

SECURITIES AND EXCHANGE COMMISSION  
WASHINGTON, DC 20549

SCHEDULE 13G  
(Rule 13d-102)

INFORMATION TO BE INCLUDED IN STATEMENTS FILED PURSUANT  
TO RULES 13d-1(b)(c), AND (d) AND AMENDMENTS THERETO FILED  
PURSUANT TO RULE 13d-2(b)

(Amendment No. 4) \*

Orchard Therapeutics plc

(Name of Issuer)

Ordinary Shares, par value £0.10 (represented by American Depositary Shares)

(Title of Class of Securities)

68570P101

(CUSIP Number)

December 31, 2021

(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)

(Page 1 of 12 Pages)

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\* 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 the disclosures provided in a prior cover page.

The information required in 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 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).

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1.	NAME OF REPORTING PERSONS I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY)	
	Deerfield Management Company, L.P.	
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5.	SOLE VOTING POWER 0
	6.	SHARED VOTING POWER 6,949,416 (1)
	7.	SOLE DISPOSITIVE POWER 0
	8.	SHARED DISPOSITIVE POWER 6,949,416 (1)
9.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 6,949,416 (1)	
10.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* <input type="checkbox"/>	
11.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 5.54%	
12.	TYPE OF REPORTING PERSON* PN	

(1) Comprised of American Depositary Shares (representing a like number of ordinary shares) held by Deerfield Private Design Fund III, L.P. and Deerfield Private Design Fund IV, L.P., of which Deerfield Management Company, L.P. is the investment advisor.

1.	NAME OF REPORTING PERSONS I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY)  Deerfield Mgmt III, L.P.	
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	CITIZENSHIP OR PLACE OF ORGANIZATION  Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5.	SOLE VOTING POWER  0
	6.	SHARED VOTING POWER  3,474,708 (2)
	7.	SOLE DISPOSITIVE POWER  0
	8.	SHARED DISPOSITIVE POWER  3,474,708 (2)
9.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON  3,474,708 (2)	
10.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* <input type="checkbox"/>	
11.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9  2.77%	
12.	TYPE OF REPORTING PERSON*  PN	

(2) Comprised of American Depositary Shares (representing a like number of ordinary shares) held by Deerfield Private Design Fund III, L.P., of which Deerfield Mgmt III, L.P. is the general partner.

1.	NAME OF REPORTING PERSONS I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY)	
	Deerfield Mgmt IV, L.P.	
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5.	SOLE VOTING POWER 0
	6.	SHARED VOTING POWER 3,474,708 (3)
	7.	SOLE DISPOSITIVE POWER 0
	8.	SHARED DISPOSITIVE POWER 3,474,708 (3)
9.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 3,474,708 (3)	
10.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* <input type="checkbox"/>	
11.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 2.77%	
12.	TYPE OF REPORTING PERSON* PN	

(3) Comprised of American Depositary Shares (representing a like number of ordinary shares) held by Deerfield Private Design Fund IV, L.P., of which Deerfield Mgmt IV, L.P. is the general partner.

1.	NAME OF REPORTING PERSONS I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY)	
	Deerfield Private Design Fund III, L.P.	
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5.	SOLE VOTING POWER 0
	6.	SHARED VOTING POWER 3,474,708 (4)
	7.	SOLE DISPOSITIVE POWER 0
	8.	SHARED DISPOSITIVE POWER 3,474,708 (4)
9.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 3,474,708 (4)	
10.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* <input type="checkbox"/>	
11.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 2.77%	
12.	TYPE OF REPORTING PERSON* PN	

(4) Comprised of American Depositary Shares (representing a like number of ordinary shares of the Issuer).

1.	NAME OF REPORTING PERSONS I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY)	
	Deerfield Private Design Fund IV, L.P.	
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	CITIZENSHIP OR PLACE OF ORGANIZATION Delaware	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5.	SOLE VOTING POWER 0
	6.	SHARED VOTING POWER 3,474,708 (5)
	7.	SOLE DISPOSITIVE POWER 0
	8.	SHARED DISPOSITIVE POWER 3,474,708 (5)
9.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 3,474,708 (5)	
10.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* <input type="checkbox"/>	
11.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 2.77%	
12.	TYPE OF REPORTING PERSON* PN	

(5) Comprised of American Depositary Shares (representing a like number of ordinary shares of the Issuer).

