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

DIVISION OF
CORPORATION FINANCE

February 12, 2019

Lee Kalowski
Chief Financial Officer
Bicycle Therapeutics Ltd.
4 Hartwell Place
Lexington, Massachusetts 02421

Re: Bicycle Therapeutics Ltd.
Draft Registration Statement on Form S-1
Filed December 21, 2018
CIK 0001761612

Dear Mr. Kalowski:

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.

DRS Form S-1

Prospectus Summary
Overview, page 1

1. Please provide the expected timing for reporting preliminary data for the Phase I part of the clinical trial of BT1718.

Introduction to Bicycles, page 2

2. We note your disclosure that the Bicycle's "renal route of elimination" minimizes liver exposure. Please provide further details as to the benefits of this route of elimination and why it does not result in increased renal exposure.

Our Pipeline, page 4

3. Please revise you pipeline table to include columns for each stage of further development and provide more specific details regarding each type of oncology indicator. In addition, we note your disclosure that BT1718 is undergoing a Phase I/IIa clinical trial; however, your table seems to indicate that BT1718 is currently undergoing a Phase I clinical trial only. Please revise or explain.

4. Your pipeline table shows that THR-149, the subject of your collaboration agreement with Oxurion, is currently undergoing a Phase I clinical trial. Please describe the Phase I trial in the Business section.

5. Please revise your pipeline table to remove the programs that are in the discovery phase. Because you have not identified a product candidate for these programs, it is premature to include them in a product pipeline table.

Implications of Being an Emerging Growth Company, page 9

6. 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.

Risk Factors

Risks Related to the Discovery, Development and Regulatory Approval of Our Product Candidates, page 19

7. Here or elsewhere in your Risk Factors section, please disclose that upon the completion of the Phase I/IIa clinical trial for BT1718, you have the right to obtain a license to the results of the clinical trial from CRUK upon the payment of a milestone, in cash and ordinary shares, and any related risks or impact on your ability to continue to develop and/or commercialize BT1718. We note your related disclosure on page 95.

Our current or future product candidates may cause undesirable side effects or have other properties when used alone... , page 24

8. We note your statement that your current and future product candidates have undergone [...] safety testing. Please revise your disclosure, if true, to state that certain of your products are currently undergoing safety testing in the form of Phase I and Phase I/IIa clinical trials, as appropriate, and none of your products have completed this testing to date.

Risks Related to Our Dependence on Third Parties

If conflicts arise with our development and commercialization collaborators or licensors, they may act in their own self-interest..., page 48

9. We note your disclosure on page 162 regarding the notices of opposition filed by Pepscan in respect of each of European patents 2 257 624 and 2 474 613. If material, please revise your Risk Factor disclosure to describe such notices of opposition, as well as any potential material consequences on your business or operations.

Risks Related to Our Intellectual Property

Cyber-attacks or other failures in telecommunications or information technology systems could result in information theft..., page 62

10. Please provide further details regarding the cyber-attack you experienced in 2018, including any material impact of the attack on your business or financial condition.

Capitalization, page 86

11. We note that your pro forma adjustments will give effect to the conversion of all outstanding preferred shares as of September 30, 2018 into ordinary shares and the effectiveness of your amended and restated memorandum and articles of association upon the closing of this offering. We also note from your disclosure on page 85 (Share Capital Reorganization...) that, pursuant to Part 17 of the Companies Act, you will reduce your share capital and that amount will be reclassified to reserves available for distribution. Please tell us if the reclassification of share capital will be disclosed in these pro forma adjustments, and if so, revise your filing to indicate that such disclosure will be made. If not, please tell us why the reclassification of share capital is not applicable to these pro forma adjustments.

Overview, page 92

12. We note that BT1718 is being developed to treat tumors with high MT1-MMP. Here or elsewhere in your prospectus, please provide further details about the percentage or volume of tumors with high MT1-MMP, and any resulting impact on the potential commercialization opportunities for BT1718. Please also provide similar details for EphA2 and Nectin-4.

