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SCHEDULE 13G

SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549

Under the Securities Exchange Act of 1934  
(Amendment No. 1)\*

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**Achilles Therapeutics plc**

(Name of Issuer)

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**Ordinary Shares, nominal value £0.001 per share**

(Title of Class of Securities)

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**00449L102\*\***

(CUSIP Number)

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**December 31, 2022**

(Date of Event which Requires Filing of this Statement)

Check the appropriate box to designate the rule pursuant to which this Schedule is filed:

Rule 13d-1(b)

Rule 13d-1(c)

Rule 13d-1(d)

\*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 (the "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

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1	<b>NAMES OF REPORTING PERSONS</b> Baker Bros. Advisors LP	
2	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	<b>SEC USE ONLY</b>	
4	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> Delaware	
	5	<b>SOLE VOTING POWER</b> 4,207,733 (1)
	6	<b>SHARED VOTING POWER</b> -0-
	7	<b>SOLE DISPOSITIVE POWER</b> 4,207,733 (1)
	8	<b>SHARED DISPOSITIVE POWER</b> -0-
9	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 4,207,733 (1)	
10	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>	
11	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 9.9% (1)(2)	
12	<b>TYPE OF REPORTING PERSON (See Instructions)</b> IA, PN	

(1) Includes 2,591,366 Ordinary Shares ("Ordinary Shares") of Achilles Therapeutics plc (the "Issuer") that are represented by 2,591,366 American Depositary Shares ("ADS") and 1,616,367 Ordinary Shares issuable upon the conversion of 1,616,367 Non-Voting Ordinary Shares (as defined in Item 4 and subject to the limitations as described therein) directly held by the Funds (as defined below). Each ADS represents one Ordinary Share of the Issuer.

(2) Based on 40,938,763 Ordinary Shares of the Issuer outstanding as of September 30, 2022, as reported in the Issuer's Form 6-K filed with the Securities and Exchange Commission ("SEC") on November 8, 2022, plus 1,616,367 Ordinary Shares issuable upon the conversion of 1,616,367 Non-Voting Ordinary Shares (as defined in Item 4 and subject to the limitations as described therein).

1	<b>NAMES OF REPORTING PERSONS</b> Baker Bros. Advisors (GP) LLC	
2	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	<b>SEC USE ONLY</b>	
4	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5	<b>SOLE VOTING POWER</b> 4,207,733 (1)
	6	<b>SHARED VOTING POWER</b> -0-
	7	<b>SOLE DISPOSITIVE POWER</b> 4,207,733 (1)
	8	<b>SHARED DISPOSITIVE POWER</b> -0-
9	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 4,207,733 (1)	
10	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>	
11	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 9.9% (1)(2)	
12	<b>TYPE OF REPORTING PERSON (See Instructions)</b> HC, OO	

- (1) Includes 2,591,366 Ordinary Shares of the Issuer that are represented by 2,591,366 ADS and 1,616,367 Ordinary Shares issuable upon the conversion of 1,616,367 Non-Voting Ordinary Shares (as defined in Item 4 and subject to the limitations as described therein) directly held by the Funds (as defined below). Each ADS represents one Ordinary Share of the Issuer.
- (2) Based on 40,938,763 Ordinary Shares of the Issuer outstanding as of September 30, 2022, as reported in the Issuer's Form 6-K filed with the SEC on November 8, 2022, plus 1,616,367 Ordinary Shares issuable upon the conversion of 1,616,367 Non-Voting Ordinary Shares (as defined in Item 4 and subject to the limitations as described therein).

