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

DIVISION OF
CORPORATION FINANCE

Mail Stop 4546

June 11, 2017

Frederick C. Beddingfield III, M.D., Ph.D.
President and Chief Executive Officer
Sienna Biopharmaceuticals, Inc.
30699 Russell Ranch Road, Suite 140
Westlake Village, California 91362

Re: Sienna Biopharmaceuticals, Inc.
Draft Registration Statement on Form S-1
Submitted May 15, 2017
CIK No. 0001656328

Dear Dr. Beddingfield:

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. We note your reference to your pipeline of "safe and effective" topical therapies in the second sentence of this section and your statement that you create topical therapies that are specifically designed to be "highly effective and safe" for chronic administration on pages 2 and 3 as well as on page 87 of the Business section. Because approval by the FDA is dependent on its determination that a drug is safe and effective and given that your product candidates have not completed clinical trials, please remove reference to your products being safe and effective throughout your filing as such a determination may only be made by the FDA.

2. Please revise your disclosure with regard to SNA-001 to identify whether the pivotal clinical trials are Phase II or Phase III trials. Similarly, on pages 3-4 and in your Business section where you describe the development of SNA-001, please identify the clinical phase of your clinical feasibility studies.

3. Please revise your charts on pages 3 and 91 to remove the Proof of Concept and Pivotal columns for SNA-001 and to extend the Phase 1, Phase 2 and Phase 3 columns so that they cover SNA-001 as well.

4. We note your disclosure on page 3 that your nonclinical studies for SNA-125 for atopic dermatitis and psoriasis are still in progress, but the location of the arrow in the chart on page 1 implies that the preclinical phase has been completed. Please revise your chart accordingly.

5. We note that you have an arrow under your Topical by Design platform for "Other research programs." Please specifically identify these research programs and the indications that they are seeking to treat. If such information has not yet been determined, please remove the "Other research programs" arrow from your charts as it is premature to include it.

Our technology platforms and product candidates
Topical by Design, page 2

6. We note your statement that SNA-120 has demonstrated statistically significant and clinically meaningful reductions in the pruritus associated with psoriasis in a Phase 2b clinical trial. Please revise your disclosure to define the terms "statistically significant" and "clinically meaningful" at their first use in this section. In doing so, please refrain from referring to p-values in this section as the discussion of p-values should be reserved for the Business section where the proper context may be given. Please also apply this comment to your disclosure under "Topical Photoparticle Therapy" on page 3.

7. Please briefly describe the pruritus visual analog scale ("VAS") and the modified Psoriasis Area and Severity Index ("mPASI") when you first reference them in this section.

8. Please clarify the "clear impact" on the diseases mentioned and the "anti-inflammatory effects" you have observed, as well as the setting in which you observed them. For instance, disclose the scope and design of the study in which these findings were made

Topical Photoparticle Therapy, page 3

9. Please describe the meaning of the terms "near-infrared," "selective photothermolysis," and "pathogenesis" when you first use them in this section.

Implications of Being an Emerging Growth Company..., page 5

10. 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
If we are unable to obtain, maintain and enforce intellectual property protection…, page 38

11. In the last paragraph of this risk factor, you state that if the nanoComposix agreement is terminated or narrowed, you could lose intellectual property rights that may be material to your Topical Photoparticle Therapy products. Please expand your disclosure in this risk factor to describe under what circumstances nanoComposix may terminate its agreement with you.

We may not be able to protect our intellectual property rights throughout the world, page 41

12. Please disclose whether you or nanoComposix is responsible for protecting the patents and patent applications you license from nanoComposix and describe the risks related to the protection of this intellectual property.

Use of Proceeds, page 62

13. Please expand your disclosure regarding the proceeds to be used for the development of SNA-125 to describe how far in the development process you estimate the allocated proceeds will enable you to reach for each indication. Similarly, for SNA-001, please clarify whether the allocated proceeds will enable you to complete the on-going clinical trials for each indication.

Management's Discussion and Analysis of Financial Condition and Operations
Critical Accounting Policies and Use of Estimates
Common Stock Valuation, page 76

14. Once you have an estimated offering price or range, please explain to us 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 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.

Business, page 87

15. Under the appropriately titled subsections, please disclose when investigational new drug applications ("INDs") were filed for the commencement of clinical trials for SNA-120, SNA-125, and SNA-001, the trial sponsor and the subject of the INDs.

SNA-120 Clinical Development
Completed Phase 2b Trial, page 98

16. When you first reference them in this section, please explain the meaning and significance of "p-values" and their relationship to "statistical significance." In doing so, please explain how "p-values" and "statistical significance" relate to the FDA's evidentiary standards of efficacy.

SNA-001 for the treatment of acne
Clinical Development Program, page 110

17. Please revise your disclosure to clarify what you mean when you describe your clinical trials of SNA-001 as "split-face," "vehicle controlled," and "split back design."

Clinical feasibility studies, page 111

18. In the second paragraph of this section, please clarify that the results were "statistically significant" rather than "significant" in both the SNA-001 and control treatment groups and if true, that the difference between SNA-001 and control treatment was not statistically significant. Please make conforming changes when discussing the trial results for SNA-001 where applicable.

Intellectual Property, page 119

19. Please provide the following information for your Topical by Design and Topical Photoparticle Therapy patent portfolio:

    - The type of patent protection provided by the patents and patent applications such as composition of matter, use or process; and
    - The foreign jurisdictions where patents are issued and patent applications are pending.

Management
Executive Officers and Employee Directors, page 139

20. Please expand the background information for Richard Peterson to provide his business experience for the past five years. See Item 401(e) of Regulation S-K.

Certain Relationships and Related Party Transactions
Promissory Note, page 167

21. Please expand to disclose the total amount outstanding as of the latest practicable date as well as the amounts of principal and interest paid, if any. Refer to Item 404(a)(5) of Regulation S-K.

Notes to Consolidated Financial Statements
Note 7. Fair Value Measurements, page F-17

22. Please revise to provide quantitative information about the significant unobservable inputs used to determine the fair value of your Level 3 IPR&D asset and contingent consideration liability in accordance with ASC 820-10-50-2bbb. If you used the third party pricing exception in determining not to disclose this information, tell us how you qualify for such exception.

You may contact Christine Torney at (202) 551-3652 or Sharon Blume at (202) 551-3474 if you have questions regarding comments on the financial statements and related matters. Please contact Johnny Gharib at (202) 551-3170 or Mary Beth Breslin at (202) 551-3625 with any other questions.

Sincerely,

/s/ Mary Beth Breslin for

Suzanne Hayes
Assistant Director
Office of Healthcare and Insurance

cc: Brian J. Cuneo, Esq.
Latham & Watkins LLP