As filed with the Securities and Exchange Commission on October 24, 2024.

UNITED STATES SECURITIES AND EXCHANGE COMMISSION Washington D.C. 20549

Washington, D.C. 20549

FORM S-1 REGISTRATION STATEMENT UNDER

THE SECURITIES ACT OF 1933

SEPTERNA, INC.

(Exact name of registrant as specified in its charter)

Delaware (State or other jurisdiction of incorporation or organization) 2834 (Primary Standard Industrial Classification Code Number) 84-3891440 (I.R.S. Employer Identification No.)

250 East Grand Avenue South San Francisco, California 94080 (650) 338-3533

(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

Copies to:

Mitchell S. Bloom Deepa M. Rich Adam V. Johnson Goodwin Procter LLP 601 Marshall Street Redwood City, California 94063 (650) 752-3100 Denny Won Charles S. Kim Kristin VanderPas Dave Peinsipp Cooley LLP 3 Embarcadero Center, 20th Floor San Francisco, California 94111 (415) 693-2000

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this registration statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, check the following box.

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. \boxtimes 333-282469

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. \Box

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. \Box

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company" and "emerging growth company" in Rule 12b-2 of the Exchange Act.

 Large Accelerated filer
 □

 Non-accelerated filer
 ⊠

 Accelerated filer
 □

 Smaller reporting company
 ⊠

 Emerging growth company
 ⊠

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 7(a)(2)(B) of the Securities Act.

The Registration Statement shall become effective upon filing in accordance with Rule 462(b) promulgated under the Securities Act of 1933, as amended.

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EXPLANATORY NOTE AND INCORPORATION BY REFERENCE

This Registration Statement is being filed pursuant to Rule 462(b) under the Securities Act of 1933, as amended (the "Securities Act"), for the sole purpose of increasing the aggregate number of shares of common stock offered by Septerna, Inc. (the "Registrant") by 830,556 shares, 108,334 of which are subject to purchase upon exercise of the underwriters' option to purchase additional shares of the Registrant's common stock. The contents of the Registration Statement on Form S-1, as amended (File No. 333-282469), filed by the Registrant with the Securities and Exchange Commission (the "Commission") pursuant to the Securities Act, which was declared effective by the Commission on October 24, 2024, including all exhibits thereto, are incorporated by reference into this Registration Statement.

The required opinion and consents are listed on an Exhibit Index attached hereto and filed herewith.

EXHIBIT INDEX

Exhibit No.	Exhibit Index
5.1	Opinion of Goodwin Procter LLP.
23.1	Consent of Independent Registered Public Accounting Firm.
23.2	Consent of Goodwin Procter LLP (included in Exhibit 5.1)
24.1*	Power of Attorney (included on signature page).

107 <u>Filing Fee Table</u>

Previously filed on the signature page to the Registrant's Registration Statement on Form S-1, as amended (File No. 333-282469), originally filed with the Securities and Exchange Commission on October 2, 2024 and incorporated by reference herein.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, as amended, the registrant has duly caused this registration statement on Form S-1 to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, California, on the 24th day of October, 2024.

SEPTERNA, INC.

By:/s/ Jeffrey Finer, M.D., Ph.D.Name:Jeffrey Finer, M.D., Ph.D.Title:President, Chief Executive Officer and Director

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement on Form S-1 has been signed by the following person in the capacities and on the date indicated.

Name	Title	Date	
/s/ Jeffrey Finer, M.D., Ph.D. Jeffrey Finer, M.D., Ph.D.	President and Chief Executive Officer (Principal Executive Officer)	October 24, 2024	
/s/ Ran Xiao, M.B.A., CFA Ran Xiao, M.B.A., CFA	Interim Chief Financial Officer, Vice President of Finance and Business Operations (Principal Financial Officer and Principal Accounting Officer)	October 24, 2024	
*	Chairman and Director	October 24, 2024	
Jeffrey Tong, Ph.D. * Abraham Bassan, M.S.	Director	October 24, 2024	
* Bernard Coulie, M.D., Ph.D., M.B.A.	Director	October 24, 2024	
* Alan Ezekowitz, M.D., D.Phil.	Director	October 24, 2024	
* Shalini Sharp, M.B.A.	Director	October 24, 2024	
* Jake Simson, Ph.D.	Director	October 24, 2024	
*By: /s/ Jeffrey Finer, M.D., Ph.D.			

