Neurocrine Biosciences and Sosei Heptares Announce Collaboration to Develop Novel Muscarinic Receptor Agonists for Schizophrenia and Other Neuropsychiatric Disorders

November 22, 2021

Neurocrine Biosciences anticipates initiating a Phase 2 study with the selective M4 agonist HTL-0016878 in schizophrenia in 2022 and Phase 1 studies for a dual M1/M4 and selective M1 agonist in 2023

Sosei Heptares receives US$100 million upfront, ongoing R&D funding, and up to US$2.6 billion in potential development, regulatory and commercial milestone payments, plus tiered sales royalties

SAN DIEGO and TOKYO and CAMBRIDGE, England, Nov. 22, 2021 /PRNewswire/ -- Neurocrine Biosciences, Inc. (Nasdaq: NBIX) and Sosei Group Corporation ("Sosei Heptares"; TSE: 4565) announce the signing of a strategic collaboration and licensing agreement to develop novel muscarinic receptor agonists, which Neurocrine Biosciences intends to study in the treatment for schizophrenia, dementia and other neuropsychiatric disorders.

Under the terms of the agreement, Neurocrine Biosciences gains development and commercialization rights to a broad portfolio of novel clinical and preclinical subtype-selective muscarinic M4, M1 and dual M1/M4 receptor agonists discovered by Sosei Heptares in development for the treatment of major neurological disorders. The most advanced program, HTL-0016878, is a selective M4 agonist. Neurocrine Biosciences plans to submit an Investigational New Drug (IND) application and initiate a placebo-controlled Phase 2 study with HTL-0016878 as a potential treatment for schizophrenia in 2022.

Sosei Heptares retains the rights to develop M1 agonists in Japan in all indications, with Neurocrine Biosciences receiving co-development and profit share options.

Muscarinic receptors are central to brain function and validated as drug targets in psychosis and cognitive disorders. Sosei Heptares has discovered selective muscarinic M4, M1 and M1/M4 dual agonists that offer the potential to deliver therapeutic effects while avoiding both the harmful side effects caused by non-selective agonists and efficacy issues experienced in some older patients caused by positive allosteric modulators that require cooperativity of diminishing levels of acetylcholine. Sosei Heptares achieved this through application of its world leading G protein-coupled receptor (GPCR) stabilized receptor platform (StaR®) and subsequent translational medicine studies.

"Our partnership collaboration with Sosei Heptares to advance their selective muscarinic agonist portfolio leverages the strengths of both our organizations with one goal in mind, to bring important medicines to patients who need better treatment options," said Kevin Gorman, Ph.D., Chief Executive Officer at Neurocrine Biosciences. "We continue to add potential best-in-class compounds to our growing pipeline, which further positions Neurocrine Biosciences as a leading neuroscience-focused biopharmaceutical company."

Shinichi Tamura, President and CEO of Sosei Heptares, added: "We are delighted to partner with Neurocrine Biosciences to advance our selective muscarinic receptor agonist portfolio. The deal highlights the significant potential value within this portfolio and brings to bear the substantial expertise of the Neurocrine team, which is highly experienced in developing and commercializing novel products for patients with neurological and psychiatric diseases globally. It also enables Sosei Heptares to retain rights in Japan, where we are confident that we can make important progress leveraging our own expertise to advance novel candidates that aim to address this major unmet need. Overall, the deal is a great example of our strategy to combine our drug design and early development capabilities with those of later stage development and commercialization partners, while also providing significant funding to expand and advance our own pipeline."

Collaboration Details

Under the terms of the agreement, Neurocrine Biosciences will be responsible for development costs associated with the programs globally, except for M1 agonists being developed in Japan. The agreement will be subject to the following terms:

- **Upfront License Payment**: Sosei Heptares will receive a total of $100 million USD in upfront cash.
- **Development and Regulatory Milestones**: Sosei Heptares is eligible to receive up to approximately $1.5 billion USD related to the successful progression of licensed candidates through to regulatory approval.
- **Commercial Milestones**: Sosei Heptares is eligible to receive up to $1.1 billion USD upon achieving certain global sales milestones of any products developed under the partnership.
- **Product Royalties**: Sosei Heptares is eligible to receive tiered royalties ranging from high single digit to mid-teen percentage on future net sales of any products developed under the partnership.

- **R&D Collaboration**: The R&D collaboration will be conducted jointly by Neurocrine Biosciences and Sosei Heptares to advance preclinical candidates through Phase 1 clinical studies. The R&D collaboration will be funded by Neurocrine Biosciences.
- **Sosei Heptares M1 Agonist Rights in Japan**: Sosei Heptares retains rights to develop M1 agonists in Japan for any indication, with Neurocrine Biosciences receiving co-development and profit share options.

This transaction is subject to customary clearances under the Hart-Scott-Rodino Antitrust Improvements Act. Assuming this transaction completes by December 31, 2021, the $100 million USD upfront payment will represent a material positive revenue impact to Sosei Heptares, and is expected to be recognized as revenue in the fourth quarter of the financial year ended December 31, 2021, subject to agreement with the Group's auditors.

BofA Securities is acting as financial advisor to Sosei Heptares. Gowling WLG and Orrick Herrington & Sutcliffe LLP are serving as legal counsel to Sosei Heptares.

Conference Call and Webcast Information

On Wednesday November 24, Sosei Heptares will host a conference call and webinar for Japanese investors at 8:00 a.m. Japan Standard Time. The live call may be accessed by pre-registration here.

A live audio webcast of the conference call will be available from the Investors section of Sosei Heptares website at www.soseiheptares.com.

