Alkermes Announces Positive Topline Results From Vibrance-2 Phase 2 Study of Once-Daily Alixorexton in Patients With Narcolepsy Type 2

November 12, 2025

– Alixorexton is the First Oral Orexin 2 Receptor Agonist to Demonstrate Efficacy in a Large Phase 2 Study in Patients With Narcolepsy Type 2, Supporting Advancement to Phase 3 –

– Alixorexton Met the Study's Dual Primary Endpoints, Demonstrating Statistically Significant and Clinically Meaningful Improvements in Wakefulness and Excessive Daytime Sleepiness Compared to Placebo in Patients With Narcolepsy Type 2 –

– Alixorexton Was Generally Well Tolerated at All Doses Tested –

– Company to Host Investor Webcast on Wednesday, Nov. 12 at 8:30 a.m. ET –

DUBLIN, Nov. 12, 2025 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today announced positive topline results from the Vibrance-2 dose-ranging phase 2 study evaluating alixorexton in patients with narcolepsy type 2 (NT2). Alixorexton, formerly referred to as ALKS 2680, is the company's novel, investigational, oral, selective orexin 2 receptor (OX2R) agonist in phase 2 development for the treatment of narcolepsy type 1 (NT1), NT2 and idiopathic hypersomnia (IH). In Vibrance-2, once-daily alixorexton met the dual primary endpoints, demonstrating statistically significant and clinically meaningful improvements from baseline compared to placebo on the Maintenance of Wakefulness Test (MWT) and Epworth Sleepiness Scale (ESS) at week eight. Alixorexton was generally well tolerated at all doses tested. Results from Vibrance-2 and the previously announced Vibrance-1 phase 2 study in patients with NT1 support rapid initiation of a global phase 3 program of alixorexton in patients with NT1 and NT2.

NT2 is a rare, chronic neurological sleep disorder that affects the brain's ability to regulate the sleep-wake cycle. NT2 is primarily characterized by excessive daytime sleepiness. The NT2 patient population is heterogeneous, with differences in symptom severity and treatment response.[1] In contrast to NT1, in which orexin deficiency is well established, the pathophysiology of NT2 remains less clearly defined and is typically associated with normal orexin levels.[2]

In Vibrance-2, patients with NT2 (n=93) were randomized (1:1:1:1) to receive a once-daily dose of alixorexton (10 mg, 14 mg or 18 mg) or placebo for eight weeks. Topline results include:

Dual Primary Endpoints

- MWT: Alixorexton demonstrated clinically meaningful improvements from baseline in mean sleep latency compared to placebo at week eight at all doses tested. Based on the pre-specified analysis, the 14 mg and 18 mg doses achieved statistical significance ($p<0.05$ adjusted for multiplicity).
- ESS[3]: Alixorexton demonstrated clinically meaningful improvements from baseline in excessive daytime sleepiness compared to placebo on the ESS at week eight at all doses tested. Based on the pre-specified analysis, the 18 mg dose achieved statistical significance ($p<0.05$ adjusted for multiplicity).

Safety

- Alixorexton was generally well tolerated across all doses tested throughout the eight-week, randomized, double-blind treatment period. Most treatment-emergent adverse events (TEAEs) were mild to moderate in severity. No serious TEAEs were reported. There were no safety signals observed in hepatic and renal parameters, vital signs or ECGs, and there were no treatment-related clinically meaningful changes on ophthalmic exams in the alixorexton-treated group.
- The most common TEAEs[4,5] were pollakiuria, insomnia, urinary urgency, dizziness and headache.
- Approximately 95% of patients completed the eight-week double-blind portion of the trial and entered into the optional five-week open-label extension, which is ongoing.

