Media Release
June 12, 2023

Idorsia launches QUVIVIQ (daridorexant) in Switzerland – a first-in-class treatment for chronic insomnia disorder to improve both nighttime symptoms and daytime functioning

- QUVIVIQ™ is indicated for the treatment of adult patients with insomnia, characterized by symptoms present for at least three months and considerable impact on daytime functioning
- QUVIVIQ, Switzerland's first approved dual orexin receptor antagonist, offers a new targeted mechanism of action that decreases nighttime overactive wakefulness in insomnia

Allschwil, Switzerland – June 12, 2023
Idorsia Ltd (SIX: IDIA) today announced that QUVIVIQ™ (daridorexant) is now available to patients in Switzerland for the treatment of adult patients with chronic insomnia characterized by symptoms present for at least three months and considerable impact on daytime functioning.[1] Chronic insomnia is one of the most prevalent sleep disorders in Switzerland, affecting 9.2% of the working-age population,[15] and impacts both physical and mental health.[3,4] According to a recent report from the RAND Corporation,[15] more than CHF 10 billion is lost from annual GDP in Switzerland due to reduced productivity associated with chronic insomnia.

QUVIVIQ is the first dual orexin receptor antagonist (DORA) available in Switzerland for the treatment of chronic insomnia disorder. Rather than inducing sleep through broad inhibition of brain activity (sedation), QUVIVIQ blocks the activation of orexin receptors[1] known for their key role in wakefulness. Consequently, QUVIVIQ decreases the wake drive, allowing sleep to occur, without altering the proportion of sleep stages.[1]

The recommended dose of QUVIVIQ is one tablet of 50 mg once per night, taken orally in the evening within 30 minutes before going to bed.[1] In certain circumstances, such as patients with moderate hepatic impairment or who are taking moderate CYP3A4 inhibitors, the recommended dose is 25 mg once per night.[1]

Jean-Paul Clozel, MD and Chief Executive Officer, commented:
"The discovery of QUVIVIQ is the result of more than 20 years of research by our own scientists at our headquarters here in Switzerland. I am very happy that QUVIVIQ is now the first dual orexin receptor antagonist available to Swiss patients suffering from chronic insomnia disorder. This offers patients a new targeted mechanism of action that decreases nighttime overactive wakefulness in insomnia, and at the recommended dose of 50 mg, improves how patients feel and function the next day. I'm confident that we can transform the way chronic insomnia disorder is treated in Switzerland."

Alice Huisman, General Manager of Idorsia Switzerland and Austria, commented:
"I am delighted that we are now able to provide Swiss patients and their physicians a new, targeted treatment option for chronic insomnia disorder. The unique characteristics of QUVIVIQ offer patients with chronic insomnia disorder not only a better night sleep, both in terms of sleep onset and duration, but also an improvement in daytime functioning. The fact that Switzerland is our home market makes this milestone particularly meaningful."

The Phase 3 program was composed of two pivotal 3-month trials and a long-term extension study, which provide clinical data for up to 12 months of nightly treatment.[1,5,17] The results of the 3-month

trials – published in The Lancet Neurology – demonstrated that at the recommended dose, QUVIVIQ significantly improved sleep onset, sleep maintenance and self-reported total sleep time in adults with chronic insomnia disorder.[5] A major focus of the trials was to evaluate the impact of QUVIVIQ on daytime functioning in patients with insomnia disorder, as assessed by IDSIQ, a patient-reported outcomes instrument. The recommended dose of QUVIVIQ demonstrated statistically significant improvement from baseline compared to placebo in the daytime sleepiness domain of IDSIQ, which means patients reported feeling less mentally and physically tired, less sleepy and more energetic during the day, at months one and three.[1]

In clinical trials, the most frequently reported adverse reactions were headache and somnolence.[1] The majority of adverse reactions were mild to moderate in intensity.[1] No evidence of a dose-relationship for the frequency or severity of adverse reactions was observed.[1] The adverse reaction profile in elderly patients was consistent with younger patients.[1] Somnolence was reported in 3% and 2% of patients treated with QUVIVIQ 25 mg and 50 mg, respectively, compared to 2% of subjects on placebo.[1] Furthermore, no rebound insomnia or withdrawal symptoms indicative of physical dependence upon treatment discontinuation were observed in clinical studies, nor was there an indication of any drug abuse potential.[1]

For more information on the marketing authorization of QUVIVIQ in Switzerland, please review the Patient Information and Information for Healthcare Professionals.

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.[3] 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.[3]

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.[8,9] Chronic insomnia is a common problem with an estimated prevalence in Switzerland of 9.2% of the working-age population.[15]

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.[3,4] It is a persistent condition with a negative impact on daytime functioning.[3] 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.[7,10] 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.[6,7] Orexin promotes wakefulness through its receptors OX1R and OX2R.[6,7] 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.[11] Under normal circumstances, orexin levels rise throughout the day as wakefulness is promoted and then fall at night.[12] Overactivity of the wake system is an important driver of insomnia.[5,10]

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 dual antagonists with the goal of rapid onset of effect and duration of action sufficient to cover the night but short enough to minimize any negative next-morning residual activity at optimally effective doses.

