Sosei Subsidiary Heptares Scientists Solve Structures of GLP-1 and Glucagon Receptors Enabling Structure-Based Design for Metabolic Disease

First structure of GLP-1 receptor in active state resolved
Novel allosteric binding site in glucagon receptor identified – published in Nature

Tokyo, Japan –25 April 2016: Sosei Group Corporation ("Sosei"; TSE Mothers Index: 4565) today announces Heptares Therapeutics ("Heptares"), has reported that its scientists have solved the high-resolution X-ray crystal structures of the GLP-1 (glucagon-like peptide 1) and glucagon receptors. Both receptors play important roles in the management of blood glucose levels and are considered to be important targets for drugs to treat metabolic diseases, such as diabetes.

The new structural information generated by Heptares from the breakthrough research on these receptors adds to the wealth of information the Company has generated using its StaR® platform on G protein-coupled receptors (GPCRs), the most important family of receptors targeted by drug developers. The unique resource, including detailed X-ray structures from more than 12 GPCRs solved by Heptares scientists, is enabling the Company to apply its structure-based design platform to develop therapeutics (small molecule and biologic) for these and structurally similar receptors that have strong links to disease.

The work by Heptares scientists in solving the X-ray structure of the full length GLP-1 receptor bound to a peptide agonist represents the first time that a receptor of this class has been resolved in its active state conformation. The availability of a high-resolution structure of the GLP-1 receptor in this conformation is expected to be important for enabling the discovery of selective small molecule oral drugs for metabolic diseases.

The findings relating to the structure of glucagon receptor have been published in Nature by Heptares scientists and describe the identification of a novel binding site distinct from the glucagon-binding site. This 'allosteric' binding site is located outside the transmembrane domain of the receptor, at the interface with the cell membrane, and is shown to inhibit the normal signalling function of the receptor when bound to a small molecule antagonist MK-0893 (Jazayeri et al, reference below).

Heptares is using the structural and physicochemical information derived from its pioneering research on the GLP-1 and glucagon receptors, and from other receptors in the same class (Class B GPCRs), including the previously solved CRF-1 receptor, to advance allosteric small molecule GLP-1 antagonists towards the clinic as potential new treatments for the rare disease congenital hyperinsulinaemia.

"Heptares continues to demonstrate the power of its StaR® technology to elucidate the structure of important GPCRs and apply this knowledge to its drug design programmes and those of it partners," said Fiona Marshall, Chief Scientific Officer at Heptares. "Our pioneering research is greatly enhancing our ability to apply our structure-based approach to

drug discovery across a wide range of GPCR targets with strong clinical validation, but which have proved difficult or impossible to access previously."

Class B GPCRs represent 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 (2016) Nature http://dx.doi.org/10.1038/nature17414
Hollenstein, K, et al Structure of class B GPCR corticotropin-releasing factor receptor 1. (2013)
Nature 499: 438–443

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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, 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.

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 further information about Sosei, please visit www.sosei.com/en.

Forward-looking statements

This press release contains forward-looking statements, including statements about the discovery, development and commercialisation of products. Various risks may cause Sosei's actual results to differ materially from those expressed or implied by the forward-looking statements, including: adverse results in clinical development programmes; failure to obtain patent protection for inventions; commercial limitations imposed by patents owned or controlled by third parties; dependence upon strategic alliance partners to develop and commercialise products and services; difficulties or delays in 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.