UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

DIVISION OF
CORPORATION FINANCE

September 5, 2018

Mark Rothera
President, Chief Executive Officer and Director
Orchard Rx Ltd
108 Cannon Street
London EC4N 6EU
United Kingdom

Re: Orchard Rx Ltd
Draft Registration Statement on Form F-1
Submitted August 6, 2018
CIK No. 0001748907

Dear Mr. Rothera:

We have reviewed your draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to these comments and your amended draft registration statement or filed registration statement, we may have additional comments.

Draft Registration Statement on Form S-1 Filed August 6, 2018

Prospectus Summary
Overview, page 1

1. We not your statement on page 21 that you may not have access to the most recent clinical data or the most recent clinical data may be limited or incomplete. For each your clinical stage product candidates, clarify whether the trail is still ongoing, the date of the most recent clinical data and whether you are aware of any limitation of the data.

2. Please further revise the discussion of OTL-103 to replace the statement that patients have

experienced a clinically meaningful reduction in bleeding and infection to present the data you used to draw this conclusion.

3. We note that you provide the maximum survival follow-up data for each of your commercial and development stage products and product candidates in your tables on pages 4 and 136. To put these figures in context, please also provide for each product or product candidate the range of treatment duration of all patients in the studies and the average survival rate of untreated patients.

4. Please revise this section to disclose that you purchased rights to Strimvelis, OTL-200 for MLD, OTL-103 for WAS and OTL-300 for TDBT from GSK in April 2018.

5. We note your disclosure on page 3 regarding your plans to submit OTL-101, OTL-200 and OTL-103 for regulatory approval in the next three years. Please revise your disclosure to discuss any additional steps you must take prior to submitting each product candidate for regulatory approval. Additionally, discuss any differences between your clinical trials and the FDA /EMA requirements and the possibility that the FDA/EMA may require additional clinical trials, a different trial design or a longer follow up period.

6. Revise the description of OTL-200 on page 3 to replace your statement that patients experienced sustained expression of the ARSA enzyme and significant long-term motor and cognitive improvements in most patients to describe the clinical trial endpoints related to the expression of ARSA enzyme and the motor and cognitive improvements and a summary of your observations. To the extent any statistical analyses were performed, these should be discussed in the business section.

7. We note your statement on page 3 that OTL-103 has achieved am overall survival rate of 100% in eight patients with a follow up of up to eight years post treatment. Are the additional seven patients included in the table on page 4 compassionate use patients? If any of these additional seven patients were trial participants, please explain why they are not counted in your statement about the results of the trial. If they are compassionate use patients, please explain whether you have data about their results. If you do not, please explain why.

8. We note your disclosure on page 144 that the EMA approved Strimvelis in May 2016 for treatment of children with ADA-SCID with no suitable HLA-matched stem cell donor. Please specify in your description of Strimvelis in this section that EMA approval is limited to the treatment of children with ADA-SCID with no suitable HLA-matched stem cell donor.

9. Please expand your disclosure on page 3 to discuss all serious adverse events observed in your ongoing trials for OTL-101, OTL-200 and OTL-103.

10. Throughout your document you make conclusory statements regarding the safety and efficacy of your product candidates. For example:

    - On page 1: "...clinical stage product candidates have accumulated compelling durable

efficacy and safety data."

- On page 2; "our long term clinical follow up across multiple diseases and vectors carrying different genes supports the safety of out autologous ex vivo gene therapy approach."
- on page 3: "OTL-200 has evidenced sustained expression of the deficient ARSA enzyme, with significant long term motor and cognitive improvements in most patients. These results exhibit the ability of our approach to target complex diseases which involve the central nervous system;" OTL-103 "clinically meaningful reductions in bleeding events and infections observed;""our clinical stage programs...continue to generate favorable safety and efficacy data in initial clinical trials."
- On page 135: "Three of our clinical-stage product candidates are currently in registrational trials and have shown compelling efficacy and safety data...;"
- On page 140: "Durable and sustained clinical benefit has been observed..."

