

September 24, 2024

Jeffrey Finer, M.D, Ph.D.  
President and Chief Executive Officer  
Septerna, Inc.  
250 East Grand Avenue  
South San Francisco, CA 94080

Re: Septerna, Inc.  
Amendment No. 1 to Draft Registration Statement on Form S-1  
Submitted September 12, 2024  
CIK No. 0001984086

Dear Jeffrey Finer M.D, Ph.D.:

We have reviewed your amended registration statement and have the following comments.

Please respond to this letter by amending your registration statement and providing the requested information. If you do not believe a comment applies 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 this letter, we may have additional comments. Unless we note otherwise, any references to prior comments are to comments in our September 5, 2024 letter.

Draft Registration Statement on Form S-1 submitted September 12, 2024  
Government Regulation, page 142

1. We note your response to prior comment 19 and re-issue the comment in part. Please expand your discussion of the Clinical Trial Notification (CTN) in Australia to clarify the applicable review and approval process. Our Solution: Our Small Molecule Single- and Multi- Incretin Receptor Agonists, page 152
2. We note the revised disclosure made in response to comment 18. However, the revisions do not put the data in the table in context. How does the data in the table demonstrate differential potency and selectivity of these compounds in their ability to activate GIPR, GLP-1R and GCGR induced intracellular signaling. An interpretation of the specific data in the table may be helpful.  
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Please contact Ibolya Ignat at 202-551-3636 or Angela Connell at 202-551-3426 if you have questions regarding comments on the financial statements and related matters. Please contact Tamika Sheppard at 202-551-8346 or Suzanne Hayes at 202-551-3675 with any other questions.

Sincerely,

Division of  
Office of Life

Corporation Finance  
Sciences  
cc: Mitchell S. Bloom