Alkermes Announces Positive Topline Results From REVITALYZ℠ Phase 3 Study Evaluating LUMRYZ® (sodium oxybate) Extended-Release in Adults With Idiopathic Hypersomnia

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– LUMRYZ Met All Primary and Key Secondary Endpoints Demonstrating Statistically Significant and Clinically Meaningful Improvements Compared to Placebo in Excessive Daytime Sleepiness and Patient-Reported Disease Severity –

– Safety Profile Consistent With Known Safety Profile of LUMRYZ –

DUBLIN--(BUSINESS WIRE)--May 12, 2026-- Alkermes plc (Nasdaq: ALKS) today announced positive topline results from the REVITALYZ℠ double-blind, placebo-controlled, randomized withdrawal, multicenter phase 3 study evaluating the investigational use of LUMRYZ® (sodium oxybate) extended-release oral suspension in adults with idiopathic hypersomnia (IH). LUMRYZ met the study's primary endpoint, demonstrating statistically significant improvements in excessive daytime sleepiness compared to placebo as measured by the change in Epworth Sleepiness Scale (ESS)[1] score (p<0.0001).

"The data from REVITALYZ demonstrate the potential utility of once-nightly LUMRYZ as an effective treatment for excessive daytime sleepiness associated with IH, building upon its established therapeutic value in narcolepsy," said Richard K. Bogan, M.D., FCCP, FAASM, Principal of Bogan Sleep Consultants, LLC and Associate Clinical Professor at the University of South Carolina School of Medicine. "This is a community with limited approved therapeutic options. These findings constitute an important contribution to the clinical understanding of treatment approaches for patients with IH, for whom disruptive symptoms present particular treatment challenges."

All study participants received LUMRYZ during an open-label dose titration period then a stable dose period, during which improvements in ESS scores were observed. At the end of the stable dose period participants were randomized to remain on LUMRYZ or switch to placebo. At the end of the double-blind randomized withdrawal period, the primary endpoint of ESS and key secondary endpoints of Patient Global Impression of Change (PGI-C)[2] and Idiopathic Hypersomnia Severity Scale (IHSS)[3] were measured for 104 participants to assess the worsening of symptoms for those participants on placebo as compared to those that remained on LUMRYZ.

From the end of the stable dose period to the end of the double-blind randomized withdrawal period, participants randomized to placebo had statistically significant worsening in ESS (p<0.0001), PGI-C (p<0.0001), and IHSS (p<0.0001) compared with participants randomized to continue treatment with LUMRYZ.

The safety profile of LUMRYZ in the REVITALYZ study was generally consistent with previously observed safety data associated with LUMRYZ, with no new safety signals observed in this population. The most common treatment-emergent adverse events (≥10% of participants) were nausea, headache, anxiety, dizziness and vomiting.

"We look forward to advancing LUMRYZ as a potential treatment for adults with idiopathic hypersomnia based on the clear and compelling outcome of the REVITALYZ study," said Craig Hopkinson, M.D. (MBChB), Chief Medical Officer and Executive Vice President, Research & Development at Alkermes. "Historically, people living with sleep disorders have had limited treatment options from which to choose, and Alkermes is motivated to contribute to the overall clinical landscape of sleep medicine through research such as this."

Alkermes plans to present detailed results from REVITALYZ at an upcoming medical meeting. Based on the positive results of this phase 3 study, Alkermes plans to file a supplemental New Drug Application (sNDA) with the U.S. Food and Drug Administration (FDA) by the end of 2026.

LUMRYZ is approved by the FDA for the treatment of excessive daytime sleepiness or cataplexy in patients 7 years of age and older with narcolepsy. LUMRYZ is not currently approved by regulatory authorities for the treatment of IH. Pursuant to the terms of a previously disclosed settlement and license agreement, Alkermes may not market, offer for sale, take orders for, distribute, promote, or provide patient support services with respect to LUMRYZ for IH before March 1, 2028, even if LUMRYZ were to receive FDA approval for IH prior to that date.

