



Sosei Subsidiary Heptares Solves First Full-length Structure of GLP-1 Receptor Bound to Peptide Agonist

New findings highlight complexity of receptor interactions and provide crucial insights for development of peptide and small molecule therapeutics – research published in Nature

Tokyo, Japan –31 May 2017: Sosei Group Corporation (“Sosei”; TSE Mothers Index: 4565) today reports that Heptares Therapeutics (“Heptares”), its wholly-owned subsidiary, has published the first high-resolution X-ray crystal structure of the full-length glucagon-like peptide-1 (GLP-1) receptor bound to a peptide agonist.

The findings, published in *Nature*, provide insight to the molecular mechanism of action of GLP-1 peptides and their interactions with the receptor. Importantly, this pioneering research further validates and enables the application of structure-based methods to the design of optimised peptide therapeutics and small molecules targeting the GLP-1 receptor, and related G protein-coupled receptors (GPCRs), for treating a range of diseases. The research was published online in *Nature* today and can be accessed at <http://dx.doi.org/10.1038/nature22800>.

GLP-1 is an important peptide hormone that regulates glucose homeostasis through control of insulin release from the pancreas. Activating the GLP-1 receptor is one of the most important and highly validated mechanisms for treating Type 2 diabetes, and awareness is increasing about the potential of this target in treating other metabolic diseases, as well as cardiovascular and neurological diseases. A number of GLP-1 peptide agonists, with improved stability and duration of action compared to native GLP-1, are already approved for treating Type 2 diabetes, including exenatide (Byetta®/Bydureon®), liraglutide (Victoza®, Saxenda®), lixisenatide (Lyxumia®), albiglutide (Tanzeum®) and dulaglutide (Trulicity®).

Fiona Marshall, Chief Scientific Officer of Heptares and Sosei, said: “The findings from this research at Heptares are ground-breaking and very exciting: they unveil a remarkably complex network of interactions between GLP-1 peptide ligands and the receptor that explains why it has been so difficult to mimic this effect with a small molecule. Understanding these interactions at a molecular level may be the breakthrough that enables the design of small molecule drugs, as well as optimised therapeutic peptides, targeting not only the GLP-1 receptor but also other closely related GPCR targets implicated in many diseases.”

The GLP-1 receptor is a member of the Class B secretin group of GPCRs, a family of structurally similar receptors for peptide hormones such as GLP-1, glucagon, corticotropin-releasing factor (CRF), calcitonin and parathyroid peptide hormone. Class B GPCRs include many therapeutic targets for cardiovascular diseases, metabolic diseases, bone diseases and migraine, but despite strong clinical validation, structural information is limited.

Reference

Jazayeri, A et al. Crystal structure of the GLP-1 receptor bound to a peptide agonist (2017) *Nature* <http://dx.doi.org/10.1038/nature22800>

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Notes to Editors

About Heptares Therapeutics

Heptares is a clinical-stage company creating transformative medicines targeting G protein-coupled receptors (GPCRs), a superfamily of 375 receptors linked to a wide range of human diseases. Heptares' proprietary StaR® technology and structure-based drug design (SBDD) capabilities enable us to engineer and develop drugs for highly validated, yet historically undruggable or challenging GPCRs. Using this approach, we are building an exciting pipeline of new medicines (small molecules and biologics) with the potential to transform the treatment of Alzheimer's disease, schizophrenia, cancer immune-oncology, migraine, addiction, metabolic disease and other indications. We have partnerships for our novel candidates and technologies with leading pharmaceutical and biotechnology companies, including Allergan, AstraZeneca, Daiichi Sankyo, Kymab, MedImmune, MorphoSys, Pfizer and Teva.

Heptares is a wholly owned subsidiary of Sosei Group Corporation. For more information, please visit www.heptares.com and www.sosei.com.

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StaR® is a registered trademark in the EU and Japan.

About Sosei

Sosei is a biopharmaceutical company originating from Japan but with global presence. Sosei's primary business model is based on identifying novel and/or differentiated product assets or technology platforms and, through supporting these in preclinical and clinical development and establishing commercial partnerships, advancing new medicines to patients worldwide. For more information about Sosei, please visit www.sosei.com.

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Forward-looking statements

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obtaining regulatory approvals to market products and services resulting from development efforts; the requirement for substantial funding to conduct research and development and to expand commercialisation activities; and product initiatives by competitors. As a result of these factors, prospective investors are cautioned not to rely on any forward-looking statements. We disclaim any intention or obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.