
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

SCHEDULE 13D/A

Under the Securities Exchange Act of 1934
(Amendment No. 2)*

ACHILLES THERAPEUTICS PLC

(Name of Issuer)

Ordinary shares, nominal value £0.001 per share

(Title of Class of Securities)

00449L102**

(CUSIP Number)

RA Capital Management, L.P.
200 Berkeley Street, 18th Floor
Boston, MA 02116
Attn: Peter Kolchinsky
Telephone: 617.778.2500

(Name, Address and Telephone Number of Person
Authorized to Receive Notices and Communications)

December 21, 2022

(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 §§ 240.13d-1(e), 240.13d-1(f) or 240.13d-1(g), check the following box.

Note: Schedules filed in paper format shall include a signed original and five copies of the schedule, including all exhibits. See Section 240.13d-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.

** There is no CUSIP number assigned to the Ordinary Shares. CUSIP number 00449L102 has been assigned to the American Depositary Shares ("ADS") of the Issuer. Each ADS represents one Ordinary Share.

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, as amended ("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).

1. Names of Reporting Persons.

RA Capital Management, L.P.

2. Check the Appropriate Box if a Member of a Group (See Instructions)

(a)

(b)

3. SEC Use Only

4. Source of Funds (See Instructions)

AF

5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)

6. Citizenship or Place of Organization

Delaware

7. Sole Voting Power

0

Number of
Shares
Beneficially
Owned by
Each
Reporting
Person With

8. Shared Voting Power

2,976,943

9. Sole Dispositive Power

0

10. Shared Dispositive Power

2,976,943

11. Aggregate Amount Beneficially Owned by Each Reporting Person

2,976,943

12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)

13. Percent of Class Represented by Amount in Row (11)

7.27%¹

14. Type of Reporting Person (See Instructions)

IA, PN

¹ The Reporting Person is the beneficial owner of 2,976,943 Ordinary Shares, represented by ADS. The percentage calculation assumes that there are 40,938,763 outstanding Ordinary Shares of the Issuer as reported in the Issuer's Form 6-K, Exhibit 99.1 filed on November 8, 2022.

1. Names of Reporting Persons.

Peter Kolchinsky

2. Check the Appropriate Box if a Member of a Group (See Instructions)

(a)

(b)

3. SEC Use Only

4. Source of Funds (See Instructions)

AF

5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)

6. Citizenship or Place of Organization

United States

7. Sole Voting Power

0

Number of
Shares
Beneficially
Owned by
Each
Reporting
Person With

8. Shared Voting Power

2,976,943

9. Sole Dispositive Power

0

10. Shared Dispositive Power

2,976,943

11. Aggregate Amount Beneficially Owned by Each Reporting Person

2,976,943

12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)

13. Percent of Class Represented by Amount in Row (11)

7.27%²

14. Type of Reporting Person (See Instructions)

HC, IN

² The Reporting Person is the beneficial owner of 2,976,943 Ordinary Shares, represented by ADS. The percentage calculation assumes that there are 40,938,763 outstanding Ordinary Shares of the Issuer as reported in the Issuer's Form 6-K, Exhibit 99.1 filed on November 8, 2022.

1. Names of Reporting Persons.

Rajeev Shah

2. Check the Appropriate Box if a Member of a Group (See Instructions)

(a)

(b)

3. SEC Use Only

4. Source of Funds (See Instructions)

AF

5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)

6. Citizenship or Place of Organization

United States

7. Sole Voting Power

0

Number of
Shares
Beneficially
Owned by
Each
Reporting
Person With

8. Shared Voting Power

2,976,943

9. Sole Dispositive Power

0

10. Shared Dispositive Power

2,976,943

11. Aggregate Amount Beneficially Owned by Each Reporting Person

2,976,943

12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)

13. Percent of Class Represented by Amount in Row (11)

7.27³

14. Type of Reporting Person (See Instructions)

HC, IN

³ The Reporting Person is the beneficial owner of 2,976,943 Ordinary Shares, represented by ADS. The percentage calculation assumes that there are 40,938,763 outstanding Ordinary Shares of the Issuer as reported in the Issuer's Form 6-K, Exhibit 99.1 filed on November 8, 2022.

1. Names of Reporting Persons.

RA Capital Healthcare Fund, L.P.

