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

DIVISION OF
CORPORATION FINANCE

January 19, 2021

Dane Saglio
Chief Financial Officer
Seneca Biopharma, Inc.
20271 Goldenrod Lane
Germantown, MD 20876

Re: Seneca Biopharma, Inc.
Registration Statement on Form S-4
Filed December 23, 2020
File No. 333-251659

Dear Mr. Saglio:

We have reviewed your 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 amending your registration statement and providing the requested information. 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 any amendment to your registration statement and the information you provide in response to these comments, we may have additional comments.

Registration Statement on Form S-4

Questions and Answers About the Merger
What is the Merger?, page 1

1. Please revise and continue to update your disclosure here and in the Exchange Ratio discussion on pages 122-23 to disclose the current and/or anticipated status of the Seneca net cash calculation. Please also provide examples of estimated percentage ownership based on Seneca's level of net cash at the Effective Time.

2. Please explain to us why you have included two separate calculations of the post-merger combined company ownership at the bottom of page 1. In particular, please explain why you have only included 50% of the shares subject to the Equity Warrants in the first calculation as well as in other calculations throughout the document, which state that pre-

Merger Seneca equity holders will hold approximately 26.2% of the combined company (assuming Seneca net cash between $4.5 million and $5.0 million).

Please also update this section to include a cross-reference to the Pre-Merger Financing discussion that appears later in the document.

3. Please revise your disclosure here and in the preceding letter to stockholders of Seneca Biopharma, Inc. and Leading BioSciences, Inc. to disclose the identity of the Investor.

4. Per your description of the CVR Agreement on page 146, please update your disclosure here and on page 18 to clarify, if true, that holders of Seneca common stock immediately prior to the effective time will only receive proceeds from Legacy Monetization Events to the extent that such proceeds exceed $300,000 in the aggregate. Please also revise to confirm whether the up-front payment of $100,000 received by Seneca for the license NSI-189, as well as any additional proceeds received by Seneca prior to the Effective Time, will be treated as a Legacy Monetization.

Prospectus Summary

Leading BioSciences , Inc., page 13

5. Please provide a more detailed, balanced summary of LBS's business including a description of its lead product candidates and the status of its current clinical programs. Refer to Item 3 of Form S-4.

6. Given that LBS has not yet initiated a Phase 2/3 or Phase 3 clinical trial for any of its product candidates, please revise your statement that LBS is a "late" clinical stage biopharmaceutical company here and on pages 185 and 231.

Nasdaq Capital Market Listing , page 24

7. Please revise your disclosure here and on the cover page to indicate whether the Nasdaq's determination regarding the initial listing application will be known at the time stockholders are asked to vote on the merger agreement and whether you have had any discussions with Nasdaq concerning the initial listing application. Please also revise to include a discussion of the potential consequences to investors, including the ability of investors to buy and sell shares of common stock, if Nasdaq does not approve the listing application of the combined company, but Seneca and LBS proceed with the merger. Finally, please revise your disclosure to indicate whether you expect Seneca's current failure to comply with Nasdaq's minimum bid price requirement to have any impact on the initial listing application of the combined company.

The Merger

Background of the Merger, page 79

8. To the extent material, please identify the individuals who participated in the meetings and discussions described in this section. For instance, please identify the representatives

of Seneca and LBS who participated negotiation calls on September 25, 2020, October 6, 2020 and October 7, 2020 as well as the representatives who negotiated on calls between November 6, 2020 and December 15, 2020.

9. We note your disclosure that you selected Solebury and Hibiscus as your financial advisors. Please provide more details regarding the selection process for financial advisors, including the qualifications considered.

Seneca Reasons for the Merger, page 93

10. We note your disclosure throughout the document that the Exchange Ratio formula is based upon an LBS valuation of $97.85 million. However, your disclosure on page 103 indicates that Cassel Salpeter's analysis of comparable public companies indicated an implied equity value reference range for LBS of $58.4-87.6 million and that Cassel Salpeter's analysis of comparable IPOs indicated an implied equity value reference range for LBS of $58.1-82.9 million.

Please revise your disclosure to discuss the reasons why Seneca's board determined that a higher LBS valuation is fair to, advisable and in the best interests of Seneca and its stockholders.

