Better Health, Brighter Future

U.S. FDA Approves Takeda's ORZEYFUL™ (oveporexton), the First and Only Medicine to Treat the Underlying Cause of Narcolepsy Type 1

- Adults Taking ORZEYFUL Experienced Significant and Meaningful Improvements Across the Full Range of Symptoms of Narcolepsy Type 1 (NT1) in Clinical Trials Compared to Those on Placebo
- As a First-in-Class Orexin Treatment, ORZEYFUL has the Potential to Redefine NT1 Care Beyond Individual Symptoms
- Takeda is Advancing U.S. Launch Preparations and Expects to Make ORZEYFUL Available Following Completion of the Drug Enforcement Administration (DEA) Scheduling Process

OSAKA, Japan and CAMBRIDGE, Massachusetts, August 5, 2026 – Takeda (TSE:4502/NYSE:TAK) announced that the U.S. Food and Drug Administration (FDA) approved ORZEYFUL™ (oveporexton), an oral orexin receptor 2 (OX2R) agonist, for the treatment of narcolepsy type 1 (NT1, narcolepsy with cataplexy) in adults.* The persistent 24-hour nature of NT1 is driven by orexin deficiency and can severely impact people's lives. As a first-in-class orexin treatment, ORZEYFUL is the only medicine indicated in the U.S. to treat the disease holistically rather than individual symptoms.

"The FDA approval of ORZEYFUL marks a new chapter for the narcolepsy type 1 community, as we introduce an entirely new class of medicine that will potentially redefine how this disease is managed and how people feel on treatment," said Julie Kim, president and chief executive officer of Takeda. "We are proud to have discovered and developed this orexin treatment innovation and will bring it to adults living with NT1 as quickly as possible."

NT1 is a rare, chronic neurological disease driven by a loss of orexin and affects an estimated 120,000 people in the U.S. People with NT1 experience excessive daytime sleepiness, cataplexy (sudden loss of muscle tone), cognitive symptoms and disrupted nighttime sleep that can severely impact multiple aspects of daily life, including work, education and social interactions.

"For those of us living with narcolepsy type 1, symptoms reshape everyday life and extend far beyond what most people understand about the condition," said Julie Flygare, President and CEO at Project Sleep and a person with NT1. "ORZEYFUL's approval is a historic moment that expands our treatment choices and gives me great hope for the future and for our community."

"Until now, people have managed narcolepsy type 1 with treatments that target symptom relief," said Dr. Emmanuel Mignot, M.D., Ph.D., principal U.S. investigator in the ORZEYFUL Phase 3 program. "As the first and only approved orexin therapy to treat the broad spectrum of the disease,

ORZEYFUL can enable a different kind of conversation in the doctor's office about treatment options."

The approval is based on a comprehensive clinical program including the global Phase 3 FirstLight (TAK-861-3001) and RadiantLight (TAK-861-3002) studies that showed oveporexton offers statistically significant improvements across the full range of symptoms of the disease. These included improvements in excessive daytime sleepiness, cataplexy and health-related quality of life. Oveporexton was generally well-tolerated with a safety profile consistent across clinical studies to date. The most common side effects include trouble sleeping (insomnia), urinary urgency, urinary frequency and excessive saliva. Learn more about the Phase 3 data results here.

"With this approval, we are turning scientific discovery into reality for adults living with narcolepsy type 1," said Andy Plump, M.D., Ph.D., President, Research & Development, Takeda. "ORZEYFUL is just the beginning. With orexin emerging as a powerful therapeutic pathway, Takeda is unlocking the potential of this new class of medicine for patients across a range of disorders."

Next Steps for ORZEYFUL Availability

The controlled substance classification for ORZEYFUL is currently under review by the Drug Enforcement Administration (DEA) and is expected within 90 days. After the controlled substance classification is determined, ORZEYFUL will be made available through a specialty pharmacy to U.S. healthcare providers and adults living with NT1. To sign up for updates visit ORZEYFUL.com.

The FDA approval is not expected to have a significant impact on the full year consolidated financial forecast for the fiscal year ending March 31, 2027.

