Alkermes to Present Positive Clinical Data From Phase 1b Study of ALKS 2680 in Patients With Narcolepsy Type 2 and Idiopathic Hypersomnia at Sleep Europe 2024

September 23, 2024

– Data From Narcolepsy Type 2 Cohort of ALKS 2680 Phase 1b Study to be Presented in Oral Presentation –

– Data From Idiopathic Hypersomnia Cohort of ALKS 2680 Phase 1b Study Accepted for Poster Presentation –

DUBLIN, Sept. 23, 2024 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today announced plans to present clinical data from its phase 1b study of ALKS 2680 in patients with narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH) at the European Sleep Research Society's (ESRS) 27th Congress, Sleep Europe 2024, taking place Sept. 24-27, 2024 in Seville, Spain. ALKS 2680 is the company's novel, investigational, oral, selective orexin 2 receptor (OX2R) agonist in development as a once-daily treatment for narcolepsy, a chronic, neurological disorder characterized by excessive daytime sleepiness.

In an oral presentation and corresponding poster presentation, the company will share data from the cohort of patients with NT2 (n=9) from the phase 1b, proof-of-concept study evaluating single-dose, oral administration of ALKS 2680. Additionally, the company will present a poster with data from the cohort of patients with IH (n=8) from the same study. As previously announced, ALKS 2680 was generally well tolerated with improved wakefulness compared to placebo in both cohorts.

"Results from the ALKS 2680 phase 1b proof-of-concept study in patients with narcolepsy type 1, narcolepsy type 2 and idiopathic hypersomnia highlight the potential of ALKS 2680 as a treatment option for people living with these sleep disorders, both with and without known orexin deficiency. Treatment with once-daily, oral ALKS 2680 was generally well tolerated with improved wakefulness compared to placebo at all doses tested across all three patient populations, supporting further clinical evaluation," said Ron Grunstein, M.D., Ph.D., Head of Sleep and Circadian Research at the Woolcock Institute of Medical Research.

The company will also present two posters at Sleep Europe 2024 detailing the study design and methods for each of the ongoing phase 2 studies, Vibrance-1 and Vibrance-2, evaluating ALKS 2680 in patients with narcolepsy type 1 and narcolepsy type 2, respectively.

"We're pleased to share the results from our ALKS 2680 phase 1b, proof-of-concept study in patients with narcolepsy type 2 and idiopathic hypersomnia at Sleep Europe 2024. These data provide further evidence of the clinical profile of ALKS 2680 in patients with sleep disorders and a strong foundation to advance the ALKS 2680 phase 2 program," said Craig Hopkinson, M.D., Chief Medical Officer and Executive Vice President of Research & Development at Alkermes. "We look forward to engaging with clinicians and researchers at this important meeting, sharing the data from our clinical development program, and discussing the design of the ongoing phase 2 studies, Vibrance-1 and Vibrance-2, which are evaluating ALKS 2680 in patients with narcolepsy type 1 and type 2, respectively."

Details of Alkermes' presentations at Sleep Europe 2024 are as follows:

The Orexin 2 Receptor Agonist ALKS 2680 in Patients with Narcolepsy Type 2: An Initial Proof of Concept Phase 1b Study

- **Presenter:** Ron Grunstein, M.D., Ph.D., Head of Sleep and Circadian Research at the Woolcock Institute of Medical Research
- **Presentation Date:** The oral presentation is scheduled to occur on Wednesday, Sept. 25, 2024 at 8:00 CEST as part of Oral Session 1 and will be available online to registered attendees. The corresponding poster (P200) will be presented on Wednesday, Sept. 25, 2024 from 16:00–17:45 CEST.

The Orexin 2 Receptor Agonist ALKS 2680 in Patients with Idiopathic Hypersomnia: An Initial Proof of Concept Phase 1b Study

- **Poster ID:** P5070
- **Presenter:** Brendon Yee, Ph.D., Professor and Respiratory and Sleep Physician at the Woolcock Institute of Medical Research
- **Presentation Date:** The poster will be presented on Thursday, Sept. 26, 2024 from 17:30–18:45 CEST.

Vibrance-1: Study Design and Methods for a Phase 2, Randomised, Placebo-Controlled, Parallel Group Study Evaluating the Safety and Efficacy of ALKS 2680 in Patients With Narcolepsy Type 1

- **Poster ID:** P797
- **Presenter:** Giuseppe Plazzi, M.D., Ph.D., Head of the Sleep Center at the Institute of Neurological Sciences of Bologna, Italy and Chair of Child Neurology at the University of Modena and Reggio Emilia
- **Presentation Date:** The poster will be presented on Thursday, Sept. 26, 2024 from 17:30–19:00 CEST.

Vibrance-2: Study Design and Methods for a Phase 2, Randomised, Placebo-Controlled, Parallel Group Study Evaluating the Safety and Efficacy of ALKS 2680 in Patients With Narcolepsy Type 2

- **Poster ID:** P5071
- **Presenter:** Sergey Yagoda, M.D., Ph.D., Alkermes
- **Presentation Date:** The poster will be presented on Thursday, Sept. 26, 2024 from 17:30–18:45 CEST.

For more information, including a complete list of abstracts, please visit the ESRS Congress website at https://esrs.eu/sleep-congress/.

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 NT1, NT2 and 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. 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 and Vibrance-2 studies in patients with NT1 and NT2, 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) and narcolepsy type 2 (Vibrance-2; NCT06555783). 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. 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 value of ALKS 2680 for the treatment of narcolepsy; and the company's expectations regarding clinical development activities for 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 ALKS 2680 could be shown to be ineffective or unsafe; potential changes in the cost, scope and duration of the ALKS 2680 development program; whether preclinical and initial clinical results for ALKS 2680 will be predictive of results of future clinical studies or real-world results; whether future clinical trials or future stages of ongoing clinical trials for ALKS 2680 will be initiated or completed on time or at all; 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, 2023 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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