Alkermes Announces Initiation of Vibrance-3 Phase 2 Study Evaluating ALKS 2680 for the Treatment of Idiopathic Hypersomnia

April 1, 2025

DUBLIN, April 1, 2025 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today announced the initiation of Vibrance-3, a phase 2 clinical study evaluating the safety and efficacy of ALKS 2680 compared to placebo in adults with idiopathic hypersomnia (IH). ALKS 2680 is the company's novel, investigational, oral, selective orexin 2 receptor (OX2R) agonist in development as a once-daily treatment for narcolepsy type 1, narcolepsy type 2 and IH – chronic, neurological disorders characterized by excessive daytime sleepiness.

"The initiation of Vibrance-3 represents an important step forward for the ALKS 2680 development program as we seek to advance a potential new treatment option for people living with idiopathic hypersomnia. There remains high unmet need for the idiopathic hypersomnia community, as evidenced by a recent survey conducted by the Sleep Consortium[1] in which more than 90% of patients surveyed indicated that IH symptoms had a moderate to high impact on their life," said Craig Hopkinson, M.D., Chief Medical Officer and Executive Vice President, Research & Development at Alkermes. "The Vibrance-3 phase 2 study builds on encouraging data from our phase 1b, proof-of-concept study of ALKS 2680 in patients with IH, and we look forward to further characterizing its safety and efficacy profile in this patient population."

Vibrance-3 is a phase 2, randomized, double-blind, dose-range-finding, placebo-controlled study evaluating the safety and efficacy of ALKS 2680 in adults with IH. Participants will be randomized to receive one of three doses of ALKS 2680 (10 mg, 14 mg or 18 mg) or placebo to be taken once-daily for eight weeks. The primary endpoint will assess, by dose level, whether participants taking ALKS 2680 experience a greater decrease in sleepiness compared to participants taking placebo alone, as measured by the change in Epworth Sleepiness Scale (ESS) score. Secondary endpoints include change in Idiopathic Hypersomnia Severity Scale (IHSS) score and incidence of adverse events. The study is expected to enroll approximately 96 patients with IH across sites in the U.S., Australia and Europe. Participants who complete the study will be eligible to continue in a long-term, open-label, safety study (NCT06767683).

More information can be found at www.clinicaltrials.gov (identifier: NCT06843590) and www.vibrancestudies.com (for U.S. audiences only).

Vibrance-1 and Vibrance-2, phase 2 studies evaluating the safety and efficacy of ALKS 2680 in adults with narcolepsy type 1 (NCT06358950) and narcolepsy type 2 (NCT06555783), respectively, are currently ongoing.

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.[2] Targeting the orexin system may address excessive daytime sleepiness across hypersomnolence disorders, whether or not deficient orexin signaling is the underlying cause of disease.[3] 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 Idiopathic Hypersomnia

Idiopathic hypersomnia (IH) is a rare, chronic, neurological sleep disorder characterized by excessive daytime sleepiness despite normal sleep durations.[4,5] Additional common symptoms can include severe sleep inertia (individuals may feel groggy or disoriented for prolonged periods after waking up), unrefreshing naps, fatigue and cognitive dysfunction.[6,7] The underlying neuropathology of idiopathic hypersomnia is unknown.[4] IH affects an estimated 40,000 people in America.[8]

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 for the treatment of narcolepsy and idiopathic hypersomnia; 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 studies or future stages of ongoing clinical studies 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, 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] The Illuminate Hypersomnia "Voice of the Patient" Report. Contains data from 811 survey respondents conducted in spring 2024.

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

[3] 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

[4] Trotti LM, Arnulf I. Idiopathic Hypersomnia and Other Hypersomnia Syndromes. Neurotherapeutics. 2021;18(1):20-31. doi:10.1007/s13311-020-00919-1

[5] American Academy of Sleep Medicine. The International Classification of Sleep Disorders. Third Edition (ICSD-3). 2014.

[6] Trotti LM. Waking up is the hardest thing I do all day: Sleep inertia and sleep drunkenness. Sleep Med Rev 2016.

[7] Vernet C, Leu-Semenescu S, Buzare MA, Arnulf I. Subjective symptoms in idiopathic hypersomnia: beyond excessive sleepiness. J Sleep Res. 2010;19:525–534

[8] Acquavella et al., J Clin Sleep Med 16:1255 (2020)

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