Media Release
January 10, 2022

Ad hoc announcement pursuant to Art. 53 LR

Idorsia receives US FDA approval of QUVIVIQ (daridorexant) 25 and 50 mg for the treatment of adults with insomnia

- The approval of QUVIVIQ™ – 25 & 50 mg – is based on a robust Phase 3 clinical program that demonstrated significant improvement versus placebo on objective measures of sleep onset and sleep maintenance, as well as patient reported total sleep time
- Idorsia's first approved medicine is a new treatment option for the approximately 25 million American adults living with insomnia[2,3,4]

Allschwil, Switzerland – January 10, 2022
Idorsia Ltd (SIX: IDIA) today announced that the US Food and Drug Administration (FDA) has approved QUVIVIQ™ (daridorexant) 25 mg and 50 mg for the treatment of adult patients with insomnia, characterized by difficulties with sleep onset and/or sleep maintenance[1]. The FDA approval of QUVIVIQ is based on an extensive clinical program that included 1,854 adults with insomnia at over 160 clinical trial sites across 18 countries. Insomnia, a serious medical condition, is the most common sleep disorder in the US.

QUVIVIQ 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.

During the Phase 3 clinical program, QUVIVIQ demonstrated significant improvement versus placebo on objective measures of sleep onset and sleep maintenance, and patient reported total sleep time. Consistent with the US prescribing information, the 50 mg dose of QUVIVIQ, which was evaluated in one of the two pivotal studies, demonstrated a significant reduction in patient reported daytime sleepiness, using a validated instrument. The most common adverse reactions (in at least 5% of patients and greater than placebo) were headache (placebo: 5%, 25 mg: 6%, 50 mg: 7%,) and somnolence or fatigue (placebo: 4%, 25 mg: 6%, 50 mg: 5%).

The FDA has recommended that QUVIVIQ be classified as a controlled substance and it is anticipated to be available to patients in May 2022, following scheduling by the US Drug Enforcement Administration.

Martine Clozel, MD and Chief Scientific Officer of Idorsia, commented:
"After more than 20 years of research and a progressive understanding of the role of orexin in sleep-wake balance and of the potential of orexin receptor antagonism, we designed daridorexant to help address several issues people with insomnia face. Daridorexant properties include a potent inhibition of both orexin receptors, a rapid absorption for sleep onset, and a pharmacokinetic profile such that around 80% of daridorexant has been eliminated after a night of sleep to help minimize residual effects."

Dr Thomas Roth, PhD, Director of the Sleep Disorder and Research Center at Henry Ford Hospital, commented:
"As noted in the definition of insomnia, the disorder is not only a problem of the night but affects a patient's ability to function during the day. Although the personal and societal burden of insomnia is well established, elevating the impact insomnia has on both the night and day remains critical in addressing patients' needs. I am encouraged to see a new advanced treatment option for the millions of adults struggling with insomnia."

Patricia Torr, President and General Manager of Idorsia US added:
"I am extremely proud to be leading the US organization of such a forward-thinking and patient-centric organization like Idorsia. With this first FDA approval for our company, QUVIVIQ provides a new treatment option that can help adults with insomnia get to sleep faster and stay asleep longer, which we know plays an important role in how they feel the next day. It's an incredibly exciting time for us and I can't wait to transform the treatment paradigm in the US. We have a differentiated product, an amazing team, and an innovative strategy, giving me absolute confidence that we can make QUVIVIQ a great success."

Guy Braunstein, MD and Head of Global Clinical Development of Idorsia, commented:
"In our investigation of daridorexant we were able to demonstrate an improvement on objective sleep parameters, as well as improvement in patient-reported outcomes. What is truly impressive, we have shown a dose response in the efficacy of daridorexant, with no increase in the rate of somnolence or fatigue with increasing doses."

Phase 3 Clinical Program

The efficacy of QUVIVIQ was evaluated in two multicenter, randomized, double-blind, placebo-controlled, parallel-group studies, Study 1 (NCT03545191) and Study 2 (NCT03575104).

