

Media Release

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New data for daridorexant in patients with insomnia disorder – including long-term safety and efficacy – to be presented at World Sleep 2022

Allschwil, Switzerland – March 10, 2022

Idorsia Ltd (SIX: IDIA) today announced that new data for daridorexant in patients with insomnia disorder, including long-term safety and efficacy data, will be presented at World Sleep 2022, a global scientific congress bringing the best of sleep medicine and research to Rome, Italy, March 11–16, 2022.

An oral presentation entitled "Long-term safety and efficacy of daridorexant in patients with insomnia disorder" will be given by Dieter Kunz, MD, Charité - Universitätsmedizin Berlin, on March 14 at 11:30am CET.

Antonio Olivieri, Senior Vice President, Head of Global Medical Affairs of Idorsia commented:

"Some patients with insomnia disorder need long-term treatment, something which is not supported by many existing treatment options. We're excited that the results for up to 12 months of treatment in the Phase 3 daridorexant program will be presented at this leading global sleep congress. The safety and efficacy of daridorexant have been well documented and these findings will shed further light on its promising long-term safety and efficacy profile."

In addition, the following posters will be presented:

- Dauvilliers Y., *et al.* Efficacy of long-term treatment with daridorexant in patients with insomnia disorder on sleep and daytime functioning: a post-hoc analysis [Poster #109]
- Di Marco T., *et al.* Effects of daridorexant and zolpidem on night wakefulness in adults with insomnia: exploratory analysis from a randomized, double-blind, placebo-controlled phase 2 trial [Poster #111]
- Heidenreich S., *et al.* A benefit-risk assessment of daridorexant for the treatment of insomnia using patient preference data from two phase 3 trials [Poster #113]
- Leger D., *et al.* Evaluating the risks of withdrawal symptoms and rebound insomnia upon discontinuation of daridorexant in patients with insomnia disorder [Poster #121]
- Fietze I., *et al.* Effects of daridorexant on sleep and daytime functioning in older patients with insomnia disorder [Poster #087]
- Zammit G., *et al.* Effects of daridorexant on total sleep time (TST) and sleep stage proportions in patients with insomnia disorder [Poster #110]

The abstracts can be found in the [Scientific Program for World Sleep 2022](#).

Notes to the editor

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.¹ 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.¹

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.^{2,3} Insomnia is a common problem with a prevalence of approximately 10% of the adult population.⁴ On this basis, and assuming a US adult population of around 250 million, there are approximately 25 million adults in the US who suffer from insomnia. In Europe, the estimated prevalence of insomnia is 6-12%⁵ and in Canada, insomnia affects an estimated 10%.⁶

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.⁷ It is a persistent condition with a negative impact on daytime functioning.¹ 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.⁸ Current recommended treatment of insomnia includes sleep hygiene recommendations, cognitive behavioral therapy, and pharmacotherapy.⁹

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.^{9,10,11} 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.¹⁰ Orexin promotes wakefulness through its receptors OX1R and OX2R.¹⁰ 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.¹² Under normal circumstances, orexin levels rise throughout the day as wakefulness is promoted and then fall at night.¹³ Overactivity of the wake system is an important driver of insomnia.^{3,9}

Daridorexant in insomnia disorder

Daridorexant is a dual orexin receptor antagonist, which blocks the binding of the wake-promoting neuropeptides orexins and is thought to turn down overactive wakefulness, as opposed to treatments that generally sedate the brain.¹⁴

The Phase 3 registration program comprised two three-month studies, together with a long-term double-blind extension study.⁸ The program enrolled around 1,850 patients with insomnia disorder.⁸ As insomnia often presents later in life, and older adults are more susceptible to experience fragmented sleep, early awakening and daytime sleepiness,¹⁵ around 40% of the recruited population was at least 65 years of age.⁸

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.⁸ 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.^{8,16}

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.¹⁷

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.⁸ 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.⁸ In all treatment groups the proportions of sleep stages were preserved, in contrast to findings reported with benzodiazepine receptor agonists.⁸

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.⁸ IDSIQ is a patient-reported outcomes instrument specifically developed and validated according to FDA guidelines, to measure daytime functioning in patients with insomnia.¹⁶ 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.⁸ Daridorexant 50 mg demonstrated highly statistically significant improvement in daytime sleepiness at month one and month three.⁸ The sleepiness domain score was not significantly improved on 25 mg in either study at either timepoint.⁸

The overall incidence of adverse events was comparable between treatment groups.⁸ Adverse events occurring in more than 5% of participants were nasopharyngitis and headache.⁸ There were no dose-dependent increases in adverse events across the dosing range, including somnolence and falls.⁸ Further, no dependence, rebound insomnia or withdrawal effects were observed

upon abrupt discontinuation of treatment.⁸ Across treatment groups, adverse events leading to treatment discontinuation were numerically more frequent with placebo than daridorexant.⁸

Regulatory status of daridorexant

Daridorexant is currently under review with Swissmedic and Health Canada. In January 2022, QUVIVIQ™ (daridorexant) was approved by the US Food and Drug Administration (FDA) for the treatment of adult patients with insomnia characterized by difficulties with sleep onset and/or sleep maintenance. In February 2022, the Committee for Medicinal Products for Human Use (CHMP), the scientific committee of the European Medicines Agency (EMA), adopted a positive opinion for the use of QUVIVIQ (daridorexant) for the treatment of adult patients with insomnia characterized by symptoms present for at least three months and considerable impact on daytime functioning.

References

- ¹ The Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM–5; American Psychiatric Association, 2013).
- ² Buysse DJ, et al. *Drug Discov Today Dis Models*. 2011;8(4):129-137.
- ³ Levenson JC, et al. *Chest*. 2015;147(4):1179-1192.
- ⁴ Schlack R, et al. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz*. 2013;56(5-6):740-748.
- ⁵ Riemann D, et al. *Sleep*. 2017;26(6):675-700.
- ⁶ Chaput, Statistics Canada; 2018 Dec 19;29(12):16-20.
- ⁷ Wardle-Pinkston S, et al. *Sleep Med Rev*. 2019;48.
- ⁸ Mignot E, et al. *Lancet Neurol*. 2022;21:125–39.
- ⁹ Muehlan, C, et al. *Expert Opin. Drug Metab. Toxicol*. 2020;16(11):1063–1078.
- ¹⁰ Muehlan, C, et al. *J Psychopharmacol*. 2020;34(3):326-335.
- ¹¹ Boof, ML, et al. *Eur J Clin Pharmacol*. 2019;75(2):195-205.
- ¹² Clifford B. Saper, et al. *Trends Neurosci*. 2001;24(12):726-31.
- ¹³ Gotter, AL, et al. *BMC Neuroscience*. 2013;14(1):14-19.
- ¹⁴ Roch, C, et al. *Psychopharmacology*. 2021;238(10):2693–2708.
- ¹⁵ Patel, D, et al. *J Clin Sleep Med*. 2018;14(06):1017–1024.
- ¹⁶ Hudgens S, et al. *Patient*. 2020. doi:10.1007/s40271-020-00474-z.
- ¹⁷ Data on file, Idorsia.

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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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