"The alixorexton data from Vibrance-2 are the first demonstration in a large, randomized phase 2 study that an orexin 2 receptor agonist can drive clinically meaningful improvements in wakefulness and excessive daytime sleepiness in patients without known orexin deficiency, with a generally well tolerated profile. These data are exciting and represent an important breakthrough in advancing a potential new treatment option for patients living with narcolepsy type 2," said Emmanuel Mignot, M.D., Ph.D., Craig Reynolds Professor of Sleep Medicine in the Department of Psychiatry and Behavioral Sciences at Stanford University and the Director of the Stanford Center for Narcolepsy.

"The positive topline results from Vibrance-2 mark a significant milestone for the narcolepsy patient community and for the alixorexton development program. In Vibrance-2, alixorexton achieved statistically significant and clinically meaningful improvements on the primary efficacy endpoints with a generally well-tolerated profile in this heterogeneous patient population. The results of this study provide critical insights that will inform our registrational program," said Craig Hopkinson, M.D., Chief Medical Officer and Executive Vice President of Research & Development at Alkermes. "Alixorexton is the first and only oral orexin 2 receptor agonist to demonstrate efficacy in large randomized, double-blind, multi-week phase 2 studies across a range of once-daily doses in patients with narcolepsy type 1 and type 2. We are proud to lead the way in translating innovative science into a potential new treatment option for patients and look forward to moving alixorexton into phase 3 development as quickly as possible."

Alkermes plans to present detailed results from the Vibrance-2 phase 2 study, including exploratory patient-reported outcomes related to cognition and fatigue, at a future scientific meeting. Alkermes plans to initiate the alixorexton narcolepsy global phase 3 program in the first quarter of 2026. Vibrance-3, a phase 2 study evaluating the safety and efficacy of alixorexton in adults with IH (NCT06843590), is currently enrolling.

Conference Call and Webcast

Alkermes will host a webcast presentation and conference call with accompanying slides for analysts and investors to share additional data from the Vibrance-2 study on Wednesday, Nov. 12, 2025, at 8:30 a.m. ET (1:30 p.m. GMT). The webcast player may be accessed on the Investors section of Alkermes' website at www.alkermes.com. To participate in the question-and-answer session, please also dial in to the conference call, which may be accessed by dialing +1 877-407-2988 for U.S. callers and +1 201-389-0923 for international callers. A replay of the webcast will be archived on the company's website for 30 days following the presentation.

About the Vibrance-2 Phase 2 Study (NCT06555783)

Vibrance-2 is a phase 2, randomized, double-blind, dose-range-finding, placebo-controlled study evaluating the safety and efficacy of alixorexton (formerly referred to as ALKS 2680) in adults with narcolepsy type 2 (NT2). Participants (n=93) were randomized to receive one of three doses of alixorexton (10 mg, 14 mg or 18 mg) or placebo to be taken once-daily for eight weeks. The dual primary endpoints assessed whether participants taking alixorexton experienced an improvement in wakefulness compared to participants taking placebo, as measured by the change from baseline in mean sleep latency on the maintenance of wakefulness test (MWT) at week eight, and a greater decrease in sleepiness as measured by the change from baseline in Epworth Sleepiness Scale (ESS) score at week eight. The secondary endpoint evaluated the safety and tolerability of alixorexton in patients with NT2, including incidence of adverse events, vital signs and clinical laboratory assessments. The study also included a number of exploratory patient-reported outcome measures, which evaluated the effect of alixorexton on participants' disease severity, fatigue and cognition. All participants in the double-blind portion of the study were eligible to continue to an optional five-week open-label safety extension portion of the study, followed by a long-term safety study.

About Alixorexton

Alixorexton (formerly referred to as ALKS 2680) is a novel, investigational, oral, selective orexin 2 receptor (OX2R) agonist in phase 2 development as a once-daily treatment for narcolepsy type 1 (NT1), narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH). Orexin, a neuropeptide produced in the lateral hypothalamus, is considered to be the master regulator of wakefulness due to its activation of multiple, downstream wake-promoting pathways that project widely throughout the brain.[6] Targeting the orexin system may address excessive daytime sleepiness across hypersomnolence disorders, whether or not deficient orexin signaling is the underlying cause of disease.[7] Once-daily oral administration of alixorexton was previously evaluated in a phase 1 study in healthy volunteers and patients with NT1, NT2 and IH, and in Vibrance-1, a phase 2 study in patients with NT1. It is currently being evaluated in the phase 2 Vibrance-2 and Vibrance-3 studies in patients with NT2 and IH, respectively.

