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Ad hoc announcement pursuant to Art. 53 LR

Idorsia and Simcere enter into a licensing agreement for daridorexant in China

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Idorsia Ltd (SIX: IDIA, "Idorsia"), specialized in the discovery, development and commercialization of small molecules to transform the horizon of therapeutic options, and Simcere Pharmaceutical Group Ltd (2096.HK, "Simcere"), an innovation and R&D-driven pharmaceutical company, announced today that they have entered into an exclusive licensing agreement for Idorsia's daridorexant in China.

Jinsheng Ren, Chairman and CEO of Simcere commented:
"This licensing agreement represents an important and exciting step in pursuing Simcere's mission of providing today's patients with medicines of the future. There are over 200 million people in China who suffer from chronic insomnia that may benefit from daridorexant. Patients are eager for a better treatment option that improves quality of sleep and next day functioning. Simcere has a proven track record of successfully developing and marketing innovative Central Nervous System therapies in China. In collaboration with Idorsia, we hope to bring another impactful medicine to millions of people."

Under the agreement, Simcere will be granted an exclusive right to develop and commercialize daridorexant in the Greater China region (Mainland China, Hong Kong, and Macau), one of the world's largest pharmaceutical markets. Simcere will be responsible for the funding and conducting of a local development program with Chinese patients. Simcere successfully commercializes Sanbexin for acute ischemic stroke and daridorexant will expand Simcere's pipeline of Central Nervous System (CNS) products in China.

According to the terms of the agreement, Idorsia will receive a US$ 30 million upfront payment, and will be eligible to receive an additional milestone payment of US$ 20 million upon regulatory approval by the National Medical Products Administration, as well as commercial milestone payments and low double-digit tiered royalties based upon future sales.

Jean-Paul Clozel, MD and Chief Executive Officer of Idorsia commented:
"Daridorexant is on track to becoming a global success, helping the millions of sufferers of insomnia around the world. Marketed as QUVIVIQ, we expect daridorexant will soon be the leading branded insomnia medication in the US in terms of new prescriptions. It is also the first dual orexin receptor antagonist available to patients in Europe, and recent positive data in Japan gives me confidence that we can make it available there too. We have been convinced of Simcere's shared enthusiasm for daridorexant, and I am confident that they are the right partner to join us on our mission of bringing an optimal treatment approach to patients with insomnia around the world by developing and commercializing daridorexant in China."

About daridorexant
Idorsia's research team has been working on the science of orexin and orexin receptors since they were first described in 1998. The team's initial work led to the conclusion that antagonism of the orexin system was the key to preserving a natural sleep architecture for patients with insomnia. With

this as the target, the team designed a dual antagonist with the goal of a rapid onset of effect and a duration of action sufficient to cover the night but short enough to avoid any negative next-morning residual activity at optimally effective doses.

Daridorexant is a dual orexin receptor antagonist, which blocks the binding of the wake-promoting neuropeptides orexins. Rather than inducing sleep through broad inhibition of brain activity, daridorexant blocks only the activation of orexin receptors. Consequently, daridorexant decreases the wake drive, allowing sleep to occur, without altering the proportion of sleep stages. The results of a Phase 3 clinical development program have been reported by Mignot, E., et al. Safety and efficacy of daridorexant in patients with insomnia disorder: results from two multicentre, randomised, double-blind, placebo-controlled, phase 3 trials, in The Lancet Neurology 2022;21:125–39.

Notes to the editor

Global regulatory status of daridorexant

In January 2022, QUVIVIQ (daridorexant) was approved by the US Food and Drug Administration (FDA) and subsequently made commercially available in May 2022. For more information about QUVIVIQ in the US, see the Full Prescribing Information (PI and Medication Guide). In April 2022, marketing authorization of QUVIVIQ was granted by the European Commission and subsequently by the Medicines and Healthcare products Regulatory Agency (MHRA) in Great Britain via the European Commission Decision Reliance Procedure. For more information about QUVIVIQ in the EU, see the Summary of Product Characteristics. Launch preparations are underway in the major European markets and QUVIVIQ was made available in both Italy and Germany in November 2022. Daridorexant is currently under review with Swissmedic and Health Canada.

About insomnia disorder

Insomnia disorder is defined as difficulty initiating or maintaining sleep, causing clinically significant distress or impairment in important areas of daytime functioning. This impact on sleep quantity or quality should be present for at least three nights per week, lasts for at least three months, and occurs despite an adequate opportunity to sleep.

Insomnia is a condition of overactive wake signaling and studies have shown that areas of the brain associated with wakefulness remain more active during sleep in patients with insomnia. It is a common problem with an estimated prevalence in China of 15% of the adult population.

Insomnia as a disorder is quite different from a brief period of poor sleep, and it can take its toll on both physical and mental health. It is a persistent condition with a negative impact on daytime functioning. Idorsia's research has shown that poor quality sleep can affect many aspects of daily life, including the ability to concentrate, mood, and energy levels.

