

October 2, 2024

VIA EDGAR

United States Securities and Exchange Commission
Division of Corporation Finance
Office of Life Sciences
100 F. Street, N.E.
Washington, D.C. 20549
Attention: Ibolya Ignat, Angela Connell, Tamika Sheppard and Suzanne Hayes

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

Dear Ladies and Gentlemen:

This letter is confidentially submitted on behalf of Septerna, Inc. (the “**Company**”), in response to the comments of the staff of the Division of Corporation Finance (the “**Staff**”) of the U.S. Securities and Exchange Commission (the “**Commission**”) with respect to the Company’s Draft Registration Statement on Form S-1, originally confidentially submitted on August 2, 2024 and resubmitted on September 12, 2024 (the “**Draft Registration Statement**”), as set forth in the Staff’s letter, dated September 24, 2024, addressed to Jeffrey Finer, M.D., Ph.D. (the “**Comment Letter**”). The Company is concurrently publicly filing the Registration Statement on Form S-1 (the “**Registration Statement**”), which includes changes to reflect responses to the Staff’s comments and other updates.

For reference purposes, the text of the Comment Letter has been reproduced herein with responses below each numbered comment. For your convenience, we have italicized the reproduced Staff comments from the Comment Letter. Unless otherwise indicated, page references in the descriptions of the Staff’s comments refer to the Draft Registration Statement, and page references in the responses refer to the Registration Statement. All capitalized terms used and not otherwise defined herein shall have the meanings set forth in the Registration Statement.

The responses provided herein are based upon information provided to Goodwin Procter LLP by the Company.

Draft Registration Statement on Form S-1

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.*

RESPONSE: The Company respectfully acknowledges the Staff's comment and advises the Staff that it has revised the disclosure on pages 142, 172 and 173 of the Registration Statement in response to the Staff's comment.

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.*

RESPONSE: The Company respectfully acknowledges the Staff's comment and advises the Staff that it has revised the disclosure on pages 152 and 153 of the Registration Statement in response to the Staff's comment.

If you should have any questions concerning the enclosed matters, please contact the undersigned at (212) 459-7072.

Enclosures

Sincerely,

/s/ Adam V. Johnson

cc: Jeffrey Finer, M.D., Ph.D., *Septerna, Inc.*
Liz Bhatt, M.S., M.B.A., *Septerna, Inc.*
Mitchell S. Bloom, *Goodwin Procter LLP*
Deepa M. Rich, *Goodwin Procter LLP*
Denny Won, *Cooley LLP*
Charles S. Kim, *Cooley LLP*
Kristin VanderPas, *Cooley LLP*
Dave Peinsipp, *Cooley LLP*