*For information regarding the submission of the new drug application for oveporexton to the U.S. FDA, please refer to Takeda's press release dated February 10, 2026, "U.S. Food and Drug Administration Accepts New Drug Application and Grants Priority Review for Takeda's Oveporexton (TAK-861) as a Potential First-in-Class Therapy for Narcolepsy Type 1".

About ORZEYFUL (oveporexton)

ORZEYFUL (oveporexton) is an oral orexin receptor 2 (OX2R) agonist, which selectively stimulates the OX2R to restore signaling and address the underlying orexin deficiency associated with narcolepsy type 1 (NT1). By activating OX2Rs, ORZEYFUL promotes wakefulness and reduces abnormal rapid eye movement (REM)-sleep like phenomena, including cataplexy (sudden and temporary loss of muscle tone), to address a range of daytime and nighttime symptoms as evaluated in clinical studies and consistent with the approved label.

INDICATION

ORZEYFUL is indicated for the treatment of narcolepsy type 1 (narcolepsy with cataplexy) in adult patients.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

ORZEYFUL is contraindicated in patients taking strong CYP3A inhibitors.

WARNINGS AND PRECAUTIONS

Insomnia: In pooled phase 3 studies in patients with NT1, 60%, 55%, and 1% of patients in the ORZEYFUL 2 mg twice daily, ORZEYFUL 1 mg twice daily, and placebo groups, respectively, developed insomnia. Prior to ORZEYFUL treatment initiation, inform patients about the risk of insomnia at initiation of treatment. If insomnia persists beyond 7 days and significantly impacts daytime functioning or quality of life, consider ORZEYFUL dosage reduction or discontinuation.

Urinary Frequency and Urgency: ORZEYFUL may cause or worsen urinary frequency and urgency. In pooled phase 3 studies in patients with NT1:

- 58%, 53%, and 5% of patients in the ORZEYFUL 2 mg twice daily, ORZEYFUL 1 mg twice daily, and placebo groups, respectively, developed urinary frequency.
- 16%, 15%, and 1% of patients in the ORZEYFUL 2 mg twice daily, ORZEYFUL 1 mg twice daily, and placebo groups, respectively, developed urinary urgency.

These lower urinary tract symptoms are consistent with ORZEYFUL's mechanism of action through agonism of the orexin receptor 2 (OX2R) on central micturition pathways. Prior to initiation of ORZEYFUL treatment, inform patients about the risk of urinary frequency and urgency and screen for lower urinary tract symptoms. Monitor ORZEYFUL-treated patients with a history of overactive bladder for worsening urinary tract symptoms.

Creatine Phosphokinase Elevations: In pooled phase 3 studies in patients with NT1, asymptomatic creatine phosphokinase elevations >5x ULN were observed in 11% (21/196) of ORZEYFUL-treated patients and 5% (4/76) of placebo treated patients. Two of these cases were characterized by markedly elevated CPK and transaminase levels; both patients discontinued treatment. None of the cases were associated with myoglobinuria or renal impairment. Advise patients to report unexplained muscle pain, weakness, or dark urine, particularly when engaging in vigorous physical activity or taking concomitant drugs associated with myotoxicity.

ADVERSE REACTIONS

The most common adverse reactions (incidence ≥5% and greater than placebo) reported in phase 3 studies with ORZEYFUL were insomnia, pollakiuria, micturition urgency, and salivary hypersecretion.

DRUG INTERACTIONS

- Concomitant use with strong or moderate CYP3A inhibitors increases oveporexton exposures, which may increase the risk of ORZEYFUL-associated adverse reactions

- Concomitant use of strong and moderate CYP3A inducers can increase oveporexton metabolism and decrease plasma levels of oveporexton, which may decrease the effectiveness of ORZEYFUL

USE IN SPECIFIC POPULATIONS

Pregnancy: There is a pregnancy exposure registry that monitors pregnancy outcomes in women who are exposed to ORZEYFUL during pregnancy. Patients should be encouraged to enroll in the ORZEYFUL pregnancy registry if they become pregnant. To enroll or obtain information from the registry, patients can call 1-877-371-0309. Available data from clinical trials with ORZEYFUL use during pregnancy are insufficient to identify a drug-associated risk of major birth defects, miscarriage, or other adverse maternal or fetal outcomes.

