Alkermes' Alixorexton Demonstrated Sustained Improvement in Wakefulness in Adults With Narcolepsy Type 1 and Type 2 in Long-Term Extension Study Interim Analysis

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—First Long-Term Study of an Orexin 2 Receptor Agonist to Demonstrate Sustained Clinically Meaningful Improvements in Wakefulness and Excessive Daytime Sleepiness for Up to Nine Months in Narcolepsy Type 1 and Type 2 —

— Improvements in Patient-Reported Cognition and Fatigue Were Also Sustained —

— Alixorexton Was Generally Well Tolerated at All Doses Tested —

DUBLIN--(BUSINESS WIRE)--Jul. 13, 2026-- Alkermes plc (Nasdaq: ALKS) today announced results from a planned interim analysis of the ongoing long-term extension (LTE) study evaluating alixorexton in adults with narcolepsy type 1 (NT1) and narcolepsy type 2 (NT2). Across all dose groups in both NT1 and NT2 participants, alixorexton demonstrated sustained clinically meaningful improvement from baseline[1] on the Maintenance of Wakefulness Test (MWT) and Epworth Sleepiness Scale (ESS) at week 24 of the LTE, approximately nine months after the first dose for participants treated with alixorexton in the randomized double-blind period of the Vibrance-1 and Vibrance-2 phase 2 studies. Alixorexton also demonstrated sustained and clinically meaningful improvement from baseline across patient-reported outcomes (PROs) evaluating cognition and fatigue at week 24. Alixorexton was generally safe and well tolerated at all doses tested. Alixorexton is a novel, investigational, oral, selective orexin 2 receptor (OX2R) agonist in development for the treatment of NT1, NT2 and idiopathic hypersomnia (IH).

"For people living with narcolepsy, symptom burden extends beyond excessive daytime sleepiness and can affect cognitive function and fatigue. It is exciting to see clinically meaningful improvements sustained across these important measures in this analysis of the long-term extension study of alixorexton in patients with narcolepsy type 1 and type 2. The consistency of the data in up to nine months of treatment provides further evidence that alixorexton, across a range of doses, has the potential to address important aspects of disease burden of narcolepsy regardless of narcolepsy type 1 or type 2 diagnosis," said Yves Dauvilliers, M.D., Ph.D., Professor of Neurology and Physiology, and Director of the Sleep-Wake Disorders Center at the University of Montpellier, France, and Coordinator of the French National Reference Center for Rare Diseases dedicated to narcolepsy and hypersomnias.

This ongoing open-label extension study is designed to evaluate the long-term safety, tolerability and durability of treatment effect of alixorexton. This interim analysis reflects safety and tolerability data as of the May 12, 2026 data cutoff and efficacy measures collected at week 24 of the LTE for participants who enrolled in the LTE after completing Vibrance-1 (NT1) or Vibrance-2 (NT2), reflecting treatment with alixorexton for up to nine months. The LTE remains ongoing and is open for enrollment for participants who complete ongoing phase 2 and phase 3 studies of alixorexton.

Narcolepsy Type 1

- As previously announced, in the Vibrance-1 phase 2 parent study, alixorexton demonstrated statistically significant and clinically meaningful improvements in wakefulness and cataplexy in participants with NT1 (n=92) randomized to receive a once-daily dose of alixorexton (4 mg, 6 mg or 8 mg) or placebo. Approximately 85% of Vibrance-1 participants (n=78) enrolled in the LTE. Dose adjustment was allowed during the first four weeks of the LTE, with most participants receiving 6 or 8 mg as their most frequent dose. As of the data cutoff, approximately 90% (n=70) of these participants remained on treatment.

Endpoints Evaluating Durability of Effect in NT1 Participants[3, 4]

- All alixorexton dose groups for NT1 achieved normative wakefulness on the MWT (mean sleep latency (MSL) ≥20 minutes) at week 24 of the LTE, with a mean observed MSL of approximately 29 minutes across LTE participants.
- Improvements in ESS[2] from baseline were sustained in the normal range (a score of ≤10) for all doses tested throughout the LTE, with a mean observed ESS of 7.5 at week 24 across LTE participants.
- Alixorexton demonstrated improvements from baseline on weekly cataplexy rate (WCR) at all LTE assessment timepoints. At week 24, the median WCR across LTE participants was 2.

