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

DIVISION OF
CORPORATION FINANCE

November 9, 2015

Via E-mail
Keith M. Gottesdiener, M.D.
Chief Executive Officer
Rhythm Pharmaceuticals, Inc.
855 Boylston Street
11th Floor
Boston, MA 02116

Re: Rhythm Pharmaceuticals, Inc.
Draft Registration Statement on Form S-1
Submitted October 13, 2015
CIK No. 0001649904

Dear Dr. Gottesdiener:

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.

Prospectus Summary
Overview, page 1

1. Please modify your description of the lack of effective or approved treatments for PWS wherever applicable to note that the FDA has approved the use of human growth hormone for children suffering from this indication.

2. Where you discuss the use of setmelanotide as a treatment for PWS-related obesity and hyperphagia, please briefly explain the impact of being designated an orphan drug. Similarly, please clarify the term “ultra-orphan disease” used in reference to POMC deficiency.

3. Please note in this summary and the risk factor concerning product development on page 16 that the Phase 2 clinical trial in POMC deficiency has only enrolled one patient to date.

4. Where you reference the previous clinical trials that enrolled over 200 patients, please note here and in the risk factor on page 16 that those trials did not demonstrate statistically significant results when setmelanotide was administered using continuous infusion, and that this led you to rely upon daily subcutaneous infection as the sole delivery method.

5. In your discussion of the use of setmelanotide for the treatment of obesity and hyperphagia in POMC deficiency and certain other indications, you state that you intend to pursue an accelerated path to approval. Please elaborate on the "accelerated path" you are referring to, including whether you intend to seek orphan drug or breakthrough therapy designations for this indication.

6. Please revise your disclosure in the Summary, and particularly when you first introduce a scientific concept or a disease target, to provide an explanation of the scientific concept that is accessible for a reader who may lack scientific training. For instance, on page 1 you discuss how MC4 deficiency may be a contributing factor in obese patients, particularly patients suffering from PWC or POMC who have MC4 deficiencies. Please revise this section to explain how MC4 deficiency may cause a patient to become obese, for instance because the body does not receive normal satiety signals. Similarly, please explain how setmelanotide works to remediate the MC4 deficiency.

7. At first use, please define the following terms or concepts:

    - "energy homeostatis;"
    - "upstream" defects or deficiencies;
    - "heterozygous deficiency;" and
    - "LepR deficiency."

Corporate Restructuring, page 12

8. Please indicate here, and wherever applicable in your Business section, which entity filed an Investigational New Drug Application for setmelanotide and approximately when that filing was made with the FDA. Please also indicate which entity has conducted or is conducting, as applicable, the clinical trials performed to date on setmelanotide.

Risk Factors
Risks Related to the Development of Our Product Candidates
"The number of patients suffering from each of the MC4 pathway deficiencies we are targeting is small . . .," page 17

9. Please remove the cross-reference to this risk factor at the end of this page, as it appears to be there in error.

"Changes in regulatory requirements, FDA guidance or unanticipated events during our clinical trial of setmelanotide may occur . . .," page 20

10. Please amend this risk factor to briefly explain what the PRO and ORO questionnaires are. Please make similar changes to your disclosure regarding the regulatory review process.

"Our product candidates may cause additional side effects . . .," page 21

11. Here, and in your disclosure on page 93, please identify the clinical trial that resulted in the serious adverse event and quantify, and briefly describe, the adverse events you have identified in your clinical testing to date.

Risks Related to Employee Matters and Managing Growth
"Following consummation of this offering, our executive officers intend to provide consulting services to the Relamorelin Company . . .," page 44

12. Please indicate, to the best of your knowledge, how much time, if any, these executive officers currently devote to the Relamorelin Company and approximately how much time they will be contractually obligated to spend on their consulting services once the agreements are in place. Please make similar changes to your disclosure on page 117.

"The indirect ownership of our executive officers…, page 44

13. Please revise this section to identify all directors who will continue to have an ownership interest in Relamorelin (or its successor Motus Therapeutics) after the offering.

Use of Proceeds, page 55

14. Please amend this disclosure to separate the amount of offering proceeds you intend to allocate toward development of setmelanotide as a treatment for Prader Willi Syndrome from the amount intended for its development as a treatment for POMC deficiency obesity.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Critical Accounting Policies and Estimates
Stock-based compensation, page 67

15. We may have additional comments on your accounting for equity issuances including stock compensation and beneficial conversion features. Once you have an estimated offering price, please provide us an analysis explaining the reasons for the differences between recent valuations of your common stock leading up to the IPO and the estimated offering price.

Business
General

16. We note your discussion in the risk factor on page 17, and again in the Market and Other Data section on page 42 regarding the limited information on the number of patients who may be impacted by PWS and POMC. Please revise your disclosure in this section to discuss in greater detail the difficulty in identifying the number of possible patients, your efforts to provide more specificity and management's view of whether those efforts are statistically valid in estimating the number of patients who might be impacted by the diseases that your therapies are targeting.

Overview, page 75

17. Please describe the consultations with the FDA you reference on page 76, including the approximate dates of any meetings and the guidance, if any, you received in each one.

Market Overview, page 78

18. Please explain on page 78 what a "hypothalamic pathway" is.

Setmelanotide: A First-in-Class Phase 2 MCAR Agonist, page 83

19. In the table on page 84, please change the clinical trial phase for POMC heterozygous deficiency and LepR deficiency from Phase 2 to Phase 1. Your disclosure should reflect the actual, and not the anticipated, clinical status of your product candidate for all its indications.

20. Where you discuss the Phase 2 clinical trials currently underway, please indicate the p-values for each that you are using to measure statistical significance, and the p-value determined for the one subject who has been tested for POMC deficiency.

21. In your discussion of the Phase 2 clinical trial for PWS on page 87, please indicate what the secondary endpoints of this trial are, if any.

22. Please indicate approximately when the Phase 1 clinical trials for setmelanotide as a treatment in connection with POMC heterozygous and LepR deficiency were performed and describe their results.

Safety and Tolerability, page 92

23. Please revise this section to clarify the differences between your current MC4 agonist (setmelanotide) and the first generation agonist that produced safety issues. Please also clarify the total number of patients involved in your Phase1b and ongoing Phase 2 trials compared to the number involved in the first generation testing.

Other Comments

24. 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.

You may contact James Peklenk at (202) 551-3661 or Joel Parker at (202) 551-3651 if you have questions regarding comments on the financial statements and related matters. Please contact Scot Foley at (202) 551-3383, Christian Windsor, Special Counsel, at (202) 551-3419 or me at (202) 551-3675 with any other questions.

Sincerely,

/s/ Christian Windsor
Special Counsel
For

Suzanne Hayes
Assistant Director
Office of Healthcare and Insurance

cc: Julio E. Vega
Laurie A. Cerveny
Morgan, Lewis & Bockius LLP
One Federal Street
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