About the REVITALYZ Study

REVITALYZ was a double-blind, placebo-controlled, randomized withdrawal, multicenter study of the efficacy and safety of LUMRYZ® (sodium oxybate) (previously referred to as FT218), a once-nightly formulation of sodium oxybate for extended-release oral suspension. Participants either initiated oxybate treatment with LUMRYZ or transitioned from oxybate therapy to LUMRYZ. After an initial screening period, all participants entered a 10-week open-label dose titration (OLDT) period with titration from a dose of 4.5 grams (g) up to a maximum dose of 9 g. The OLDT was followed by a 2-week stable dose (SD) period, after which 104 participants entered a subsequent 2-week double-blind, randomized withdrawal (DBRW) period. The primary efficacy endpoint was a measure of change in the least squares mean score on the ESS[1] from the end of the SD period to the end of the DBRW period. Key secondary endpoints included the proportion of participants reporting worsening of symptoms on the PGI-C[2] at the end of the DBRW period, and change in total IHSS[3] scores from the end of the SD period to the end of the DBRW period. The study also included additional secondary and exploratory endpoints evaluating disease severity and functional outcomes.

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 the U.S.[8]

About LUMRYZ® (sodium oxybate) for extended-release oral suspension

LUMRYZ (sodium oxybate) for extended-release oral suspension is a central nervous system depressant indicated for the treatment of cataplexy or excessive daytime sleepiness (EDS) in patients 7 years of age and older with narcolepsy.

IMPORTANT SAFETY INFORMATION

WARNING: CENTRAL NERVOUS SYSTEM (CNS) DEPRESSION and ABUSE AND MISUSE

Central Nervous System Depression
LUMRYZ™ (sodium oxybate) is a CNS depressant. Clinically significant respiratory depression and obtundation may occur in patients treated with LUMRYZ at recommended doses. Many patients who received LUMRYZ during clinical trials in narcolepsy were receiving CNS stimulants.

Abuse and Misuse
LUMRYZ (sodium oxybate) is the sodium salt of gamma-hydroxybutyrate (GHB). Abuse or misuse of illicit GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreased consciousness, coma, and death.

Because of the risks of CNS depression and abuse and misuse, LUMRYZ is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called the LUMRYZ REMS.

CONTRAINDICATIONS
LUMRYZ is contraindicated for use in:

- combination with sedative hypnotics or alcohol
- patients with succinic semialdehyde dehydrogenase deficiency

WARNINGS AND PRECAUTIONS
Central Nervous System Depression
The concurrent use of LUMRYZ with other CNS depressants, including but not limited to opioid analgesics, benzodiazepines, sedating antidepressants or antipsychotics, sedating antiepileptic drugs, general anesthetics, muscle relaxants, and/or illicit CNS depressants, may increase the risk of respiratory depression, hypotension, profound sedation, syncope, and death. If use of these CNS depressants in combination with LUMRYZ is required, dose reduction or discontinuation of one or more CNS depressants (including LUMRYZ) should be considered. In addition, if short-term use of an opioid (eg, post- or perioperative) is required, interruption of treatment with LUMRYZ should be considered.

After first initiating treatment and until certain that LUMRYZ does not affect them adversely (eg, impair judgment, thinking, or motor skills), caution patients against engaging in hazardous activities requiring complete mental alertness or motor coordination such as operating hazardous machinery, including automobiles or airplanes. Also caution patients against engaging in these hazardous activities for at least six (6) hours after taking LUMRYZ. Patients should be queried about CNS depression-related events upon initiation of LUMRYZ therapy and periodically thereafter.

Abuse and Misuse
LUMRYZ is a Schedule III controlled substance. The active ingredient of LUMRYZ, sodium oxybate, is the sodium salt of gamma-hydroxybutyrate (GHB), a Schedule I controlled substance. Abuse of illicit GHB, either alone or in combination with other CNS depressants, is associated with CNS adverse reactions, including seizure, respiratory depression, decreases in the level of consciousness, coma, and death. The rapid onset of sedation, coupled with the amnestic features of GHB, particularly when combined with alcohol, has proven to be dangerous for the voluntary and involuntary user (eg, assault victim). Physicians should carefully evaluate patients for a history of drug abuse and follow such patients closely.

LUMRYZ REMS
LUMRYZ is available only through a restricted distribution program called the LUMRYZ REMS because of the risks of central nervous system depression and abuse and misuse.

