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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): February 18, 2025

SEPTERNA, INC.
(Exact name of Registrant as Specified in Its Charter)

Delaware	**001-42382**	**84-3891440**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

Septerna, Inc.
250 East Grand Avenue
South San Francisco, CA **94080**
(Address of Principal Executive Offices) **(Zip Code)**

Registrant's Telephone Number, Including Area Code: (650) 338-3533

Not Applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.001 par value per share	SEPN	The Nasdaq Global Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

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 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On February 18, 2025, Septerna, Inc. (the "Company") issued a press release entitled "Septerna Announces Discontinuation of SEP-786 Phase 1 Clinical Trial and Plans to Advance Next-Generation Oral Small Molecule PTH1R Agonist." A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K.

The information furnished under this Item 7.01, including Exhibit 99.1 hereto, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

99.1	Press Release issued by Septerna, Inc. on February 18, 2025, furnished herewith.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Septerna, Inc.

Date: February 18, 2025

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

Exhibit 99.1

Septerna Announces Discontinuation of SEP-786 Phase 1 Clinical Trial and Plans to Advance Next-Generation Oral Small Molecule PTH1R Agonist

Trial decision follows unanticipated events of elevated unconjugated bilirubin levels

Company advancing multiple next-generation PTH1R agonists with distinct and unrelated chemical structures relative to SEP-786

SOUTH SAN FRANCISCO, Calif., Feb. 18, 2025 – Septerna, Inc. (Nasdaq: SEPN), a clinical-stage biotechnology company pioneering a new era of GPCR drug discovery, today announced its decision to discontinue the Phase 1 single- and multiple-ascending dose (SAD/MAD) clinical trial of SEP-786 in healthy volunteers. SEP-786 is an oral small molecule agonist of the parathyroid hormone 1 receptor (PTH1R) being developed for the treatment of hypoparathyroidism.

Septerna's decision follows the observation of two unanticipated severe (Grade 3) events of elevated unconjugated bilirubin in the MAD portion of the Phase 1 trial, both of which were without elevations in ALT, AST, and GGT liver enzyme levels. Dosing was discontinued for both study participants, and the bilirubin elevations were reversible. Importantly, there were no events of liver injury, cholestasis, or hemolysis across all participants, and there were no serious adverse events (SAEs) in the Phase 1 trial.

"After careful evaluation of SEP-786 and in the context of our robust PTH1R agonist program, we've made the decision to discontinue the SEP-786 Phase 1 trial. We observed early signals of on-target pharmacological activity with SEP-786, with increases in serum calcium and corresponding decreases in endogenous PTH, reinforcing our commitment to developing an oral small molecule PTH1R agonist for hypoparathyroidism," said Jeffrey Finer, M.D., Ph.D., chief executive officer and co-founder of Septerna. "Strategically, for each of our programs, we identify a diverse portfolio of follow-on compounds that are chemically distinct. We have multiple attractive PTH1R agonists from which we plan to select a next-generation candidate to accelerate toward the clinic later this year to quickly regain momentum with our PTH1R program."

In completed 28-day preclinical toxicology studies, SEP-786 was generally well-tolerated, without predicted risk of bilirubin elevation. In response to these Phase 1 events, Septerna has initiated non-clinical studies to investigate the underlying mechanism behind the observed effect.

"Our extensive preclinical research and toxicology studies did not predict the risk of this off-target effect of SEP-786," said Jae B. Kim, M.D., Chief Medical Officer of Septerna. "We plan to expeditiously progress our PTH1R program with a next-generation candidate. In addition, we are on-track with SEP-631, our selective oral small molecule MRGPRX2 negative allosteric modulator for mast cell diseases, which we are preparing for clinical initiation later this year. We look forward to sharing more on our progress in the future."

The Company's cash, cash equivalents, and marketable securities totaled $137.5 million as of September 30, 2024. Together with the $302.6 million in net proceeds from the company's IPO completed in October 2024, Septerna expects its current cash position to support its planned operations into at least the second half of 2027.

About Septerna

Septerna, Inc. is a clinical-stage biotechnology company pioneering a new era of GPCR drug discovery powered by its proprietary Native Complex Platform™. Its industrial-scale platform aims to unlock the full potential of GPCR therapies and has led to the discovery and development of its deep pipeline of oral small molecule product candidates focused initially on treating patients in three therapeutic areas: endocrinology, immunology and inflammation, and metabolic diseases. Septerna was launched by preeminent drug discovery company builders and scientific leaders in the biochemistry, structural biology, and pharmacology of GPCRs. For more information, please visit www.septerna.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements about Septerna's beliefs and expectations regarding: the continued development and advancement of Septerna's oral small molecule GPCR-targeted programs; its ability to demonstrate, and the timing of, preclinical proof-of-concept in vivo and ex vivo for multiple programs including Septerna's plan to select a next-generation PTH1R product candidate to accelerate toward the clinic later this year; its ability to advance any product candidates that it may identify and successfully complete any clinical studies; the initiation, timing, progress, and results of conducting its research and development programs including its plans to initiate a clinical trial for SEP-631 later this year; the potential of its proprietary Native Complex Platform™; its expectations regarding the implementation of its business model, strategic plans for its business, product candidates, and technology, and the accuracy of its estimates regarding expenses and capital requirements, including its expected cash runway into at least the second half of 2027. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "objective," "ongoing," "plan," "predict," "project," "potential," "should," or "would," or the negative of these terms, or other comparable terminology are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks associated with: uncertainties related to Septerna's product candidates entering clinical trials; the authorization, initiation, and successful completion of preclinical and Investigational New Drug (IND)-enabling studies to support future clinical development of potential product candidates (including those for the PTH1R program), including uncertainties related to opening INDs and obtaining regulatory approvals; risks related to clinical development outcomes including unexpected safety or efficacy findings; the results of preclinical studies, or clinical studies not being predictive of future results in connection with future studies; the scope of protection Septerna is able to establish and maintain for intellectual property rights covering its Native Complex Platform™ and its product candidates; Septerna's ability to identify and enter into future license agreements and collaborations; and general economic, industry and market

conditions. These and other risks and uncertainties are described in greater detail in the section entitled “Risk Factors” in Septerna’s most recent Quarterly Report on Form 10-Q, as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent Septerna’s views only as of today and should not be relied upon as representing its views as of any subsequent date. Septerna explicitly disclaims any obligation to update any forward-looking statements subject to any obligations under applicable law. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

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