Jeffrey Finer, M.D., Ph.D. Attorney-in-Fact

Re: <u>Securities Registered under Registration Statement on Form S-1</u>

We have acted as counsel to you in connection with your filing of (i) a Registration Statement on Form S-1 (File No. 333-282469) (as amended or supplemented, the "Initial Registration Statement") pursuant to the Securities Act of 1933, as amended (the "Securities Act"), and (ii) a second Registration Statement on Form S-1 filed pursuant to Rule 462(b) promulgated under the Securities Act (the "462(b) Registration Statement," and together with the Initial Registration Statement, the "Registration Statement"). This opinion letter is being furnished to you in connection with your filing of the 462(b) Registration Statement relating to the registration of the offering by Septerna, Inc., a Delaware corporation (the "Company"), of up to 830,556 shares (the "Shares") of the Company's Common Stock, \$0.001 par value per share, including Shares purchasable by the underwriters upon their exercise of an option to purchase additional shares granted to the underwriters by the Company. The Shares are being sold to the several underwriters named in, and pursuant to, an underwriting agreement among the Company and such underwriters (the "Underwriting Agreement").

We have reviewed such documents and made such examination of law as we have deemed appropriate to give the opinions set forth below. We have relied, without independent verification, on certificates of public officials and, as to matters of fact material to the opinion set forth below, on certificates of officers of the Company.

The opinion set forth below is limited to the Delaware General Corporation Law.

Based on the foregoing, we are of the opinion that the Shares have been duly authorized and, when delivered and paid for in accordance with the terms of the Underwriting Agreement, will be validly issued, fully paid and non-assessable.

This opinion letter and the opinion it contains shall be interpreted in accordance with the Core Opinion Principles as published in 74 *Business Lawyer* 815 (Summer 2019).

We hereby consent to the inclusion of this opinion as Exhibit 5.1 to the 462(b) Registration Statement and to the references to our firm under the caption "Legal Matters" in the Initial Registration Statement. In giving our consent, we do not admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations thereunder.

Very truly yours,

/s/ Goodwin Procter LLP GOODWIN PROCTER LLP

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the Registration Statement on Form S-1 filed pursuant to Rule 462(b) of the Securities Act of 1933 of the reference to our firm under the caption "Experts" and to the incorporation by reference of our report dated August 2, 2024 (except for the eleventh paragraph of Note 1, as to which the date is October 21, 2024), with respect to the financial statements of Septerna, Inc. included in Amendment No.2 to the Registration Statement (Form S-1 No. 333-282469) and related Prospectus of Septerna, Inc. for the registration of its common stock.

/s/ Ernst & Young LLP

San Mateo, California October 24, 2024

Calculation of Filing Fee Table

Form S-1

(Form Type)

Septerna, Inc.

(Exact Name of Registrant as Specified in its Charter)

Table 1: Newly Registered Securities

	Security Type	Security Class Title	Fee Calculation or Carry Forward Rule	Amount Registered	Proposed Maximum Offering Price per Unit	Proposed Maximum Aggregate Offering Price ⁽¹⁾⁽²⁾	Fee Rate	Amount of Registration Fee			
NEWLY REGISTERED SECURITIES											
Fees to Be Paid	Equity	Common Stock, par value \$0.001 per share	457(a)	830,556(1)	\$18.00(1)	\$14,950,008.00	0.00015310	\$2,288.85			
Fees Previously Paid			_	_	_			_			
CARRY FORWARD SECURITIES											
Carry Forward Securities	_	_	_	_		_					
	Total Offering Amounts					\$14,950,008.00		\$2,288.85			
	Total Fees Previously Paid Total Fee Offsets Net Fee Due							—			
								_			
								\$2,288.85(3)			

(1)Represents only the additional number of shares being registered and includes 108,334 shares of common stock that the underwriters have the option to purchase. Does not include the securities that the Registrant previously registered on the Registration Statement on Form S-1 (File No. 333-282469), as amended (the "Prior Registration Statement").

(2)Estimated solely for the purpose of computing the registration fee in accordance with Rule 457(a) under the Securities Act of 1933, as amended (the "Securities Act").

(3)The registration fee is calculated in accordance with Rule 457(a) under the Securities Act based on the proposed maximum aggregate offering price. The registrant previously registered securities on the Prior Registration Statement having a proposed maximum aggregate offering price of \$316,249,992.00, which was declared effective by the Securities and Exchange Commission on October 24, 2024. In accordance with Rule 462(b) under the Securities Act, an additional amount of securities having a proposed maximum aggregate offering price of \$14,950,008.00 is hereby registered, which includes shares issuable upon the exercise of the underwriters' option to purchase additional shares.