Better Health, Brighter Future

News Release

Takeda Intends to Rapidly Initiate the First Global Phase 3 Trials of TAK-861, an Oral Orexin Agonist, in Narcolepsy Type 1 in First Half of Fiscal Year 2024

- ***Primary and Key Secondary Endpoints Were Met in Narcolepsy Type 1 Phase 2b Trial***
- ***TAK-861 Was Found to be Generally Safe and Well-Tolerated***
- ***Results Will be Presented at an Upcoming Scientific Congress***

OSAKA, Japan, and CAMBRIDGE, Massachusetts, February 8, 2024 – Takeda ***(*****TSE:4502/NYSE:TAK)** today announced positive topline results from a randomized, double-blind, placebo-controlled, multiple dose Phase 2b trial evaluating TAK-861, an oral orexin receptor 2 (OX2R) agonist, in patients with narcolepsy type 1.

Narcolepsy is a chronic, rare neurological disorder of central hypersomnolence with significant unmet need despite multiple approved therapies. It is currently classified into two different types: narcolepsy type 1 (NT1) caused by significant loss of orexin neurons with resulting lack of orexin, and narcolepsy type 2 (NT2) where orexin levels are generally normal. Stimulating the orexin receptor 2 in NT1 patients targets the underlying pathophysiology of the disease to restore orexin signaling. Two separate Phase 2b studies were conducted in NT1 (NCT05687903) and NT2 (NCT05687916).

The NT1 trial TAK-861-2001 evaluating TAK-861 in 112 patients demonstrated statistically significant and clinically meaningful improvement in objective and subjective measures of wakefulness compared to placebo at week 8 including on the primary endpoint Maintenance of Wakefulness Test (MWT) ($p < 0.001$). Improvements in key secondary endpoints including Epworth Sleepiness Scale (ESS) and Weekly Cataplexy Rate (WCR) were statistically significant and clinically meaningful, consistent with the primary endpoint. The majority of patients who completed the trial entered a long-term extension study. Based on these results, and in consultation with global health authorities, Takeda plans to initiate global Phase 3 trials of TAK-861 in NT1 rapidly in the first half of its fiscal year 2024.

At this time, Takeda does not plan to advance TAK-861 in NT2. Data are being further analyzed to determine next steps in orexin normal populations. Takeda is progressing multiple orexin agonists in patient populations with normal levels of orexin neuropeptides such as NT2 and other indications where orexin biology is implicated.

TAK-861 was generally safe and well tolerated in both trials. No treatment related serious adverse events were reported. In addition, no cases of hepatotoxicity or visual disturbances were reported in the Phase 2b trials or in the ongoing TAK-861 long-term extension trial.

“We are thrilled to announce these clear and compelling results from the TAK-861 trial in narcolepsy type 1 that allows us to rapidly initiate Phase 3 trials this year as we work to deliver a medicine to patients that could address the underlying pathophysiology of the disease,” said Sarah Sheikh M.Sc., B.M., B.Ch, MRCP, Head, Neuroscience Therapeutic Area Unit and Head, Global Development at Takeda. “Takeda thanks the patients, caregivers and investigators who participated in our orexin agonist trials. We will continue to apply our deep and growing understanding of orexin biology

as we work to develop and deliver transformative treatments to people across a range of indications who could benefit from this mechanism."

Results from both trials will be presented at an upcoming scientific congress.

Results from the Phase 2b trials have no impact on the full year consolidated reported forecast for the fiscal year ending March 31, 2024 (Fiscal Year 2023).

About Takeda
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