Media Release
April 20, 2020

Idorsia announces positive results in the first Phase 3 study of daridorexant with improved overall sleep and daytime performance of patients with insomnia

- Idorsia to host an investor webcast to discuss the first Phase 3 results today at 14:00hrs CEST

Allschwil, Switzerland – April 20, 2020
Idorsia Ltd (SIX: IDIA) today announced positive top-line results of the first pivotal Phase 3 study investigating 25 and 50 mg doses of its dual orexin receptor antagonist, daridorexant, in 930 adult and elderly patients (39.1% ≥ 65 years) with insomnia. The study demonstrated efficacy of treatment with daridorexant on objective and subjective sleep parameters and daytime performance with no residual effect in the morning, and no evidence of rebound or withdrawal symptoms upon treatment discontinuation.

Daridorexant at both 25 and 50 mg significantly improved **sleep onset** and **sleep maintenance** as measured objectively in a sleep lab by polysomnography. Daridorexant also significantly improved **subjective total sleep time** as measured daily with a patient diary at home. The results were consistently statistically significant at month 1 and at month 3, indicating sustained benefit. Furthermore, treatment with daridorexant improved patients' **daytime performance** from baseline at month 1 and month 3.

Jean-Paul Clozel, MD and Chief Executive Officer of Idorsia, commented:
"While we designed daridorexant to have the optimal profile for a sleep medicine, I am none-the-less stunned by the results. Once approved, by providing daridorexant to the millions of patients with insomnia, Idorsia will have a major impact on this medical, social, and economic problem. It has struck me particularly in these times of confinement that we are living through, that sleep problems are a major issue and require an extremely safe and effective drug that can be used by the many. With these results Idorsia is entering into a new era; less than 3 years since its creation, Idorsia is taking a huge step forward in delivering on the vision to become a fully-fledged biopharmaceutical company."

Dr. Thomas Roth, PhD, Director of the Sleep Disorder and Research Center at Henry Ford Hospital, commented:
"Pharmacological treatment for insomnia should not only help patients to fall asleep quickly and to stay asleep but also address the negative impact of poor sleep on daytime functioning. I believe that the optimal way to achieve this is through blocking the action of orexin and therefore turning down overactive wakefulness seen among insomnia disorder patients. This will allow patients to sleep throughout the night, while avoiding the adverse effects, associated with many sleep medications that act through broad sedation of the brain. The excellent results seen in this Phase 3 study of 3-month duration suggests that daridorexant can fulfil this significant need for patients with insomnia."

Guy Braunstein, MD and Head of Global Clinical Development of Idorsia, commented:
"When designing our program, we had to show the effect of daridorexant on objective sleep measures. It was also very important to us to deliver on what the patient really needs. The program therefore aimed to determine whether daridorexant improved patients' perception of their sleep and their performance during the day. To measure this, we developed and validated a specific patient reported outcome instrument. It was a big commitment, and we were confident that if any drug could show a positive impact it was daridorexant. We knew that this information was missing from the science of sleep."

Primary and secondary efficacy endpoints overview

Daridorexant significantly improved sleep onset as measured by a decrease in latency to persistent sleep (LPS) from baseline compared to placebo. Daridorexant significantly improved sleep maintenance as measured by a decrease in wake time after sleep onset (WASO) from baseline compared to placebo. Total sleep time subjectively (sTST) assessed daily by patients increased significantly from baseline compared to placebo. All of these sleep measures were significantly improved with both 50 mg and 25 mg daridorexant at both 1- and 3-month timepoints. The impact of insomnia on patients' daytime performance was measured daily using the sleepiness domain score from the Insomnia Daytime Symptoms and Impacts Questionnaire (IDSIQ) a Patient Reported Outcome (PRO) instrument, validated according to the US Food and Drug Administration (FDA) Guidance for Industry. Daridorexant improved daytime performance, as measured by patients feeling less physically and mentally tired, less sleepy and more energetic during the day. The results were significant with 50 mg and showed a numerical trend with 25 mg, at both month 1 and month 3. Overall, the primary and secondary endpoints analyses showed consistency across doses, objective and subjective endpoints, through both night and day, and the effect was maintained over time.

