Alkermes Showcases Research From Psychiatry and Sleep Portfolios at the Neuroscience Education Institute Fall Congress

November 5, 2026

– Real-World Assessment of Impact of Initiating LYBALVI® (olanzapine and samidorphan) on Acute Care Events in Patients with Schizophrenia or Bipolar I Disorder and Comorbid Alcohol Use Disorder –

– Results from the ASPIRE Study Exploring Associations Between Depression and Disease Burden in Adults Living with Narcolepsy and Idiopathic Hypersomnia –

DUBLIN--(BUSINESS WIRE)--Nov. 5, 2026-- Alkermes plc (Nasdaq: ALKS) today announced plans to present data from across its psychiatry and sleep medicine portfolios at the Neuroscience Education Institute (NEI) Fall Congress, taking place Nov. 5-8, 2026 in Colorado Springs, Colo. The company will present data related to LYBALVI® (olanzapine and samidorphan), ARISTADA® (aripiprazole lauroxil) and LUMRYZ® (sodium oxybate) extended-release oral suspension, as well as alixorexton, the company's 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).

"As we wrap up a year of robust scientific exchange across the globe, Alkermes is proud of our continued contributions to expanding the body of evidence in neuroscience and progressing care for people living with complex and difficult-to-treat psychiatric and neurological disorders," said Craig Hopkinson, M.D. (MBChB), Chief Medical Officer and Executive Vice President, Research & Development at Alkermes. "As a company with an industry-leading portfolio in both psychiatry and sleep, we are especially proud of the work our team has done to understand the real-world experiences of people living with schizophrenia, bipolar I, narcolepsy and idiopathic hypersomnia, as well as the real-world impact of our medicines. This research is essential in informing healthcare providers' complex clinical decision making and supporting patients as they navigate their diagnosis and treatment journeys."

Highlights of accepted presentations include:

- Results of a real-world assessment of acute care events—including inpatient admissions and emergency department visits —among patients living with schizophrenia or bipolar I disorder and comorbid alcohol use disorder in the 12 months before and after initiating LYBALVI.
- A plain language summary explaining the combination of olanzapine and samidorphan that constitutes LYBALVI and providing an overview of clinical data supporting its use in the early and sustained treatment of schizophrenia and bipolar I disorder.
- Research exploring associations between depression and disease burden in adults living with narcolepsy and idiopathic hypersomnia using data from the ASPIRE study, a real-world, patient-centered online survey.

In addition to NEI, Alkermes also presented research this fall at Psych Congress, September 15–19 in New Orleans; the Annual Conference of the International Society for Bipolar Disorders (ISBD), September 28-30 in Vancouver, Canada; and the Academy of Managed Care Pharmacy (AMCP) Nexus, October 26–29 in San Diego.

The full list of Alkermes' presentations by meeting is as follows:

Neuroscience Education Institute

- Poster 16: Orexin 2 Receptor Agonists as a Potential Therapeutic Approach to the Treatment of Sleep-wake Disturbance, Fatigue, and Cognitive Deficit in Neuropsychiatric Disease
- Poster 20: Understanding the Lexicon and Experience of "Brain Fog" in Online Narcolepsy and Idiopathic Hypersomnia Communities: A Social Listening Analysis
- Poster 34: Participant-Reported Cognitive Function and Fatigue in Participants with Narcolepsy Type 2 Treated With Alixorexton, an Orexin 2 Receptor Agonist, in the Vibrance-2 Study
- Poster 35: Alixorexton Improved Patient-Reported Cognitive Functioning and Fatigue in Participants with Narcolepsy Type 1 in the Vibrance-1 Study
- Poster 40: Long-Term Safety and Efficacy of Olanzapine/Samidorphan in a Subgroup of Early-in-Illness Patients
- Poster 41: Use of an Aripiprazole Lauroxil Injection Administered Once Every Month, 6 Weeks, or 2 Months in People With Schizophrenia: A Clinician-Focused Summary of Study Data
- Poster 42: Olanzapine and Samidorphan Combination For Early and Sustained Treatment of Schizophrenia and Bipolar I Disorder: A Plain Language Summary
- Poster 48: Inpatient Initiation of the Long-Acting Injectable Antipsychotic Aripiprazole Lauroxil for the Treatment of Acute Exacerbations of Schizophrenia
- Poster 49: Safety and Efficacy of Aripiprazole Lauroxil in an Outpatient Setting After Initiation During Hospitalization for an

Acute Exacerbation of Schizophrenia
- Poster 60: Real-World Persistence on Olanzapine/Samidorphan Versus Other Oral Second-Generation Antipsychotics in Patients With Schizophrenia
- Poster 61: Acute Care Events Following Initiation of Combined Olanzapine/Samidorphan Among Patients With Schizophrenia or Bipolar I Disorder and Comorbid Alcohol Use Disorder
- Poster 76: Nighttime Symptom Experience and Treatment Challenges: Perspectives From People With Narcolepsy
- Poster 102: Association Between Depression and Disease Burden in Narcolepsy and Idiopathic Hypersomnia: Patient-Centered Results from the ASPIRE Study
- Poster 133: REFRESH Real-World Experience in Narcolepsy: Burden of Twice-Nightly Oxybate and Changes in Symptoms and Quality of Life With Extended-Release, Once-Nightly Sodium Oxybate

