

☐ Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See Instruction 1(b).

☐ Check this box to indicate that a transaction was made pursuant to a contract, instruction or written plan for the purchase or sale of equity securities of the issuer that is intended to satisfy the affirmative defense conditions of Rule 10b5-1(c). See Instruction 10.

STATEMENT OF CHANGES IN BENEFICIAL OWNERSHIP

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934 or Section 30(h) of the Investment Company Act of 1940

OMB APPROVAL	
OMB Number:	3235-0287
Estimated average burden hours per response:	0.5

1. Name and Address of Reporting Person * <u>Simson Jake</u> (Last) (First) (Middle) <u>C/O SEPTERNA, INC.</u> <u>250 EAST GRAND AVENUE</u> (Street) <u>SOUTH SAN FRANCISCO</u> <u>CA</u> <u>94080</u> (City) (State) (Zip)	2. Issuer Name and Ticker or Trading Symbol <u>Septerna, Inc. [SEPN]</u> 3. Date of Earliest Transaction (Month/Day/Year) <u>06/26/2026</u> 4. If Amendment, Date of Original Filed (Month/Day/Year)	5. Relationship of Reporting Person(s) to Issuer (Check all applicable) ☒ Director 10% Owner Officer (give title below) Other (specify below) 6. Individual or Joint/Group Filing (Check Applicable Line) ☒ Form filed by One Reporting Person Form filed by More than One Reporting Person
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Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned

1. Title of Security (Instr. 3)	2. Transaction Date (Month/Day/Year)	2A. Deemed Execution Date, if any (Month/Day/Year)	3. Transaction Code (Instr. 8)		4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5)			5. Amount of Securities Beneficially Owned Following Reported Transaction(s) (Instr. 3 and 4)	6. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	7. Nature of Indirect Beneficial Ownership (Instr. 4)
			Code	V	Amount	(A) or (D)	Price			

Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities)

1. Title of Derivative Security (Instr. 3)	2. Conversion or Exercise Price of Derivative Security	3. Transaction Date (Month/Day/Year)	3A. Deemed Execution Date, if any (Month/Day/Year)	4. Transaction Code (Instr. 8)		5. Number of Derivative Securities Acquired (A) or Disposed of (D) (Instr. 3, 4 and 5)		6. Date Exercisable and Expiration Date (Month/Day/Year)		7. Title and Amount of Securities Underlying Derivative Security (Instr. 3 and 4)		8. Price of Derivative Security (Instr. 5)	9. Number of derivative Securities Beneficially Owned Following Reported Transaction(s) (Instr. 4)	10. Ownership Form: Direct (D) or Indirect (I) (Instr. 4)	11. Nature of Indirect Beneficial Ownership (Instr. 4)
				Code	V	(A)	(D)	Date Exercisable	Expiration Date	Title	Amount or Number of Shares				
Stock Option (Right to Buy)	\$37.34	06/26/2026		A		15,000		(1)	06/25/2036	Common Stock	15,000	\$0	15,000	D ⁽²⁾	

Explanation of Responses:

1. The shares underlying the stock option vest in full upon the earlier of (i) June 26, 2027 or (ii) the date of the Issuer's next annual meeting of stockholders, subject to the Reporting Person's continued service to the Issuer through such vesting date.

2. Under the Reporting Person's arrangement with RA Capital Management, L.P. (the "Adviser"), the Reporting Person holds the option for the benefit of the R.A. Capital Healthcare Fund, L.P. (the "Fund") and R.A. Capital Nexus Fund III, L.P. (the "Nexus Fund III"). The Reporting Person is obligated to turn over to the Adviser any net cash or stock received upon exercise of the option, which will offset advisory fees owed by the Fund and the Nexus Fund III to the Adviser. The Reporting Person therefore disclaims beneficial ownership of the option and underlying common stock.

Remarks:

Exhibit 24.2 - Substitute Power of Attorney

/s/ Mark A. Wilson, Attorney-in-Fact 06/30/2026

** Signature of Reporting Person Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

* If the form is filed by more than one reporting person, see Instruction 4 (b)(v).

** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.

SUBSTITUTE POWER OF ATTORNEY

Under the terms of powers of attorney (each, a "Power of Attorney") previously filed with the U.S. Securities and Exchange Commission, the undersigned was appointed an attorney-in-fact for the below listed individuals to, among other things, execute for and on behalf of the following individuals any Form 3, Form 4, Form 5, Schedule 13D, or Schedule 13G, or any amendment(s) thereto, in accordance with Section 13 or Section 16 of the Securities Exchange Act of 1934, as amended, and the rules and regulations promulgated thereunder:

Abraham Bassan
Liz Bhatt
Bernard Coulie
Alan Ezekowitz
Jeffrey Finer
Jae B. Kim
Uwe Klein
Daniel D. Long
Shalini Sharp
Jake Simson
Samira Shaikhly
Jeffrey K. Tong

In accordance with the authority granted under each Power of Attorney, including the full power of substitution, the undersigned hereby appoints each of Gil M. Labrucherie and Mark A. Wilson, as substitute attorneys-in-fact, on behalf of the individuals listed above, with the power to exercise and execute all of the powers granted or conferred in the original Power of Attorney. For the avoidance of doubt, the foregoing appointment shall not serve as a revocation of the powers granted to the undersigned herself in each Power of Attorney.

This substitute Power of Attorney shall remain in full force and effect with respect to each Power of Attorney until such underlying Power of Attorney is revoked or terminated, unless earlier revoked by the undersigned in a signed writing.

Date: February 10, 2026

By: /s/ Ran Xiao
Name: Ran Xiao
Title: Attorney-in-Fact