About safety in the study

The rate of adverse events was comparable between placebo and daridorexant at both treatment doses. Treatment-emergent adverse events (TEAEs) during the double-blind study period were reported in 37.7% and 37.7% of the patients treated with 25 and 50 mg daridorexant, respectively (34.0% for placebo). The most frequent TEAE reported over 3% incidence and higher than placebo was nasopharyngitis, headache. The number of serious adverse events were higher in the placebo group compared to the daridorexant treatment groups (25 mg, 2 patients; 50 mg, 3 patients; placebo, 7 patients). Based on independent, blinded adjudication, potential narcolepsy-like symptoms denoting excessive daytime sleepiness were balanced across all groups (four patients in total), and those describing complex sleep behavior were observed in three patients in total. There was no next-morning residual effect assessed by a visual analog scale every morning. There was no rebound insomnia, or withdrawal symptoms upon discontinuation, and no suicide, suicidal ideation or self-injury were observed.

Guy Braunstein continued:
"I want to say a big thank you to the study team, both at the investigation sites and at Idorsia and all the study participants, for delivering a comprehensive and robust study, which has given us a wealth of data to judge the strength of daridorexant. The results from this pivotal study are truly remarkable for the consistency of the benefit in sleep measures. Moreover, this is the first study to demonstrate an insomnia product can improve how the patient feels during the day. If you ask anybody who suffers from insomnia that is what they want – to sleep longer and feel better during day. Daridorexant is addressing real patient problems. The results are made even more remarkable when you see that the efficacy is achieved without compromising safety. We now look forward to the results from the second pivotal study of daridorexant 10 and 25 mg."

Martine Clozel, MD and Chief Scientific Officer of Idorsia, commented:
"Our research team has been working on the science of orexin and orexin receptors since their first description in 1998. Our initial work led us to the conclusion that antagonism of the orexin system was the key to providing a natural sleep architecture for patients with insomnia. We did not discover daridorexant by chance – we have worked very hard preclinically and clinically to find the ideal compound to unlock this amazing potential. We wanted a dual antagonist with a rapid effect, and a duration of action sufficient for the night but short enough to avoid any negative residual activity the following morning. The results we share today have made it all worthwhile and prove that we were right to persevere for over 20 years on the project. It just shows what can be achieved with tailored drug design. I am incredibly proud of the discovery team that created daridorexant."

Simon Jose, Chief Commercial Officer of Idorsia, commented:
"The millions of people suffering from insomnia are seeking new treatment options to help them sleep well at night and – very importantly – perform well during the day. This is the first time a sleep medicine has demonstrated not only an improvement in sleep onset and sleep maintenance, but also in daytime performance. We look forward to bringing this medication to patients with difficulty sleeping, after review by regulatory authorities. We are confident that with such a wealth of evidence we can make this unique non-sedating sleep medication a huge success and are excited by the opportunity to lead the transformation and modernization of the sleep market."

Detailed study results will be made available through scientific disclosure at upcoming congresses and in peer reviewed publications.

About the Phase 3 registration program

The Phase 3 registration program comprises two confirmatory studies of 3-month duration, together with a 40-week extension study which has recruited around 1,800 patients with insomnia (900 in each study) from over 160 sites across 18 countries.

The confirmatory multi-center, double-blind, randomized, placebo-controlled, parallel-group, polysomnography studies assess the efficacy and safety of daridorexant on objective and subjective sleep and daytime performance parameters in adult and elderly patients with insomnia. The first study, reported here, evaluated treatment with 25 mg and 50 mg doses over 3 months, while the second study will measure treatment with 10 mg and 25 mg doses over 3 months and is expected to report results in the third quarter of 2020. The 40-week extension study will measure the effect of all three doses, generating data for long-term treatment of insomnia.