1.	NAME OF REPORTING PERSONS I.R.S. IDENTIFICATION NO. OF ABOVE PERSONS (ENTITIES ONLY)	
	James E. Flynn	
2.	CHECK THE APPROPRIATE BOX IF A MEMBER OF A GROUP* (a) <input type="checkbox"/> (b) <input checked="" type="checkbox"/>	
3.	SEC USE ONLY	
4.	CITIZENSHIP OR PLACE OF ORGANIZATION United States	
NUMBER OF SHARES BENEFICIALLY OWNED BY EACH REPORTING PERSON WITH	5.	SOLE VOTING POWER 0
	6.	SHARED VOTING POWER 6,949,416 (6)
	7.	SOLE DISPOSITIVE POWER 0
	8.	SHARED DISPOSITIVE POWER 6,949,416 (6)
9.	AGGREGATE AMOUNT BENEFICIALLY OWNED BY EACH REPORTING PERSON 6,949,416 (6)	
10.	CHECK BOX IF THE AGGREGATE AMOUNT IN ROW (9) EXCLUDES CERTAIN SHARES* <input type="checkbox"/>	
11.	PERCENT OF CLASS REPRESENTED BY AMOUNT IN ROW 9 5.54%	
12.	TYPE OF REPORTING PERSON* IN	

(6) Comprised of American Depositary Shares (representing a like number of ordinary shares) held by Deerfield Private Design Fund III, L.P. and Deerfield Private Design Fund IV, L.P.

Item 1(a). Name of Issuer:

Orchard Therapeutics plc

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Item 1(b). Address of Issuer's Principal Executive Offices:

108 Cannon Street,  
London EC4N 6EU  
United Kingdom

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Item 2(a). Name of Person Filing:

James E. Flynn, Deerfield Mgmt III, L.P., Deerfield Mgmt IV, L.P., Deerfield Management Company, L.P., Deerfield Private Design Fund III, L.P. and Deerfield Private Design Fund IV, L.P.

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

James E. Flynn, Deerfield Mgmt III, L.P., Deerfield Mgmt IV, L.P., Deerfield Management Company, L.P., Deerfield Private Design Fund III, L.P. and Deerfield Private Design Fund IV, L.P., 345 Park Avenue South, 12th Floor, New York, NY 10010

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Item 2(c). Citizenship:

Deerfield Mgmt III, L.P., Deerfield Mgmt IV, L.P., Deerfield Management Company, L.P., Deerfield Private Design Fund III, L.P. and Deerfield Private Design Fund IV, L.P. - Delaware limited partnerships;

James E. Flynn – United States citizen

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

Ordinary Shares, par value £0.10 (represented by American Depositary Shares)

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Item 2(e). CUSIP Number:

68570P101

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Item 3. If This Statement is Filed Pursuant to Rule 13d-1(b), or 13d-2(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.
  - (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);
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- (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;
- (j)  A non-U.S. institution in accordance with Rule 13d-1(b)(1)(ii)(J);
- (k)  Group, in accordance with Rule 13d-1(b)(1)(ii)(K).

If filing as a non-U.S. institution in accordance with Rule 13d-1(b)(1)(ii)(J), please specify the type of institution: \_\_\_\_\_

Item 4. Ownership.

Provide the following information regarding the aggregate number and percentage of the class of securities of the issuer identified in Item 1.

- (a) Amount beneficially owned\*\*:

Deerfield Mgmt III, L.P. – 3,474,708 shares  
 Deerfield Mgmt IV, L.P. – 3,474,708 shares  
 Deerfield Management Company, L.P. - 6,949,416 shares  
 Deerfield Private Design Fund III, L.P. – 3,474,708 shares  
 Deerfield Private Design Fund IV, L.P. – 3,474,708 shares  
 James E. Flynn – 6,949,416 shares

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- (b) Percent of class\*\*:

Deerfield Mgmt III, L.P. – 2.77%  
 Deerfield Mgmt IV, L.P. – 2.77%  
 Deerfield Management Company, L.P. – 5.54%  
 Deerfield Private Design Fund III, L.P. – 2.77%  
 Deerfield Private Design Fund IV, L.P. – 2.77%  
 James E. Flynn – 5.54%

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- (c) Number of shares as to which such person has\*\*:

- |  |  |
|--|--|
| (i) Sole power to vote or to direct the vote:                | <u>All Reporting Persons - 0</u>   |
| (ii) Shared power to vote or to direct the vote:             | Deerfield Mgmt III, L.P. – 3,474,708 shares<br>Deerfield Mgmt IV, L.P. – 3,474,708 shares<br>Deerfield Management Company, L.P. - 6,949,416 shares<br>Deerfield Private Design Fund III, L.P. – 3,474,708 shares<br>Deerfield Private Design Fund IV, L.P. – 3,474,708 shares<br>James E. Flynn – 6,949,416 shares |
| (iii) Sole power to dispose or to direct the disposition of: | <u>All Reporting Persons - 0</u>   |
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(iv) Shared power to dispose or to direct the disposition of:

Deerfield Mgmt III, L.P. – 3,474,708 shares  
Deerfield Mgmt IV, L.P. – 3,474,708 shares  
Deerfield Management Company, L.P. - 6,949,416 shares  
Deerfield Private Design Fund III, L.P. – 3,474,708 shares  
Deerfield Private Design Fund IV, L.P. – 3,474,708 shares  
James E. Flynn – 6,949,416 shares

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\*\*See footnotes on cover pages which are incorporated by reference herein.

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 .

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Item 6. Ownership of More Than Five Percent on Behalf of Another Person.

