Mail Stop 6010 April 27, 2007

Mr. Christoph Westphal
Chief Executive Officer
Sirtris Pharmaceuticals, Inc.
790 Memorial Drive
Cambridge, Massachusetts 02139

Re: Sirtris Pharmaceuticals, Inc.
Registration Statement on Form S-1
Amendment nos. 3 and 4 filed April 18 and 19, 2007
File No. 333-140979

Dear Mr. Westphal:

We have reviewed your filing and have the following comments. Where indicated, we think you should revise your document in response to these comments. If you disagree, we will consider your explanation as to why our comment is inapplicable or a revision is unnecessary. Please be as detailed as necessary in your explanation. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure. After reviewing this information, we may raise additional comments.

Please understand that the purpose of our review process is to assist you in your compliance with the applicable disclosure requirements and to enhance the overall disclosure in your filing. We look forward to working with you in these respects. We welcome any questions you may have about our comments or any other aspect of our review. Feel free to call us at the telephone numbers listed at the end of this letter.

FORM S-1

Initial clinical strategy and regulatory status, page 4

1. Please expand the discussion to clarify the status of your application and ability to conduct clinical studies in the United States pending resolution of any outstanding issues with the FDA, e.g. if your application is currently on hold pending resolution of issues and you cannot conduct clinical trials in the United States, so state. Also, please indicate the nature of the additional information requested, when you anticipate providing this information, and the anticipated time frame, if determinable, for clinical testing in the United States to begin.

2. Please clarify the effect the delay in approval of your IND, or possible non-approval of the IND, may have on your future prospects. If applicable, this information should also be presented in the risk factor section.

Capitalization, page 33

3. Please delete the cash line item from the Capitalization table.

Critical Policies and Estimates, page 45

Stock-based compensation, page 46

4. We note your response to comment 3. Please address the following:
   - On page 48 and F-12 of your filing, you disclose that, for the IPO market approach scenario, you selected the comparable companies based on similar factors; including the number of drug candidates under development, the status of clinical trials, the status of the intellectual property portfolios and the status of partnerships and collaborations with large pharmaceutical companies. Based on the information provided in Exhibit A, the population used is a wide variety of biotech companies. Please be more specific regarding the factors used in determining comparable companies.
   - Please tell us why you believe it is appropriate to include companies with products in Phase 3 clinical trials and Phase 2 clinical trial in your comparable companies considering that your products are in pre-clinical and Phase 1 clinical trials.
   - It appears that you are using the same comparables for each valuation date. Please tell us why that is appropriate given that the stage of development and milestones change with time.
   - Please explain what the IPO Pre-money amount in Exhibit A represents and how it was derived. If the amount represents the enterprise value, please confirm that. If not, please explain the significance of the value and how it was used in your valuation of your common and preferred stock.
   - Please tell us why you believe that the market values of companies whose IPO dates occurred several years prior to your proposed IPO accurately represent the current industry IPO market conditions for your industry and should be included in your comparable companies.
   - Please confirm that you are only using non-public entities as comparables.

5. Refer to your response to comment 3. We do not believe that your method of using the median in determining the value of your company is appropriate. The population you are using is not based on comparable companies with similar products, marketability of products, stages of development, collaborative partnerships, etc. In addition, it appears based on the information you provided that the company you are using for the median has completed phase 2 in one indication and went effective over a year ago when the market for your industry may have been different. It is unclear to us why this would represent a comparable company.

6. Please update the table on page 47 to include any options, warrants, or other equity instruments granted/issued in 2007. Disclose any anticipated compensation expense to be recorded as a result of equity issuances.

Initial clinical strategy and regulatory status, page 61

7. Please expand the discussion to indicate when you received the favorable response referred to in the carryover paragraph on the top of page 62.

8. Please indicate when the FDA requested the non-rodent toxicity study and the amount of additional time you anticipate will be required to complete this study.

Note 14. Subsequent event, page F-34

9. We note your response to comment 6. Please revise your disclosure to clarify that the shares of Series C-1 redeemable convertible preferred stock issued on January 22 and February 1, 2007 are convertible at $8.82 per share. In addition, please tell us and disclose in the filing what events occurred to increase the fair value of the underlying shares from the $4.62 amount at December 2006 to $6 at the time of issuance in January 22, 2007 and February 1, 2007 and what events led to the increase from the issuance of the C-1 redeemable convertible preferred stock price of $6 to the IPO range of $9-11. We note your response states that 73% of the Series C-1 redeemable convertible preferred stock offering was funded by independent investors yet on page 98 you disclose that 5,520,833 or 73% of the shares were sold to the directors, officers and five percent shareholders. Please explain this inconsistency.

* * *

As appropriate, please amend your registration statement in response to these comments. You may wish to provide us with marked copies of the amendment to expedite our review. Please furnish a cover letter with your amendment that keys your responses to our comments and provides any requested information. Detailed cover

letters greatly facilitate our review. Please understand that we may have additional comments after reviewing your amendment and responses to our comments.

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 all information required under the Securities Act of 1933 and that they have provided all information investors require for an informed investment decision. 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 the company requests acceleration of the effective date of the pending registration statement, it should furnish a letter, at the time of such request, 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.

In addition, please be advised that the Division of Enforcement has access to all information you provide to the staff of the Division of Corporation Finance in connection with our review of your filing or in response to our comments on your filing.

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. We will act on the request and, pursuant to delegated authority, grant acceleration of the effective date.

We direct your attention to Rules 460 and 461 regarding requesting acceleration of a registration statement. Please allow adequate time after the filing of any amendment for further review before submitting a request for acceleration. Please provide this request at least two business days in advance of the requested effective date.

You may contact Dana Hartz at (202) 551-3648 or Mary Mast at (202) 551-3613 if you have questions regarding comments on the financial statements and related matters. Please contact John Krug at (202) 551-3862, Suzanne Hayes, Branch Chief, at (202) 551- 3675, or me at (202) 551-3715 with any other questions.

Sincerely,

Jeffrey Riedler
Assistant Director

cc: Marc Rubenstein, Esq.
Richard D. Truesdell, Jr., Esq.