Durability of Effect in NT1 Participants

		4 mg	6 mg	8 mg
Most frequent dose in the LTE		n=4	n=24	n=50
Mean Observed MSL on MWT[3] (minutes)	At Baseline[1]	1.7	2.2	3.4
	At Week 24 of LTE	**35.3**	**30.7**	**28.1**
Mean Observed ESS[4]	At Baseline[1]	19.0	19.0	18.4
	At Week 24 of LTE	**4.3**	**7.0**	**8.1**

Median WCR[4]	At Baseline[1]	19.8	18.2	15.8
	At Week 24 of LTE	**6.0**	**1.2**	**4.0**

Exploratory Endpoints in NT1 Participants: Cognition and Fatigue

- Improvements from baseline in exploratory PROs evaluating cognition and fatigue were generally maintained across dose groups in the LTE. At week 24, most NT1 participants across all doses had cognitive functioning scores within the normal range, as measured by the British Columbia – Cognitive Complaints Inventory (BC-CCI)[5], and mean fatigue scores were within the normal range, as measured by PROMIS-Fatigue[6], across all doses. Prior to treatment with alixorexton in the parent study, participants reported mean scores of moderate cognitive impairment and fatigue.

Safety in NT1 Participants

- Alixorexton was generally safe and well tolerated across all doses tested in the LTE.
- No serious treatment-emergent adverse events (TEAEs) were reported. Most TEAEs were mild to moderate in severity. The most common TEAEs[7] in the LTE were headache, micturition urgency, pollakiuria, and nasopharyngitis.

Narcolepsy Type 2

- As previously announced, in the Vibrance-2 phase 2 parent study, alixorexton demonstrated statistically significant and clinically meaningful improvements in wakefulness in participants with NT2 (n=93) randomized to receive a once-daily dose of alixorexton (10 mg, 14 mg or 18 mg) or placebo. Approximately 70% of Vibrance-2 participants (n=63) enrolled in the LTE. Dose adjustment was allowed during the first four weeks of the LTE, with most participants receiving 14 or 18 mg as their most frequent dose. As of the data cutoff, approximately 80% (n=51) of these participants remained on treatment.

Endpoints Evaluating Durability of Effect in NT2 Participants[3,4]

- All alixorexton dose groups for NT2 demonstrated further improvement on the MWT at week 24 of the LTE, with mean observed MSL of approximately 18 minutes across LTE participants.
- Improvements in ESS were sustained in the normal range (a score of ≤10) for the 14 mg and 18 mg dose groups throughout the LTE. Across LTE participants, the mean observed ESS was 8.9 at week 24.

Durability of Effect in NT2 Participants

		10 mg	**14 mg**	**18 mg**
Most frequent dose in the LTE		n=3	n=25	n=34
Mean Observed MSL on MWT[3] (minutes)	At Baseline[1]	2.0	4.8	5.2
	At Week 24 of LTE[8]	**21.1**	**18.0**	**17.3**
Mean Observed ESS[4]	At Baseline[1]	16.7	16.8	18.1
	At Week 24 of LTE	**12.5**	**8.1**	**9.3**

Exploratory Endpoints in NT2 Participants: Cognition and Fatigue

- Improvements from baseline in exploratory PROs evaluating cognition and fatigue were generally maintained in NT2 participants across dose groups in the LTE. At week 24, most NT2 participants across all doses had cognitive functioning scores within the normal or mild range, as measured by the BC-CCI[5], and mean fatigue scores were within the normal range, as measured by PROMIS-Fatigue[6], across all doses. Prior to treatment with alixorexton in the parent study, participants reported overall mean scores of moderate cognitive impairment and fatigue.

Safety in NT2 Participants

- Alixorexton was generally safe and well tolerated across all doses tested in the LTE.
- No serious TEAEs were reported. Most TEAEs were mild to moderate in severity. The most common TEAEs[7] in the LTE were insomnia, headache, pollakiuria, and upper respiratory tract infection.

