Septerna to Present Preclinical Data from GPCR Drug Discovery Engine at ENDO 2024

05.20.24

Native Complex Platform™ has rapidly produced multiple GPCR-targeted programs approaching clinical development

Oral, small molecule parathyroid hormone 1 receptor (PTH1R) agonist for hypoparathyroidism preparing to enter Phase 1 trials in late 2024

Oral, thyroid stimulating hormone receptor (TSHR) program part of advanced, multi-asset preclinical pipeline

SOUTH SAN FRANCISCO, Calif. – May 20, 2024 – Septerna, a biotechnology company discovering and advancing novel, oral small molecule medicines targeting G protein-coupled receptors (GPCRs), today announced that the company will present the first preclinical data on the company's parathyroid hormone 1 receptor (PTH1R) and thyroid stimulating hormone receptor (TSHR) programs at the Endocrine Society's Annual Meeting (ENDO 2024) held June 1-4 in Boston.

"We are excited to present for the first time new preclinical findings from our breakthrough GPCR Native Complex Platform TM at ENDO 2024, marking a significant moment in our evolution to a clinical-stage company," said Jeffrey Finer, M.D., Ph.D., Chief Executive Officer and Co-founder of Septerna. "Led by our PTH1R program, which has the potential to be the first oral replacement therapy for hypoparathyroidism, these promising preclinical data validate our approach to discover novel GPCR-targeted medicines and reaffirm our dedication to deliver transformative therapies to patients in need of better treatment options."

Presentation Details

Title: Characterization of a Novel Oral Small Molecule PTH1R Agonist: Proof of Concept for an Alternative to Injectable Peptide-based Therapy for Hypoparathyroidism
Poster Presentation (MON-372): Monday, June 3 at 12:00 PM – 1:30 PM ET
Poster Session (P085): Bone and Mineral Metabolism: Clinical Osteoporosis
Rapid-Fire Presentation (RF14-03): Monday, June 3 at 1:55 PM – 2:00 PM ET
Oral Abstract and Rapid-Fire Session (OR14): Bone and Mineral Metabolism: PTH, Calcium, and Phosphate Metabolism
Presenter: Jun Zhang, Ph.D., Senior Director of Disease Biology, Septerna

Title: A Novel, Oral Small Molecule Antagonist Targeting TSHR Improves Hyperthyroidism in an *in vivo* Model of Graves' Disease
Poster Presentation (MON-589): Monday, June 3 at 12:00 PM – 1:30 PM ET
Poster Session (P096): Thyroid: Thyroid Autoimmunity II
Presenter: Amer Mirza, Ph.D., Vice President, Disease Biology and Translational Sciences, Septerna

About Septerna
Septerna, Inc. is a biotechnology company focused on advancing novel, oral small molecule medicines targeting the entire class of G protein-coupled receptors (GPCRs). The company's Native Complex Platform TM recapitulates GPCRs with their native structure, function, and dynamics outside of the cellular environment to rapidly apply new technologies for industrial-scale drug discovery to address both validated GPCRs and many GPCRs that have been undruggable and unexploited to date. Septerna is building a pipeline of GPCR-targeted, oral small molecule drug candidates, led by its program targeting the parathyroid hormone 1 receptor (PTH1R) for the treatment of hypoparathyroidism. Septerna was launched in 2022 by scientific founders who have made groundbreaking GPCR discoveries. For more information, please visit www.septerna.com.

About the PTH1R Program and Hypoparathyroidism
Septerna is developing a novel, first-in-class, oral small molecule parathyroid hormone 1 receptor (PTH1R) agonist designed to treat patients with hypoparathyroidism, a harmful condition characterized by a deficiency of the parathyroid hormone (PTH). Hypoparathyroidism results in a wide range of debilitating symptoms, including fatigue, brain fog, muscle weakness, and in severe cases can lead to seizures, heart arrhythmias, and kidney failure. Current available treatments include supplements that only partially address PTH deficiency or PTH peptide replacements, which require daily injections. Septerna's investigational PTH1R agonist has been shown to normalize serum calcium levels in preclinical studies and has the potential to be the first oral alternative to injectable hypothyroidism treatments.

About the TSHR Program and Graves' disease
Septerna is developing a novel, investigational, oral small molecule thyroid stimulating hormone receptor (TSHR) antagonist for the treatment of Graves' disease and thyroid eye disease (TED). Graves' disease is an autoimmune condition in which the body produces antibodies that bind to and activate the TSH receptor on thyroid cells. These antibodies stimulate the thyroid gland to produce too much thyroid hormone, resulting in hyperthyroidism. Additionally, in TED, the antibodies can cause swelling of the

muscles behind the eyes, which can result in eye bulging, pain and blurred vision. Current standard-of-care treatments for Graves' disease are inadequate and focus on the thyroid (surgery, radioactive iodine, and antithyroid medicines) while failing to prevent progression to Graves' eye disease. Septerna's TSHR antagonist is designed to shut down all Graves' autoactivating antibodies with a single drug.

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