1	<b>NAMES OF REPORTING PERSONS</b> Felix J. Baker	
2	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	<b>SEC USE ONLY</b>	
4	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> United States	
<b>NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH</b>	5	<b>SOLE VOTING POWER</b> 4,207,733 (1)
	6	<b>SHARED VOTING POWER</b> -0-
	7	<b>SOLE DISPOSITIVE POWER</b> 4,207,733 (1)
	8	<b>SHARED DISPOSITIVE POWER</b> -0-
9	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 4,207,733 (1)	
10	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>	
11	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 9.9% (1)(2)	
12	<b>TYPE OF REPORTING PERSON (See Instructions)</b> IN, HC	

- (1) Includes 2,591,366 Ordinary Shares of the Issuer that are represented by 2,591,366 ADS and 1,616,367 Ordinary Shares issuable upon the conversion of 1,616,367 Non-Voting Ordinary Shares (as defined in Item 4 and subject to the limitations as described therein) directly held by the Funds (as defined below). Each ADS represents one Ordinary Share of the Issuer.
- (2) Based on 40,938,763 Ordinary Shares of the Issuer outstanding as of September 30, 2022, as reported in the Issuer's Form 6-K filed with the SEC on November 8, 2022, plus 1,616,367 Ordinary Shares issuable upon the conversion of 1,616,367 Non-Voting Ordinary Shares (as defined in Item 4 and subject to the limitations as described therein).

1	<b>NAMES OF REPORTING PERSONS</b> Julian C. Baker	
2	<b>CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP (See Instructions)</b> (a) <input type="checkbox"/> (b) <input type="checkbox"/>	
3	<b>SEC USE ONLY</b>	
4	<b>CITIZENSHIP OR PLACE OF ORGANIZATION</b> United States	
	5	<b>SOLE VOTING POWER</b> 4,207,733 (1)
	6	<b>SHARED VOTING POWER</b> -0-
	7	<b>SOLE DISPOSITIVE POWER</b> 4,207,733 (1)
	8	<b>SHARED DISPOSITIVE POWER</b> -0-
9	<b>AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON</b> 4,207,733 (1)	
10	<b>CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES (See Instructions)</b> <input type="checkbox"/>	
11	<b>PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9</b> 9.9% (1)(2)	
12	<b>TYPE OF REPORTING PERSON (See Instructions)</b> IN, HC	

- (1) Includes 2,591,366 Ordinary Shares of the Issuer that are represented by 2,591,366 ADS and 1,616,367 Ordinary Shares issuable upon the conversion of 1,616,367 Non-Voting Ordinary Shares (as defined in Item 4 and subject to the limitations as described therein) directly held by the Funds (as defined below). Each ADS represents one Ordinary Share of the Issuer.
- (2) Based on 40,938,763 Ordinary Shares of the Issuer outstanding as of September 30, 2022, as reported in the Issuer's Form 6-K filed with the SEC on November 8, 2022, plus 1,616,367 Ordinary Shares issuable upon the conversion of 1,616,367 Non-Voting Ordinary Shares (as defined in Item 4 and subject to the limitations as described therein).

### Amendment No. 1 to Schedule 13G

This Amendment No. 1 to Schedule 13G amends and restates the previously filed Schedule 13G 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.

**Item 1(a) Name of Issuer:**

Achilles Therapeutics plc (the “Issuer”)

**Item 1(b) Address of Issuer’s Principal Executive Offices:**

245 Hammersmith Road

London W6 8PW United Kingdom

**Item 2(a) Name of Person Filing:**

This Schedule 13G is being filed jointly by the Reporting Persons.

**Item 2(b) Address of Principal Business Office or, if None, Residence:**

The business address of each of the Reporting Persons is:

c/o Baker Bros. Advisors LP

860 Washington Street, 3<sup>rd</sup> Floor

New York, NY 10014

(212) 339-5690

**Item 2(c) Citizenship:**

The Adviser is a limited partnership organized under the laws of the State of Delaware. The Adviser GP is a limited liability company organized under the laws of the State of Delaware. The citizenship of each of Julian C. Baker and Felix J. Baker is the United States of America.

**Item 2(d) Title of Class of Securities:**

Ordinary Shares, nominal value £0.001 per share (“Ordinary Shares”).

