
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

SCHEDULE 13D

Under the Securities Exchange Act of 1934
(Amendment ___)*

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)

April 6, 2021

(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 ("ADSs") of the Issuer. Each ADS represents one Ordinary Shares.

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

5,014,687

9. Sole Dispositive Power

0

10. Shared Dispositive Power

5,014,687

11. Aggregate Amount Beneficially Owned by Each Reporting Person

5,014,687

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

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

12.34%¹

14. Type of Reporting Person (See Instructions)

IA, PN

¹ Represents an aggregate of 5,014,687 Ordinary Shares of the Issuer held by the Fund and the Nexus Fund which constitutes approximately 12.34% of the class outstanding. The percentage calculation assumes that there are currently 40,621,751 outstanding Ordinary Shares of the Issuer, based upon the closing of the Issuer's initial public offering of ADSs, as reported in the Issuer's prospectus filed with the SEC on March 31, 2021.

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

5,014,687

9. Sole Dispositive Power

0

10. Shared Dispositive Power

5,014,687

11. Aggregate Amount Beneficially Owned by Each Reporting Person

5,014,687

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

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

12.34%²

14. Type of Reporting Person (See Instructions)

HC, IN

² Represents an aggregate of 5,014,687 Ordinary Shares of the Issuer held by the Fund and the Nexus Fund which constitutes approximately 12.34% of the class outstanding. The percentage calculation assumes that there are currently 40,621,751 outstanding Ordinary Shares of the Issuer, based upon the closing of the Issuer's initial public offering of ADSs, as reported in the Issuer's prospectus filed with the SEC on March 31, 2021.

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

5,014,687

9. Sole Dispositive Power

0

10. Shared Dispositive Power

5,014,687

11. Aggregate Amount Beneficially Owned by Each Reporting Person

5,014,687

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

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

12.34%³

14. Type of Reporting Person (See Instructions)

HC, IN

³ Represents an aggregate of 5,014,687 Ordinary Shares of the Issuer held by the Fund and the Nexus Fund which constitutes approximately 12.34% of the class outstanding. The percentage calculation assumes that there are currently 40,621,751 outstanding Ordinary Shares of the Issuer, based upon the closing of the Issuer's initial public offering of ADSs, as reported in the Issuer's prospectus filed with the SEC on March 31, 2021.

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

4,050,972

9. Sole Dispositive Power

0

10. Shared Dispositive Power

4,050,972

11. Aggregate Amount Beneficially Owned by Each Reporting Person

4,050,972

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

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

9.97%⁴

14. Type of Reporting Person (See Instructions)

PN

⁴ Represents 4,050,972 Ordinary Shares of the Issuer held by the Fund which constitutes approximately 9.97% of the class outstanding. The percentage calculation assumes that there are currently 40,621,751 outstanding Ordinary Shares of the Issuer, based upon the closing of the Issuer's initial public offering of ADSs, as reported in the Issuer's prospectus filed with the SEC on March 31, 2021.