Notable requirements of the LUMRYZ REMS include the following:

- Healthcare providers who prescribe LUMRYZ are specially certified.
- LUMRYZ will be dispensed only by pharmacies that are specially certified.
- LUMRYZ will be dispensed and shipped only to patients who are enrolled in the LUMRYZ REMS with documentation of safe use conditions.

Further information is available at www.LUMRYZREMS.com or by calling 1-877-453-1029.

Respiratory Depression and Sleep-Disordered Breathing
LUMRYZ may impair respiratory drive, especially in patients with compromised respiratory function. In overdoses of oxybate with illicit use of GHB, life-threatening respiratory depression has been reported. Increased apnea and reduced oxygenation may occur with LUMRYZ administration. A significant increase in the number of central apneas and clinically significant oxygen desaturation may occur in patients with obstructive sleep apnea treated with LUMRYZ. Prescribers should be aware that sleep-related breathing disorders tend to be more prevalent in obese patients, in men, in postmenopausal women not on hormone replacement therapy, and among patients with narcolepsy.

Depression and Suicidality
Depression, and suicidal ideation and behavior, can occur in patients treated with LUMRYZ. In an adult clinical trial in patients with narcolepsy

(n=212), there were no suicide attempts, but one patient with a history of depression and anxiety developed suicidal ideation in the LUMRYZ-treated group. In a clinical trial in pediatric narcolepsy patients administered immediate-release sodium oxybate, one patient experienced suicidal ideation and two patients reported depression. The emergence of depression in patients treated with LUMRYZ requires careful and immediate evaluation. Patients with a previous history of a depressive illness and/or a suicide attempt should be monitored carefully for the emergence of depressive symptoms while taking LUMRYZ.

Other Behavioral or Psychiatric Adverse Reactions
Other behavioral and psychiatric adverse reactions can occur in patients taking LUMRYZ. During adult clinical trials in patients with narcolepsy administered LUMRYZ, 2% of 107 patients treated with LUMRYZ experienced a confusional state. No patients treated with LUMRYZ discontinued treatment because of confusion. Anxiety occurred in 7.5% of 107 patients treated with LUMRYZ in the adult trial in patients with narcolepsy. Other psychiatric reactions reported in adult clinical trials in patients with narcolepsy administered LUMRYZ included irritability, emotional disorder, panic attack, agitation, delirium, and obsessive thoughts. Other neuropsychiatric reactions reported in adult clinical trials in patients with narcolepsy administered immediate-release sodium oxybate and in the postmarketing setting for immediate-release sodium oxybate include hallucinations, paranoia, psychosis, aggression, and agitation. In a clinical trial in pediatric patients administered immediate-release sodium oxybate, neuropsychiatric reactions including acute psychosis, confusion, and anxiety were reported. The emergence or increase in the occurrence of behavioral or psychiatric events in patients taking LUMRYZ should be carefully monitored.

Parasomnias
Parasomnias can occur in patients taking LUMRYZ. Sleepwalking, defined as confused behavior occurring at night and at times associated with wandering, was reported in 3% of 107 adult patients with narcolepsy treated with LUMRYZ. No patients treated with LUMRYZ discontinued due to sleepwalking. Episodes of sleepwalking should be fully evaluated and appropriate interventions considered.

Use in Patients Sensitive to High Sodium Intake
LUMRYZ has a high sodium content. In patients sensitive to sodium intake (eg, those with heart failure, hypertension, or renal impairment), consider the amount of daily sodium intake in each dose of LUMRYZ.

MOST COMMON ADVERSE REACTIONS
Most common adverse reactions (incidence ≥5% and greater than placebo) reported for any dose of LUMRYZ in a trial of adults with narcolepsy were nausea, dizziness, enuresis, headache, and vomiting. Similarly, in a trial of pediatric narcolepsy patients receiving immediate-release sodium oxybate, the most commonly observed adverse reactions (incidence ≥5%) were nausea, enuresis, vomiting, headache, decreased weight, decreased appetite, dizziness, and sleepwalking.

