



## Media Release

### June 13, 2019

## Efficacy and safety data with Idorsia's dual orexin receptor antagonist presented at SLEEP 2019 in San Antonio

### **Allschwil, Switzerland – June 13, 2019**

Idorsia Ltd (SIX: IDIA) today announced that efficacy and safety data from two Phase 2 studies of ACT-541468, Idorsia's dual orexin receptor antagonist, for the treatment of adult and elderly patients with insomnia, have been presented at SLEEP 2019 in San Antonio (Texas, USA).

A poster presentation entitled "*ACT-541468, a New Dual Orexin Receptor Antagonist, to Treat Insomnia Disorder: A Randomized, Double-Blind, Placebo-Controlled, Active-Comparator Phase 2 Study*", highlighted the positive results of a Phase 2 study in 360 adult patients with insomnia disorder.

An oral presentation entitled "*ACT-541468, a Dual Orexin Receptor Antagonist, for the Treatment of Insomnia Disorder in the Elderly*" in the "*Novel Treatment Targets and Approaches for Insomnia Disorder*" session by Gary Zammit, PhD & Associate Professor at the Icahn School of Medicine at Mount Sinai, highlighted the positive results of a Phase 2 study in 58 elderly patients with insomnia disorder.

### **Conclusions of the Phase 2 results presented**

- Treatment with ACT-541468 dose-dependently improved sleep onset and sleep maintenance in adult and elderly patients with insomnia disorder, with significant reductions in LPS (latency to persistent sleep) and WASO (wake after sleep onset), at the time points measured
- Treatment with ACT-541468 in adults and elderly was generally well tolerated across all doses, with no narcolepsy-like symptoms, no evidence of suicidal ideation, no complex sleep behaviors, and no dose-limiting safety events
- There was no residual next-morning effect at any dose (as measured by e.g. the Karolinska sleepiness scale)
- Self-reported next-day functioning (daytime alertness, morning sleepiness, daytime ability to function) assessed by a visual analog scale was improved across all dose groups in elderly patients

### **Gary Zammit, PhD and Associate Professor, Icahn School of Medicine at Mount Sinai, commented on the results in elderly patients:**

"Developing a new therapy is particularly important for the elderly as they have higher rates of insomnia and a greater risk for adverse events. The results presented show promotion of sleep onset and sleep maintenance in elderly patients with insomnia disorder. The ongoing Phase 3 program with ACT-541468 will include both adults and elderly patients. If the positive results observed in the Phase 2 clinical program are confirmed, ACT-541468 has the potential to bring significant benefits to these patients."

### **Guy Braunstein, MD and Head of Global Clinical Development, commented:**

"ACT-541468 is a potent and selective dual orexin receptor antagonist selected for development because of its favorable PK and PD profile. We were very pleased to observe the efficacy profile in these studies, covering the full night, with no indication of residual effect in the morning, across the dose range tested. This is assumed to be related to the elimination half-life in both adult and elderly volunteers, with minimal residual plasma level in the morning, as shown in Phase 1 clinical trials. Now we're looking forward to seeing the results of the Phase 3 program in the first half of 2020."

In addition to the Phase 2 data, two poster presentations highlighted the results of the Phase 1 studies with ACT-541468 in Japanese and Caucasian volunteers "*Clinical Pharmacology of the Dual Orexin Receptor Antagonist ACT-541468 in Japanese and Caucasian Subjects*", and in elderly volunteers "*Clinical Pharmacology of the Dual Orexin Receptor Antagonist ACT-541468 in Elderly Subjects*".

Manuscripts are currently in preparation and will be published in scientific journals.

#### **About the Phase 2 study in adults**

The multi-center, double-blind, randomized, placebo-controlled, active-reference, parallel-group, polysomnography dose-response Phase 2 study to assess the efficacy and safety of ACT-541468 (5, 10, 25, 50 mg) in 360 adult patients (64% female; ranging from 18 to 64 years) with insomnia disorder showed a significant ( $p \leq 0.0007$ ) dose-dependent decrease in WASO at Days 1 & 2 (average decrease of wake time after sleep onset from baseline on the first 2 nights of treatment, measured by polysomnography). Observed mean reductions from baseline to Days 1 & 2 for WASO were -28.99, -33.75, -39.64, and -45.49 min for ascending ACT-541468 doses (placebo, -20.98 min; zolpidem, -31.23 min), and were sustained at Days 28 & 29 (-37.76, -43.74, -39.84, -46.97 min for ascending ACT-541468 doses; placebo, -33.80 min; zolpidem, -37.08 min).