Item 1.	Security and Issuer
<p>This Schedule 13D relates 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.</p>	
Item 2.	Identity and Background
<p>(a) This Schedule 13D is being filed on behalf of RA Capital Management, L.P. (“<u>RA Capital</u>”), Peter Kolchinsky, Rajeev Shah, and RA Capital Healthcare Fund, L.P. (the “<u>Fund</u>”), which are collectively referred to herein as the “<u>Reporting Persons</u>.” The agreement among the Reporting Persons to file this Schedule 13D jointly in accordance with Rule 13d-1(k) of the Securities Exchange Act of 1934, as amended (the “<u>Exchange Act</u>”), is attached hereto as Exhibit 1.</p> <p>The Ordinary Shares reported herein includes 2,719,349 Ordinary Shares and 1,331,623 American Depositary Shares (“ADSs”), each representing one Ordinary Share, held by the Fund, and 906,450 Ordinary Shares and 57,265 ADSs held by RA Capital Nexus Fund, L.P. (the “<u>Nexus Fund</u>”). 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 shares of the Issuer’s Common Stock 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 Schedule 13D Statement (the “<u>Statement</u>”) 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, the Account (as defined below), 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 3.	Source and Amount of Funds or Other Consideration
<p>Prior to the Issuer's initial public offering (the "IPO"), in September 2019 the Reporting Persons caused the Fund, a separately managed account (the "Account"), and the Nexus Fund to purchase an aggregate of 8,350,731 Series B Preferred Shares (the "<u>Series B Preferred Shares</u>") of the Issuer in a private placement for an aggregate purchase price of £16,000,000.59. In October 2020, the Reporting Persons caused the Fund, the Account, and the Nexus Fund to purchase an aggregate of 4,175,365 Series B Preferred Shares (the "<u>Series B Preferred Shares</u>") of the Issuer in a private placement for an aggregate purchase price of £7,999,999.34. In October 2020, the Reporting Persons caused the Fund, the Account, and the Nexus Fund to purchase an aggregate of 1,830,251 Series C Preferred Shares (the "<u>Series C Preferred Shares</u>") of the Issuer in a private placement for an aggregate purchase price of £3,951,328.89. The Series B Preferred shares and the Series C preferred shares automatically converted into 3,625,799 Ordinary Shares upon completion of the IPO. The Fund, the Account, and the Nexus Fund also purchased 1,388,888 ADSs from the underwriters of the IPO for an aggregate purchase price of \$24,999,984. All purchases were for cash and were funded by working capital of the Fund, the Account, and the Nexus Fund.</p>	
Item 4.	Purpose of Transaction
<p>The Reporting Persons acquired beneficial ownership of the Ordinary Shares reported herein for investment purposes and not with an intent, purpose or effect of changing control of the Issuer. Although the Reporting Persons currently have no plan or proposal to acquire any additional Ordinary Shares or to dispose of any of the Ordinary Shares reported herein, the Reporting Persons may acquire additional Ordinary Shares from time to time or dispose of Ordinary Shares they beneficially own, consistent with their investment purposes and in amounts to be determined by the Reporting Persons based upon a number of factors, including, without limitation, their ongoing assessment of the Issuer's business prospects, prevailing market conditions, the availability of other investment opportunities, and/or other considerations.</p> <p>In addition, consistent with their investment purpose, the Reporting Persons may engage in communications with persons associated with the Issuer, including shareholders of the Issuer, officers of the Issuer and/or members of the board of directors of the Issuer, to discuss matters regarding the Issuer, including but not limited to its operations and strategic direction. Derek DiRocco, a Partner of RA Capital, currently serves as a director of the Issuer and therefore will engage in regular discussions with the Issuer's board of directors and management as part of his duties as a director.</p> <p>The Reporting Persons have no plans or proposals that relate to, or could result in, any of the matters referred to in paragraphs (a) through (j), inclusive, of the instructions to Item 4 of Schedule 13D.</p> <p>The Reporting Persons may, however, change their purpose and formulate and implement plans or proposals with respect to the Issuer at any time and from time to time. Any such action may be made by the Reporting Persons alone or in conjunction with other shareholders, potential acquirers, financing sources and/or other third parties and could include one or more purposes, plans or proposals that relate to or would result in actions required to be reported herein in accordance with Item 4 of Schedule 13D.</p>	
Item 5.	Interest in Securities of the Issuer
<p>(a) The information set forth in rows 11 and 13 of the cover pages to this Schedule 13D is incorporated by reference. The percentage set forth in row 13 is based on 40,621,751 outstanding Ordinary Shares, as reported by the Issuer in its prospectus supplement filed with the Securities and Exchange Commission (the "<u>SEC</u>") on March 31, 2021.</p> <p>(b) The information set forth in rows 7 through 10 of the cover pages to this Schedule 13D and Item 2 above is incorporated by reference.</p> <p>(c) Schedule A sets forth all transactions with respect to the shares of Common Stock effected during the past sixty days by any Reporting Person and is incorporated herein by reference.</p> <p>(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 shares of Common Stock subject to this Schedule 13D.</p> <p>(e) Not applicable.</p>	

Item 6.	Contracts, Arrangements, Understandings or Relationships with Respect to Securities of the Issuer
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Lock-up Agreement

The 3,625,799 Ordinary shares acquired prior to the closing of the Issuer's initial public offering as well as the shares reported on this Schedule 13D are subject to a lock-up agreement (the "Lock-Up Agreement"), as referenced in the Issuer's prospectus supplement filed with the SEC on March 31, 2021. Pursuant to the Lock-Up Agreement, the Fund, Nexus Fund and the Account may not, with limited exceptions, for a period of 180 days from the date of the prospectus, offer, sell or otherwise transfer or dispose of any of the Issuer's securities, without the prior written consent of J.P. Morgan Securities LLC, BofA Securities, Inc. and Piper Sandler & Co.

Shareholders Agreement

On February 7, 2021, the Issuer, the Fund, the Nexus Fund, the Account, and certain other parties entered into the amended and restated registration rights agreement (the "Shareholders Agreement"). Beginning 180 days after the effectiveness of the Issuer's registration statement filed in connection with its initial public offering, the Shareholders Agreement provides the parties thereto with certain demand registration rights, including shelf registration rights, in respect of the shares of Common Stock issued to it upon conversion of the Preferred Shares, subject to certain conditions. The registration rights will expire, with respect to any particular Holder, the earlier of i) such time as such holder holds less than 1% of the Company's outstanding Ordinary Shares (treating all shares of Investor Shares on an as-converted basis) or ii) such time as the Company has completed its Initial Offering and all Registrable Securities of the Company issuable or issued upon conversion of the Shares held by and issuable to such Holder (and its Affiliates) may be sold pursuant to Rule 144 without registration and without limitation thereunder as to volume or manner of sale. The Shareholders Agreement contains customary cross-indemnification provisions, pursuant to which the Issuer is obligated to indemnify the Fund and other parties in the event of material misstatements or omissions in the registration statement attributable to the Issuer or any violation or alleged violation whether by action or inaction by the Issuer under certain securities laws and the Fund is obligated to indemnify the Issuer for material misstatements or omissions in the registration statement attributable to it.

