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

DIVISION OF
CORPORATION FINANCE

May 10, 2012

Via E-mail
Mr. Donald J. Santel
Chief Executive Officer
601 Gateway Boulevard
Suite 200
South San Francisco, CA 94080

Re: Hyperion Therapeutics, Inc.
Registration Statement on Form S-1
Filed April 13, 2012
File No. 333-180694

Dear Mr. Santel:

We have reviewed your 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 amending your registration statement and providing the requested information. 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 any amendment to your registration statement and the information you provide in response to these comments, we may have additional comments.

FORM S-1

General

1. Please provide updated financial statements and financial information throughout the filing. Refer to Rule 3-12 of Regulation S-X.

2. We note that you intend to submit a number of confidential treatment requests in relation to certain agreements you intend to file by amendment to the registration agreement. Please note that you will be receiving comments to the confidential treatment requests under separate cover and that all confidential treatment issues must be resolved before we will consider a request for acceleration of the registration statement. Please file these agreements, your confidential treatment requests and all other exhibits as soon as possible.

3. Since you appear to qualify as an "emerging growth company," as defined in the Jumpstart Our Business Startups Act ("the Act"), please disclose on your prospectus cover page that you are an emerging growth company, and revise your prospectus to provide the following additional disclosures:

    - Describe how and when a company may lose emerging growth company status;
    - A brief description of the various exemptions that are available to you, such as exemptions from Section 404(b) of the Sarbanes-Oxley Act of 2002 and Section 14A(a) and (b) of the Securities Exchange Act of 1934; and
    - Your election under Section 107(b) of the Act:
        - If you have elected to opt out of the extended transition period for complying with new or revised accounting standards pursuant to Section 107(b) of the Act, include a statement that the election is irrevocable; or
        - If you have elected to use the extended transition period for complying with new or revised accounting standards under Section 102(b)(2)(B) of the Act, provide a risk factor explaining that this election allows you to delay the adoption of new or revised accounting standards that have different effective dates for public and private companies until those standards apply to private companies. Please state in your risk factor that, as a result of this election, your financial statements may not be comparable to companies that comply with public company effective dates. Include a similar statement in your critical accounting policy disclosures in MD&A.

In addition, consider describing the extent to which any of these exemptions are available to you as a Smaller Reporting Company.

4. Please note that when you file a pre-effective amendment containing pricing-related information, we may have additional comments. As you are likely aware, you must file this amendment prior to circulating the prospectus.

5. Please note that when you file a pre-effective amendment that includes your price range, it must be bone fide. We interpret this to mean that your range may not exceed $2 if you price below $10 and 20% if you price above $10.

6. Please note that where we provide examples to illustrate what we mean by our comments, they are examples and not exhaustive lists. If our comments are applicable to portions of the filing that we have not cited as examples, make the appropriate changes in accordance with our comments.

7. Please provide us proofs of all graphic, visual or photographic information you will provide in the printed prospectus prior to its use, for example in a preliminary prospectus. Please note that we may have comments regarding this material.

Prospectus Summary
Our Company, page 1

8. Please clarify which company currently manufactures and sells BUPHENYL commercially.

Ravicti Clinical Development, page 2

9. Please explain what is meant by the term “non-inferiority” from a scientific/clinical perspective.

10. Please disclose here that under your Special Protocol Assessment, non-inferiority would be demonstrated if the mean value of ammonia in patients taking Ravicti was not more than 25% higher than that seen on Buphenyl.

Risk Factors Associated with Our Business, page 3

11. Please reference the arbitration proceedings with Ucyclyd. Please include an appropriate risk factor in the Risk Factors section. The risk factor should describe the dispute between you and Ucyclyd, address the risks associated with an unfavorable outcome to the arbitration proceeding, including the risk that you could lose your rights to Ravicti and your potential purchase rights to Buphenyl and Ammonul and an assessment of the potential consequences to your ability to continue as a going concern. We are also asking you to reference these proceedings in the Legal section of the Business section as well. See comment 40 below.

Risk Factors, page 10
Risks Related to Development, Commercialization and Regulatory Approval

"To obtain regulatory approval to market Ravicti…" page 12

12. To the extent you have experienced a delay, suspension or premature termination relating to your product candidate, please expand your disclosure to describe and provide the reasons for the relevant delay, suspension or premature termination.

"Serious adverse events or other safety risks…" page 12

13. Please expand your disclosure to disclose any known undesirable side effects or adverse effects that have been associated with your product candidate.

"If our competitors are able to develop and market products…" page 16

14. You disclose that you face competition from established pharmaceutical and biotechnology companies, as well as from academic institutions, government agencies and private and public research institutions. Please expand your disclosure to name, in addition to Ucyclyd and its products, the entities and products from which you believe you will face competition in the UCD and HE market.

Risks Related to Our Financial Position and Need for Additional Capital
"We may need to obtain additional financing to fund our operations…" page 23

15. Please expand this risk factor to describe the nature and amount of payments you may receive from Ucyclyd beginning in January 2013 if Ravicti is not approved by the FDA prior to January 2013.

