares were traded in multiple transactions at a prices ranging from \$13.32 to \$13.50. The Reporting Persons undertake to provide the staff of the Securities and Exchange Commission (the "Staff"), upon request, full information regarding the number of shares traded at each separate price within the ranges set forth in this footnote.

(2) The reported price is a weighted average price. These shares were traded in multiple transactions at prices ranging from \$13.42 to \$13.89. The Reporting Persons undertake to provide the Staff, upon request, full information regarding the number of shares traded at each separate price within the ranges set forth in this footnote.

(3) The reported price is a weighted average price. These shares were traded in multiple transactions at prices ranging from \$13.44 to \$13.81. The Reporting Persons undertake to provide the Staff, upon request, full information regarding the number of shares traded at each separate price within the ranges set forth in this footnote.

(4) The reported price is a weighted average price. These shares were traded in multiple transactions at prices ranging from \$13.48 to \$14.00. The Reporting Persons undertake to provide the Staff, upon request, full information regarding the number of shares traded at each separate price within the ranges set forth in this footnote.

(5) The reported price is a weighted average price. These shares were traded in multiple transactions at prices ranging from \$15.11 to \$15.49. The Reporting Persons undertake to provide the Staff, upon request, full information regarding the number of shares traded at each separate price within the ranges set forth in this footnote.

(d) Certain securities of the Issuer are held directly by 667, a limited partnership the sole general partner of which is Baker Biotech Capital, L.P., a limited partnership the sole general partner of which is Baker Biotech Capital (GP), LLC. Julian C. Baker and Felix J. Baker are the managing members of Baker Biotech Capital (GP), LLC.

Certain securities of the Issuer are held directly by Life Sciences, a limited partnership the sole general partner of which is Baker Brothers Life Sciences Capital, L.P., a limited partnership the sole general partner of which is Baker Brothers Life Sciences Capital (GP), LLC. Julian C. Baker and Felix J. Baker are the managing members of Baker Brothers Life Sciences Capital (GP), LLC.

(e) Not applicable.

SIGNATURE

After reasonable inquiry and to the best of my knowledge and belief, I certify that the information set forth in this statement is true, complete and correct.

Dated: December 17, 2024

BAKER BROS. ADVISORS LP

By: Baker Bros. Advisors (GP) LLC, its general partner

By: /s/ Scott L. Lessing

Name: Scott L. Lessing
Title: President

BAKER BROS. ADVISORS (GP) LLC

By: /s/ Scott L. Lessing

Name: Scott L. Lessing
Title: President

/s/ Julian C. Baker

Julian C. Baker

/s/ Felix J. Baker

Felix J. Baker
