



Media Release

June 11, 2018

Idorsia initiates a Phase 3 registration program with nemorexant (ACT-541468) for the treatment of insomnia

- [Idorsia to host an investor webcast to discuss the Phase 3 program today at 14:00hrs CEST](#)

Allschwil, Switzerland – June 11, 2018

Idorsia Ltd (SIX: IDIA) today announced that the first patients have been enrolled into the Phase 3 registration program with nemorexant (proposed INN for ACT-541468), a dual orexin receptor antagonist, for the treatment of adult and elderly patients with insomnia. The Phase 3 program aims to confirm the positive results observed in the comprehensive Phase 2 clinical program in both adult and elderly patients with insomnia and is based on interaction with Health Authorities.

The registration program comprises two confirmatory studies together with a long-term extension study, which will recruit a total of 1,800 patients with insomnia from over 160 sites across 18 countries and is anticipated to run for around 2 years. As insomnia often presents later in life, around 40% of the recruited population will be aged 65 years and older. The program will investigate three doses (10 mg, 25 mg, and 50 mg), which were all effective and well tolerated in both adult and elderly patients studied in Phase 2. Patients will be treated for three months in the two trials, with the opportunity to continue treatment in a 40-week extension study.

Insomnia is defined as a combination of dissatisfaction with sleep and a significant negative impact on daytime functioning. 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.

Dr. Thomas Roth, PhD, Director of the Sleep Disorder and Research Center at Henry Ford Hospital, commented:

“Good quality sleep is vital to our physical and mental health. Poor quality sleep can affect many aspects of daily life, including the ability to concentrate, work effectively, and can impact social activities. Insomnia is a distinct disorder and not merely a symptom of other disorders. It is important to take it seriously and to help patients to fall asleep and stay asleep for the right amount of time thereby positively impacting their quality of life. There are treatments available to help insomnia but they may be associated with side effects, have limited efficacy, or are not suitable for long-term use.”

Martine Clozel, MD and Chief Scientific Officer, commented:

“Dual orexin receptor antagonism specifically targets excessive alertness, in contrast to treatments of insomnia that act via broad sedation of the CNS. As a result, nemorexant offers the potential to induce a normal sleep architecture with a maintained efficacy in chronic insomnia patients. The pharmacokinetic/pharmacodynamic profile of nemorexant, observed in patients with insomnia, is a direct result of our targeted approach, based on early use of modeling, to identify a compound with the optimal profile for a sleep medication.”

Idorsia has worked closely with patients to design the registration program through the development of a tailored Patient Reported Outcome instrument. This validated tool will be used to measure the

impact of nemorexant on daytime performance. Idorsia will continue its patient focus through the conduct of a patient preference study. The aim of the study is to collect information on what patients consider important with regards to safety and efficacy of a sleep therapy.

Guy Braunstein, MD and Head of Global Clinical Development, added:

“As shown in the Phase 2 study, nemorexant has the potential to offer the combination of fast onset of sleep, maintained efficacy throughout the night, without next-day residual effects. Our confirmatory Phase 3 registration program goes one step further: we will follow patients throughout the night and during the day, which will help us to characterize the impact of the condition on the daytime performance and how it is affected by the treatment. With the patient preference study, we will further the understanding of what is important to patients, in essence we will have a preferred benefit-risk profile from the patient's perspective.”

About the Phase 3 registration program

The Phase 3 registration program comprises two confirmatory studies together with a 40-week extension study which will recruit a total of 1,800 patients with insomnia from over 160 sites across 18 countries and is anticipated to run for around 2 years.

The confirmatory multi-center, double-blind, randomized, placebo-controlled, parallel-group, polysomnography studies will assess the efficacy and safety of nemorexant on objective and subjective sleep and daytime functioning parameters in adult and elderly patients with insomnia disorder. The first study will evaluate 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. The 40-week extension study will measure 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 functioning. 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 sleeping disorder. By 2020, it is estimated that there will be approximately 13 million insomnia patients being treated with pharmaceutical-grade insomnia medications in the US alone, according to research by GlobalData Ltd in 2015.

The impacts of insomnia on physical and mental health may include fatigue, daytime sleepiness, poor concentration, depressed mood, or impaired ability to perform social or occupational tasks.

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

Data supporting nemorexant (ACT-541468) in insomnia

The safety and efficacy of nemorexant in adult and elderly patients with insomnia was evaluated in a comprehensive Phase 2 program, comprising two studies and included zolpidem 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, nemorexant significantly decreased LPS (latency to persistent sleep) in a dose-dependent manner. Treatment with nemorexant was generally well tolerated. There were no reports of serious adverse events related to nemorexant.

The positive readouts of the second Phase 2 study, conducted in 58 elderly patients (ranging from 65 to 85 years), were consistent with the efficacy and safety profile of nemorexant for this patient population. The results of this study also showed a significant decrease in WASO and LPS at Day 1 & 2 in a dose-dependent manner.

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 Orexins

Orexins are neuropeptide modulators - small protein-like molecules used by nerve cells (or neurons) to communicate with each other in the brain. Orexins act functionally at the interface of alertness, energy homeostasis and reward: aversion systems, essentially to regulate vigilance and alertness states. Defects of the orexin peptides, or their receptors, are associated with wakefulness and sleep disorders.

The anatomical distribution of orexin receptors in the brain supports the essential role that orexin plays in promoting alertness and maintaining wakefulness under situations of high motivational relevance, e.g. circadian vigilance states, reward opportunities or exposure to threats. Orexins and their receptors are highly conserved across vertebrate species.

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 Nathaniel 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.

References

- Brisbare-Roch C. et al. Nat Med. 13(2):150-5; 2007.
- Roth T. 2007;3 Suppl 5:S7-10.
- Treiber A. et al. J. Pharmacol. Exp. Ther July 7, 2017.
- Muehlan C, et. al. Clin Pharmacol Ther. 2018 Feb 15.

Investor webcast

An investor conference call and webcast will be held to discuss the Phase 3 program. The call will start with presentations by senior management, followed by a Q&A session (live access to the speakers).

Date: **Monday June 11, 2018**
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 company, 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 650 highly qualified specialists dedicated to realizing our ambitious targets.

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