Better Health, Brighter Future

Statement

Statement on Inadvertent Abstract Disclosure for Opevorexton (TAK-861) by World Sleep Congress

Osaka, JAPAN and CAMBRIDGE, Massachusetts, July 31, 2025 – An embargoed version of an abstract for our Phase 3 TAK-861-3002 study (RadiantLight) of oveporexton (TAK-861) in narcolepsy type 1, which is slated to be presented at the upcoming World Sleep 2025 congress in September, was inadvertently published by the World Sleep Congress on their website. Once we became aware, we reached out to World Sleep and they have since removed the abstract.

This abstract is only one of several abstracts from our Phase 3 studies that will be presented at the conference. We look forward to sharing the positive results from both of our Phase 3 studies at World Sleep, which, as previously disclosed, met all of the primary and secondary endpoints across all doses at week 12. These results reinforce the potential of oveporexton to transform the standard of care for people with narcolepsy type 1.

In the spirit of transparency, we are also providing the abstract that was inadvertently published as an attachment.

Takeda does not anticipate any significant impact on its consolidated financial results as a result of this matter.

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(Attachment)

Title

Efficacy and Safety of Oveporexton (TAK-861) for the Treatment of Narcolepsy Type 1: Results from a Phase 3 Randomized Study in Asia, Australia and Europe.

Authors

Yves Dauvilliers[1,2,3], Jakub Antczak[4], Erik Buntinx[5], Rafael del Rio Villegas[6,7], Seung-Chul Hong[8], Sheila Sivam[9], Shuqin Zhan[10], Elena Koundourakis[11], Rachel Neuwirth[11], Tina Olsson[11], Sarah Sheikh[11], Philipp von Rosenstiel[11], Baiyun Yao[11], Alice Cai[11]*, Giuseppe Plazzi[12,13]*

Affiliations

[1]Sleep-Wake Disorders Center, Department of Neurology, Gui-de-Chauliac Hospital, CHU, Montpellier, France; ydauvilliers@yahoo.fr

[2]Institute of Neurosciences of Montpellier, INSERM, University of Montpellier, France

[3]National Reference Network for Narcolepsy, Montpellier, France

[4]Jagiellonian University, Kraków, Poland; jakub.antczak@uj.edu.pl

[5]ANIMA Research, Alken, Belgium; erik.buntinx@anima-alken.be

[6]Neurophysiology and Sleep Disorders Unit, Vithas Hospitals, Madrid, Spain; rafaeldelrio@movistar.es

[7]Universidad CEU San Pablo, CEU Universities, Madrid, Spain

[8]Department of Psychiatry, St. Vincent's Hospital, College of Medicine, The Catholic University of Korea, Suwon, Korea; hscjohn@hotmail.com

[9]Woolcock Institute of Medical Research and Royal Prince Alfred Hospital, Sydney, NSW, Australia; sheila.sivam@sydney.edu.au

[10]Department of Neurology, Xuanwu Hospital, Capital Medical University, Beijing, China; shqzhan@hotmail.com

[11]Takeda Development Center Americas, Inc., Cambridge, MA, USA; Elena.Koundourakis@Takeda.com; Rachel.Neuwirth@Takeda.com; tina.olsson@takeda.com; sarah.sheikh@takeda.com; baiyun.yao@takeda.com; alice.cai@takeda.com

[12]Department of Biomedical, Metabolic and Neural Sciences, University of Modena and

Reggio-Emilia, Modena, Italy; giuseppe.plazzi@unibo.it
[13]IRCCS, Istituto delle Scienze Neurologiche, Bologna, Italy

*Shared last author
Presenter: Yves Dauvilliers

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Introduction

Narcolepsy type 1 (NT1) is a chronic, rare, neurologic disorder of hypersomnolence caused by loss of orexin-producing neurons in the hypothalamus, which regulate wakefulness, sleep, and attention through activation of orexin receptors. NT1 results in a range of symptoms including excessive daytime sleepiness, sudden muscle weakness (cataplexy), disrupted nighttime sleep, sleep paralysis, hypnagogic/hypnopompic hallucinations, and cognitive symptoms. Orexin receptor agonists are promising treatments for NT1 as currently available therapies do not target orexin deficiency. Oveporexton (TAK-861) is an investigational oral orexin receptor 2 (OX2R)-selective agonist that stimulates OX2R to restore signaling and address the underlying orexin deficiency. In a previous phase 2b study, oveporexton delivered improvements across the spectrum of NT1 symptoms, assessed by both objective and patient-reported measures, and was generally well tolerated. Here, we report first results from a phase 3 study that evaluated the efficacy, safety and impact on functioning, quality of life and cognition of oveporexton in participants with NT1.

Materials and methods

In this double-blind, placebo-controlled, phase 3 study (TAK-861-3002) participants were randomized 2:1 to oral oveporexton 2 mg or placebo twice daily at least 3 hours apart for 12 weeks. At the end of treatment, participants either entered the long-term extension or completed 4 weeks of follow up. Key inclusion criteria included: age 16–70 years; International Classification of Sleep Disorders, Third Edition (ICSD-3) or ICSD-3-text revision diagnosis of NT1 supported by polysomnography, multiple sleep latency testing (MSLT) or orexin cerebrospinal fluid (CSF) concentrations ≤110 pg/mL; Epworth Sleepiness Scale (ESS) score ≥11; and ≥4 partial/complete episodes of cataplexy/week. The primary endpoint was change from baseline in mean sleep latency on the Maintenance of Wakefulness Test (MWT) at week 12. Secondary endpoints included change from baseline in ESS total score at week 12, weekly cataplexy rate (WCR) at week 12, and occurrence of treatment-emergent adverse events (TEAE).

Results

Overall, 105 participants (50 [47.6%] female) were enrolled across Asia, Australia, and Europe; 70 were randomized to oveporexton 2 mg/2 mg and 35 to placebo. At baseline, mean age was 30.7 years, mean ESS score was 17.5, mean MWT sleep latency was 4.5 minutes and median WCR was 23.5 attacks/week. At week 12, significant least square (LS) mean (95% CI) changes from baseline were achieved with oveporexton 2mg/2mg vs placebo in MWT sleep latency (20.09 [16.57, 23.61] minutes, P<0.001 vs placebo). Significant changes vs placebo were also achieved at week 12 for ESS total score (LS mean [95% CI] change from baseline: -9.53 [-11.10, -7.97], P<0.001) and WCR (Incidence rate ratio [95% CI] vs placebo: 0.25 [0.15, 0.42], P<0.001). Sixty (85.7%) oveporexton-treated participants experienced ≥1 TEAEs vs 15 (42.9%) placebo-treated participants; there were no serious TEAEs. The most common TEAEs with oveporexton were pollakiura (43 [61.4%]) and insomnia (40 [57.1%]). 101 (96.2%) completed study treatment, of which 100 (99.0%) enrolled into the long-term extension.

Conclusions

In this phase 3 study, oveporexton treatment resulted in significant improvements on measures of sleepiness and cataplexy frequency with oveporexton versus placebo, and was generally well tolerated.

Acknowledgments

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