Nxera Pharma Notes Positive Phase 2 Data for Partnered Schizophrenia Candidate NBI-1117568

- NBI-1117568 is an oral, muscarinic M4 selective receptor agonist discovered by Nxera advancing through clinical development under a multi-program collaboration with Neurocrine Biosciences
- The once-daily 20 mg dose efficacy, safety and tolerability Phase 2 results support advancement to Phase 3 in schizophrenia in early 2025
- The once-daily 20 mg dose met the primary endpoint, demonstrating a statistically significant 7.5-point improvement (p=0.011, 0.61 effect size) in the PANSS total score compared to placebo at week 6 with an 18.2-point PANSS total score improvement from baseline
- The once-daily 20 mg dose met additional endpoints, demonstrating statistically significant improvements in Clinical Global Impression of Severity Scale and Marder Factor Score Positive Symptom Change and Negative Symptom Change
- NBI-'568 was generally safe and well tolerated at all doses studied
- Neurocrine to host conference call/webcast at 8am EDT / 1pm BST / 9pm JST

Tokyo, Japan and Cambridge, UK, 28 August 2024 – Nxera Pharma Co., Ltd. ("Nxera" or "the Company"; TSE 4565) – formerly known as Sosei Group or Sosei Heptares – notes the announcement by its partner Neurocrine Biosciences Inc. ("Neurocrine"; Nasdaq: NBIX) that NBI-1117568 (NBI-'568) has delivered positive topline results from its Phase 2 clinical study in adults with schizophrenia. NBI-'568 is the first investigational, oral, muscarinic M4 selective agonist in development for the treatment of schizophrenia.

NBI-'568 is the most advanced candidate from a broad portfolio of novel clinical and preclinical subtype-selective muscarinic M4, M1 and dual M1/M4 receptor agonists discovered by Nxera and advancing under a 2021 global collaboration with Neurocrine for the treatment of major neurological disorders. To date, Nxera has received multiple, significant payments from Neurocrine including those based on developmental progress of four candidates in clinical trials and is eligible to receive development, regulatory and commercial milestones of up to US$2.6 billion, plus product royalties, provided the criteria under the agreement are satisfied. Nxera retains rights to develop M1 agonists advancing under this collaboration in Japan in all indications, subject to certain exceptions.

The NBI-'568-SCZ2028 dose-finding study met its primary endpoint for the once-daily 20 mg dose. It

demonstrated a clinically meaningful and statistically significant reduction from baseline in the Positive and Negative Syndrome Scale (PANSS) total score at Week 6 with a placebo-adjusted mean reduction of 7.5 points (p=0.011 and effect size of 0.61) and an 18.2-point reduction from baseline. The once-daily 20 mg dose also demonstrated a statistically significant improvement for additional endpoints, including improvement in the Clinical Global Impression of Severity (CGI-S) scale, Marder Factor Score – Positive Symptom Change, and Marder Factor Score – Negative Symptom Change.

Matt Barnes, EVP, President of Nxera Pharma UK and Head of R&D, commented: "These Phase 2 data reported by our partner Neurocrine represent an important milestone and strong clinical validation of the power of Nxera's NxWave™ discovery platform. We believe these data show that NBI-1117568 has a competitive product profile and could be an important new therapy option for patients with schizophrenia potentially with a once-daily pill. Furthermore, with four development candidates in clinical trials from the portfolio of selective muscarinic agonists discovered and licensed by Nxera to Neurocrine in 2021, offering multiple shots on goal across complex neurological and neuropsychiatric disorders, we look forward to further progress under this highly productive partnership."

"This Phase 2 dose-finding study delivered on our goal of identifying a once-daily, well tolerated dosing regimen with a compelling and competitive benefit-risk profile," **said Eiry Roberts, M.D., Chief Medical Officer at Neurocrine Biosciences**. "We recognize the significant need for new and innovative medicines to treat schizophrenia and look forward to advancing NBI-'568, the first M4 selective agonist, into Phase 3 development early next year."

NBI-'568 was generally safe and well-tolerated at all doses studied in the Phase 2 clinical trial. Treatment discontinuation rates due to adverse events were similar between NBI-'568 and placebo. Adverse events with the highest incidence were somnolence, dizziness, and headache. Gastrointestinal adverse events including nausea and constipation were low in frequency and similar to placebo. Cardiovascular-related events were also low in frequency and were not deemed to have clinical relevance at any dose tested. NBI-'568 was not associated with a greater increase in weight than placebo. Few extrapyramidal symptoms adverse events were reported.