ADDITIONAL ADVERSE REACTIONS
Additional adverse reactions that occurred in ≥2% of adult patients with narcolepsy treated with LUMRYZ and were more frequent in the LUMRYZ treatment group than with placebo were vomiting, nausea, decreased weight, decreased appetite, dizziness, somnolence, headache, enuresis, anxiety, and somnambulism.

DRUG INTERACTIONS
LUMRYZ is contraindicated for use in combination with alcohol or sedative hypnotics. Use of other CNS depressants may potentiate the CNS-depressant effects of LUMRYZ.

PREGNANCY AND LACTATION
There are no adequate data on the developmental risk associated with the use of sodium oxybate in pregnant women. LUMRYZ should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. GHB is excreted in human milk after oral administration of sodium oxybate. There is insufficient information on the risk to a breastfed infant, and there is insufficient information on milk production in nursing mothers. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for LUMRYZ and any potential adverse effects on the breastfed infant from LUMRYZ or from the underlying maternal condition.

PEDIATRIC USE
LUMRYZ has not been studied in a pediatric clinical trial for narcolepsy. The safety and effectiveness of LUMRYZ in the treatment of cataplexy or excessive daytime sleepiness in pediatric patients 7 years of age and older with narcolepsy is supported by evidence from a double-blind, placebo-controlled, randomized-withdrawal study of immediate-release sodium oxybate. Safety and effectiveness of LUMRYZ in pediatric patients below the age of 7 years have not been established.

GERIATRIC USE
Dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

HEPATIC IMPAIRMENT
LUMRYZ should not be initiated in patients with hepatic impairment because appropriate dosage adjustments for initiation cannot be made with the available dosage strengths. Patients with hepatic impairment who have been titrated to a maintenance dosage of another oxybate product can be switched to LUMRYZ if the appropriate dosage strength is available.

DEPENDENCE AND TOLERANCE
There have been case reports of withdrawal, ranging from mild to severe, following discontinuation of illicit use of GHB at frequent repeated doses (18 g to 250 g per day) in excess of the recommended dosage range. Signs and symptoms of GHB withdrawal following abrupt discontinuation included insomnia, restlessness, anxiety, psychosis, lethargy, nausea, tremor, sweating, muscle cramps, tachycardia, headache, dizziness, rebound fatigue and sleepiness, confusion, and, particularly in the case of severe withdrawal, visual hallucinations, agitation, and delirium. These symptoms generally abated in three (3) to fourteen (14) days. In cases of severe withdrawal, hospitalization may be required. The discontinuation effects of LUMRYZ have not been systematically evaluated in controlled clinical trials.

Tolerance to LUMRYZ has not been systematically studied in controlled clinical trials. There have been some case reports of symptoms of tolerance developing after illicit use at dosages far in excess of the recommended LUMRYZ dosage regimen.

Please see full Prescribing Information, including BOXED Warning.

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 announcement 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 LUMRYZ; and plans and expectations regarding submission of an sNDA for LUMRYZ for the treatment of IH. 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 high degrees 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 an sNDA for LUMRYZ for the treatment of IH will be submitted in a timely manner; once an sNDA is submitted, whether the clinical results for LUMRYZ for the treatment of IH will meet the regulatory requirements for approval by the FDA; whether the clinical results for LUMRYZ will be predictive of future clinical results or real-world results; whether the FDA agrees with the company's regulatory approval strategies; whether LUMRYZ could be shown to be ineffective or unsafe; 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] 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).

[2] PGI-C: Self-administered, single item questionnaire assessing how a patient's condition has changed on a 7-point scale (very much worse, much worse, minimally worse, no change, minimally improved, much improved, very much improved). The key secondary endpoint analysis examined the proportion of subjects who reported worsening of their condition between the end of the stable dose period to the end of the double-blind randomized withdrawal period.

[3] IHSS: Self-administered, 14-item questionnaire (score range: 0-50) that assesses the frequency, intensity and consequences of 3 IH symptoms (excessive daytime sleepiness, prolonged nighttime sleep, and sleep inertia), with higher scores indicating greater severity of IH symptoms over the past month.

[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. Prevalence of narcolepsy and other sleep disorders and frequency of diagnostic tests from 2013-2016 in insured patients actively seeking care. J Clin Sleep Med. 16:1255 (2020).

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