



First Subject Dosed in Phase 1 Clinical Study of Novel Selective Muscarinic M₄ Agonist in Development to Treat Major Symptoms of Alzheimer's Disease

Tokyo, Japan –1 September 2017: Sosei Group Corporation ("Sosei"; TSE Mothers Index: 4565) today reported that Heptares Therapeutics ("Heptares"), the wholly-owned subsidiary of Sosei, announces that the first healthy subject has been dosed with the first-in-class, selective muscarinic M₄ receptor agonist HTL0016878 in a Phase 1 clinical study. The Phase 1 study dosing triggers a US\$15 million milestone payment by Allergan to Heptares under a global R&D and commercialisation partnership announced in April 2016.

Heptares and Allergan are developing HTL0016878, an orally available, small molecule drug candidate with potential to treat certain neurobehavioural symptoms of Alzheimer's disease. The compound stimulates M₄ receptor activity in the brain with high selectivity, and offers the possibility for an improved safety profile over previous muscarinic receptor agonists, which have been associated with adverse effects elsewhere in the body leading to safety and tolerability issues.

HTL0016878 was designed by Heptares using its proprietary structure-based drug design platform and is the first compound, selected from a series of selective M₄ agonists, to progress into clinical studies. The double-blind, randomised first-in-human study is being conducted in the UK by Heptares and will assess safety, tolerability and pharmacokinetics of single and multiple oral doses of HTL0016878 in up to 106 healthy subjects. Preliminary results are expected in the first half of 2018.

Tim Tasker, Heptares' Chief Medical Officer, said: "The start of this new clinical trial marks the progression of the fourth compound designed by Heptares into clinical studies and follows the advancing clinical studies with selective M₁ agonists under our partnership with Allergan. The target selectivity we can build into molecules increasingly highlights the potential of our approach to create new medicines with significantly improved clinical profiles for addressing a range of diseases. In creating the first selective M₄ agonist to enter human studies, we are a step closer to our goal of developing a new therapeutic approach to ease the considerable burden and distress caused by diseases such as Alzheimer's."

Under the terms of the 2016 global R&D and commercialisation partnership, Allergan licensed exclusive global rights to Heptares' broad portfolio of novel subtype-selective muscarinic receptor agonists (M₁, M₄ and dual M₁/M₄ agonists) for the treatment of major neurological disorders, including Alzheimer's disease. In addition to the new clinical programme with HTL0016878, a selective M₄ agonist, announced today, the companies are advancing a programme evaluating selective M₁ agonists through clinical studies as a potential treatment for symptomatic cognitive deficits in Alzheimer's patients; and are assessing the potential of dual M₁/M₄ agonists with potential to treat both cognitive and neurobehavioural symptoms through preclinical studies.

This milestone will be going to be reported as revenue in the second quarter of FY2017.

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Contact for Sosei Group Corporation
Harumi BANSE, Investor Relations
+81-(0)3-5210-3399
hbanse@sosei.com

About Muscarinic receptors

Muscarinic receptors are G protein-coupled receptors (GPCRs) found in multiple tissues. Until now, attempts to develop medicines that target M₁ and M₄ receptors have been unsuccessful because of side effects caused by the activation of M₂ and M₃ receptors. Selective M₁ or M₄ agonists that do not activate M₂ or M₃ therefore are highly sought after, and expected to address blockbuster markets.

About Alzheimer's Disease¹

There is significant unmet medical need and heavy economic burden across multiple diseases characterized by dementia. In Alzheimer's disease (AD), currently available drugs provide limited and transient effects. Healthcare costs associated with AD and dementia (estimated at over \$640 billion for North America, Western Europe and Asia-Pacific) including nursing home care, continue to grow dramatically and new therapies with better and more durable efficacy are urgently needed. It is estimated that over 45 million people worldwide have dementia (4.8 million in North America, 7.5 million in Western Europe, 3.6 million in Asia-Pacific) and this is expected to increase to over 130 million in 2050. Alzheimer's disease is the most common cause of dementia and may contribute to 60–70% of cases.

Although AD is usually considered a cognitive disorder, almost all AD patients develop neurobehavioural symptoms at some stage during disease progression, ranging from mild to severe. These symptoms are associated with patient and caregiver distress, increased rates of institutionalisation, and increased mortality.

¹Sources: World Health Organization, Alzheimer's Disease International, National Institute of Mental Health.

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, MorphoSys, Peptidream, 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/en/

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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/en/