A total of 1854 patients with Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5®) insomnia were randomized to receive QUVIVIQ or placebo once daily, in the evening, for 3 months. Study 1 randomized 930 subjects to QUVIVIQ 50 mg (N = 310), 25 mg (N = 310) or placebo (N = 310). Study 2 randomized 924 subjects to QUVIVIQ 25 mg (N = 309), 10 mg (N = 307), or placebo (N = 308). The 10 mg dose is not an approved dose.

At the end of the 3-month treatment period, both studies included a 7-day placebo run-out period, after which patients could enter a 9-month, double-blind, placebo-controlled extension study (Study 3, NCT03679884). A total of 600 subjects were treated for at least 6 months of cumulative treatment, including 373 treated for at least 12 months.

Primary efficacy endpoints for both studies were the change from baseline to Month 1 and Month 3 in Latency to Persistent Sleep (LPS) and Wake After Sleep Onset (WASO), measured objectively by polysomnography in a sleep laboratory. LPS is a measure of sleep induction and WASO is a measure of sleep maintenance.

Secondary endpoints included in the statistical testing hierarchy with Type I error control were patient-reported Total Sleep Time (sTST), evaluated every morning at home using a validated Sleep Diary Questionnaire (SDQ).

In Study 1, doses of 25 and 50 mg QUVIVIQ showed a statistically significant improvement vs placebo on polysomnography (LPS, WASO) and self-reported total sleep (sTST), at Month 1 and Month 3.

In Study 2, QUVIVIQ 25 mg showed a statistically significant improvement vs placebo on WASO and sTST at Month 1 and Month 3. QUVIVIQ 10 mg did not show a statistically significant improvement on LPS, WASO, or sTST at Month 1 or Month 3.

The efficacy of QUVIVIQ was similar across subgroups based on age, sex, race, and region.

The 50 mg dose of QUVIVIQ, which was evaluated in one of the two pivotal studies, also demonstrated significant reduction in daytime sleepiness compared to placebo, as measured by the sleepiness domain score from the Insomnia Daytime Symptoms and Impacts Questionnaire (IDSIQ)[7] at month 1 and month 3 (key secondary endpoint). Results on this endpoint for the 25mg dose did not reach statistical significance in either study at both timepoints.

The most common reported adverse reactions (in at least 5% of patients and greater than placebo) were headache (placebo: 5%, 25 mg: 6%, 50 mg: 7%,) and somnolence or fatigue (placebo: 4%, 25 mg: 6%, 50 mg: 5%).

For more information see the **Full Prescribing Information** (PI and Medication Guide).

Important Safety Information

QUVIVIQ is a prescription medicine for adults who have trouble falling asleep or staying asleep (insomnia).

Do not take QUVIVIQ if you fall asleep often at unexpected times (narcolepsy).

QUVIVIQ may cause serious side effects, including:

- **Decreased awareness and alertness.** The morning after you take QUVIVIQ, your ability to drive safely and think clearly may be decreased. You may also have sleepiness during the day.
  - Do not take more QUVIVIQ than prescribed.
  - Do not take QUVIVIQ unless you are able to stay in bed for at least 7 hours before you must be active again.
  - Take QUVIVIQ at night within 30 minutes before going to bed.

QUVIVIQ is a federally controlled substance because it can be abused or lead to dependence.

Before taking QUVIVIQ, tell your healthcare provider about all of your medical conditions, including if you:

- have a history of depression, mental illness, or suicidal thoughts or actions; drug or alcohol abuse or addiction; a sudden onset of muscle weakness (cataplexy); daytime sleepiness
- have lung or breathing problems, including sleep apnea
- have liver problems
- are pregnant or plan to become pregnant
- are breastfeeding or plan to breastfeed

Tell your healthcare provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements

- Taking QUVIVIQ with certain medicines can cause serious side effects. QUVIVIQ may affect the way other medicines work and other medicines may affect the way QUVIVIQ works.
- **Do not take QUVIVIQ with other medicines that can make you sleepy unless instructed by your healthcare provider.**

What should I avoid while taking QUVIVIQ?

- Do not drink alcohol while taking QUVIVIQ. It can increase the effects of alcohol, which can be dangerous.
- Do not drive, operate heavy machinery, do anything dangerous, or do other activities that require clear thinking if you do not feel fully awake, or you have taken QUVIVIQ and have less than a full night of sleep (at least 7 hours), or if you have taken more QUVIVIQ than prescribed.