“These long-term results represent a significant contribution to our understanding of alixorexton as a potential new treatment option for patients with narcolepsy. We are particularly encouraged by the durability of effect observed across multiple dimensions of the disease, including wakefulness, cognition and fatigue, together with a safety profile that continued to be generally well tolerated. These data also underscore the importance of dosing flexibility to meet individual needs across narcolepsy patients with known orexin deficiency as well as patients with normal orexin tone,” said Craig Hopkinson, M.D., (MBChB), Chief Medical Officer and Executive Vice President, Research & Development at Alkermes. “We are excited to continue advancing enrollment in the phase 3 Brilliance Studies and work toward completing the Vibrance-3 phase 2 study in IH later this year.”

Alkermes plans to present these results at an upcoming medical meeting. Alixorexton is currently being evaluated in the phase 3 Brilliance Studies in adults with NT1 and NT2, and in the phase 2 Vibrance-3 study in adults with IH (Brilliance NT1 – Study 302: NCT07455383; Brilliance NT2 – Study 303: NCT07502443; Brilliance NT1 – Study 304: NCT07540897; Vibrance-3: NCT06843590).

About Alixorexton
Alixorexton (formerly referred to as ALKS 2680) is a novel, investigational, oral, selective orexin 2 receptor (OX2R) agonist in development for the treatment of 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.[9] Targeting the orexin system may address excessive daytime sleepiness across hypersomnolence disorders, whether or not deficient orexin signaling is the underlying cause of disease.[10] Alixorexton is currently being evaluated in the phase 3 Brilliance Studies in patients with NT1 and NT2, and in the phase 2 Vibrance-3 study in patients with IH. The U.S. Food and Drug Administration (FDA) has granted alixorexton Breakthrough Therapy designation for the treatment of NT1 and Orphan Drug Designation (ODD) for the treatment of IH. The European Commission has granted ODD to alixorexton for the treatment of narcolepsy.

About Alkermes plc
Alkermes plc (Nasdaq: ALKS), 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, bipolar I disorder and narcolepsy. Alkermes' pipeline includes late-stage clinical candidates in development for narcolepsy and idiopathic hypersomnia, and orexin 2 receptor agonists in early clinical development for other neurological disorders, including attention-deficit hyperactivity disorder (ADHD) and fatigue associated with multiple sclerosis and Parkinson's disease. 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 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: clinical study results for alixorexton may not be predictive of results of future stages of ongoing clinical studies, future clinical studies or real-world results; clinical studies for alixorexton may not be initiated or completed on expected timelines or at all; alixorexton may be shown to be ineffective or unsafe; the FDA may not agree with the company's regulatory strategies or components of its development program for alixorexton, including clinical trial designs, conduct and methodologies; 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, 2025 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] For efficacy/durability endpoints and disease characteristics, baseline values are defined as the parent study baseline. For safety endpoints, baseline values are defined as end of treatment in the parent study (rollover), or prior to the first dose of LTE (re-entry).

[2] ESS: Self-administered, 8-item questionnaire (score range: 0-24) that measures severity of excessive daytime sleepiness over the past 7 days (score ≤10 = normative; 11-12 = mild; 13-15 = moderate; 16-24 = severe).

[3] For MSL on MWT, results are summarized by the dose that participants received on the day of the MWT assessment at week 24.

[4] For ESS and WCR, results are summarized by the most frequent dose participants received during the LTE.

[5] 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; 5-8 = mild; 9-14 = moderate; 15-18 = severe).

[6] PROMIS-Fatigue: 6-item self-administered questionnaire assessing the severity of a patient's fatigue over the past 7 days. Items are scored and transformed to T-scores (<55 = normative; 55-<60 = mild; 60-<70 = moderate; ≥70 = severe).

[7] TEAEs in ≥10% of all alixorexton-treated patients with symptom onset during the LTE.

[8] MWT data for four NT2 participants that had completed 24 weeks of treatment was outstanding at the time of, and therefore not included in, the data analysis.

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

[10] 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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