Opinion of the Financial Advisor to the Seneca Transaction Committee
Financial Analysis of Seneca, page 102

11. Please revise your disclosure to provide the implied equity value reference range for Seneca on an aggregate basis.

Interests of the Seneca Directors and Executive Officers in the Merger, page 105

12. Please update your disclosure to discuss whether the report commissioned from Radford - Aon Rewards Consulting, Inc. included a discussion or recommendation with respect to the compensation payable to the executive officers discussed in this section, including the compensation that may be paid to executive officers in exchange for the cancellation of their options.

13. Please define the term "Accrued Obligations."

Material U.S. Federal Income Tax Consequences of the Merger, page 113

14. Please revise your prospectus disclosure to provide a firm conclusion regarding treatment of the transaction under Section 368(a) and remove language stating that it is intended that, or generally, certain material tax consequences will apply. In addition, please clearly state that the conclusion is the opinion of counsel. Please also remove any statement that assumes the material tax consequences at issue (e.g., "If the Merger qualifies as a reorganization within the meaning of Section 368(a) of the Code"). Refer to Section III of Staff Legal Bulletin No. 19 for guidance.

Agreements Related to the Merger
Pre-Merger Financing, page 142

15. Please revise your disclosure in the "*Securities Purchase Agreement (Equity Financing)*" subsection to describe the circumstances under which the Converted Additional Shares would not be delivered to the Investor by the 136th day following the Effective Time.

    Please also update your disclosure to clarify, if true, that any Converted Additional Shares not delivered to the Investor from escrow will be distributed to the holders of LBS capital stock at the Effective Time.

Contingent Value Rights Agreement, page 144

16. Please revise your disclosure to (i) explain the role of the CVR Agent and (ii) discuss how the CVR Holders' Representative will be selected. Please also revise to clarify whether Seneca's obligations pursuant to the CVR Agreement will become the obligations of the combined company following the Effective Time.

17. We note your disclosure that (i) Seneca will be entitled to use all or a portion of the Ongoing Support Funding ($500,000) for expenses related to a Legacy Monetization, (ii) that Seneca will pay $500,000 (i.e. the entire amount of the Ongoing Support Funding) to the CVR Holders' Representative at the Effective Time and that (iii) the CVR Holders' Representative will be entitled to be reimbursed from a segregated escrow account for costs related to any Legacy Monetization.

    Please update your disclosure to clarify (A) whether the intent of the arrangement is that the CVR Holders' Representative's fee will be reduced by amounts used by Seneca for expenses related to a Legacy Monetization and (B) the amount of funds that will be placed in the segregated escrow account and the identity of the escrow agent.

18. We note your disclosure that each CVR will entitle its holder to receive a pro rata portion of 80% of the net proceeds from any Legacy Monetization. We further note that "net proceeds" is defined as gross proceeds less deductions. Please revise your disclosure to explain how the remaining 20% of net proceeds from any Legacy Monetization will be allocated.

    We further note your disclosure on page 146 that the gross proceeds of any monetization will be reduced by the amount of the Ongoing Support Funding. Please update your disclosure here and in the Q&A in your document to clarify, if true, that the $500,000 of Ongoing Support Funding must be repaid before the net proceeds of any Legacy Monetization are distributed to legacy Seneca stockholders.

Description of Seneca's Business
Employees, page 183

19. Please revise your disclosure here and on page 221 to provide a description of your human capital resources as required by Item 101(c)(2)(ii) of Regulation S-K.

Description of LBS's Business
Overview, page 186

20. Please update LBS's pipeline chart to clarify whether each of the product candidates in the chart is wholly-owned or licensed from a third party.

    In addition, we note the inclusion of an oral protease inhibitor for glucose control and autoimmune disease in LBS's pipeline table. Given the status of development and the limited disclosure in the prospectus regarding these programs it seems premature to highlight theses program prominently in LBS's pipeline table. Accordingly, please revise to remove these programs from the pipeline table or advise.

21. We note the disclosure throughout this section stating that "evidence suggests that digestive enzyme leakage...", "genetic evidence supporting the association of proteases...", "there is building evidence that...", "multiple lines of evidence implicate aberrant protease activity", etc. Please revise these and similar statements to clearly described where this evidence was observed and whether it was based on studies or trials conducted by LBS or by a third party.

Our Strategy, page 187

22. Please update this section, or another part of the Description of LBS's Business as appropriate, to discuss whether you have identified the first indication(s) for which you anticipate seeking marketing approval for LB1148 and the clinical trials that you will be required to conduct to support your initial application(s) for marketing approval.

23. Please remove the statement that LBS intends to "rapidly" develop LB1148 as well as any other statements that state or imply that you will be successful in developing and progressing your product candidates in a rapid or accelerated manner as these statements are inherently speculative.

