

## PRESS RELEASE

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# Saniona announces new preclinical data reinforcing SAN2465's potential as a rapid-acting antidepressant

**Saniona (OMX: SANION), a clinical-stage biopharmaceutical company focused on neurological and psychiatric disorders, today announces that SAN2465 significantly enhanced hippocampal synaptic plasticity in preclinical studies, providing mechanistic evidence for its potential as a rapid-acting antidepressant.**

"These findings provide important additional mechanistic support for SAN2465 and complement the rapid and sustained antidepressant-like effects we have previously demonstrated in animal models," said Karin Sandager Nielsen, Chief Scientific Officer of Saniona. "Together, these results strengthen the scientific rationale for developing SAN2465 as a differentiated, oral rapid-acting antidepressant. We are excited to advance this promising asset towards first-in-human clinical studies."

Long-term potentiation (LTP) is a well-established experimental measure of synaptic plasticity, reflecting the brain's ability to strengthen communication between neurons in response to activity, a process fundamental to learning, memory and adaptive brain function. Impaired synaptic plasticity has been associated with chronic stress and depression, while restoration of synaptic function is increasingly recognized as an important component of antidepressant action, including the effects of rapid-acting antidepressants such as ketamine [1].

Saniona has completed the key toxicology and CMC activities for SAN2465 and is preparing an Investigational New Drug (IND) application to the U.S. Food and Drug Administration (FDA), expected to be submitted to the FDA by the end of October 2026. The planned Phase 1 study will evaluate the safety, tolerability and pharmacokinetics of SAN2465 in healthy volunteers. The study is also designed to assess pharmacodynamic biomarkers that may support future clinical development and dose selection.

## More about the LTP study and results

The study employed an established LTP model using mouse hippocampal brain slices [2] to measure SAN2465's effect on synaptic plasticity and potentiation. SAN2465 was found to significantly enhance synaptic potentiation following burst stimulation, reaching 43.5% above baseline compared with 26.5% for vehicle ( $p=0.022$ ). The  $\alpha 5$ -selective reference compound  $\alpha 5$ 1A, previously shown to enhance hippocampal LTP and cognitive performance in rodents [3] and reduce alcohol-induced memory impairment in humans [4], produced a comparable response of 40.0%. No statistically significant difference was observed between SAN2465 and  $\alpha 5$ 1A.

Negative modulation of  $\alpha 5$ -containing GABA-A receptors has previously been shown to restore excitatory synaptic strength and reverse stress-induced depressive-like behavior, including cognitive impairment, in preclinical models [5]. Together with Saniona's previous findings showing rapid and sustained antidepressant-like effects of SAN2465 following a single oral dose, the new LTP data further support the potential of selective GABA-A  $\alpha 5$  modulation as a differentiated approach to address both mood symptoms and cognitive dysfunction associated with major depressive disorder.

## More about Major Depressive Disorder

Depression affects hundreds of millions of people worldwide [6]. Conventional antidepressants have a delayed onset of effect, low remission rates, and more than 30% of patients do not respond adequately, leading to treatment-resistant depression [7]. Esketamine (Spravato®), the first approved rapid-acting antidepressant, reached worldwide sales of USD 1.7 billion in 2025 [8], highlighting the demand for fast-acting treatment options. However, due to risks including sedation, dissociation and respiratory depression, esketamine is only available through a restricted Risk Evaluation and Mitigation Strategy (REMS) program requiring administration and monitoring in a certified healthcare setting [9].

## More about SAN2465

SAN2465 is a GABA-A  $\alpha 5$  negative allosteric modulator designed to deliver ketamine-like rapid onset without the limitations associated with ketamine and esketamine. In the chronic mild stress model, a well-established animal model of depression [10], a single oral dose of SAN2465 produced a rapid and sustained reversal of chronic stress-induced depressive-like symptoms, including anhedonia, anxiety and cognitive impairment. The onset and magnitude of the effects were comparable to ketamine. SAN2465 has also been shown to significantly enhance hippocampal synaptic plasticity (LTP). GABA-A  $\alpha 5$  receptors are highly expressed in the hippocampus and related limbic regions, brain regions involved in emotional control, mood and cognition [11,12]. Through selective modulation of these receptors, SAN2465 has the potential to provide rapid antidepressant efficacy without the dissociative and other adverse effects associated with NMDA receptor antagonists, potentially enabling convenient oral treatment without the need for in-clinic administration and monitoring.

[1] Duman RS et al. Nat Med 2016;22(3):238–249

[2] Seabrook GR et al. Neuropharmacology 1997;36(6):823–830

[3] Dawson GR et al. J Pharmacol Exp Ther 2006;316(3):1335–1345

[4] Nutt DJ et al. Neuropharmacology 2007;53(7):810–820

[5] Fischell J et al. Neuropsychopharmacology 2015;40(11):2499–2509

[6] World Health Organization. Depression fact sheet (September 2026).  
<https://www.who.int/news-room/fact-sheets/detail/depression>

[7] Zhdanova M et al. J Clin Psychiatry 2021;82(2):20m13699

[8] Johnson & Johnson. Q4 and full-year 2025 results, January 2026

[9] SPRAVATO® (esketamine) US Prescribing Information, revised March 2026

[10] Willner P. Neurobiol Stress 2017;6:78–93

[11] Sur C et al. Brain Res 1999;822(1-2):265–270 [12] Atack JR. Pharmacol Ther 2010;125(1):11–26

## About Saniona

Saniona is a clinical-stage biopharmaceutical company focused on discovering, developing, and delivering innovative treatments for neurological and psychiatric disorders. The company's internal pipeline includes SAN2668 for pediatric epilepsy syndromes and SAN2465 for major depressive disorder. Saniona has established strategic collaborations with leading pharmaceutical companies, including Jazz Pharmaceuticals, which holds global rights to SAN2355 for epilepsy, Acadia Pharmaceuticals, which holds worldwide rights to ACP-711 for essential tremor, and with Medix, which holds rights to tesofensine for obesity in Mexico, and Argentina. Saniona's ion channel discovery platform is further validated through research collaborations with Boehringer Ingelheim, Cephalgenix and AstronauTx, which holds worldwide rights to ATX0926. Headquartered in Copenhagen, Saniona is listed on the Nasdaq Stockholm Main Market.

For more information, visit [www.saniona.com](http://www.saniona.com).

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**Attachments**

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