Alkermes Presents Detailed Positive Results from Vibrance-1 Phase 2 Study of Alixorexton in Patients with Narcolepsy Type 1 at World Sleep Congress 2025

September 8, 2025

– First Orexin 2 Receptor Agonist to Demonstrate Clinically Meaningful and Statistically Significant Impact on Wakefulness, Cognition and Fatigue with Once-Daily Dosing Across a Range of Doses –

– Alixorexton Was Generally Well Tolerated at All Doses Tested –

– Company to Host Investor Webcast on Monday, Sept. 8 at 8:00 a.m. ET –

DUBLIN, Sept. 8, 2025 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today announced detailed positive results from the Vibrance-1 phase 2 study evaluating alixorexton in patients with narcolepsy type 1 (NT1). Alixorexton, formerly ALKS 2680, is a novel, investigational, oral, selective orexin 2 receptor (OX2R) agonist in phase 2 development as a once-daily treatment for NT1, narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH). The randomized, placebo-controlled, six-week, double-blind phase 2 study conducted in 92 patients with NT1 demonstrated clinically meaningful and statistically significant improvements in wakefulness, cognition and fatigue that were sustained over the six-week treatment period. Alixorexton was generally well tolerated at all doses tested (4 mg, 6 mg and 8 mg).

"The detailed Vibrance-1 dataset presented at World Sleep highlights the robust efficacy of once-daily alixorexton in improving wakefulness and reducing excessive daytime sleepiness in patients with narcolepsy type 1, along with its generally well tolerated safety profile. The improvements in patient-reported outcomes, especially those related to fatigue and cognitive function, suggest that alixorexton may offer meaningful relief across a spectrum of symptoms that impact patients," said Giuseppe Plazzi, M.D., Ph.D., Neurologist, Director of the Narcolepsy Center at the IRCCS of the Neurological Sciences of Bologna and Professor of Childhood Neuropsychiatry at the University of Modena and Reggio Emilia. "These data underscore alixorexton's potential to be an important new treatment option for narcolepsy type 1 and to reduce the broader disease burden of this complex neurological disorder."

The data were presented in three oral presentations at World Sleep Congress, taking place Sept. 5-10, 2025 in Singapore. Prespecified analyses are included in the table below. Key highlights include:

- Once-daily alixorexton met the primary endpoint across all doses tested, demonstrating statistically significant, clinically meaningful and dose-dependent improvements from baseline compared to placebo in mean sleep latency (MSL) on the Maintenance of Wakefulness Test (MWT) at week six. Patients had a mean sleep latency of approximately 3 minutes at baseline. All alixorexton dose groups achieved normative wakefulness on the MWT (mean sleep latency ≥20 minutes), with observed mean sleep latency of approximately 24 minutes, 26 minutes and 28 minutes for the 4, 6 and 8 mg doses, respectively.
- Alixorexton demonstrated robust and clinically meaningful improvements on the key secondary endpoint evaluating change from baseline versus placebo on the Epworth Sleepiness Scale (ESS) at week six.[1] Patients had a mean ESS score of 18.5 at baseline. Improvements in ESS were sustained in the normal range (a score of ≤10) for all doses tested across all timepoints during the six-week double-blind treatment period and the subsequent open-label extension period through week 13.[2]
- On the key secondary endpoint evaluating mean weekly cataplexy rates, alixorexton demonstrated numerical and clinically meaningful improvements across all doses compared to placebo at weeks five and six[3] and, on the pre-specified analysis, achieved statistical significance at the 6 mg dose. More than 40% of patients at the 6 mg and 8 mg doses achieved 100% reduction in cataplexy during week six of the study.
- Vibrance-1 also included a range of exploratory patient-reported outcome measures. Alixorexton drove statistically significant and clinically meaningful improvements from baseline compared to placebo in disease severity, fatigue and cognitive impairment. At week six, most patients receiving alixorexton reported mild narcolepsy severity.[4] Across all timepoints and all alixorexton dose groups, mean cognitive impairment scores fell within the lowest severity category of "none or minimal" impairment and mean fatigue scores fell into the "normal" range—effectively achieving normalization across both cognition and fatigue.[5,6]

Primary and Key Secondary Endpoints *Reported p-values adjusted for multiplicity*				
Change from Baseline at Week 6 vs. Placebo	**Placebo**	**4 mg**	**6 mg**	**8 mg**
	*LSM**	*LSM vs. placebo*		
MSL on MWT (minutes)	-0.6	22.2 **p=0.01**	24.1 **p<0.0001**	26.0 **p<0.0001**

ESS	-3.1	-6.4 **p=0.01**	-8.7 **p<0.0001**	-8.3 **p<0.0001**
Weekly Cataplexy Rate (Rate ratio vs. placebo at weeks 5 and 6)[3]	--	0.49 **p=0.169**	0.31 **p=0.01**	0.64 **p=0.452**