If any other person 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, such securities, a statement to that effect should be included in response to this item and, if such interest relates to more than five percent of the class, such person should be identified. A listing of the shareholders of an investment company registered under the Investment Company Act of 1940 or the beneficiaries of employee benefit plan, pension fund or endowment fund is not required.

N/A

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

If a parent holding company or Control person has filed this schedule, pursuant to Rule 13d-1(b)(1)(ii)(G), so indicate under Item 3(g) and attach an exhibit stating the identity and the Item 3 classification of the relevant subsidiary. If a parent holding company or control person has filed this schedule pursuant to Rule 13d-1(c) or Rule 13d-1(d), attach an exhibit stating the identification of the relevant subsidiary.

N/A

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Item 8. Identification and Classification of Members of the Group.

If a group has filed this schedule pursuant to ss.240.13d-1(b)(1)(ii)(J), so indicate under Item 3(j) and attach an exhibit stating the identity and Item 3 classification of each member of the group. If a group has filed this schedule pursuant to ss.240.13d-1(c) or ss.240.13d-1(d), attach an exhibit stating the identity of each member of the group.

See Exhibit B

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Item 9. Notice of Dissolution of Group.

Notice of dissolution of a group may be furnished as an exhibit stating the date of the dissolution and that all further filings with respect to transactions in the security reported on will be filed, if required, by members of the group, in their individual capacity. See Item 5.

N/A

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## Item 10. Certifications.

"By signing below I certify that, to the best of my knowledge and belief, the securities referred to above 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, other than activities solely in connection with a nomination under §240.14a-11."

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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.

DEERFIELD MANAGEMENT COMPANY, L.P.

By: Flynn Management LLC, General Partner

By: /s/ Jonathan Isler

Jonathan Isler, Attorney-In-Fact

DEERFIELD MGMT III, L.P.

By: J.E. Flynn Capital III, LLC, General Partner

By: /s/ Jonathan Isler

Jonathan Isler, Attorney-In-Fact

DEERFIELD MGMT IV, L.P.

By: J.E. Flynn Capital IV, LLC, General Partner

By: /s/ Jonathan Isler

Jonathan Isler, Attorney-In-Fact

DEERFIELD PRIVATE DESIGN FUND III, L.P.

By: Deerfield Mgmt III, L.P., General Partner

By: J.E. Flynn Capital III, LLC, General Partner

By: /s/ Jonathan Isler

Jonathan Isler, Attorney-In-Fact

DEERFIELD PRIVATE DESIGN FUND IV, L.P.

By: Deerfield Mgmt IV, L.P., General Partner

By: J.E. Flynn Capital IV, LLC, General Partner

By: /s/ Jonathan Isler

Jonathan Isler, Attorney-In-Fact

JAMES E. FLYNN

/s/ Jonathan Isler

Jonathan Isler, Attorney-In-Fact

Date: February 11, 2022

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Exhibit List

Exhibit A. Joint Filing Agreement.

Exhibit B. Item 8 Statement.

Exhibit C. Power of Attorney (1).

(1) Power of Attorney previously filed as Exhibit 24 to a Form 4 with regard to DA32 Life Science Tech Acquisition Corp. filed with the Securities and Exchange Commission on August 3, 2021 by Deerfield Partners, L.P., Deerfield Mgmt, L.P., Deerfield Management Company, L.P. and James E. Flynn.

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Exhibit A

Joint Filing Agreement

The undersigned agree that this Schedule 13G, and all amendments thereto, relating to the Ordinary Shares, par value £0.10 (represented by American Depositary Shares) of Orchard Therapeutics plc shall be filed on behalf of the undersigned.

DEERFIELD MANAGEMENT COMPANY, L.P.

By: Flynn Management LLC, General Partner

By: /s/ Jonathan Isler

Jonathan Isler, Attorney-In-Fact

DEERFIELD MGMT III, L.P.

By: J.E. Flynn Capital III, LLC, General Partner

By: /s/ Jonathan Isler

Jonathan Isler, Attorney-In-Fact

DEERFIELD MGMT IV, L.P.

By: J.E. Flynn Capital IV, LLC, General Partner

By: /s/ Jonathan Isler

Jonathan Isler, Attorney-In-Fact

DEERFIELD PRIVATE DESIGN FUND III, L.P.

By: Deerfield Mgmt III, L.P., General Partner

By: J.E. Flynn Capital III, LLC, General Partner

By: /s/ Jonathan Isler

Jonathan Isler, Attorney-In-Fact

DEERFIELD PRIVATE DESIGN FUND IV, L.P.

By: Deerfield Mgmt IV, L.P., General Partner

By: J.E. Flynn Capital IV, LLC, General Partner

By: /s/ Jonathan Isler

Jonathan Isler, Attorney-In-Fact

JAMES E. FLYNN

/s/ Jonathan Isler

Jonathan Isler, Attorney-In-Fact

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Exhibit B

Due to the relationships between them, the reporting persons hereunder may be deemed to constitute a “group” with one another for purposes of Section 13(d)(3) of the Securities Exchange Act of 1934.