Media Release
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Idorsia Japan confirms daridorexant dose response in Japanese patients with insomnia – preparation for a local registration program advancing

Allschwil, Switzerland, and Tokyo, Japan – August 6, 2020
Idorsia Ltd (SIX: IDIA), Idorsia Pharmaceuticals Japan today announced the positive conclusion of a dose-confirmation study for daridorexant, Idorsia's dual orexin receptor antagonist, in Japanese patients with insomnia. On the basis of the positive results, preparation of registration studies in Japan is now on-going.

The Phase 2 study was a multicenter, double-blind, randomized, placebo-controlled, 4-period, 4-treatment crossover polysomnography dose response study to investigate the efficacy and safety of daridorexant on the first 2 days of each treatment period in Japanese patients with insomnia. In addition, the 4th double-blind treatment period was followed by a treatment duration of 12 days to investigate subjective efficacy variables and safety data.

Treatment with daridorexant in 47 adult patients (ranging from 16 to 64 years) showed a significant dose-dependent decrease in WASO at Day 1 & 2 (average decrease of wake time after sleep onset from baseline on the 2 nights of treatment, measured by polysomnography). In addition, daridorexant significantly decreased LPS (latency to persistent sleep) in a dose-dependent manner. Furthermore, daridorexant showed significant improvements on subjective sleep parameters such as sWASO (subjective wake after sleep onset), sLSO (subjective latency to sleep onset) and sTST (subjective total sleep time). Treatment with daridorexant was generally well tolerated. Most of the adverse events were mild. There were no reports of serious adverse events and withdrawals related to daridorexant.

Jean-Paul Clozel, MD and Chief Executive Officer of Idorsia, commented:
"Our Japanese team, under the leadership of Dr Satoshi Tanaka, has done an outstanding job to advance the development of daridorexant for Japanese patients so rapidly. The results we see in this Phase 2 dose-confirmation study, extend the excellent profile of daridorexant seen in two large pivotal global studies to a Japanese population. This will enable initiation of the registration study in Japan so that Japanese patients can benefit from daridorexant as soon as possible."

Dr Satoshi Tanaka, President of Idorsia Pharmaceuticals Japan, commented:
"It is very satisfying to see the results of the first randomized trial run by the Idorsia team in Japan. The team has delivered robust, high-quality data which clearly support the development of daridorexant for Japanese patients with insomnia. We are now working very hard with our partner Mochida to prepare for the Phase 3 registration studies in Japan."

In April and July 2020, Idorsia reported positive results in each of the two pivotal Phase 3 studies of **daridorexant** in patients with insomnia. The program demonstrated efficacy of treatment with daridorexant on objective and subjective sleep parameters, and daytime functioning, with patients reporting no morning sleepiness, and no evidence of rebound or withdrawal symptoms upon

treatment discontinuation. More details and commentary can be found in the dedicated press releases (first study), (second study) and the investor webcasts (first study), (second study) which are available for replay on the corporate website.
In December 2019, Idorsia and Mochida Pharmaceutical Co., Ltd. entered into an exclusive license agreement for the supply, co-development and co-marketing of daridorexant for insomnia and related disorders in Japan.

Notes to the editor

About insomnia

Insomnia is a condition of overactive wake signaling that can have a profound effect on the lives of patients. Insomnia can be defined as difficulty falling asleep and / or staying asleep, occuring at least three times a week for a minimum of three months.

It is estimated that as many as one in ten people suffer from insomnia 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 functioning, 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-morning residual effects, anterograde amnesia, and risk of tolerance and dependence.

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 and consolidate wakefulness. There are two forms of orexin neuropeptides – Orexin A and Orexin B. Orexin promotes wakefulness through its receptors OX_1R and OX_2R. In combination, these neuropeptides and receptors comprise the orexin system. The orexin system stimulates target neurons in the wake system – leading to the release of several chemicals (Dopamine, Serotonin, Histamine, Acetylcholine, Norepinephrine) which promote wakefulness. Under normal circumstances, orexin levels rise throughout the day as wakefulness is promoted and then consolidated and fall at night. Overactivity of the orexin system is thought to be an important driver of insomnia.

Idorsia's research team has been working on the science of orexin and orexin receptors since they were first described in 1998. The teams 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 started to design 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 at optimally effective doses.

About dual orexin receptor antagonism

Dual orexin receptor antagonists – or DORAs – are an entirely different approach to treating insomnia than previous drug classes, turning down overactive wakefulness by blocking the activity of orexin. DORAs specifically target the orexin system by competitively binding with both receptors and thereby reversibly blocking the activity of orexin. It is hypothesized that blocking orexin receptors reduces the downstream activity of the other wake promoting neurotransmitters that are overactive in insomnia, leading to the clinical efficacy demonstrated by orexin receptor antagonists.

References

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About Mochida

Mochida Pharmaceutical Co., Ltd. has been committed to research and development of innovative pharmaceutical products since its establishment thereby providing distinctive medicines to the medical field. Currently, the core pharmaceutical business focuses resources on the targeted areas of cardiovascular medicine, obstetrics and gynecology, dermatology, psychiatry and gastroenterology, while also providing medicine for intractable disease as well as generics including biosimilars, to meet medical needs. For more information on Mochida Pharmaceutical Co., Ltd., please see http://www.mochida.co.jp/

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.

Idorsia Pharmaceuticals Japan was established, under the leadership of Dr Satoshi Tanaka, in 2018 to conduct clinical development and prepare the commercialization of Idorsia's innovative and promising compounds for patients in Japan.

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