Septerna Presents New Preclinical Data at ASBMR 2024 Highlighting Therapeutic Potential of Oral Small Molecule Parathyroid Hormone 1 Receptor (PTH1R) Agonists for Hypoparathyroidism

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In addition to maintaining serum calcium control, PTH1R agonists upregulated bone turnover biomarkers and active Vitamin D levels over 28 days of dosing in a preclinical model

Septerna's lead product candidate, SEP-786, now in Phase 1 clinical development

SOUTH SAN FRANCISCO, Calif. – September 30, 2024 – Septerna, a clinical-stage biotechnology company pioneering a new era of GPCR-targeted drug discovery, presented new preclinical data from its parathyroid hormone 1 receptor (PTH1R) program in a poster presentation at the American Society for Bone and Mineral Research (ASBMR) 2024 Annual Meeting held from September 27-30, 2024, in Toronto, ON, Canada.

The data demonstrate that Septerna's PTH1R small molecule agonists activate PTH1R and elicit downstream effects on bone and kidney by regulating key genes important for calcium homeostasis in a manner similar to native parathyroid hormone (PTH). In addition, building on data presented at the Endocrine Society's Annual Meeting (ENDO), Septerna's PTH1R agonists demonstrated sustained control of serum calcium and phosphate levels and upregulation of bone turnover biomarkers and increases in active Vitamin D levels over 28 days with daily oral administration. Septerna is dosing healthy volunteers in a Phase 1 clinical trial to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of its lead oral small molecule PTH1R agonist product candidate, SEP-786.

"We are pleased to highlight data from the preclinical studies of our PTH1R small molecule agonists demonstrating activity similar to native PTH, which support the initiation of our clinical trial and affirm our belief that our lead product candidate, SEP-786, has the potential to reshape the treatment paradigm for patients with hypoparathyroidism," said Jeffrey Finer, M.D., Ph.D., Chief Executive Officer and Co-founder of Septerna. "The progress of this program is an excellent illustration of the ability of our Native Complex Platform™ to unlock difficult-to-drug GPCRs and discover novel small molecules with the potential to address numerous disorders in endocrinology and beyond."

Data Summary

The poster, entitled "Characterization of a Novel Oral Small Molecule PTH1R Agonist: Sustained Control of Serum Calcium and Modulation of Bone Biomarkers in TPTx Rats", is summarized below.

- Primary human renal proximal epithelial cells and a human osteoblast cell line treated with PTH and a small molecule agonist of PTH1R suggest similar pathway engagement.
- Comparable on target bone activities (anabolic and catabolic) were observed in mouse bones treated with PTH peptide and a PTH1R small molecule agonist.
- Daily oral administration of a PTH1R agonist resulted in sustained, dose dependent regulation of serum calcium and phosphate levels over a 28-day period.
- New data were presented demonstrating that daily dosing of a PTH1R agonist upregulated bone turnover biomarkers and active Vitamin D levels in a dose-dependent manner over 28 days.

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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