About Alkermes plc

Alkermes plc, a mid-cap growth and value equity, is a global biopharmaceutical company that seeks to develop innovative medicines in the field of neuroscience. The company has a portfolio of proprietary commercial products for the treatment of alcohol dependence, opioid dependence, schizophrenia and bipolar I disorder, and a pipeline of clinical and preclinical candidates in development for neurological disorders, including narcolepsy and idiopathic hypersomnia. Headquartered in Ireland, Alkermes also has a corporate office and research and development center in Massachusetts and a manufacturing facility in Ohio. For more information, please visit Alkermes' website at www.alkermes.com.

Note Regarding Forward-Looking Statements

Certain statements set forth in this press release constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, but not limited to, statements concerning: the potential therapeutic and commercial value of alixorexton (formerly referred to as ALKS 2680) and the company's expectations, including timelines, related to the alixorexton development program. The company cautions that forward-looking statements are inherently uncertain. Although the company believes that such statements are based on reasonable assumptions within the bounds of its knowledge of its business and operations, the forward-looking statements are neither promises nor guarantees and they are necessarily subject to a high degree of uncertainty and risk. Actual performance and results may differ materially from those expressed or implied in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: whether initial clinical results for alixorexton will be predictive of results of future stages of ongoing clinical studies, future clinical studies or real-world results; whether ongoing or future clinical studies for alixorexton will be initiated or completed on expected timelines or at all; whether alixorexton could be shown to be ineffective or unsafe; potential changes in the cost, scope and duration of the alixorexton development program; and those risks and uncertainties described under the heading "Risk Factors" in the company's Annual Report on Form 10-K for the year ended Dec. 31, 2024 and in subsequent filings made by the company with the U.S. Securities and Exchange Commission (SEC), which are available on the SEC's website at www.sec.gov. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. Except as required by law, the company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release.

[1] Ruoff C, Rye D. The ICSD-3 and DSM-5 guidelines for diagnosing narcolepsy: clinical relevance and practicality. Curr Med Res Opin. 2016;32(10):1611-1622. doi:10.1080/03007995.2016.1208643

[2] Bassetti CLA, Adamantidis A, Burdakov D, et al. Narcolepsy – clinical spectrum, aetiopathophysiology, diagnosis and treatment. Nat Rev Neurol. 2019;15(9):519-539.

[3] Epworth Sleepiness Scale: 8-item self-administered questionnaire that measures severity of excessive daytime sleepiness across multiple conditions over the past 7 days (≤10 = normative).

[4] TEAEs in ≥10% among all alixorexton-treated patients.

[5] Data cutoff as of the end of the double-blind randomized treatment period. Safety data collection is ongoing, and data are subject to change.

[6] Buysse, D. Diagnosis and assessment of sleep and circadian rhythm disorders. *Journal of Psychiatric Practice*. 2005; 11(2):102-115

[7] Ten-Blanco M, Flores A, Cristino L, Pereda-Perez I. Targeting the orexin/hypocretin system for the treatment of neuropsychiatric and neurodegenerative diseases: From animal to clinical studies. Frontiers in Neuroendocrinology. 2023;69(101066). https://www.sciencedirect.com/science/article/pii/S0091302223000146

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View original content to download multimedia:https://www.prnewswire.com/news-releases/alkermes-announces-positive-topline-results-from-vibrance-2-phase-2-study-of-once-daily-alixorexton-in-patients-with-narcolepsy-type-2-302612317.html

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