Notes to the editor

About insomnia

Insomnia is defined as a combination of dissatisfaction with sleep and a significant negative impact on daytime performance. Dissatisfaction with sleep refers to the difficulty to initiate and/or maintain sleep on at least three nights per week for at least three months, despite adequate opportunity to sleep.

Insomnia is, worldwide, the most commonly reported sleep disorder and its impact is often underestimated. In reality, it can be a distressing condition that can impair quality of life. Sleepless nights can leave people feeling irritable and out of sorts – this may affect many aspects of daily life, from studying and employment to social activities and relationships. People who suffer from insomnia may lack the energy or motivation to exercise or to take part in social activities. It can also have a significant economic impact as it increases the risk of accident and injury on the road or in the workplace, and is a leading cause of absenteeism and reduced productivity at work. People with insomnia are more likely to experience feeling down or depressed, lack concentration, and suffer from poor energy levels during the day compared with people who sleep well. In addition, worrying about sleep can cause stress and may lead to negative thought patterns which may in turn make it more difficult to sleep, setting up a vicious circle. Chronic insomnia is associated with cardiovascular and cerebrovascular diseases, and increased mortality.

The goal of treatments for insomnia is to improve sleep quality and quantity, as well as reducing insomnia-related impaired daytime performance, while avoiding adverse events and next morning residual effect. Current treatment of insomnia includes cognitive behavioral therapy, sleep hygiene recommendations, and pharmacotherapy. The most widely prescribed products on the market that are indicated for insomnia enhance the effects of gamma-aminobutyric acid (GABA), the major inhibitory neurotransmitter in the central nervous system. Such medications are only approved for short-term use and are associated with side effects such as next-day effects, anterograde amnesia, and risk of tolerance and dependence.

Data supporting daridorexant in insomnia

The safety and efficacy of daridorexant in adult and elderly patients with insomnia was evaluated in a comprehensive Phase 2 program, comprising two studies, one of which included zolpidem 10 mg as an active reference. Both studies showed the desired effect on sleep maintenance and onset, with a significant dose-response relationship; treatment was generally well tolerated.

The first Phase 2 study in 360 adults (ranging from 18 to 64 years), with a treatment duration of 4 weeks, showed a significant dose dependent decrease in WASO at Day 1 & 2 (average decrease of wake-time after sleep onset from baseline on the first 2 nights of treatment, measured by polysomnography). In addition, daridorexant significantly decreased LPS (latency to persistent sleep) in a dose-dependent manner. Treatment with daridorexant was generally well tolerated. There were no reports of serious adverse events related to daridorexant.

The positive findings of the second Phase 2 study, conducted in 58 elderly patients (≥ 65 years), were consistent with the efficacy and safety profile of daridorexant observed in the adult population. The results of this study also showed a significant decrease in WASO and LPS at Day 1 & 2 in a dose-dependent manner. Treatment with daridorexant was generally well tolerated. There were no reports of serious adverse events related to daridorexant.

Data from an extensive Phase 1 program showed an optimal pharmacokinetic and pharmacodynamic profile for a sleep medication, together with excellent safety and tolerability.

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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Investor webcast

An investor conference call and webcast will be held to discuss the Phase 3 results with senior management.

Date: Monday April 20, 2020
Time: 14:00 CEST | 13:00 BST | 08:00 EDT

Webcast participants should visit Idorsia's website www.idorsia.com 10-15 minutes before the webcast is due to start.
Conference call participants should start calling the number below 10-15 minutes before the conference is due to start.

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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 one of Europe's leading biopharmaceutical companies, with a strong scientific core.

Headquartered in Switzerland - a biotech-hub of Europe - Idorsia is specialized in the discovery and development of small molecules, to transform the horizon of therapeutic options. Idorsia has a broad portfolio of innovative drugs in the pipeline, an experienced team, a fully-functional research center, and a strong balance sheet – the ideal constellation to bringing R&D efforts to business success.

Idorsia was listed on the SIX Swiss Exchange (ticker symbol: IDIA) in June 2017 and has over 800 highly qualified specialists dedicated to realizing our ambitious targets.

For further information, please contact

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