PRESS RELEASE

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Saniona advances SAN2465 as a novel rapid-onset clinical candidate for major depressive disorder

Saniona (OMX: SANION), a clinical-stage biopharmaceutical company, today announces the selection of its proprietary GABAA α5 Negative Allosteric Modulator (NAM) lead compound, SAN2465, as a clinical candidate for major depressive disorder. This decision follows encouraging results obtained from a rodent model, specifically the chronic mild stress model of depression. SAN2465 demonstrated rapid and sustained reversal of chronic stress-induced depressive-like symptoms, including anhedonia, anxiety, and cognitive impairment. This positions SAN2465 as an innovative and rapid-acting approach to treating major depressive disorder and its associated comorbidities.

Originally discovered through collaboration with Boehringer Ingelheim for schizophrenia, SAN2465 is a highly potent and selective negative allosteric modulator of GABAA α5. Saniona holds exclusive global rights to the program following the termination of the collaboration with Boehringer Ingelheim in November 2020. SAN2465 is now poised for pre-clinical development as a rapid-acting antidepressant for collaboration with a partner.

SAN2465 was rigorously tested in the chronic mild stress model of depression in the laboratory of Professor Mariusz Papp, Maj Institute of Pharmacology, Polish Academy of sciences, Krakow, Poland. The chronic mild stress model is widely acknowledged as the most valid animal model of depression with translational potential to human disease [1]. Results indicate that a single oral treatment of SAN2465, administered 24 and 48 hours before testing, effectively reversed depressive-like symptoms, as assessed by stress-induced reduction of sucrose intake. Furthermore, SAN2465 reversed the anxiogenic-like behaviors and cognitive impairments induced by stress after a single oral treatment administered 48 hours and 72 hours before testing, respectively. Importantly, the onset and robustness of the effect are comparable to the NMDA antagonist ketamine, suggesting a potential new mechanism of action with a differentiated side effect profile.

Karin Sandager Nielsen, CSO of Saniona, commented, “These data strongly suggest that SAN2465 may induce rapid antidepressant effects similar to those observed with esketamine (Spravato™), which has demonstrated clinical response within hours after the first dose in patients [2,3].”

The rapid antidepressant effect of esketamine is believed to stem from fast onset neuroplastic changes in molecular signaling cascades in relevant brain regions [4,5]. Similar changes have been observed through pharmacological negative allosteric modulation of the GABAA α5 receptors in rodent studies [5,6] suggesting that this mechanism could have a comparable rapid antidepressant effect in humans. Importantly, unlike NMDA receptor blockade with esketamine, negative modulation of GABAA α5 receptors is not anticipated to lead to significant adverse effects, as the expression of these receptors is more localized and mainly restricted to limbic areas [7,8]. Use of esketamine is restricted by a Risk Evaluation and Mitigation Strategy (REMS) Program.

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Thomas Feldthus, CEO of Saniona, expressed excitement about these promising findings, stating, “We are looking forward to sharing the results with potential partners. This innovative approach for the treatment of major depressive disorder differs substantially from conventional antidepressant drugs in its mechanism of action, and it has the potential to become a first-in-class rapid-acting antidepressant without the significant adverse effects associated with esketamine [9].”

More about Major Depressive Disorder
Depressive disorders affect 280 million people globally and stand as the leading cause of disability [10]. Current conventional treatment relies on modulation of the monoaminergic system such as selective serotonin reuptake inhibitors, monoamine oxidase inhibitors and tricyclic antidepressants. However, existing conventional therapies exhibit delayed clinical responses, low remission rates, and a substantial portion of patients (more than 30%) do not respond adequately, leading to treatment-resistant depression [11]. In 2019, the FDA approved esketamine (Spravato™), the first prescription NMDA-antagonist-based fast-acting antidepressant. However, esketamine is associated with significant risks, including sedation, dissociation, respiratory depression, and abuse and misuse. Therefore, SPRAVATO® is only available through a restricted program called the SPRAVATO® Risk Evaluation and Mitigation Strategy (REMS) Program. Because of the risk associated with esketamine, there is a significant medical need for improved safe treatment options with rapid-onset and clinical response devoid of the use limitations associated with esketamine, in the large population of treatment-resistant patients.

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This information is information that Saniona AB (publ) is obliged to make public pursuant to the EU Market Abuse Regulation. The information was submitted for publication, through the agency of the contact persons set out above, at 2024-01-02 08:00 CET.

About Saniona
Saniona (OMX: SANION) is a clinical-stage biopharmaceutical company leading the way in ion channel modulation for the treatment of epilepsy and other neurological disorders. Saniona’s epilepsy pipeline features SAN711, a Phase 2-ready candidate drug targeting absence seizures, SAN2219 for acute repetitive seizures, and SAN2355, addressing refractory focal onset seizures. Beyond epilepsy, Saniona oversees four clinical programs poised for collaboration. Tesofensine, Saniona’s most advanced candidate, is progressing towards regulatory approval for obesity in Mexico through a partnership with Medix. Tesomet™ is ready for Phase 2b, targeting rare eating disorders, while SAN903 is ready for Phase 1 for inflammatory bowel disease and SAN2465 is set for preclinical development for major depressive disorder. Saniona has esteemed partners, including Boehringer Ingelheim GmbH, Productos Medix, S.A de S.V, AstronauTx Limited, and Cephagenix ApS. Saniona is based in Copenhagen and listed on Nasdaq Stockholm Main Market. For more information, please visit **www.saniona.com**.

Attachments

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