24. Please remove here and throughout to remove any statements that LBS's product candidates are "best-in-class" or "first-in-class" because the term suggests that the product candidates are effective and likely to be approved by the FDA. If your use of the term was designed to convey your belief that your product candidates are based on a differentiated technology or approach, you may further discuss how your technology or approach differs from those of your competitors.

25. We note your statements that a "similarly designed" open-label clinical trial provide evidence that LB1148 can reduce the time to return to bowel function in GI surgery and

that three patients treated with LB1148 who were assessed for postoperative adhesions did not develop postoperative adhesions.

Please balance your disclosure to disclose the stage of these trials, whether the trials were powered for efficacy, and any relevant limitations. We further note that your disclosure on page 194 regarding the postoperative adhesions assessment states that the surgeon for one of the three patients was not an investigator and that postoperative adhesions were not formally assessed. Please revise your statements on page 187 to reflect the discussion on page 194.

Unmet Needs in Intestinal Barrier Dysfunction and the Opportunity for LB1148, page 187

26. We note your statement here that LB1148 "is expected to confer multiple benefits" as well as your statement elsewhere that LB1148 "is expected to improve patient outcomes." We similarly note your statements that data suggest that LB1148 may prevent postoperative adhesions in surgical patients, that LB1148 may offer distinguishing benefits for patients providers and that LB1148 may reduce overall length of stay in both the hospital and ICU settings. These are just examples.

Please revise your disclosure throughout your prospectus to revise these and similar statements to eliminate conclusions or predictions that LB1148 is or will be effective as determinations of efficacy are solely within the authority of the FDA. You may provide a summary of the objective data from your preclinical studies and clinical trials without including conclusions related to efficacy.

Clinical Development of LB1148, page 192

27. Please update your disclosure to include a explanation of statistical significance.

CV Surgery Phase 1, LBS-IST-CVS-101, page 192

28. Please update your disclosure to discuss whether the clinical trial of LB1148-Z can be used to support an eventual NDA filing with the FDA.

PB101, page 200

29. Please revise your disclosure to state whether PB101 is wholly-owned by LBS or in-licensed. Please also revise your disclosure to clarify whether you conducted the studies referenced later in this section or if they were conducted by a third-party. Further, please present more detailed information regarding the studies in animal models that indicate that PB101 can preserve intestinal issue following intestinal injury. Alternatively, explain to us why this disclosure would not be material.

Finally, please revise your disclosure to indicate the status of a potential IND filing for PB101 or explain to us why this would not be practicable.

Protease Activity and IBD, page 201

30. Please revise and simplify your disclosure in the first seven sentences of this paragraph. Your disclosure should clearly explain the role of proteases and should clearly convey the potential relationship between protease activity and GI diseases.

Intellectual Property, page 206

31. Please update this section to discuss your IP coverage for PB101.

Co-Development Agreement with Newsoara, page 209

32. Please update your disclosure in this section to clarify if LB1148 and PB101 are subject to the agreement.

Government Regulation and Product Approval, page 210

33. Please update your disclosure in this section to include a discussion of the regulation of polyethylene glycol 3350 ("PEG") referenced on page 47 of your registration statement. In your revisions, please disclose whether you have discussed the classification of PEG in LB1148 with the FDA or other regulatory agencies. Please also explain why an FDA decision that LB1148 is a combination product would require additional clinical trials "for which there is not currently a feasible clinical trial design."

Description of Seneca Capital Stock
Amended and Restated Certificate of Incorporation and Amended and Restated Bylaws, page 272

34. We note that Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder, and Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. We further note your disclosure on page 280 that your exclusive forum provision does not apply to Securities Act or Exchange Act claims. Please revise your disclosure here to clarify, if true, that the exclusive forum provision described here does not apply to Securities Act or Exchange Act claims.

We remind you that the company and its management are responsible for the accuracy and adequacy of their disclosures, notwithstanding any review, comments, action or absence of action by the staff.

Refer to Rules 460 and 461 regarding requests for acceleration. Please allow adequate time for us to review any amendment prior to the requested effective date of the registration statement.

You may contact Christine Torney at 202-551-3652 or Kevin Kuhar at 202-551-3662 if you have questions regarding comments on the financial statements and related matters. Please contact Alan Campbell at 202-551-4224 or Celeste Murphy at 202-551-3257 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Life Sciences

cc: Raul Silvestre