Patient-reported Outcomes *Exploratory endpoints; Reported p-values are nominal*				
Change from Baseline at Week 6 vs. Placebo	**Placebo** *LSM*	**4 mg** *LSM vs. placebo*	**6 mg**	**8 mg**
Narcolepsy Severity Scale for Clinical Trials (NSS-CT)[4]	-7.1	-9.1 **p=0.0008**	-12.4 **p<0.0001**	-11.0 **p<0.0001**
PROMIS-Fatigue[5]	-3.3	-8.7 **p=0.0018**	-12.4 **p<0.0001**	-12.9 **p<0.0001**
British Columbia Cognitive Complaints Inventory (BC-CCI)[6]	-1.2	-3.5 **p<0.0001**	-3.7 **p<0.0001**	-4.8 **p<0.0001**
*Least-squares mean difference				

- Alixorexton was generally well tolerated across all doses tested throughout the six-week, randomized, double-blind treatment period. No serious treatment-emergent adverse events (TEAEs) were reported. There were no clinically meaningful changes in hepatic and renal parameters, vital signs, ECGs or ophthalmic exams in the alixorexton-treated group.
- Most TEAEs were mild to moderate in severity. The most common TEAEs[7] were pollakiuria, insomnia, salivary hypersecretion, urinary urgency and blurred vision. Events of insomnia largely occurred and resolved within the first week of dosing. Events of blurred vision were mostly mild and intermittent and largely occurred and resolved within the first three days of treatment.
- More than 95% of patients who participated in the six-week double-blind portion of the trial entered into the seven-week open-label extension.

"As we seek to unlock a new era of innovation in neuroscience, the compelling results from Vibrance-1 underscore the strength of Alkermes' orexin program. These data represent a significant new contribution to the evidence base supporting the utility of orexin 2 receptor agonists in central disorders of hypersomnolence and support exploration of the broader therapeutic potential of the class across a range of psychiatric and neurological conditions," said Richard Pops, Chief Executive Officer of Alkermes. "We believe orexin-targeted therapeutics represent a significant opportunity for growth. We look forward to advancing alixorexton into phase 3 as soon as possible, and ALKS 4510 and ALKS 7290 into first-in-human studies this year, with the goal of delivering novel and differentiated new treatments across a broad range of disorders."

Based on these results, Alkermes plans to initiate a global phase 3 program for alixorexton in the first quarter of 2026. Vibrance-2, a phase 2 study evaluating the safety and efficacy of alixorexton in adults with NT2 (NCT06555783), recently completed enrollment. 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 on Monday, Sept. 8, 2025, at 8:00 a.m. ET (8:00 p.m. SGT) to discuss these data. 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-1 Phase 2 Study (NCT06358950)

Vibrance-1 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 1 (NT1). Participants (n=92) were randomized to receive one of three doses of alixorexton (4 mg, 6 mg or 8 mg) or placebo to be taken once-daily for six weeks. The primary endpoint 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 six. Secondary endpoints included change from baseline in Epworth Sleepiness Scale (ESS) score at week six and mean weekly cataplexy rate (WCR) at weeks five and six, and incidence of adverse events. 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 a seven-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 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.[8] Targeting the orexin system may address excessive daytime sleepiness across hypersomnolence disorders, whether or not deficient orexin signaling is the underlying cause of disease.[9] 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 is currently being evaluated in the phase 2 Vibrance-1, Vibrance-2 and Vibrance-3 studies in patients with NT1, NT2 and IH, respectively.

About Alkermes plc

Alkermes plc (Nasdaq: ALKS) is a mid-cap growth and value equity 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 and the company's other orexin 2 receptor agonists, and the company's expectations, including timelines, regarding the company's orexin development programs. 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] ESS: 8-item self-administered questionnaire that measures severity of excessive daytime sleepiness across multiple conditions over the past 7 days (≤10 = normative).

[2] Week 13 data reflects data from the subset of patients who had completed the Week 13 visit of the open-label extension period as of the July 1, 2025 data snapshot (n=59). Not all patients had completed the open-label extension as of July 1, 2025.

[3] Weekly cataplexy rate was derived at Week 6 from patients' cataplexy diaries over Weeks 5 and 6.

[4] NSS-CT: 15-item self-administered questionnaire (score: 0-57) that assesses the severity and consequences of the five major narcolepsy symptoms such as daytime sleepiness, cataplexy, hallucinations, sleep paralysis, and disturbed nighttime sleep over the past 7 days.

[5] PROMIS-Fatigue: 6-item self-administered questionnaire assessing the severity of a patients' fatigue over the past 7 days. Items are scored and transformed to T-scores (<55 = normative).

[6] BC-CCI: 6-item self-administered questionnaire (score: 0-18) assessing perceived problems with concentration, memory, expressing thoughts, word finding, slow thinking, and difficulty solving problems over the past 7 days (≤4 = normative).

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

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

[9] 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

Alkermes Contacts:
For Investors: Sandy Coombs, +1 781 609 6377
For Media: Gretchen Murphy, +1 781 609 6419

View original content to download multimedia:https://www.prnewswire.com/news-releases/alkermes-presents-detailed-positive-results-from-vibrance-1-phase-2-study-of-alixorexton-in-patients-with-narcolepsy-type-1-at-world-sleep-congress-2025-302548610.html

SOURCE Alkermes plc