Risks Related to Our Reliance on Third Parties
"We have no manufacturing capacity…" page 25

16. Please identify here the third-party manufacturers upon whom you are substantially dependent, disclose the material terms of your supply contracts with any such manufacturers in the Business section and file the related contracts as exhibits to your registration statement.

"We use a single manufacturer for fill/finish of Ravicti…" page 25

17. Please identify the single contract manufacturer that supplies your finished Ravicti drug product. Please disclose the material terms of your supply contract and file the supply contract as an exhibit to your registration statement.

Risks Related to Our Intellectual Property, page 28
"We may not be able to protect our proprietary technology…" page 30

18. Here and in the page 31 regarding your intellectual property rights throughout the world, please disclose any known infringement of your intellectual property by third parties.

"We may infringe the intellectual property rights of others…" page 31

19. Disclose whether any third parties have asserted that you are infringing their intellectual property rights. Disclose whether you are involved in any pending litigation regarding infringement of third party intellectual property.

Risks Related to Our Business Operations and Industry, page 32
"We depend upon our key personnel…" page 32

20. If any of your key personnel intend to retire or resign in the near future, please revise to address such departure and the potential impact on your organization.

"We will need to significantly increase the size of our organization…" page 33

21. To the extent that you have experienced any difficulties to date managing growth, including retaining a sufficient number of skilled personnel, please expand this risk factor to describe these challenges.

Use of Proceeds, page 41

22. We note that you intend to use the net proceeds of this offering to complete the clinical development of Ravicti for UCD; for repayment over eight quarters of up to principal amount of $22.0 million of a potential loan from Ucyclyd; royalty and license payments under your license with Brusilow; royalty and license payments to Ucyclyd; and for general corporate purposes. Please revise your disclosure:

- to specifically and separately identify the amount of proceeds you intend to use to fund the completion of the clinical development of Ravicti for UCD;
- to separately identify the amount of proceeds you intend to use to make royalty and license payments to Brusilow, royalty and license payments to Ucyclyd, and general corporate purposes; and
- to identify the amount of proceeds you intend to allocate for the commercialization of the product and the nature of such expenses.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Financial Overview, page 51

23. For businesses in the development stage, the discussion of the operating results should address cumulative information from inception. Amounts discussed should be reconciled to the cumulative amounts reported in your consolidated financial statements. Please revise throughout the document as applicable.

Critical Accounting Policies and Estimates
Stock-Based Compensation, page 55

24. Regarding your valuation methodology, please address the following:

- You disclose on page 58 that you use the Income and/or Market approach for valuing your stock. However, your disclosure on page 59 appears to indicate that for each of the periods discussed you only used an income approach. Please clarify in what circumstances you use each method and what dates each method was used.
- If you used both the Income and Market valuation methods clarify in the filing how you determined the final valuation and why you believe it is appropriate. In addition, clarify if the methods resulted in similar valuations or if significantly different, how the final valuation was determined.
- Tell us why you believe the Income approach is appropriate considering the uncertainty of receiving regulatory approval for Ravicti.
- If you continue to believe the income approach is appropriate, clarify in the filing how the uncertainty was factored into the discount rate in the income approach.

Discuss each significant factor contributing to the difference between the fair value as of the date of each grant and the estimated IPO price.

25. You state on page 58 that in the Market approach you used market multiples of comparable publicly traded companies in your industry or similar lines of business which are based on key metrics implied by the enterprise values or acquisition values of comparable publicly traded companies. Clarify in the filing what similar lines of business you used and why. Also clarify in the filing what

specific factors you used to determine the companies you selected and why their use was considered appropriate (i.e. phase of development, number of products, collaboration agreements, size, etc.).

26. In order for us to fully understand the equity fair market valuations reflected in your financial statements, please revise the tabular disclosure presented on page 56 to include an itemized chronological schedule covering all equity instruments, including preferred stock and warrants, issued since January 1, 2011 through the date of your response. Please provide the following information separately for each equity issuance:
    - The date of the transaction,
    - The number of options or warrants granted or shares issued,
    - The exercise price of the options or warrants or the per share amount paid,
    - Management's estimated fair market value per share and how the estimate was made,
    - The identity of the recipient, indicating if the recipient was a related party,
    - The nature and terms of concurrent transactions; and,
    - The amount of any compensation or interest expense element.

27. Please note that because the initial filing did not include an estimated offering price we are deferring evaluation of common stock related compensation expenses until you specify the estimated offering price.

Business, page 69

28. Please briefly describe and provide an overview of the development of your business over the past five years, including a description of your relationship with Ucyclyd. Please include a description of the various collaboration agreements you have entered into with Ucyclyd, including the material terms of such agreements. We note your description on page F-14 of the registration statement. Please provide similar disclosure here.

29. We note that you purchased the worldwide rights to Ravicti from Ucyclyd in March 2012. However, your disclosure in this section indicates that you submitted an NDA to the FDA for Ravicti in December 2011. Please reconcile or explain this discrepancy. Please clarify which entity owned the rights to Ravicti at the time of the NDA submission.

