Alkermes to Present New Research Related to ALKS 2680 at SLEEP 2025

May 29, 2025

– Company to Present Eight Posters and Two Oral Presentations, Including New Analyses From ALKS 2680 Phase 1 Study –

– New Research Evaluating the Clinical, Economic and Humanistic Burden of Narcolepsy and Findings From In-Depth Qualitative Patient Interviews on the Burden of Idiopathic Hypersomnia Will Also Be Presented –

DUBLIN, May 29, 2025 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today announced plans to present new research related to ALKS 2680 at SLEEP 2025, the 38th annual meeting of the Associated Professional Sleep Societies (APSS), taking place June 8-11, 2025 in Seattle. ALKS 2680 is the company's novel, investigational, oral 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).

Seven abstracts were accepted for poster presentation. The one abstract selected for dual presentation (oral and poster) describes quantitative electroencephalography (qEEG) exploratory results from the phase 1b study of ALKS 2680 in patients with NT1, NT2 and IH. Findings demonstrated a statistically significant, wake-associated qEEG profile with ALKS 2680 compared to placebo. In addition, in an oral presentation, Marcus Yountz, M.D., Alkermes' Vice President of Clinical Development, will provide an overview of the ALKS 2680 development program and Alkermes' broader orexin portfolio during the general session: *Advances in the Development of Orexin Agonists*.

Additional presentation highlights include:

- Pooled data from the phase 1b study which showed that single doses of ALKS 2680 were generally well tolerated and led to statistically significant, clinically meaningful improvements in mean sleep latency at all doses tested in patients with NT1, NT2 or IH.
- Results from a cardiac safety analysis in healthy volunteers, which demonstrated a lack of any effects of ALKS 2680 on QTc prolongation, heart rate or cardiac conduction.
- Study design and methods for Vibrance-3, a recently initiated phase 2 clinical study evaluating the safety and efficacy of ALKS 2680 compared to placebo in patients with IH.
- Findings from a retrospective, cross-sectional analysis of the 2021/2023 U.S. National Health and Wellness Survey evaluating the clinical, economic and humanistic burden of narcolepsy.

"Alkermes is at the forefront of development in the orexin 2 receptor agonist therapeutic category; this new investigational mechanism has the potential to transform the treatment paradigm for central disorders of hypersomnolence. The breadth of posters that Alkermes is presenting at this year's SLEEP meeting underscores this potential and demonstrates our leadership in orexin biology as we execute the clinical development program for ALKS 2680 in narcolepsy and idiopathic hypersomnia and advance our broader portfolio of orexin 2 receptor agonists in other neuropsychiatric and neurological disorders," said Craig Hopkinson, M.D., Chief Medical Officer and Executive Vice President, Research & Development at Alkermes. "We remain focused on the successful execution of the phase 2 Vibrance Studies across narcolepsy type 1, narcolepsy type 2 and idiopathic hypersomnia, and look forward to sharing topline results from Vibrance-1 in early Q3."

The SLEEP 2025 abstracts are available on the SLEEP Meeting website: https://www.sleepmeeting.org/abstract-supplements/

Details of Alkermes' accepted presentations at SLEEP 2025 are as follows:

Oral presentations

"Investigational Orexin-2 Receptor Agonists for Narcolepsy Types 1 and 2, Idiopathic Hypersomnia, and Beyond"

- **Session:** S-19
- **Presenter:** Marcus Yountz, M.D., Alkermes
- **Presentation Date/Time:** The oral presentation is scheduled to occur on Wednesday, June 11, 2025 during the *Advances in the Development of Orexin Agonists* session (8:30 – 9:00 a.m. PT).

"Effects of the Orexin 2 Receptor Agonist ALKS 2680 on qEEG in Patients with Narcolepsy and Idiopathic Hypersomnia"

- **Abstract ID:** 830
- **Poster Board Number:** 392
- **Presenter:** Julia Chapman, Ph.D., Woolcock Institute of Medical Research
- **Presentation Date/Time:** The oral presentation is scheduled to occur on Wednesday, June 11, 2025 during the *Hypersomnia: New Drugs and New Data* session (4:15 – 4:30 p.m. PT). A corresponding poster will be presented on Wednesday, June 11, 2025 from 10:00 – 11:45 a.m. PT, during session P-51.

Poster presentations

"The Clinical and Humanistic Burden of Narcolepsy: Matched Analysis of US National Health and Wellness Survey Data"

- **Abstract ID:** 805
- **Poster Board Number:** 323
- **Presenter:** Michael Doane, Ph.D., Alkermes
- **Presentation Date:** The poster will be presented on Monday, June 9, 2025 from 10:00 – 11:45 a.m. PT, during session P-15.

"The Economic Burden of Narcolepsy: Matched Analysis of US National Health and Wellness Survey Data"

- **Abstract ID:** 806
- **Poster Board Number:** 324
- **Presenter:** Michael Doane, Ph.D., Alkermes
- **Presentation Date:** The poster will be presented on Monday, June 9, 2025 from 10:00 – 11:45 a.m. PT, during session P-15.