Statements regarding efficacy and safety are determinations that only the FDA or a foreign government equivalent has the authority to make. Please revise your disclosure throughout your document, including but not limited to the statements noted, to eliminate your conclusions or any suggestions that your product candidates have been or will ultimately be determined safe and/or effective or have demonstrated safety and/or efficacy for purposes of granting approval by the FDA or comparable agency. You may present the objective data from the clinical trials without drawing a conclusion from the results. For example, you may note that a candidate was well tolerated, the absence of serious adverse events or the number of trial participants who met the identified trial endpoints.

11. Additionally, we note your statements about the long-term safety and efficacy appear to contradict your statement on page 22 that there is limited data concerning the safety and efficacy following treatment with your product candidates. Please revise your disclosure to address these inconsistencies.

12. With respect to table on page 2, please explain the following:

- the distinction between "Preclinical" and "Clinical proof of concept;" and
- the meaning of "registrational trial."

Additionally, revise the table to include separate columns for Phase I, Phase II and Phase III clinical trials and disclose the current trial phase in the discussion section. Alternatively, tell us why you believe that "registrational trial" is a better description of the current developmental stage for each of your product candidates. This explanation should address whether you are relying on an approval process that differs from your discussion on pages 169-172 and how the stage of development and the process compares to the competitive approaches presented on page 167.

13. Please explain the basis for your belief that the total addressable market potential in the diseases underlying your five lead programs could be greater than $2 billion annually. Your response should include your material assumptions underlying this prediction.

Implications of being an emerging growth company and a foreign private issuer , page 6

14. Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications.

Favorable results fromcompassionate use programs may not establish proof-of-concept..., page 22

15. To the extent that any of the results presented in the Summary or Business sections are the results of compassionate use programs, please revise the discussion to identify the results as such.

Capitalization, page 106

16. You disclose on page 106 that the capitalization table on a pro forma basis gives effect to the conversion of all outstanding preferred shares as of December 31, 2017 into an aggregate of 41,581,513 ordinary shares upon the closing of this offering. You also disclose on page 105 that the conversion ratio of each class of preferred shares of Orchard Therapeutics plc into ordinary shares of Orchard Therapeutics plc will be determined based on the final price per ADS in this offering. In this regard, it is not clear how the conversion of the preferred shares presented in the capitalization table was calculated. Please advise.

17. Please revise all pro forma balance adjustments to present them on a gross rather than a net basis. In this regard, we note that the adjustments to cash and equity accounts are comprised of multiple pro forma adjustments. Each adjustment should be separately presented and disclosed. This same comment also applies to pro forma consolidated balance sheet data on page 11 as applicable.

18. Please revise the table in this section to reflect your capitalization as of a date no earlier than 60 days prior to the date of your registration statement. Refer to Item 3.B of Part I of Form 20-F, and Item 4 of Part I of Form F-1.

Dilution, page 108

19. Please revise the dilution table to separately present the pro forma impact of the corporate reorganization and the offering so that readers could understand the impact of each of these transactions. Also disclose in the footnote the total number of shares of common

stock outstanding used to calculate each pro forma net tangible book value. Refer to Instruction (6) related to Item 11-02-02(b)(6) of Regulation S-X.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Recent Developments, page 113

20. We note your disclosure on page 114 that under the GSK Agreement, you are required to make Strimvelis commercially available in the European Union until such time as an alternative gene therapy, such as your OTL-101 product candidate, is commercially available for patients in the European Union. Please clarify in your disclosure whether you intend to continue to sell Strimvelis once OTL-101 is commercially available in the European Union.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Components of Our Results of Operations
Income Tax (Expense) Benefit, page 118

21. You disclose here that your income tax credit recognized represents the sum of the R&D tax credits recoverable in the United Kingdom and income tax payable in the United States. You also disclose on page 131 that you record U.K. R&D tax credits as a reduction to R&D expense in the year in which the expenditures were incurred. To the extent you classify part of your U.K. tax credits as R&D expenses and part as income tax benefits, please revise to clearly disclose the fact. In addition, disclose whether the tax credits depend on your generation of future taxable income or your ongoing tax status or tax positon, and how you determine the classification of these R&D tax credits between R&D expense and income tax benefits.

Share-Based Compensation, page 128

22. Once you have an estimated offering price or range, please explain to us how you determined the fair value of the common stock underlying your equity issuances and the reasons for any differences between the recent valuations of your common stock leading up to the IPO and the estimated offering price.

