PRESS RELEASE

Boehringer Ingelheim and Sosei Heptares join forces to develop first-in-class treatments targeting all symptoms of schizophrenia

- *Single-target agreement focused on development of novel, small molecule agonists of GPR52 discovered by Sosei Heptares with the potential to simultaneously address positive, negative and cognitive symptoms of schizophrenia*
- *Sosei Heptares will receive EUR 25 million upfront from Boehringer Ingelheim and is eligible for an option exercise payment of EUR 60 million and further milestone payments totaling up to EUR 670 million plus tiered royalties*

Ingelheim, Germany, Tokyo, Japan and Cambridge, UK, 11 March 2024 – Today, Boehringer Ingelheim and Sosei Group Corporation ("Sosei Heptares"; TSE: 4565) announced they have entered a global collaboration and exclusive option-to-license agreement. At the center is a joint mission to develop and commercialize Sosei Heptares' portfolio of first-in-class GPR52 agonists, a novel G protein-coupled receptor (GPCR) target, with the intent to improve patient outcomes by simultaneously addressing positive, negative, and cognitive symptoms of schizophrenia[1,2,3].

Schizophrenia is a serious condition that affects about 1 in 100 people worldwide[4]. It is characterized by three clusters of symptoms[5,6]:

- 'Positive' symptoms – such as psychosis, delusions and hallucinations
- 'Negative' symptoms – such as social withdrawal and apathy
- Cognitive symptoms – such as attention, planning and memory deficits

The impact of these symptoms on people's ability to cope with normal day-to-day life is significant and the related burden on carers and society at large is substantial, especially since the age of onset of the disease is typically in the 20s[7]. While 'positive' symptoms can be stabilized with antipsychotics, some of which can have side effects, there are currently no approved medicines for 'negative' or cognitive symptoms.

The development of a new schizophrenia treatment targeting GPR52 has the potential to address all three aspects of schizophrenia[1,2] providing a novel precision treatment. This is based on the location of the receptor in the two areas of the brain that drive the positive (the striatum) and the negative and cognitive symptoms (the prefrontal cortex). The GPR52 agonism calms the striatum while boosting frontal cortical function, which achieves further precision in treatment[8].

"We're very excited to enter this partnership with Sosei Heptares with this novel approach, which aims to address a huge unmet need of those living with schizophrenia. This partnership is highly complementary to our other development programs aiming to bring a new precision medicine approach to the treatment of mental health disorders with therapies, which we hope will transform the lives of those living with schizophrenia," states Hugh Marston, Global Head CNS Discovery Research at Boehringer Ingelheim.

Matt Barnes, President of Heptares Therapeutics and Head of UK R&D at Sosei Heptares, commented: "This collaboration highlights the significant potential GPR52 has shown in preclinical research as a novel, first in class target for the treatment of schizophrenia and related neurological disorders. We're delighted to partner with Boehringer Ingelheim and leverage its leading expertise in neurological disease research and innovation. Together, we will focus on accelerating the development of this highly innovative program, which is currently in a Phase 1 clinical study, towards patients in need."

About the Agreement

Sosei Heptares will receive an upfront payment of EUR 25 million from Boehringer Ingelheim upon signing and is eligible for an option exercise payment of EUR 60 million and further development, regulatory and commercialization milestone payments totaling up to EUR 670 million plus customary tiered royalties for a clinical-stage asset on future Boehringer Ingelheim product sales.

Under the terms of the agreement, Boehringer Ingelheim has the exclusive option to license Sosei Heptares' portfolio of GPR52 agonists following the completion of Sosei Heptares' ongoing Phase 1 and subsequent Phase 1b trial and further Phase 2 enabling activities with HTL0048149, a first-in-class GPR52 agonist. Sosei Heptares will retain control and act as sponsor of these trials until option exercise, estimated in 2025. The licensed portfolio will include HTL0048149 as well as multiple differentiated back-up compounds designed by Sosei Heptares using its StaR® technology and structure-based drug design (SBDD) platform.

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About GPR52 and HTL0048149

GPR52 is an orphan G protein-coupled receptor (GPCR) highly expressed in the brain, especially in the striatum and the prefrontal cortex, and represents a potential emerging therapeutic target for a range of neurological and neuropsychiatric disorders[9].

Sosei Heptares has developed a portfolio of selective GPR52 agonists and modulators leveraging proprietary insights from its StaR® technology SBDD platform, the most advanced of which (HTL0048149) entered in a first-in-human clinical trial in 2023[10].

HTL'149 has been designed to selectively target GPR52 as a once-daily, oral drug with an antipsychotic and pro-cognitive profile. Uniquely, HTL'149 aims to treat positive symptoms (e.g. psychosis, delusions, hallucinations), negative symptoms (e.g. social withdrawal and apathy) and cognitive impairment (e.g. attention, planning and memory deficits) associated with schizophrenia and to minimize adverse effects associated with some of the available antipsychotic drugs[9,11,12,13].

Through this novel mechanism of action, HTL'149 aims to address the significant proportion of schizophrenia patients who do not respond to existing treatments or are unable to tolerate some of the side effects of antipsychotics, which potentially results in a lack of compliance to antipsychotic treatments. Furthermore, current antipsychotic drugs do not effectively treat the negative or cognitive symptoms of disease.

HTL'149 is under investigation in a Phase 1a/b randomized, double-blind, placebo-controlled, single- and multiple-ascending dose study to assess its safety, pharmacokinetics, and pharmacodynamics in healthy volunteers aged 18-55 years. The trial is being conducted in the UK and initial data are expected in 2025[9,14].

About Boehringer Ingelheim

Boehringer Ingelheim is working on breakthrough therapies that transform lives, today and for generations to come. As a leading research-driven biopharmaceutical company, the company creates value through innovation in areas of high unmet medical need. Founded in 1885 and family-owned ever since, Boehringer Ingelheim takes a long-term, sustainable perspective. More than 53,000 employees serve over 130 markets in the two business units Human Pharma and Animal Health. Learn more at www.boehringer-ingelheim.com (global) or www.boehringer-ingelheim.com/uk (for UK)

Boehringer Ingelheim has an innovative mental health pipeline focused on precision psychiatry approaches in indications of high unmet patient need. In pivotal trials, it includes a glycine transporter type-1 (GlyT1) inhibitor with iclepertin, addressing cognitive impairment associated with schizophrenia (CIAS) (NCT04846868, NCT04846881)[15],[16] and a prescription digital therapeutic (PDT), CT-155, for people experiencing negative symptoms of schizophrenia (NCT05838625)[17].

About Sosei Heptares

Sosei Heptares is a fully integrated biopharmaceutical company focused on bringing life-changing medicines based on world-class science to patients globally. Our vision is to become one of Japan's global biopharmaceutical champions.

Our global business combines our world-leading GPCR-targeted StaR® technology, structure-based drug design and early development capabilities in the UK with a highly experienced clinical development capability and a commercial operation in Japan. We are leveraging these capabilities to generate and advance a broad and deep pipeline of novel medicines across multiple therapeutic areas, including neurology, immunology, gastroenterology and inflammatory diseases. We intend to develop these opportunities for patients in Japan and globally both internally and through our partnerships with global biopharmaceutical companies and emerging technology companies.

Sosei Heptares operates from key locations in Tokyo and Osaka (Japan), London and Cambridge (UK), Basel (Switzerland) and Seoul (South Korea).

For more information, please visit https://soseiheptares.com/
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