Septerna Announces Initiation of Phase 1 Clinical Trial of SEP-479, an Oral Small Molecule PTH1R Agonist for the Treatment of Hypoparathyroidism

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Trial Designed to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of SEP-479 in Healthy Volunteers

Data Anticipated in Late 2026 or Early 2027

SOUTH SAN FRANCISCO, Calif., April 13, 2026 (GLOBE NEWSWIRE) -- Septerna, Inc. (Nasdaq: SEPN), a clinical-stage biotechnology company pioneering a new era of G protein-coupled receptor (GPCR) drug discovery, today announced the dosing of the first participants in its Phase 1 clinical trial of SEP-479, its potent oral small molecule PTH1R agonist being developed for the treatment of patients with hypoparathyroidism. The Phase 1 clinical trial is a single-ascending dose (SAD) and multiple-ascending dose (MAD) clinical trial to evaluate the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of SEP-479 in healthy adult volunteers.

“Hypoparathyroidism is a lifelong condition that patients must manage with either high doses of calcium supplements several times a day or daily parathyroid hormone (PTH) injections, both of which can place a substantial burden on patients over time,” said Jeffrey Finer, M.D., Ph.D., Chief Executive Officer and Co-founder of Septerna. “We are encouraged by the preclinical data for SEP-479, which underscore its potential to be a disease modifying therapy for hypoparathyroidism by directly targeting the PTH receptor to provide patients full-day calcium control and relief from their debilitating symptoms. Based on these findings, we believe SEP-479 has the potential to be differentiated as a once-daily oral therapy for patients, and we look forward to advancing our Phase 1 trial as rapidly as possible.”

The randomized, placebo-controlled Phase 1 clinical trial is expected to enroll up to 150 healthy adult participants. Dosing is underway in the SAD portion of the clinical trial, which will evaluate the safety and tolerability of SEP-479 at escalating oral doses. The MAD portion of the clinical trial is designed to evaluate the safety and tolerability of once-daily oral dosing of SEP-479 over multiple days of treatment, with secondary and exploratory endpoints including PK and PD, with the latter assessed by changes in endogenous PTH and serum calcium, as well as other biomarkers. Septerna anticipates reporting data from the trial in late 2026 or early 2027.

About SEP-479
Septerna is developing SEP-479, a potent oral small molecule parathyroid hormone 1 receptor (PTH1R) agonist, for the treatment of patients with hypoparathyroidism. In preclinical studies, SEP-479 demonstrated activity comparable to PTH peptides in cell-based assays and in vivo models, normalized serum calcium in a rat model of hypoparathyroidism and increased serum calcium with reductions in endogenous PTH in a non-human primate PK/PD study. SEP-479 was generally well tolerated in 28-day GLP toxicology studies in rats, dogs and non-human primates.

About Hypoparathyroidism
Hypoparathyroidism is a debilitating endocrine disease caused by a deficiency of the parathyroid hormone (PTH) that results in a range of symptoms, including muscle cramps, fatigue, cognitive dysfunction, and life-threatening complications, such as cardiac arrhythmias, seizures, and renal failure. Current therapies include high doses of calcium and vitamin D supplements orally several times daily or daily PTH injections. There remains a need for treatment options designed to functionally replace PTH that offer more convenient modes of administration for patients compared to lifelong daily injections.

About Septerna
Septerna, Inc. is a clinical-stage biotechnology company with a world-class team of GPCR experts and drug developers advancing cutting-edge science to unlock the full potential of GPCR therapies for patients with significant unmet needs. The company’s proprietary Native Complex Platform® is designed to enable new approaches to GPCR drug discovery and has led to the development of a diverse pipeline of novel oral small molecule drug candidates. Septerna is advancing programs in endocrinology, immunology and inflammation, metabolic diseases and additional therapeutic areas, both independently and with partners. 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 potential of SEP-479 preclinical data to translate into similar clinical safety, pharmacokinetic, and pharmacodynamic findings; the estimated availability of SEP-479 Phase 1 clinical data in late 2026 or early 2027; the potential for SEP-479 to be a differentiated once-daily oral therapy for patients with hypoparathyroidism; the potential of its proprietary Native Complex Platform®; the size and growth potential of the markets for its current and future product candidates; its expectations regarding strategic plans for its business, product candidates, and technology; and the scope of protection it is able to establish and maintain for intellectual property rights covering its Native Complex Platform® and its product candidates. 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: the risk that SEP-479 preclinical data does not turn out to be predictive of future clinical outcomes for SEP-479; risks related to clinical development outcomes for SEP-479 including unexpected safety, pharmacokinetic, or pharmacodynamic findings; risks related to the actual timing of future availability of clinical data for SEP-479 including that the actual timing of enrollment and completion of the study may differ from management’s current estimates; the scope of protection Septerna is able to establish and maintain for intellectual property rights covering its Native Complex Platform® and its product candidates (including SEP-479); 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 Annual Report on Form 10-K for the year ended December 31, 2025, 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.

Investor Contact:
Renee Leck, THRUST
renee@thrustsc.com

Media Contact:
Carly Scaduto, THRUST
carly@thrustsc.com