13. To the extent material, please disclose the Materials Transfer Agreement into which you entered in October 2018, along with the material terms and conditions of such Agreement. In this regard, we note your disclosure in Note 17 to your Consolidated Financial Statements on page F-59.

Financial Overview, page 93

14. Please clarify the breakdown of revenues produced by each of your collaboration agreements. In addition, please clarify whether or not the $20.5 million in revenue cumulatively earned from your collaboration agreements includes the $5.0 million to be paid in January 2019 pursuant to the terms of your collaboration agreement with AstraZeneca.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Components of Our Results of Operations
Expenses, page 95

15. We note your disclosure regarding your Clinical Trial and License Agreement with CRTL and CRUK pursuant to which you are entitled to receive revenue sharing of a "mid to high double digit percentage of the net revenue." Please revise your disclosure to present a range of not more than 10 percentage points. Please similarly revise your disclosure regarding your potential tiered royalty payments pursuant to the terms of the Bioverativ collaboration agreement on page 139 and the Oxurion collaboration agreement on page 141.

Results of Operations
Research and Development Expenses, page 102

16. We note from your disclosure here that you have incurred research and development costs for several product candidates (i.e. BT1718 (MT1), BT5528 (EphA2) and BT8009 (Nectin-4)), and your lead product candidate, BT1718 (MT1), has incurred these costs since at least 2016. Please revise your filing to disclose research and development costs for each of your product candidates incurred from inception to date.

Business
Properties of Bicycles as Therapeutic Agents, page 121

17. Please clarify whether you can always identify a compound for development in only six to 12 months after a target has been selected, or if this is an average amount of time.

Our Oncology Programs, page 124

18. To the extent not disclosed, please provide the endpoint for each of your clinical trials and preclinical studies.

Preclinical Experience, page 127

19. We note your disclosure that, in the docetaxel resistant model, BT1718 at both doses tested was associated with significant responses. Please clarify whether this response was statistically significant, and if so, please indicate the p-value by which you measured

statistical significance. Please also explain how "p-value" is used to measure statistical significance.

Founder Royalty Arrangements, page 142

20. Please provide further details about each of your founder royalty agreements, including the parties to each agreement and any other material terms. In this regard, we note your disclosure in Note 12 to your Consolidated Financial Statements on page F-55.

Intellectual Property, page 142

21. Please expand your disclosure regarding your patent portfolio to disclose the type of patent protection provided by the patents or patent applications (e.g., composition of matter, method of use).

Executive Compensation
Employment Agreements with Our Named Executive Officers, page 172

22. We note that pursuant to the terms of their respective employment agreements, each of Kevin Lee, Lee Kalowski and Maria Koehler are entitled to annual discretionary cash bonuses if certain performance targets are met. Please provide further details regarding such performance targets.

Note 2 - Summary of Significant Accounting Policies
Share-based Compensation, page F-20

23. You disclose at the top of page F-21 four factors used to determine the fair value of your ordinary shares at each grant date. Once you have an estimated offering price or range, please explain to us in further detail 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 initial public offering and the estimated offering price. This information will help facilitate our review of your accounting for equity issuances of stock compensation.

Note 7 - Warranty Liability, page F-29

24. We note that your warrants are remeasured to fair value at each reporting date. We also note that your warrants are classified within Level 3 of the fair value hierarchy. Please revise your filing to disclose the following:

- Quantitative information about the significant unobservable inputs used in the fair value measurement of these warrants (e.g. risk-adjusted discount rate, present value periods, equity values calculated under the OPM, et al); and
- A narrative description of the sensitivity of the fair value measurement to changes in the unobservable inputs.

Refer to ASC 820-10-50-2(bbb)(2) and 50-2(g), respectively.

General

25. 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. Please note that we may have comments regarding this material.

You may contact Jim Dunn at (202) 551-3724 or Isaac Esquivel at (202) 551-3395 if you have questions regarding comments on the financial statements and related matters. Please contact Liz Walsh at (202) 551-3696 or Chris Edwards at (202) 551-6761 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Healthcare & Insurance

cc: Jonathan Schur