2. Check the Appropriate Box if a Member of a Group (See Instructions)

(a)

(b)

3. SEC Use Only

4. Source of Funds (See Instructions)

WC

5. Check if Disclosure of Legal Proceedings Is Required Pursuant to Items 2(d) or 2(e)

6. Citizenship or Place of Organization

Delaware

7. Sole Voting Power

0

Number of
Shares
Beneficially
Owned by
Each
Reporting
Person With

8. Shared Voting Power

2,404,839

9. Sole Dispositive Power

0

10. Shared Dispositive Power

2,404,839

11. Aggregate Amount Beneficially Owned by Each Reporting Person

2,404,839

12. Check if the Aggregate Amount in Row (11) Excludes Certain Shares (See Instructions)

13. Percent of Class Represented by Amount in Row (11)

5.87⁴

14. Type of Reporting Person (See Instructions)

PN

⁴ The Reporting Person is the beneficial owner of 2,404,839 Ordinary Shares, represented by ADS. The percentage calculation assumes that there are 40,938,763 outstanding Ordinary Shares of the Issuer as reported in the Issuer's Form 6-K, Exhibit 99.1 filed on November 8, 2022.

Item 1.	Security and Issuer
<p>Item 1 of the Statement is hereby amended and supplemented as follows:</p> <p>This Amendment No. 2 amends and supplements the statement on Schedule 13D originally filed with the Securities and Exchange Commission on April 16, 2021, as amended by Amendment No. 1 filed on December 15, 2022 (as so amended, the “Statement”) by the Reporting Persons with respect to the Ordinary Shares, nominal value £0.001 per share per share (“<u>Ordinary Shares</u>”) of Achilles Therapeutics plc, a public limited company incorporated under the laws of England and Wales (the “<u>Issuer</u>”), which has its principal executive offices at 245 Hammersmith Road, London W6 8PW, United Kingdom. Unless otherwise defined herein, capitalized terms used in this Amendment No. 2 shall have the meanings ascribed to them in the Statement. Unless amended or supplemented below, the information in the Statement remains unchanged.</p>	
Item 2.	Identity and Background
<p>Item 2 of the Statement is hereby amended and restated as follows:</p> <p>(a) This Schedule 13D is being filed on behalf of RA Capital Management, L.P. (“RA Capital”), Peter Kolchinsky, Rajeev Shah, and RA Capital Healthcare Fund, L.P. (the “Fund”) who are collectively referred to herein as the “Reporting Persons”.</p> <p>The ADS reported herein include 2,404,839 ADS held by the Fund and 572,104 ADS held by RA Capital Nexus Fund, L.P. (the “Nexus Fund”). All options (right to purchase), that were previously held by Dr. Derek DiRocco for the benefit of RA Capital expired unexercised as of November 3, 2022.</p> <p>RA Capital Healthcare Fund GP, LLC is the general partner of the Fund and RA Capital Nexus Fund GP, LLC is the general partner of the Nexus Fund. The general partner of RA Capital is RA Capital Management GP, LLC, of which Dr. Kolchinsky and Mr. Shah are the controlling persons. RA Capital serves as investment adviser for the Fund and the Nexus Fund, and may be deemed a beneficial owner, for purposes of Section 13(d) of the Exchange Act, of any securities of the Issuer held by the Fund or the Nexus Fund. The Fund and the Nexus Fund have delegated to RA Capital the sole power to vote and the sole power to dispose of all securities held in the Fund’s and the Nexus Fund’s portfolio, including the ADS reported herein. Because the Fund and the Nexus Fund have divested themselves of voting and investment power over the reported securities they hold and may not revoke that delegation on less than 61 days’ notice, the Fund and the Nexus Fund disclaim beneficial ownership of the securities they hold for purposes of Section 13(d) of the Act and therefore disclaim any obligation to report ownership of the reported securities under Section 13(d) of the Exchange Act. As managers of RA Capital, Dr. Kolchinsky and Mr. Shah may be deemed beneficial owners, for purposes of Section 13(d) of the Act, of any securities of the Issuer beneficially owned by RA Capital. RA Capital, Dr. Kolchinsky, and Mr. Shah disclaim beneficial ownership of the securities reported in this Statement other than for the purpose of determining their obligations under Section 13(d) of the Act, and the filing of the Statement shall not be deemed an admission that either RA Capital, Dr. Kolchinsky, or Mr. Shah is the beneficial owner of such securities for any other purpose.</p> <p>(b) The address of the principal business office of each of the Reporting Persons is 200 Berkeley Street, 18th Floor, Boston, MA 02116.</p> <p>(c) The Fund is a private investment vehicle. RA Capital provides investment management services to the Fund and the Nexus Fund. The principal occupation of Dr. Kolchinsky and Mr. Shah is investment management.</p> <p>(d) During the last five years, none of the Reporting Persons has been convicted in a criminal proceeding (excluding traffic violations or similar misdemeanors).</p> <p>(e) During the last five years, none of the Reporting Persons has been a party to a civil proceeding of a judicial or administrative body of competent jurisdiction and as a result of such proceeding was or is subject to a judgment, decree of final order enjoining future violations of, or prohibiting or mandating activities subject to, federal or state securities laws or finding any violation with respect to such laws.</p> <p>(f) See row 6 of the cover pages.</p>	