A replay of the webcast will be available on Sosei Heptares' website after the conclusion of the event and will be archived for approximately one month.

About Muscarinic Receptors

Muscarinic receptors are G protein-coupled receptors (GPCRs) found in multiple tissues including the brain, cardiovascular system, and gastrointestinal tract. Selective activation of M4 and M1 receptors in the brain is a clinically validated approach to treating cognitive and neuropsychological symptoms of neurological diseases, including schizophrenia, dementia associated with Alzheimer's disease, Parkinson's disease, and others. Until now, attempts to develop medicines that selectively target M4 and M1 receptors have been unsuccessful because of side effects caused by the activation of M2 and M3 receptors. Highly selective M4 or M1 agonists that do not activate M2 or M3 therefore are highly sought after and expected to have the potential to address major unmet medical needs with blockbuster potential.

About Programs in the Collaboration Agreement

HTL-0016878

HTL-0016878 ("878") is an oral, investigational M4 selective agonist that has completed multiple Phase 1 studies and Neurocrine Biosciences is preparing to initiate Phase 2 studies in schizophrenia in 2022. As a selective M4 orthosteric agonist, '878 offers the potential for an improved safety profile without the need of combination therapy to minimize side effects and avoids the need of cooperativity with acetylcholine (ACh) when compared to non-selective muscarinic agonists and positive allosteric modulators in development. Studies completed to date have shown '878 to be generally well tolerated.

Preclinical Programs

The collaboration includes rights to multiple preclinical programs which include selective muscarinic compounds targeting M1, M4 receptors and a dual M1/M4 receptor candidate. In combination with '878, the programs offer the ability to leverage M1 and M4 selectivity to address the unmet need for patients suffering from psychosis and cognitive-related diseases.

After signing a R&D and commercialization partnership in 2016, Allergan returned all program rights to '878 and the preclinical programs to Sosei Heptares in Q1 2021.

About Neurocrine Biosciences

Neurocrine Biosciences is a neuroscience-focused, biopharmaceutical company dedicated to discovering, developing and delivering life-changing treatments for people with serious, challenging and under-addressed neurological, endocrine and psychiatric disorders. The company's diverse portfolio includes FDA-approved treatments for tardive dyskinesia, Parkinson's disease, endometriosis*, uterine fibroids* and clinical programs in multiple therapeutic areas. For nearly three decades, Neurocrine Biosciences has specialized in targeting and interrupting disease-causing mechanisms involving the interconnected pathways of the nervous and endocrine systems. For more information, visit neurocrine.com, and follow the company on LinkedIn. (*in collaboration with AbbVie).

About Sosei Heptares

We are an international biopharmaceutical group focused on the discovery and early development of new medicines originating from our proprietary GPCR-targeted StaR® technology and structure-based drug design platform capabilities. We are advancing a broad and deep pipeline of novel medicines across multiple therapeutic areas, including neurology, immunology, gastroenterology,

and inflammatory diseases.

We have established partnerships with some of the world's leading pharmaceutical companies and multiple emerging technology companies, including AbbVie, AstraZeneca, Biohaven, Genentech (Roche), GSK, Neurocrine Biosciences, Pfizer, and Takeda. Sosei Heptares is headquartered in Tokyo, Japan with corporate and R&D facilities in Cambridge, UK.

"Sosei Heptares" is the corporate brand and trademark of Sosei Group Corporation, which is listed on the Tokyo Stock Exchange (ticker: 4565). Sosei, Heptares, the logo and StaR® are trademarks of Sosei Group companies.

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

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Neurocrine Biosciences Forward-looking statements

In addition to historical facts, this press release contains forward-looking statements that involve a number of risks and uncertainties. These statements include, but are not limited to, statements related to the benefits to be derived from transactions with Sosei Group Corporation; our potential milestone and royalty payments to Sosei Heptares; the development of our product candidates and the timing of completion of our clinical, regulatory, and other development activities; Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are: the possibility that the transaction with Sosei Heptares is not consummated on the expected timeline or at all or the possibility that regulatory approvals of the proposed transaction will impose conditions or are not obtained; risks and uncertainties associated with the scale and duration of the COVID-19 pandemic and resulting global, national, and local economic and financial disruptions; risks and uncertainties related to any COVID-19 quarantines, shelter-in-place and similar government orders that are currently in place or that may be put in place in the future, including the impact of such orders on our business operations and the business operations of the third parties on which we rely; our future financial and operating performance; risks or uncertainties related to the development of the our product candidates; risks that the FDA or other regulatory authorities may make adverse decisions regarding our product candidates; risks that clinical development activities may not be completed on time or at all; risks that clinical development activities may be delayed for regulatory, manufacturing, or other reasons, may not be successful or replicate previous clinical trial results, may fail to demonstrate that our product candidates are safe and effective, or may not be predictive of real-world results or of results in subsequent clinical trials; risks and uncertainties relating to competitive products and technological changes that may limit demand for a product candidate; risks that the benefits of the agreements with Sosei Heptares may never be realized; risks that our product candidates may be precluded from commercialization by the proprietary or regulatory rights of third parties, or have unintended side effects, adverse reactions or incidents of misuse; and other risks described in our periodic reports filed with the SEC, including without limitation our quarterly report on Form 10-Q for the quarter ended September 30, 2021. Neurocrine disclaims any obligation to update the statements contained in this press release after the date hereof.

Sosei Group Corporation Forward-looking statements

This press release contains forward-looking statements, including statements about the discovery, development, and commercialization of products. Various risks may cause Sosei Group Corporation's actual results to differ materially from those expressed or implied by the forward-looking statements, including: adverse results in clinical development programs; 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 commercialize 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 commercialization 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.

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