Lactation: There are no data available on the presence of oveporexton in human milk, the effects on the breastfed infant, or the effects on milk production. Animal studies indicate that oveporexton was present in the milk of lactating rats. When a drug is present in animal milk, it is likely that the drug will be present in human milk.

Hepatic Impairment: Avoid use of ORZEYFUL in patients with severe hepatic impairment (Child-Pugh C), as it has not been studied in this population.

Renal Impairment: Avoid use of ORZEYFUL in patients with severe renal impairment on dialysis (eGFR <15 mL/minute), as it has not been studied in this population.

DRUG ABUSE AND DEPENDENCE

ORZEYFUL contains oveporexton. Controlled substance schedule to be determined after review by the Drug Enforcement Administration.

ORZEYFUL has potential for abuse and misuse. Carefully evaluate patients for a recent history of drug abuse, especially those with a history of CNS stimulant, and follow such patients closely, observing them for signs of misuse or abuse of ORZEYFUL.

Important Note: Prescribing Information is subject to change pending DEA scheduling and final label publication.

Please click for Full Prescribing Information.

About Takeda's Orexin Franchise

Takeda is the leader in orexin science with a tailored portfolio of investigational orexin agonists in pre-clinical and clinical stages for multiple-sleep wake disorders and other indications where orexin plays a role including respiration, mood and metabolism. ORZEYFUL (oveporexton) is the lead orexin receptor 2 (OX2R) agonist asset in Takeda's orexin franchise and has been approved by regulatory bodies in China and the United States for the treatment of narcolepsy type 1 (NT1). The company is also investigating other oral orexin agonists, including TAK-360 being investigated for the treatment of NT1, narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH), as well as TAK-495.

About Takeda

Takeda is focused on creating better health for people and a brighter future for the world. We aim to discover and deliver life-transforming treatments in our core therapeutic and business areas, including gastrointestinal and inflammation, rare diseases, plasma-derived therapies, oncology, neuroscience and vaccines. Together with our partners, we aim to improve the patient experience and advance a new frontier of treatment options through our dynamic and diverse pipeline. As a leading values-based, R&D-driven biopharmaceutical company headquartered in Japan, we are guided by our commitment to patients, our people and the planet. Our employees in approximately 80 countries and regions are driven by our purpose and are grounded in the values that have defined us for more than two centuries. For more information, visit www.takeda.com.

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This press release and any materials distributed in connection with this press release may contain forward-looking statements, beliefs or opinions regarding Takeda's future business, future position and results of operations, including estimates, forecasts, targets and plans for Takeda. Without limitation, forward-looking statements often include words such as "targets", "plans", "believes", "hopes", "continues", "expects", "aims", "intends", "ensures", "will", "may", "should", "would", "could", "anticipates", "estimates", "projects", "forecasts", "outlook" or similar expressions or the negative thereof. These forward-looking statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those expressed or implied by the forward-looking statements: the economic circumstances surrounding Takeda's global business, including general economic conditions in Japan and the United States and with respect to international trade relations; competitive pressures and developments; changes to applicable laws and regulations, including tax, tariff and other trade-related rules; challenges inherent in new product development, including uncertainty of clinical success and decisions of regulatory authorities and the timing thereof; uncertainty of commercial success for new and existing products; manufacturing difficulties or delays; fluctuations in interest and currency exchange rates; claims or concerns regarding the safety or efficacy of marketed products or product candidates; the impact of health crises, like the novel coronavirus pandemic; the success of our environmental sustainability efforts, in enabling us to reduce our greenhouse gas emissions or meet our other environmental goals; the extent to which our efforts to increase efficiency, productivity or cost-savings, such as the integration of digital technologies, including artificial intelligence, in our business or other initiatives to restructure our operations will lead to the expected benefits; and other factors identified in Takeda's most recent Annual Report on Form 20-F and Takeda's other reports filed with the U.S. Securities and Exchange Commission, available on Takeda's website at: https://www.takeda.com/investors/sec-filings-and-security-reports/ or at www.sec.gov. Takeda does not undertake to update any of the forward-looking statements contained in this press release or any other forward-looking statements it may make, except as required by law or stock exchange rule. Past performance is not an indicator of future results and the results or statements of Takeda in this press release may not be indicative of, and are not an estimate, forecast, guarantee or projection of Takeda's future results.

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