Primary Endpoints Results Summary

Week 6 (Day 42)	**Placebo (N=68)**	**20 mg QD (N=35)**	**40 mg QD (N=38)**	**60 mg QD (N=34)**	**30 mg BID (N=26)**
PANSS Total Score LS Mean Change from Baseline*	-10.8	-18.2	-12.6	-13.7	-15.8
LS Mean Difference vs Placebo*	-	-7.5 (p=0.011)	-1.9 (p=0.282)	-2.9 (p=0.189)	-6 (p=0.090)
Effect Size**	-	0.61	0.27	0.39	0.23

**Least-squares (LS) means are from a mixed models for repeated measures (MMRM), which includes treatment group, visit, and study period as fixed effects; treatment group-by-visit interaction; baseline PANSS total score as a covariate; and subject as a random effect.*
***Effect size (Cohen's D) is based on observed data.*

Status of Neurocrine's Muscarinic Portfolio Licensed from Nxera

Neurocrine is advancing an industry leading portfolio of muscarinic agonists in clinical development with potential to treat a range of neurological and neuropsychiatric conditions. The four candidates progressing from its partnership with Nxera, are:

Compound	Primary Mechanism	Phase	Therapeutic Areas	Potential Areas for Development
NBI-1117568	M4 agonist	2	Psychosis Cognition	Alzheimer's Disease Bipolar Disorder Parkinson's Disease Lewy Body Dementia Schizophrenia
NBI-1117569	M4 agonist	1		
NBI-1117567*	M1 agonist	1		
NBI-1117570	M1/M4 dual agonist	1		

**Nxera retains rights to develop M1 agonists advancing under this collaboration in Japan in all indications, subject to certain exceptions*.

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About NBI-1117568
NBI-1117568 is the first and only M4 selective orthosteric agonist in clinical development. It was discovered by Nxera Pharma and licensed to Neurocrine in 2021 as part of a portfolio of muscarinic receptor agonists with potential to treat a range of neurological and neuropsychiatric conditions. There are five muscarinic acetylcholine receptors involved in neurotransmission. As an M4 selective agonist, NBI-1117568 offers the potential for an improved safety profile without the need of combination therapy to minimize off-target pharmacology-related side effects, while also not being dependent on the presence of acetylcholine for efficacy.

About the NBI-1117568-SCZ2028 Phase 2 Clinical Study
The Phase 2, multicenter, randomized, double-blind, placebo-controlled, multi-arm, multi-stage inpatient dose-finding study was designed and conducted by Neurocrine to assess the efficacy, safety, tolerability, and pharmacokinetics (PK) of NBI-'568 compared with placebo in adult subjects with a primary diagnosis of schizophrenia who are experiencing an acute exacerbation or relapse of symptoms. The study enrolled 210 participants. For more information about this study, visit ClinicalTrials.gov.

About the Agreement with Neurocrine Biosciences
Nxera Pharma and Neurocrine entered a collaboration and licensing agreement in November 2021 to develop a portfolio of novel muscarinic receptor agonists for the treatment of schizophrenia, dementia and other neuropsychiatric disorders.

Under the terms of the agreement, Neurocrine gained 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 Nxera. Neurocrine is responsible for development costs associated with the programs globally, except for M1 agonists being developed in Japan. Nxera retains rights to develop M1 agonists in Japan for any indication, with Neurocrine receiving co-development and profit share options.

Nxera is eligible to receive R&D funding plus development, regulatory and commercial milestones of up to US$2.6 billion, with further product royalties, provided the criteria under the agreement are satisfied.

About Neurocrine Biosciences
Neurocrine Biosciences is a leading neuroscience-focused, biopharmaceutical company with a simple purpose: to relieve suffering for people with great needs, but few options. Neurocrine Biosciences is dedicated to discovering and developing life-changing treatments for patients with under-addressed neurological, neuroendocrine, and neuropsychiatric disorders. The company's diverse portfolio includes FDA-approved treatments for tardive dyskinesia, chorea associated with Huntington's disease, endometriosis* and uterine fibroids*, as well as a robust pipeline including multiple compounds in mid- to late-phase clinical development across its core therapeutic areas. For three decades, Neurocrine Biosciences has applied its unique insight into neuroscience and the interconnections between brain and body systems to treat complex conditions. The company relentlessly pursues medicines to ease the burden of debilitating diseases and disorders, because you deserve brave science. For more information, visit neurocrine.com, and follow the company on LinkedIn, X (Formerly Twitter), and Facebook.
(**in collaboration with AbbVie*)

About Nxera Pharma
Nxera Pharma (formerly Sosei Heptares) is a technology powered biopharma company, in pursuit of new specialty medicines to improve the lives of patients with unmet needs in Japan and globally.

In addition to several products being commercialized in Japan, we are advancing an extensive pipeline of over 30 active programs from discovery through to late clinical stage internally and in partnership with leading pharma and biotech companies. This pipeline is focused on addressing major unmet needs in some of the fastest-growing areas of medicine across neurology, GI and immunology, metabolic disorders and rare diseases, and leverages the power of our unique and industry leading GPCR-targeted structure-based drug discovery "NxWave™" platform to provide a sustainable source of best- or first-in-class candidates.

Nxera employs over 350 talented people at key locations in Tokyo and Osaka (Japan), London and Cambridge (UK), Basel (Switzerland) and Seoul (South Korea) and is listed on the Tokyo Stock Exchange (ticker: 4565).

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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.