Septerna Announces Initiation of Phase 1 Clinical Trial with SEP-786, a Novel Oral Small Molecule PTH1R Agonist for the Treatment of Hypoparathyroidism

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Trial Initiation Marks Septerna's Transition to a Clinical-Stage Company Developing a Portfolio of Oral Small Molecule GPCR-Targeted Medicines

Phase 1 Clinical Trial Designed to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of SEP-786 in Healthy Volunteers

SOUTH SAN FRANCISCO, Calif. – September 27, 2024 – Septerna, a clinical-stage biotechnology company pioneering a new era of GPCR-targeted drug discovery, today announced the dosing of the first participants in its Phase 1 clinical trial of SEP-786, its novel, potent and selective, oral small molecule parathyroid hormone 1 receptor (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-786 in healthy adult volunteers.

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. Conventional therapy requires patients take high doses of calcium and Vitamin D supplements orally several times daily or life-long daily injections of PTH replacement therapy.

"GPCR-targeted drugs have been the most productive target class in drug discovery history, with about one-third of all FDA-approved drugs targeting these receptors. Our proprietary Native Complex Platform™ fuels the discovery of oral small molecule compounds for a wide range of GPCRs, such as PTH1R, a validated receptor target for hypoparathyroidism," said Jeffrey Finer, M.D., Ph.D., Chief Executive Officer and Co-founder of Septerna. "An oral small molecule PTH1R agonist has transformative potential as a convenient, disease-modifying treatment option that could provide patients with full-day calcium control, while resolving the serious effects of low blood calcium levels due to PTH deficiency. We look forward to assessing the safety of SEP-786 and its potential to normalize serum calcium levels, as we have seen in preclinical models, in this Phase 1 clinical trial. I am very proud of the rapid execution by our R&D team in achieving this milestone, which underscores the power of our Native Complex Platform™ to take on GPCR targets which have been historically challenging for small molecule drug discovery."

The randomized, placebo-controlled, SAD and MAD Phase 1 clinical trial is expected to enroll up to 180 healthy adult participants. Dosing is underway in the SAD portion of the clinical trial, which will evaluate the safety and tolerability of SEP-786 at escalating oral doses. The MAD portion of the clinical trial is designed to evaluate the safety and tolerability of once-daily and twice-daily oral dosing of SEP-786 over multiple days of treatment with secondary endpoints including PK, changes in serum calcium and urinary calcium, and other biomarkers.

About SEP-786 and Hypoparathyroidism

Septerna is developing SEP-786, a novel, potent and selective oral small molecule parathyroid hormone 1 receptor (PTH1R) agonist for the treatment of patients with hypoparathyroidism, a rare endocrine disease characterized by a deficiency of the parathyroid hormone (PTH). Hypoparathyroidism results in a wide range of debilitating symptoms, including muscle cramps, fatigue, cognitive dysfunction and life-threatening complications, such as cardiac arrhythmias, seizures, and renal failure. Currently available treatments include supplements that only partially address PTH deficiency, or PTH peptide replacements, which require daily injections. Preclinical safety studies support that SEP-786 has demonstrated the ability to normalize serum calcium and was generally well-tolerated in 28-day Good Laboratory Practice toxicology studies. SEP-786 has the potential to be a differentiated treatment for hypoparathyroidism.

About Septerna

Septerna, Inc. is a clinical-stage biotechnology company pioneering a new era of G protein-coupled receptor (GPCR) oral small molecule drug discovery powered by its proprietary Native Complex PlatformTM. 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 product candidates focused initially on treating patients in three therapeutic areas: endocrinology, immunology and inflammation, and metabolic diseases. Septerna was launched in 2022 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.

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