Septerna Announces Selection of SEP-204 as Development Candidate for Graves' Disease and TED and Reports Preclinical Data at the 2026 American Thyroid Association Annual Meeting

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Potent, selective TSHR NAM with pre-clinical activity demonstrated across biochemical, thyroid and ocular endpoints

Favorable PK profile anticipated to support once-daily oral dosing in humans

Phase 1 clinical trial initiation planned for the first quarter of 2027

SOUTH SAN FRANCISCO, Calif., Nov. 04, 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 selection of SEP-204 as its potential first-in-class development candidate for the treatment of Graves' disease and thyroid eye disease (TED) and reported initial preclinical data ahead of a poster presentation at the 2026 American Thyroid Association (ATA) Annual Meeting on November 5.

SEP-204 is a potent and selective oral small molecule thyroid-stimulating hormone receptor (TSHR) negative allosteric modulator (NAM). SEP-204 inhibited TSHR activation in Graves' disease animal models and has pharmacokinetic properties to support once daily dosing. A Phase 1 trial in healthy volunteers is anticipated to initiate in the first quarter of 2027.

"Based on the pre-clinical data we have generated to date, we believe SEP-204 has the potential to change the treatment paradigm for Graves' disease and TED, two serious autoimmune endocrine diseases that can profoundly affect patients' health and quality of life," said Rajiv Patni, chief medical officer of Septerna. "We look forward to working closely with disease experts and the patient community to advance SEP-204 into clinical development and build upon these promising preclinical findings with clinical results."

Preclinical studies of SEP-204 demonstrated the following key findings:

- Potent TSHR inhibition with desirable drug-like properties and a high level of selectivity over the closely related follicle-stimulating hormone receptor (FSHR) and luteinizing hormone receptor (LHR).
- Inhibition of thyroid-stimulating antibody (TSAb) activation of TSHR in human thyrocyte cell assays.
- In Graves' disease animal models, findings included restoration of normal thyroid hormone T4 levels and reductions in thyroid enlargement and orbital proptosis.
- Dose-dependent increases in TSH levels followed by decreases in thyroid hormone levels were observed across preclinical species.
- Generally well tolerated in 28-day GLP toxicology studies in rats and dogs.
- High oral bioavailability and low clearance across preclinical species, with a projected human half-life of approximately 20-40 hours, which is anticipated to support once-daily oral dosing in humans.

About SEP-204, Graves' Disease and Thyroid Eye Disease

SEP-204 is an investigational oral small molecule thyroid-stimulating hormone receptor (TSHR) negative allosteric modulator (NAM) being developed as a potential disease-modifying treatment for Graves' disease and thyroid eye disease (TED). It is designed to block the overactivation of TSHR caused by patients' autoantibodies in thyroid cells and orbital fibroblasts and has the potential to address both conditions. Graves' disease is an autoimmune condition in which antibodies activate TSHR, stimulating excess thyroid hormone production and causing hyperthyroidism. Some patients also develop TED, a serious, potentially vision-threatening autoimmune condition affecting tissues behind the eyes that can cause eye bulging, swelling, pain and blurred or double vision. Current standard-of-care treatments do not address the shared underlying cause of both Graves' disease and TED.

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 translation of preclinical findings to clinical outcomes in patients; the potential of SEP-204 to be a first-in-class, disease-modifying treatment for Graves' disease and TED; advancing SEP-204 into a Phase 1 clinical study and the timing thereof; SEP-204's potential for once daily dosing; the potential of its proprietary Native Complex Platform ®; 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; among others. 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: SEP-204 successfully entering and advancing through clinical trials including uncertainties related to opening investigational new drug applications and obtaining other regulatory approvals; risks related to clinical development outcomes including unexpected safety or efficacy findings; the results of preclinical studies not being predictive of future clinical outcomes; risks related to the timing of initiating clinical studies; and the scope of protection Septerna is able to establish and maintain for intellectual property rights covering its Native Complex Platform® and its product candidates; among others. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in Septerna's Quarterly Report on Form 10-Q for the three months ended June 30, 2026, 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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