**Item 2(e) CUSIP Number:**

00449L102

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**Item 3** If this statement is filed pursuant to §§240.13d-1(b) or (c), check whether the person filing is a:

- (a)  Broker or dealer registered under Section 15 of the Exchange Act.
- (b)  Bank as defined in section 3(a)(6) of the Exchange Act.
- (c)  Insurance company as defined in section 3(a)(19) of the Exchange Act.
- (d)  Investment company registered under section 8 of the Investment Company Act of 1940.
- (e)  An investment adviser in accordance with Rule 13d-1(b)(1)(ii)(E).
- (f)  An employee benefit plan or endowment fund in accordance with Rule 13d-1(b)(1)(ii)(F).
- (g)  A parent holding company or control person in accordance with Rule 13d-1(b)(1)(ii)(G).
- (h)  A savings association as defined in Section 3(b) of the Federal Deposit Insurance Act.
- (i)  A church plan that is excluded from the definition of an investment company under section 3(c)(14) of the Investment Company Act of 1940.
- (j)  Group, in accordance with Rule 13d-1(b)(1)(ii)(J).

**Item 4** **Ownership:**

Items 5 through 9 and 11 of each of the cover pages to this Amendment No. 1 are incorporated herein by reference.

Set forth below is the aggregate number of Ordinary Shares represented by American Depositary Shares of the Issuer (“ADS”) directly held by each of Baker Brothers Life Sciences, L.P. (“Life Sciences”) and 667, L.P. (“667”, and together with Life Sciences, 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 Class A non-voting Ordinary Shares (“Non-Voting Ordinary Shares”) convertible at any time without consideration on a 1-for-1 basis, subject to the limitations on conversion described below. Each ADS represents one Ordinary Share of the Issuer.

The information set forth below is based on 40,938,763 Ordinary Shares outstanding as of September 30, 2022, as reported in the Issuer’s Form 6-K filed with the Securities and Exchange Commission on November 8, 2022, plus 1,616,367 Ordinary Shares issuable upon the conversion of 1,616,367 Non-Voting Ordinary Shares, subject to the limitations on conversion described below. Such percentage figures are calculated in accordance with Rule 13d-3 under the Securities Exchange Act of 1934, as amended (the “Exchange Act”).

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Name	Number of Ordinary Shares we own or have the right to acquire within 60 days	Percent of Class Outstanding
667, L.P.	323,112	0.8%
Baker Brothers Life Sciences, L.P.	3,884,621	9.1%
<b>Total</b>	<b>4,207,733</b>	<b>9.9%</b>

The Non-Voting Ordinary Shares are only convertible 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 9.99% of the outstanding Ordinary Shares (the “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.

Pursuant to the management agreements, as amended, among the Adviser, 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.

The Adviser GP, Felix J. Baker and Julian C. Baker as managing members of the Adviser GP, and the Adviser may be deemed to be beneficial owners of securities of the Issuer directly held by the Funds.

**Item 5 Ownership of Five Percent or Less of a Class:**

If this statement is being filed to report the fact that as of the date hereof the reporting person has ceased to be the beneficial owner of more than five percent of the class of securities, check the following . N/A



**Item 6 Ownership of More than Five Percent on Behalf of Another Person:**

N/A

**Item 7 Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on by the Parent Holding Company or Control Person:**

The information in Item 4 is incorporated herein by reference.

**Item 8 Identification and Classification of Members of the Group:**

N/A

**Item 9 Notice of Dissolution of Group:**

N/A

**Item 10 Certification:**

By signing below I certify that, to the best of my knowledge and belief, the securities referred to above were acquired and are held in the ordinary course of business and were not acquired and are not held for the purpose of or with the effect of changing or influencing the control of the issuer of the securities and were not acquired and are not held in connection with or as a participant in any transaction having that purpose or effect.

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**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.

February 14, 2023

**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

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