Item 5.	Interest in Securities of the Issuer
<p>Item 5 of the Statement is amended and restated as follows:</p> <ul style="list-style-type: none">(a) The information set forth in rows 11 and 13 of the cover pages to this Statement is incorporated herein by reference. The percentages set forth in row 13 of the cover pages are based on 40,938,763 outstanding Ordinary Shares of the Issuer as reported in the Issuer's Form 6-K, Exhibit 99.1 filed with the Securities and Exchange Commission ("<u>SEC</u>") on November 8, 2022.(b) The information set forth in rows 7 through 10 of the cover pages to this Statement and Item 2 above is incorporated herein by reference.(c) Schedule A sets forth all transactions with respect to the ADS that have not previously been reported during the past sixty days by any Reporting Person and is incorporated herein by reference.(d) No person (other than the Reporting Persons) is known to have the right to receive or the power to direct the receipt of dividends from, or the proceeds from the sale of, the ADS subject to this Statement.(e) Not applicable.	
Item 7.	Material to be Filed as Exhibits
Exhibit 1 Joint Filing Agreement	

SIGNATURES

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 23, 2022

RA CAPITAL MANAGEMENT, L.P.

By: /s/ Peter Kolchinsky
Name: Peter Kolchinsky
Title: Authorized Signatory

PETER KOLCHINSKY

/s/ Peter Kolchinsky

RAJEEV SHAH

/s/ Rajeev Shah

RA CAPITAL HEALTHCARE FUND, L.P.

By: RA Capital Healthcare Fund GP, LLC
Its: General Partner

By: /s/ Peter Kolchinsky
Name: Peter Kolchinsky
Title: Manager

SCHEDULE A

Name	Date of Transaction	Number of Shares Acquired / (Disposed)	Transaction	Price per Share
RA Capital Healthcare Fund, L.P.	12/16/22	156,717 ADS	Sell	\$ 1.06
RA Capital Healthcare Fund, L.P.	12/19/22	117,876 ADS	Sell	\$ 0.86
RA Capital Healthcare Fund, L.P.	12/20/22	42,804 ADS	Sell	\$ 0.84
RA Capital Healthcare Fund, L.P.	12/21/22	43,984 ADS	Sell	\$ 0.80
RA Capital Healthcare Fund, L.P.	12/22/22	149,525 ADS	Sell	\$ 0.81
RA Capital Healthcare Fund, L.P.	12/23/22	402,388 ADS	Sell	\$ 0.81
RA Capital Nexus Fund, L.P.	12/16/22	37,283 ADS	Sell	\$ 1.06
RA Capital Nexus Fund, L.P.	12/19/22	28,042 ADS	Sell	\$ 0.86
RA Capital Nexus Fund, L.P.	12/20/22	10,183 ADS	Sell	\$ 0.84
RA Capital Nexus Fund, L.P.	12/21/22	10,464 ADS	Sell	\$ 0.80
RA Capital Nexus Fund, L.P.	12/22/22	35,572 ADS	Sell	\$ 0.81
RA Capital Nexus Fund, L.P.	12/23/22	95,727 ADS	Sell	\$ 0.81

JOINT FILING AGREEMENT

This Joint Filing Agreement, dated as of December 23, 2022, is by and among RA Capital Management, L.P., Peter Kolchinsky, Rajeev Shah, and RA Capital Healthcare Fund, L.P. (the foregoing are collectively referred to herein as the “Filers”).

Each of the Filers may be required to file with the United States Securities and Exchange Commission a statement on Schedule 13G and/or 13D with respect to Ordinary Shares, nominal value £0.001 per share of Achilles Therapeutics plc beneficially owned by them from time to time.

Pursuant to and in accordance with Rule 13(d)(1)(k) promulgated under the Securities Exchange Act of 1934, as amended, the Filers hereby agree to file a single statement on Schedule 13G and/or 13D (and any amendments thereto) on behalf of each of such parties, and hereby further agree to file this Joint Filing Agreement as an exhibit to such statement, as required by such rule.

This Joint Filing Agreement may be terminated by any of the Filers upon one week’s prior written notice or such lesser period of notice as the Filers may mutually agree.

Executed and delivered as of the date first above written.

RA CAPITAL MANAGEMENT, L.P.

By: /s/ Peter Kolchinsky
Name: Peter Kolchinsky
Title: Authorized Signatory

PETER KOLCHINSKY

/s/ Peter Kolchinsky

RAJEEV SHAH

/s/ Rajeev Shah

RA CAPITAL HEALTHCARE FUND, L.P.

By: RA Capital Healthcare Fund GP, LLC
Its: General Partner

By: /s/ Peter Kolchinsky
Name: Peter Kolchinsky
Title: Manager