About QUVIVIQ (daridorexant) in insomnia disorder

Studies over the past decades have shown that hyperarousal processes in the brain play a key role in the pathology of insomnia.[6] Chronic insomnia disorder is the result of continued brain hyperarousal that requires sustained management with therapy suitable for daily use over months.[7] Orexin is a neuropeptide, a small protein-like molecule, produced by the brain that

promotes wakefulness.[1,6] QUVIVIQ reduces nocturnal hyperarousal to improve sleep (onset and maintenance) without next-morning residual effects in insomnia patients, and thus improves daytime functioning.[5]

Global regulatory status of QUVIVIQ

In January 2022, QUVIVIQ 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. 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. Marketing authorization of QUVIVIQ was granted by Swissmedic in December 2022, and made available to patients in Switzerland in June 2023. For more information about QUVIVIQ in Switzerland, see the Patient Information and Information for Healthcare Professionals. In April 2023, Health Canada approved QUVIVIQ in Canada. For more information on the marketing authorization of QUVIVIQ in Canada, see the Product Monograph.

The daridorexant Phase 3 registration program[5]

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,[13] around 40% of the recruited population was at least 65 years of age.[16]

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.[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. 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.[14] 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.[1] The most frequently reported adverse reactions were headache and somnolence and, overall, the majority of adverse reactions were mild to moderate in intensity.[1] No evidence of a dose-relationship for the frequency or severity of adverse reactions was observed.[1]

References

1. QUVIVIQ™ Patient Information and Information for Healthcare Professionals. May 2022.
2. Riemann, D., et al. Sleep. 2017;26(6):675-700.
3. The Diagnostic and Statistical Manual of Mental Disorders (5th ed.; DSM–5; American Psychiatric Association, 2013).
4. Wardle-Pinkston S., et al. Sleep Med Rev. 2019;48.
5. Mignot, E., et al. Lancet Neurol. 2022;21:125–39.
6. Muehlan, C., et al. Expert Opin. Drug Metab. Toxicol. 2020;16(11):1063–1078.
7. Muehlan, C., et al. J Psychopharmacol. 2020;34(3):326-335.
8. Buysse, D.J., et al. Drug Discov Today Dis Models. 2011;8(4):129-137.
9. Levenson, J.C., et al. Chest. 2015;147(4):1179-1192.
10. Boof, M.L., et al. Eur J Clin Pharmacol. 2019;75(2):195-205.
11. Clifford, B.S., et al. Trends Neurosci. 2001;24(12).726-31.
12. Gotter, A.L., et al. BMC Neuroscience. 2013;14(1):14-19.
13. Patel, D., et al. J Clin Sleep Med. 2018;14(06):1017–1024.
14. Hudgens, S., et al. Patient. 2020. doi:10.1007/s40271-020-00474-z.

15. Hafner, M., et al. The Societal and Economic Burden of Insomnia in Adults: An International Study. Santa Monica, CA: RAND Corporation, 2023.
16. Fietze I., et al. 2022 Oct;39(10):795-810.
17. Kunz D, et al. CNS Drugs. 2022 Dec 9.

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 20-year heritage of drug discovery, a broad portfolio of innovative drugs in the pipeline, an experienced team of professionals covering all disciplines from bench to bedside, and commercial operations in Europe, Japan, and the US – the ideal constellation for bringing innovative medicines to patients.

Idorsia was listed on the SIX Swiss Exchange (ticker symbol: IDIA) in June 2017 and has over 1,300 highly qualified specialists dedicated to realizing our ambitious targets.

For further information, please contact

Andrew C. Weiss
Senior Vice President, Head of Investor Relations & Corporate Communications
Idorsia Pharmaceuticals Ltd, Hegenheimermattweg 91, CH-4123 Allschwil
+41 58 844 10 10
investor.relations@idorsia.com
media.relations@idorsia.com
www.idorsia.com

The above information contains certain "forward-looking statements", relating to the company's business, which can be identified by the use of forward-looking terminology such as "estimates", "believes", "expects", "may", "are expected to", "will", "will continue", "should", "would be", "seeks", "pending" or "anticipates" or similar expressions, or by discussions of strategy, plans or intentions. Such statements include descriptions of the company's investment and research and development programs and anticipated expenditures in connection therewith, descriptions of new products expected to be introduced by the company and anticipated customer demand for such products and products in the company's existing portfolio. Such statements reflect the current views of the company with respect to future events and are subject to certain risks, uncertainties and assumptions. Many factors could cause the actual results, performance or achievements of the company to be materially different from any future results, performances or achievements that may be expressed or implied by such forward-looking statements. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those described herein as anticipated, believed, estimated or expected.