30. Please disclose the amount of gross sales in 2011 for each of BUPHENYL and AMMONUL separately.

31. Please provide more details regarding the pivotal study for AMMONUL that you reference here. Identify the study, the entity which funded it, the size of the patient population that participated and when and where the study was conducted.

Key Advantages of Ravicti, page 73

32. Please clarify specifically what you mean by the terms “non-inferior” and “directionally favorable”. Specifically discuss the pooled results of the Phase II and Phase III clinical trials and explain how the data demonstrated statistically significant lower ammonia levels. Please revise your disclosure to specify how many fewer HA crises patients on Ravicti experienced on average rather than state that the results were “numerically fewer.”

Ravicti Clinical Development in UDC Patients, page 74

33. Please revise your disclosure to explain how it was determined that Ravicti would be demonstrated to be non-inferior to BUPHENYL if the mean value of ammonia on Ravicti was not more than 25% higher than that seen on BUPHENYL. Clarify whether this determination was made in consultation with the FDA and whether such factors as the lower sodium content of Ravicti and other potential benefits were considered in arriving at the threshold mean value.

Pediatric Study Under 6 Years, page 78

34. Please revise to disclose the specific concerns raised by the FDA during your pre-NDA meeting.

Ravicti Nonclinical Development, page 79

35. Please revise to disclose the specific basis for the conclusion of the panel that the results of the rat study were not predictive of human risk. Please disclose whether the FDA has issued any formal or informal response to the white paper summarizing the outcome of the expert panel review.

HE, page 80
Current Therapies and Limitations, page 80

36. Please identify the manufacturer of Rifaximin 550mg tablets.

Ravicti Clinical Development in HE Patients, page 81

37. Please identify who conducted the pivotal study for rifaximin, what the key results were and what the essential features are of that study which your Phase II Part B study shares.

Manufacturing, page 85

38. Please disclose whether you are substantially dependent upon any of the suppliers referenced in this section. If so, please describe the material terms of your contract with any such supplier and file the agreement as an exhibit to your Form S-1. Please disclose whether you have identified any alternate suppliers.

Competition, page 86

39. Please identify any competitors who have pre-clinical or clinical products that would compete directly with Ravicti, BUPHENYL or AMMONUL.

Legal Proceedings, page 99

40. We note your description on page 59 of the MD&A section of your filing of the demand for arbitration you filed with respect to your rights and obligations under the collaboration agreement with Ucyclyd. Please reference those proceedings in this section. Your disclosure should include a description of the specific matters in dispute, the dates of adjudication, any material findings and the final results of the arbitration proceedings. If the proceedings are still ongoing, please note this.

Exhibits

41. Please file the following as exhibits to your filing:

    - the license agreement with Brusilow;
    - the research agreement with Dr. Summar; and
    - the original collaboration agreement with Ucyclyd and all amendments thereto.

Financial Statements
8. Commitments and Contingencies, page F-23

42. You state on page 59 that you were in arbitration discussions with Ucyclyd relating to your rights to Ravicti, including the filing of the NDA for UCD. You filed your NDA in December 2011. Please tell us why the nature of this contingency and the disclosures required by ASC 450-20-50 have not been provided. If the arbitration proceedings were resolved and the revised agreement disclosed in Note 16 is a result of those proceedings, please clarify in the filing and update the filing to disclose the result of the arbitration proceedings.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes the information the Securities Act of 1933 and all applicable Securities Act rules require. Since the company and its management are in possession of all facts relating to a company's disclosure, they are responsible for the accuracy and adequacy of the disclosures they have made.

Notwithstanding our comments, in the event you request acceleration of the effective date of the pending registration statement please provide a written statement from the company acknowledging that:

- should the Commission or the staff, acting pursuant to delegated authority, declare the filing effective, it does not foreclose the Commission from taking any action with respect to the filing;

- the action of the Commission or the staff, acting pursuant to delegated authority, in declaring the filing effective, does not relieve the company from its full responsibility for the adequacy and accuracy of the disclosure in the filing; and

- the company may not assert staff comments and the declaration of effectiveness as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

Please refer to Rules 460 and 461 regarding requests for acceleration. We will consider a written request for acceleration of the effective date of the registration statement as confirmation of the fact that those requesting acceleration are aware of their respective responsibilities under the Securities Act of 1933 and the Securities Exchange Act of 1934 as they relate to the proposed public offering of the securities specified in the above registration statement. Please allow adequate time for us to review any amendment prior to the requested effective date of the registration statement.

You may contact Ibolya Ignat at (202) 551-3656 or Mary Mast at (202) 551-3613 if you have questions regarding comments on the financial statements and related matters. Please contact Nandini Acharya at (202) 551-3495, John Krug at (202) 551-3862 or me at (202) 551-3715 with any other questions.

Sincerely,

/s/ Daniel Greenspan for

Jeffrey Riedler
Assistant Director

Via E-mail
cc: Laura A. Berezin, Esq.
Hogan Lovells US LLP
525 University Avenue
Palo Alto, CA 94301