

SCHEDULE 13G

Amendment No. 2
ORCHARD THERAPEUTICS PLC
COMMON STOCK
Cusip #68570P101

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)

Cusip #68570P101
Item 1: Reporting Person - FMR LLC
Item 2: (a)
(b)
Item 4: Delaware
Item 5: 12,244,590
Item 6: 0
Item 7: 12,244,590
Item 8: 0
Item 9: 12,244,590
Item 11: 12.686%
Item 12: HC

Cusip #68570P101
Item 1: Reporting Person - Abigail P. Johnson
Item 2: (a)
(b)
Item 4: United States of America
Item 5: 0
Item 6: 0
Item 7: 12,244,590
Item 8: 0
Item 9: 12,244,590
Item 11: 12.686%
Item 12: IN

Item 1(a). Name of Issuer:

ORCHARD THERAPEUTICS PLC

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

108 CANNON STREET
LONDON, X0 EC4N 6EU
ENGLAND

Item 2(a). Name of Person Filing:

FMR LLC

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

245 Summer Street, Boston, Massachusetts 02210

Item 2(c). Citizenship:

Not applicable

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

COMMON STOCK

Item 2(e). CUSIP Number:

68570P101

Item 3. Not Applicable

Item 4. Ownership

(a) Amount Beneficially Owned: 12,244,590

(b) Percent of Class: 12.686%

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

(i) sole power to vote or to direct the vote: 12,244,590

(ii) shared power to vote or to direct the vote: 0

(iii) sole power to dispose or to direct the disposition of: 12,244,590

(iv) shared power to dispose or to direct the disposition of: 0

Item 5. Ownership of Five Percent or Less of a Class.

Not applicable.

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

One or more other persons are 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 COMMON STOCK of ORCHARD THERAPEUTICS PLC.

The interest of F-Prime Capital Partners Healthcare Fund IV LP, in the COMMON STOCK of ORCHARD THERAPEUTICS PLC, amounted to 6,122,295 shares or 6.343% of the total outstanding COMMON STOCK at December 31, 2020.

The interest of F-Prime Capital Partners Healthcare Fund IV-A LP, in the COMMON STOCK of ORCHARD THERAPEUTICS PLC, amounted to 6,122,295 shares or 6.343% of the total outstanding COMMON STOCK at December 31, 2020.

Item 7. Identification and Classification of the Subsidiary Which Acquired the Security Being Reported on By the Parent Holding Company.

See attached Exhibit A.

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

Not applicable.

Item 9. Notice of Dissolution of Group.

Not applicable.

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.

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 5, 2021

Date

/s/ Kevin M. Meagher

Signature

Kevin M. Meagher

Duly authorized under Power of Attorney effective as of September 28, 2018, by and on behalf of FMR LLC and its direct and indirect subsidiaries*

* This power of attorney is incorporated herein by reference to Exhibit 24 to the Schedule 13G filed by FMR LLC on October 9, 2018, accession number: 0000315066-18-002414.

Exhibit A

Pursuant to the instructions in Item 7 of Schedule 13G, the following table lists the identity and Item 3 classification, if applicable, of each relevant entity that beneficially owns shares of the security class being reported on this Schedule 13G.

Entity ITEM 3 Classification

IMPRESA MANAGEMENT LLC * IA

* Entity beneficially owns 5% or greater of the outstanding shares of the security class being reported on this Schedule 13G.

Abigail P. Johnson is a Director, the Chairman and the Chief Executive Officer of FMR LLC.

Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC.

This filing reflects the securities beneficially owned, or that may be deemed to be beneficially owned, by FMR LLC, certain of its subsidiaries and affiliates, and other companies (collectively, the "FMR Reporters"). This filing does not reflect securities, if any, beneficially owned by certain other companies whose beneficial ownership of securities is disaggregated from that of the FMR Reporters in accordance with Securities and Exchange Commission Release No. 34-39538 (January 12, 1998).

RULE 13d-1(k) (1) AGREEMENT

The undersigned persons, on February 5, 2021, agree and consent to the joint filing on their behalf of this Schedule 13G in connection with their beneficial ownership of the COMMON STOCK of ORCHARD THERAPEUTICS PLC at December 31, 2020.

FMR LLC

By /s/ Kevin M. Meagher
Kevin M. Meagher

Duly authorized under Power of Attorney effective as of September 28, 2018, by and on behalf of FMR LLC and its direct and indirect subsidiaries*

Abigail P. Johnson

By /s/ Kevin M. Meagher
Kevin M. Meagher

Duly authorized under Power of Attorney effective as of September 30, 2018, by and on behalf of Abigail P. Johnson*

* This power of attorney is incorporated herein by reference to Exhibit 24 to the Schedule 13G filed by FMR LLC on October 9, 2018, accession number: 0000315066-18-002414.