ACT-541468 also significantly ( $p < 0.05$ ) decreased LPS (latency to persistent sleep) at doses 10 mg and higher in a dose-dependent manner. Observed changes in mean LPS from baseline to Days 1 & 2 were -26.88, -29.31, -36.14, and -36.41 min for ascending ACT-541468 doses (placebo, -22.02 min; zolpidem, -45.12 min). Reductions in LPS were sustained at Days 28 & 29.

ACT-541468 treatment was well tolerated at all doses, with no evidence of dose-dependent adverse effects. Treatment-emergent adverse events (TEAEs) were reported in 35%, 38%, 38%, and 34% of the patients treated with 5, 10, 25, and 50 mg ACT-541468, respectively (30% for placebo; 40% for zolpidem). The main TEAEs across all groups were headache, somnolence, and nasopharyngitis. No signs of next-morning residual effects or rebound insomnia were observed, and there were no reports of serious adverse events related to ACT-541468.

#### **About the Phase 2 study in elderly**

In this multi-center, double-blind, randomized, placebo-controlled, 5-period, 5-treatment crossover, polysomnography dose-response Phase 2 study to assess the efficacy and safety of ACT-541468 (5, 10, 25, 50 mg) in elderly patients with insomnia disorder, 58 patients (67% female; ranging from 65-85 years) were randomized.

A dose-response relationship was demonstrated for WASO ( $p \leq 0.0001$ ) and LPS ( $p \leq 0.025$ ). Observed mean reductions from baseline to Days 1 & 2 for ascending doses for WASO were; (placebo, -14.13), -18.43, -32.37, -44.20, and -61.11 min, and for LPS were; (placebo, -33.88), -37.92, -44.61, -44.81, and -44.88 min.

Self-reported next-day functioning was improved across all groups. The most frequent treatment-emergent adverse events were fatigue, nasopharyngitis, gait disturbance, and headache (all  $\leq 7\%$ ), with no apparent relationship to dose (except fatigue [50 mg], 7%).

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## Notes to the editor

### About the Phase 3 program

In June 2018, Idorsia initiated a Phase 3 registration program with ACT-541468 for the treatment of adult and elderly patients with insomnia. 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 disorder at over 160 sites across 18 countries. As insomnia often presents later in life, around 40% of the recruited population will be aged 65 years or older. The confirmatory studies will investigate three doses (10 mg, 25 mg, and 50 mg), on objective and subjective sleep and daytime functioning parameters. Patients will be treated for three months in the two trials, with the opportunity to continue treatment in a 40-week extension study.

The Phase 3 program aims to confirm the positive results observed in the Phase 2 clinical program. The program is on track to report results in the first half of 2020. In addition, a comprehensive clinical pharmacology program is to be conducted in parallel.

### About Gary Zammit

Gary Zammit, PhD, is the President & CEO of Clinilabs, a full-service CRO that provides clinical drug development to industry, focusing on CNS therapeutics. He also is an Associate Clinical Professor of Psychiatry, Icahn School of Medicine at Mount Sinai (New York, NY). Dr. Zammit earned a Ph.D. degree in clinical psychology from the University of Toledo (Toledo, OH), where he won both the Turin Service Award and the Leckie Scholar Award. He completed an internship and clinical research fellowship in the Department of Psychiatry at the New York Hospital - Cornell University Medical College (White Plains, NY), where he won the Alumni Award for Excellence. Dr. Zammit has authored two books and over 160 articles and abstracts that have appeared in medical journals.

### References

- SLEEP, Volume 42, Abstract Supplement, 2019

### 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 750 highly qualified specialists dedicated to realizing our ambitious targets.

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