"Vibrance-3: Study Design and Methods for a Phase 2, Randomized, Placebo-Controlled, Parallel-Group Study Evaluating the Safety and Efficacy of ALKS 2680 in Patients With Idiopathic Hypersomnia"

- **Abstract ID:** 1661
- **Poster Board Number:** 538
- **Presenter:** David T. Plante, M.D., Ph.D., Associate Professor of Psychiatry at the University of Wisconsin-Madison
- **Presentation Date:** The poster will be presented on Tuesday, June 10, 2025 from 10:00 – 11:45 a.m. PT, during session P-37.

"Evaluation of Cardiac Safety Profile of ALKS 2680 in Healthy Subjects: Concentration-QTc Relationship of ALKS 2680"

- **Abstract ID:** 837
- **Poster Board Number:** 399
- **Presenter:** Jahnavi Kharidia, Ph.D., Alkermes
- **Presentation Date:** The poster will be presented on Wednesday, June 11, 2025 from 10:00 – 11:45 a.m. PT, during session P-51.

"The Orexin 2 Receptor Agonist ALKS 2680 in Patients with Narcolepsy or Idiopathic Hypersomnia: A Phase 1b Study"

- **Abstract ID:** 838
- **Poster Board Number:** 400
- **Presenter:** Ron Grunstein, M.D., Ph.D., Head of Sleep and Circadian Research at the Woolcock Institute of Medical Research
- **Presentation Date:** The poster will be presented on Wednesday, June 11, 2025 from 10:00 – 11:45 a.m. PT, during session P-51.

"Evaluation of the Novel Orexin 2 Receptor Agonist ALKS 2680 on Measures of Arousal Circuit Activation in Rodents"

- **Abstract ID:** 848
- **Poster Board Number:** 410
- **Presenter:** Julie Brooks, Ph.D., Alkermes
- **Presentation Date:** The poster will be presented on Wednesday, June 11, 2025 from 10:00 – 11:45 a.m. PT, during session P-51.

"Diagnosis Journey, Symptoms, and Burden of Idiopathic Hypersomnia: Patient Perspectives from Qualitative Interviews"

- **Abstract ID:** 849
- **Poster Board Number:** 411
- **Presenter:** Trey Williams, Ph.D., Alkermes
- **Presentation Date:** The poster will be presented on Wednesday, June 11, 2025 from 10:00 – 11:45 a.m. PT, during session P-51.

About the ALKS 2680 Phase 1 Study

The phase 1 study for ALKS 2680 included single-ascending dose and multiple-ascending dose evaluations in healthy volunteers, and double-blind, crossover treatment in patients with narcolepsy type 1 (NT1), narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH).

In the healthy volunteer phase of the study, each cohort included eight participants, six of whom were randomized to receive ALKS 2680 and two of whom received placebo. In the single-dose portion, ALKS 2680 was dosed from 1 mg to 50 mg. In the multiple-dose portion, participants received single daily doses of ALKS 2680 ranging from 3 mg to 25 mg strengths for up to 10 days. The objectives of this part of the study were to assess ALKS 2680's safety, tolerability, pharmacokinetics (PK) and pharmacodynamics.

The phase 1b proof-of-concept part of the study enrolled patients with NT1 (n=10), NT2 (n=9) or IH (n=8). Following an initial two-week washout period of existing medications, patients received single doses of three active dose levels of ALKS 2680 (1 mg, 3 mg and 8 mg for NT1; 5 mg, 12 mg and 25 mg for NT2 and IH) and placebo in a randomized sequence in a four-way crossover design, with washout periods between each treatment in the sequence. The objectives were to assess safety and tolerability, and changes from baseline in average sleep latency, as measured through the Maintenance of Wakefulness Test (MWT) at each crossover period, along with plasma PK, and patient-reported measures of alertness on the Karolinska Sleepiness Scale (KSS).

About ALKS 2680

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.[1] Targeting the orexin system may address excessive daytime sleepiness across hypersomnolence disorders, whether or not deficient orexin signaling is the underlying cause of disease.[2] Once-daily oral administration of ALKS 2680 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 the Vibrance Studies

The Vibrance Studies are phase 2, randomized, double-blind, dose-range-finding studies evaluating the safety and efficacy of ALKS 2680 compared to placebo in patients with narcolepsy type 1 (Vibrance-1; NCT06358950), narcolepsy type 2 (Vibrance-2; NCT06555783) and idiopathic hypersomnia (Vibrance-3, NCT06843590). More information can be found at www.vibrancestudies.com (for U.S. audiences only).

About Alkermes plc

Alkermes plc 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 ALKS 2680 and the company's portfolio of orexin 2 receptor agonists; and the company's expectations regarding execution and timelines for its phase 2 Vibrance studies of ALKS 2680. 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 future clinical studies or future stages of ongoing clinical studies for ALKS 2680 will be initiated or completed on time or at all; whether ALKS 2680 could be shown to be ineffective or unsafe; potential changes in the cost, scope and duration of the ALKS 2680 development program or the development program for the company's other orexin assets; whether preclinical and initial clinical results will be predictive of results of future clinical studies or real-world results; 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] Buysse, D. Diagnosis and assessment of sleep and circadian rhythm disorders. *Journal of Psychiatric Practice*. 2005; 11(2):102-115

[2] 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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