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

DIVISION OF
CORPORATION FINANCE

August 17, 2017

David Fellows
Chief Executive Officer
Nightstar Therapeutics Limited
215 Euston Road
London NW1 2BE
United Kingdom

Re: Nightstar Therapeutics Limited
Draft Registration Statement on Form F-1
Submitted July 21, 2017
CIK No. 0001711675

Dear Mr. Fellows:

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 F-1 submitted July 21, 2017

Prospectus Summary, page 1

1. Your chart on page 87 indicates that enrollment is on-going for your Phase 2 REGENERATE trial and that you will conduct a separate Phase 2 trial to assess bilateral treatment. Accordingly, please revise your pipeline chart on page 1 concerning NSR-REP1 to clarify the need to conduct this Phase 2 work. Also, tell us whether you are awaiting data from the REGENERATE trial in order to commence the planned Phase 3 trial.

2. Please tell us your basis for disclosing that NSR-REP1 represents the "most clinically advanced product candidate" for the treatment of CHM.

Risks Associated with Our Business, page 4

3. We note your disclosure on page 12 indicating that FDA has not approved any gene therapy products to date. Please revise the fourth bullet point in this section to clarify the risk.

Use of Proceeds, page 58

4. We note your disclosure that part of the proceeds will fund the clinical development of NSR-REP1 for the treatment of CHM, including the initiation of your planned Phase 3 clinical trial, and fund the preclinical development of NSR-003 for a rare inherited macular dystrophy, including the planned initiation of a Phase 1 clinical trial. Please expand your disclosure to include the amount you will need to complete each of these clinical trials. See Item 3.C.1. of Form 20-F.

Dilution, page 63

5. Your disclosure on page F-17 indicates that as of December 31, 2016 you had outstanding Tranche Obligations to issue 8,070,314 Class A ordinary shares in connection with prespecified milestones. Please revise and update your Dilution and Capitalization sections to discuss the impact of any issuances or potential issuances stemming from these obligations.

Critical Accounting Policies and Significant Judgments and Estimates
Valuation of Share-Based Compensation and Tranche Obligations
Determination of Fair Value of Ordinary Shares, page 75

6. Once you have an estimated offering price or range, please explain to us the reasons for any differences between the recent valuations of your common stock leading up to the IPO and the estimated offering price. This information will help facilitate our review of your accounting for equity issuances including stock compensation and beneficial conversion features.

Management's Discussion and Analysis of Financial Condition and Results of Operations
JOBS Act, page 78

7. 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.

Clinical Development of NSR-REP1, page 87

8. Your risk disclosure on page 12 indicates that FDA guidelines provide that a BLA application must be supported by two well-controlled pivotal Phase 3 trials. Accordingly, please tell us why your chart on page 87 does not reflect a second future Phase 3 trial.

Safety Observations from Clinical Trials of NSR-REP1, page 91

9. We note your disclosure concerning the clinical investigator's determinations concerning whether the serious adverse effects were or were not treatment-related. Please refer to Rule 436(a) and revise to identify the clinical investigator and file a consent for the summarization. For additional guidance, you may refer to Compliance Disclosure Interpretations, Securities Act Rules, Q. 233.02.

Clinical Development of NSR-RPGR, page 92

10. Please revise to identify the jurisdiction(s) where you are conducting the Phase 1/2 clinical trial and indicate whether you have submitted an IND to FDA. To the extent that you have submitted an IND, disclose when you submitted it and identify the IND sponsor(s) and the specific indications listed therein. If you are conducting the trial in the United States and believe that no INDs are required for this product candidate and/or indication at this time, please disclose this information in the prospectus.

Principal Shareholders, page 125

11. Please revise to identify the person(s) with voting or dispositive control of the shares held by Syncona Porfolio Limited.

Differences in Corporate Law, page 133

12. You may not qualify your disclosure by reference to state or national laws. Accordingly, please remove or revise the third sentence under the heading.

Notes to Consolidated Financial Statements
1. Nature of Business, page F-7

13. Please refer to the first paragraph herein and address the following:

- Tell us why the form of the report of the independent registered public accounting firm that will be signed upon the completion of reorganization described herein is appropriate. In this regard, Nightstar Therapeutics Limited was not incorporated until July 2017 and the reorganization has not been reflected in a period covered by financial statements included in the filing. If this form of report is not appropriate, it would appear that separate audited financial statements of both Nightstar Therapeutics Limited and NightstaRx Limited are required to be included in the filing.
- Tell us whether any shares of Nightstar Therapeutics Limited will be outstanding

prior to the reorganization, and, if so, how many, and to whom.

- If the financial statements in the filing are presumably presenting that of Nightstar Therapeutics Limited, tell us why the capital structure as presented within the consolidated balance sheets and consolidated statements of shareholders' equity as well as that described throughout the notes to the consolidated financial statements appears to be that of NightstaRx Limited.
- Disclose the accounting treatment to be afforded to the reorganization and its rationale. Tell us the accounting literature to which you rely to support the accounting treatment.
- The use of the word "Company" within this and other notes is confusing considering that it can be used to represent Nightstar Therapeutics Limited or NightstaRx Limited depending on the time frame, which may not always be obvious.
- Tell us whether the re-register of Nightstar Therapeutics Limited as a public limited company and the renaming of it as Nightstar Therapeutics plc will occur before effectiveness of the registration statement. If so, tell us how you intend to account for and disclose these changes within the financial statements.

Exhibits

14. We refer to your disclosure on page 93 concerning the manufacturing of NSR-REP1 and NSR-RPGR. Please file as an exhibit the non-exclusive license from NCH for the manufacturing process and supporting analytical technology. Also, disclose the material terms of the license in your Business section.

You may contact Sasha Parikh at 202-551-3627 or Jim Rosenberg, Senior Assistant Chief Accountant, at 202-551-3679 if you have questions regarding comments on the financial statements and related matters. Please contact Irene Paik at 202-551-6553 or Joseph McCann at 202-551-6262 with any other questions.

Division of Corporation Finance
Office of Healthcare & Insurance