Sosei subsidiary Heptares announces positive outcome of Phase 1a study with first-ever selective muscarinic M1 receptor agonist for improving cognition in patients with Alzheimer's disease

Early evidence of enhanced brain activity seen at dose levels that are well tolerated

Tokyo, Japan – 17 June 2015: Sosei Group Corporation (“Sosei”; TSE Mothers Index: 4565) is pleased to announce that its wholly-owned subsidiary Heptares Therapeutics (“Heptares”) has reported the positive outcome of its Phase 1a study with HTL9936, the first-ever fully selective muscarinic M1 receptor agonist to enter clinical development.

The Phase 1a study assessed the safety, tolerability and pharmacokinetics of HTL9936 in relation to dose in 84 healthy volunteers, while also evaluating preliminary signs of efficacy (increase in brain activity). Key findings were:

- Early evidence of increased brain activity, as measured by electroencephalography (EEG), was seen after dosing and gave signals similar to those seen with other cognitive enhancing agents1,2.

- HTL9936 was well tolerated at drug levels that result in the increased brain activity observed without side effects.

- HTL9936 demonstrates good penetration into the brain, as indicated by levels found in cerebrospinal fluid.

- M1 selectivity was demonstrated with, unlike earlier muscarinic agonists3, no adverse effects seen from stimulation of other muscarinic receptors.

These preliminary data suggest that the selective M1 agonist product profile of HTL9936 predicted from preclinical studies translates to humans. Heptares is now putting in place a series of further clinical studies with the objective of demonstrating clinical proof of concept in patients, and moreover is advancing its diverse portfolio of follow-on selective muscarinic agonists that target M1, M4, and both M1/M4 to the clinic.

“HTL9936 was designed and developed specifically to be a first-in-class oral agent to improve cognitive function (memory and thinking abilities) in patients with serious neurological diseases, such as Alzheimer’s disease and dementia,” said Tim Tasker, Chief Medical Officer of Heptares. “We are therefore delighted with the outcome of this first clinical study, the results of which provide important validation of our GPCR-directed structure-based design platform and approach to create important new medicines in areas of unmet need. We look forward to advancing HTL9936 and the M1 agonist programme into further clinical studies to confirm the efficacy and safety observed.”

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Notes to Editors

About M1 Receptor Agonism
M1 receptor agonism is a well-validated mechanism of action for treating cognitive impairment and a valuable pharmacological profile that the pharmaceutical industry has endeavored to create for decades. The principal challenge has been to engineer selective compounds that activate the M1 receptor subtype without also activating the M2 or M3 receptors, which are associated with undesirable side effects. All previous compounds have been discontinued due to inadequate selectivity. Using a new structure-guided approach, Heptares scientists determined for the first time the x-ray crystal structure of the M1 receptor in its agonist conformation and used these unique insights into the receptor drug binding site to identify new chemistries with fully selective M1 agonist profiles.

About Alzheimer's Disease and Other Disorders of Cognitive Impairment
Today there is significant unmet medical need and heavy economic burden across multiple diseases characterised by cognitive impairment and dementia. In Alzheimer’s disease, currently available drugs provide limited and transient effects on cognition. Healthcare costs associated with the epidemic of AD, including nursing home care, continue to grow dramatically and new therapies with better and more durable efficacy are urgently needed. In addition, an estimated 80% of schizophrenics suffer from cognitive impairment and 1.3 million patients in the US suffer from Lewy body dementia. Currently there are no approved therapies for treating cognitive impairment in schizophrenia or for treating Lewy body dementia.

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. Its proprietary structure-based drug design technology enables Heptares to engineer drugs for highly validated, yet historically undruggable or challenging GPCRs. Using this approach, Heptares has built an exciting pipeline of new medicines with the potential to transform the treatment of Alzheimer’s disease, schizophrenia, ADHD, migraine, addiction, metabolic disease and other indications. Heptares pharmaceutical partners include Cubist, MorphoSys, Takeda, AstraZeneca and MedImmune. For more information about Heptares, please visit www.heptares.com and www.sosei.com.

HEPTARES is a registered trademark in the EU, Switzerland, US 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.

References:
5. Lewy Body Dementia Association, Inc. www.lbda.org

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.