The goal of treatments for insomnia is to improve sleep quality and quantity, as well as daytime functioning, while avoiding adverse events and next-morning residual effects. Current recommended treatment of insomnia includes sleep hygiene therapy, cognitive behavioral therapy, and pharmacotherapy.

About the orexin system

Wake and sleep signaling is regulated by intricate neural circuitry in the brain. One key component of this process is the orexin system, which helps promote wakefulness. There are two forms of orexin neuropeptides – small protein-like molecules used by nerve cells (neurons) to communicate with each other in the brain – orexin A and orexin B. Orexin promotes wakefulness through its receptors OX1R and OX2R. Together, these neuropeptides and receptors make up the orexin system. The orexin system stimulates targeted neurons in the wake system – leading to the release of several chemicals (serotonin, histamine, acetylcholine, norepinephrine) – to promote wakefulness. Under normal circumstances, orexin levels rise throughout the day as wakefulness is promoted and then fall at night. Overactivity of the wake system is an important driver of insomnia.

The daridorexant clinical development program

The Phase 3 registration program comprised two three-month studies, together with a long-term double-blind extension study. The program enrolled a total of 1,854 patients with insomnia disorder. As insomnia often presents later in life, and older adults are more susceptible to experience fragmented sleep, early awakening and daytime sleepiness, around 40% of the recruited population was at least 65 years of age.

The placebo-controlled studies investigated the effects of three doses of daridorexant (10 mg, 25 mg, and 50 mg) on sleep and daytime functioning parameters, objectively in a sleep lab by polysomnography and subjectively with a daily patient diary at home. The impact of insomnia on patients' daytime functioning was measured daily using the sleepiness domain score from the Insomnia Daytime Symptoms and Impacts Questionnaire (IDSIQ©) – a patient-reported outcome (PRO) instrument developed and validated according to the FDA Guidance for Industry.

More than 800 patients continued treatment in the 40-week extension study, which measured the effect of all three doses vs. placebo, generating data for long-term treatment of insomnia disorder.

Phase 3 data has been reported in The Lancet Neurology: The pivotal studies demonstrated that daridorexant 50 mg significantly improved sleep onset, sleep maintenance and self-reported total sleep time at months one and three compared to placebo. The largest effect was observed with the highest dose (50 mg), followed by 25 mg, while the 10 mg dose did not have a significant effect. In all treatment groups the proportions of sleep stages were preserved, in contrast to findings reported with benzodiazepine receptor agonists.

A major focus of the trials was to evaluate the impact of daridorexant on daytime functioning in patients with insomnia disorder, as assessed by the IDSIQ. IDSIQ is a patient-reported outcomes instrument specifically developed and validated according to FDA guidelines, to measure daytime functioning in patients with insomnia. The sleepiness domain score of the IDSIQ was evaluated as a key secondary endpoint in both pivotal studies and comparisons to placebo included type I error control for multiplicity. Daridorexant 50 mg demonstrated highly statistically significant improvement in daytime sleepiness at month one and month three. The sleepiness domain score was not significantly improved on 25 mg in either study at either timepoint.

The overall incidence of adverse events was comparable between treatment groups. The most frequently reported adverse reactions were headache and somnolence and, overall, the majority of adverse reactions were mild to moderate in intensity. There was no evidence of dose-dependent increases in adverse events across the dosing range. Further, no dependence, rebound insomnia or evidence of abuse or withdrawal symptoms indicative of physical dependence upon treatment discontinuation was observed in clinical studies.

Key literature

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About Simcere

Simcere Pharmaceutical Group Limited (2096.HK) is an innovation and R&D-driven pharmaceutical company. The company focuses on three therapeutic areas, oncology, central nervous system and autoimmune diseases, with a forward-looking vision toward disease areas that may have significant clinical needs in the future, aiming to achieve the mission of "providing today's patients with medicines of the future." Leveraging its R&D capability and commercialization excellence, Simcere has built a market-leading product portfolio in China. Its vigorous in-house R&D efforts and extensive R&D collaborations have made it a strategic cooperation partner with world leading innovative companies and research institutes.

For more information, please visit: http://en.simcere.com/
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About Idorsia

Idorsia Ltd is reaching out for more – We have more ideas, we see more opportunities and we want to help more patients. In order to achieve this, we will develop Idorsia into a leading biopharmaceutical company, with a strong scientific core.

Headquartered near Basel, Switzerland – a European biotech-hub – Idorsia is specialized in the discovery, development and commercialization of small molecules to transform the horizon of therapeutic options. Idorsia has a broad portfolio of innovative drugs in the pipeline, an experienced team of professionals covering all disciplines from bench to bedside, state-of-the-art facilities, and a strong balance sheet – the ideal constellation to translate R&D efforts into business success.

Idorsia was listed on the SIX Swiss Exchange (ticker symbol: IDIA) in June 2017 and has over 1,200 highly qualified specialists dedicated to realizing our ambitious targets.

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