Business
Our Strategy, page 141

23. We note your disclosure on page 141 that your programs OTL-200 for MLD and OTL-103 for WAS have both achieved their primary endpoints in registrational trials. We also note your disclosure elsewhere that your clinical trials for OTL-200 for MLD and OTL-103 for WAS are ongoing and not complete. Please revise your disclosure here to clarify that you have not completed the registrational trials for these programs.

24. Please revise the first bullet point to put into context your statement concerning your goal to "rapidly advance" your five clinical-stage product candidates towards marketing

approval and "rapidly progress" OTL-102 and OTL-300 through clinical development to regulatory filing. In this regard, we note your risk factor disclosures on pages 20 - 24 which indicates that you may need to perform additional clinical trials and clinical testing is expensive, time-consuming and uncertain as to outcome and that you may find it difficult to enroll patients in your clinical trials, which could delay or prevent you from proceeding with clinical trials of your product candidates.

Supportive Trial with GOSH, page 146

25. Please identify on page 147 the one SAE that was assessed as being possibly related to protocol treatment or procedures.

Ongoing Clinical Trial with UCLA (with Cryopreserved Formulation), page 147

26. Please revise to disclose how many patients you expect to evaluate as part of your comparability analysis.

License Agreements, page 164

27. Please describe the material terms of and file as exhibits the license, development and supply agreement with Oxford Biomedica, the UCLB/UCLA License Agreement and the license agreement with Généthon, or tell us why they are not material to your business. Refer to Item 10.C of Form 20-F and Item 601(b)(10) of Regulation S-K.

28. Please revise the description of your agreement with GSK to provide the range of the tiered royalties for the MLD and WAS products and provide more specific information about the highest royalty tier for TDBT sales, such as teens, twenties, thirties, etc.

Related Party Transactions, page 200

29. Please file the transitional services agreement with GSK entered into on April 11, 2018, or tell us the basis for your belief that it is not required. Refer to Item 601(b)(10) of Regulation S-K.

Registration Rights, page 207

30. You disclose that upon completion of the offering, the holders of the shares of your ordinary share issuable upon the conversion of your preferred shares will be entitled to registration rights. Please disclose if you anticipate whether there will be any maximum cash penalties under the registration rights agreements or additional penalties that may result from delays in registering these securities. Refer to ASC 825-20-50-1.

Description of American Depositary Shares
Governing Law/Waiver of Jury Trial, page 236

31. We note your disclosure that as a party to the deposit agreement, investors waive their

rights to trial by jury in any legal proceeding arising out of the deposit agreement or the ADRs against the company and/or the depositary. Please provide a risk factor regarding the impact of this provision of the deposit agreement on the rights of ADS holders. In addition, address potential enforceability issues. Finally, clarify that by agreeing to the provision, investors will not be deemed to have waived the company's or the depositary's compliance with U.S. federal securities laws and the rules and regulations promulgated thereunder and ensure that the deposit agreement includes a specific statement to that effect.

Financial Statements
Consolidated Statements of Operations and Comprehensive Loss, page F-4

32. Please tell us what consideration was given to including pro forma earnings per share information on the face of your historical financial statements to give effect to the corporate reorganization. Refer to SAB Topic 4:C. In addition, please revise to include pro forma earnings per share in your summary selected financial data on page 11.

2. Summary of Significant Accounting Policies
Segment Information, page F-11

33. You disclose that you operate as a single operating segment. Please tell us and disclose how you have assessed whether your two geographic regions, the United Kingdom and United States, represent operating segments under ASC 280-10-50-1. Describe the frequency and contents of the discreet financial information for the geographic regions that is regularly reviewed by the CODM to make decisions about resources to be allocated and assess performance. Please also revise to include entity-wide information about geographic areas. Refer to ASC 280-10-50-38 through 42 as applicable.

General

34. Please provide us proofs of all graphics, visual, or photographic information you will provide in the printed prospectus prior to its use, for example in a preliminary prospectus.

You may contact Sisi Cheng at 202-551-5004 or Sharon Blume at 202-551-3474 if you have questions regarding comments on the financial statements and related matters. Please contact Irene Paik at 202-551-6553 or Suzanne Hayes at 202-551-3675 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Healthcare & Insurance