QUVIVIQ may cause other serious side effects, including:

- **Worsening depression and suicidal thoughts.** Call your healthcare provider right away if you have any worsening depression or thoughts of suicide or dying**.**
- **Temporary inability to move or talk (sleep paralysis) for up to several minutes, or hallucinations while you are going to sleep or waking up.**
- **Complex sleep behaviors** such as sleep-walking, sleep-driving, preparing and eating food, making phone calls, having sex or doing other activities while not fully awake that you may not remember the next morning. Stop taking QUVIVIQ and call your healthcare provider right away if you experience a complex sleep behavior.

The most common side effects of QUVIVIQ are headache and sleepiness**.**

These are not the only side effects of QUVIVIQ. Call your doctor for advice about side effects.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Notes to the editor

About Insomnia

According to the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5®), insomnia is defined as a combination of difficulty obtaining sufficient sleep and dissatisfaction with sleep combined with a significant negative impact on daytime functioning. Chronic insomnia is defined as difficulty initiating and/or maintaining sleep on at least three nights per week for at least three months, despite adequate opportunity to sleep.

Insomnia is a condition of overactive brain activity during sleep, and studies have shown that areas of the brain associated with wakefulness remain more active during sleep in patients with insomnia.

Insomnia is the most common sleep disorder, affecting more than 25 million adults in the US.[2] Poor quality or insufficient sleep can affect many aspects of the daily lives of people with trouble sleeping including the ability to concentrate, mood and energy levels.[3] In the long-term, insomnia is associated with numerous serious health conditions, such as psychiatric disorders, cardiovascular disease, type 2 diabetes, substance abuse and dementia.[4,5,6]

About Dr. Thomas Roth, PhD

Dr. Roth has been the Director of the Sleep Disorders and Research Center at Henry Ford Hospital in Detroit, since 1978. Dr. Roth is also a Professor in the Department of Psychiatry at Wayne State University, School of Medicine in Detroit, Michigan, and serves as a Clinical Professor in the Department of Psychiatry at the University of Michigan, College of Medicine in Ann Arbor.

After serving as president of the Sleep Research Society, and the founding president of the National Sleep Foundation (NSF), Dr. Roth became chairman of the National Center on Sleep Disorders Research advisory board. In addition, he was a member of the board of directors of the Associated Professional Sleep Societies (APSS), chaired the Association's Scientific Program Committee and the governing board of the World Federation of Sleep Research Societies.

Dr. Roth was instrumental in the formation of the Association of Sleep Disorders Center (ASDC) and served as the organization's second president. He is also the former Chairman of the World Health Organization's worldwide project on sleep and health. In addition to authoring and co-authoring numerous articles, Dr. Roth serves as past editor-in-chief of the journal Sleep. He currently sits on the editorial boards of Sleep Reviews, Stress Medicine, and Advances in Therapy and Human Psychopharmacology.

In 2002, Dr. Roth received the NSF's Lifetime Achievement Award for his accomplishments and contributions to sleep science, sleep medicine and public health. He received a Distinguished Research Award from the Sleep Research Society as well as the Nathanial Kleitman Award from the Academy of Sleep Medicine. Dr. Roth's contributions to the sleep field are expansive, ranging from prolific research productivity and scholarship to multiple national leadership positions, as well as the mentoring of many students and colleagues. Dr. Roth serves as a consultant to Idorsia.

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About Idorsia US

Idorsia US, an affiliate of Idorsia, is reaching out for more – we have more ideas, we see more opportunities, and we want to help more patients. To achieve this, we will help develop Idorsia into a leading biopharmaceutical company, with a strong scientific core. With commercial operations based outside of Philadelphia, PA, one of densest communities of life sciences talent in the world, we are helping to realize the company's ambition of bringing innovative medicines from bench to bedside. Our goal is to build a commercial footprint that will deliver Idorsia's deep pipeline of products from its R&D engine to the US market – with the potential to change the lives of many patients.

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 1'000 highly qualified specialists dedicated to realizing our ambitious targets.

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