The description of the of the Lock-Up Agreement and Shareholders Agreement contained in this Item 6 is qualified in its entirety by reference to the full text of the agreements, which are filed as Exhibit 2 and Exhibit 3 hereto, respectively.

Item 7.	Material to be Filed as Exhibits
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Exhibit 1 Joint Filing Agreement

Exhibit 2 Form of Lock-up Agreement (incorporated by reference to Exhibit D of Exhibit 1.1 to the Issuer's Amendment No. 3 to Registration Statement on Form F-1 (File No. 333-253735))

Exhibit 3 Form of Amended and Restated Registration Rights Agreement (incorporated by reference to Exhibit 10.4 to the Issuer's Amendment No. 3 to Registration Statement on Form F-1 (File No. 333-253735))

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: April 16, 2021

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 GP, LLC

By: /s/ Peter Kolchinsky

Name: Peter Kolchinsky

Title: Manager

SCHEDULE A

Name	Date of Transaction	Number of Shares Acquires / (Disposed)	Transaction	Price per Share
RA Capital Healthcare Fund, L.P.	9/2/19	5,319,429 Series B Preferred	Purchase	£ 1.916
RA Capital Healthcare Fund, L.P.	11/17/20	2,659,715 Series B Preferred	Purchase	£ 1.916
RA Capital Healthcare Fund, L.P.	11/19/20	1,252,330 Series C Preferred	Purchase	£ 2.1589
RA Capital Healthcare Fund, L.P.	4/1/21	387,874 Ordinary Shares (1)	(1)	\$ 16.55(1)
RA Capital Healthcare Fund, L.P.	4/6/21	103,610 ADSs (2)	(2)	\$ 16.55(2)(4)
RA Capital Healthcare Fund, L.P.	4/6/21	2,331,475 Ordinary Shares	Conversion	(3)
RA Capital Healthcare Fund, L.P.	4/6/21	1,228,013 ADSs	Purchase	\$ 18.00(4)
RA Capital Nexus Fund, L.P.	9/2/19	2,087,683 Series B Preferred	Purchase	£ 1.916
RA Capital Nexus Fund, L.P.	11/17/20	1,043,841 Series B Preferred	Purchase	£ 1.916
RA Capital Nexus Fund, L.P.	11/19/20	457,563 Series C Preferred	Purchase	£ 2.1589
RA Capital Nexus Fund, L.P.	4/6/21	906,450 Ordinary Shares	Conversion	(3)
RA Capital Nexus Fund, L.P.	4/6/21	57,265 ADSs	Purchase	\$ 18.00(4)
Account	9/2/19	943,619 Series B Preferred (5)	Purchase	£ 1.916
Account	11/17/20	471,809 Series B Preferred (5)	Purchase	£ 1.916
Account	11/19/20	120,358 Series C Preferred (5)	Purchase	£ 2.1589
Account	4/1/21	(387,874 Ordinary Shares) (1)	(1)	\$ 16.55(1)
Account	4/6/21	103,610 ADSs	Purchase	\$ 18.00(4)
Account	4/6/21	(103,610 ADSs) (2)	(2)	\$ 16.55(2)

- (1) On April 1, 2021, the Fund acquired a participation interest in the reported shares as part of a reorganization of the assets of the Account (the "Reorganization"). The reported shares reflect preferred shares of the Issuer that converted into Ordinary Shares on April 6, 2021 upon the closing of the Issuer's initial public offering, on an as converted basis.
- (2) Represents shares purchased by the Account that were acquired by the Fund at the closing of the Issuer's initial public offering pursuant to the Reorganization.
- (3) Each share of Series B Preferred Stock and Series C Preferred Stock automatically converted into Ordinary Shares upon the closing of the Issuer's initial public offering for no additional consideration, on a one-for-0.2526 reverse split basis.
- (4) The shares were acquired in the Issuer's initial public offering.
- (5) The Fund acquired a participation interest in the reported shares pursuant to the Reorganization.

JOINT FILING AGREEMENT

This Joint Filing Agreement, dated as of April 16, 2021, 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 Common Stock, 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 GP, LLC

By: /s/ Peter Kolchinsky

Name: Peter Kolchinsky

Title: Manager