Psych Congress

- Poster 22: Inpatient Initiation of the Long-Acting Injectable Antipsychotic Aripiprazole Lauroxil for the Treatment of Acute Exacerbations of Schizophrenia
- Poster 23: Safety and Efficacy of Aripiprazole Lauroxil in an Outpatient Setting After Initiation During Hospitalization for an Acute Exacerbation of Schizophrenia
- Poster 25: Real-World Persistence on Olanzapine/Samidorphan Versus Other Oral Second-Generation Antipsychotics in Patients With Schizophrenia
- Poster 26: Acute Care Events Following Initiation of Olanzapine/Samidorphan Among Patients With Schizophrenia or Bipolar I Disorder and Comorbid Alcohol Use Disorder
- Poster 27: Use of an Aripiprazole Lauroxil Injection Administered Once Every Month, 6 Weeks, or 2 Months in People With Schizophrenia: A Clinician-Focused Summary of Study Data
- Poster 28: Long-Term Safety and Efficacy of Olanzapine/Samidorphan in a Subgroup of Early-in-Illness Patients
- Poster 29: Olanzapine and Samidorphan Combination For Early and Sustained Treatment of Schizophrenia and Bipolar I Disorder: A Plain Language Summary
- Poster 71: Orexin 2 Receptor Agonists as a Potential Therapeutic Approach to the Treatment of Sleep-Wake Disturbance, Fatigue, and Cognitive Deficit in Neuropsychiatric Disease
- Poster 151: Association Between Depression and Disease Burden in Narcolepsy and Idiopathic Hypersomnia: Patient-Centered Results From the ASPIRE Study
- Poster 152: Alixorexton Improved Patient-Reported Cognitive Functioning and Fatigue in Patients With Narcolepsy Type 1 in the Vibrance-1 Study
- Poster 164: Nighttime Symptom Experience and Treatment Challenges: Perspectives From People With Narcolepsy
- Poster 165: REFRESH Real-World Experience in Narcolepsy: Burden of Twice-Nightly Oxybate and Changes in Symptoms and Quality of Life With Extended-Release, Once-Nightly Sodium Oxybate

The Annual Conference of the International Society for Bipolar Disorders

- Poster M99: Healthcare Resource Utilization and Treatment Patterns 12 Months After Initiating Olanzapine/Samidorphan: Subgroup Analysis of Patients With Bipolar I Disorder
- Poster M100: Real-World Comparison of Olanzapine/Samidorphan vs Olanzapine: An Assessment of Treatment Patterns and Acute Care Events Among Patients With Bipolar I Disorder
- T103: Real-World Impact of Olanzapine/Samidorphan on Rates of Relapse Among Young Adults With Schizophrenia or Bipolar I Disorder

Academy of Managed Care Pharmacy (AMCP) Nexus

- Poster 213: Real-World Comparison of Olanzapine/Samidorphan vs Olanzapine: An Assessment of Treatment Patterns and Acute Care Events Among Patients With Schizophrenia or Bipolar I Disorder
- Poster 214: Real-World Persistence on Olanzapine/Samidorphan Versus Other Oral Second-Generation Antipsychotics in Patients With Schizophrenia

About LYBALVI® (olanzapine and samidorphan)

LYBALVI® (olanzapine and samidorphan) is a once-daily, oral atypical antipsychotic drug approved in the U.S. for the treatment of adults with schizophrenia and for the treatment of adults with bipolar I disorder, as a maintenance monotherapy or for the acute treatment of manic or mixed episodes, as monotherapy or as adjunct to lithium or valproate. LYBALVI is a combination of olanzapine, an atypical antipsychotic, and samidorphan, an opioid antagonist, in a single bilayer tablet. LYBALVI is available in fixed dosage strengths composed of 10 mg of samidorphan and 5 mg, 10 mg, 15 mg or 20 mg of olanzapine.

IMPORTANT SAFETY INFORMATION for LYBALVI® (olanzapine and samidorphan)

Boxed Warning: Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. LYBALVI is not approved for the treatment of patients with dementia-related psychosis.

Contraindications: LYBALVI is contraindicated in patients who are using opioids or are undergoing acute opioid withdrawal. If LYBALVI is administered with lithium or valproate, refer to the lithium or valproate Prescribing Information for the contraindications for these products.

Cerebrovascular Adverse Reactions in Elderly Patients with Dementia-Related Psychosis, including stroke, transient ischemia attack, and fatalities. See Boxed Warning.

Precipitation of Severe Opioid Withdrawal in Patients who are Physiologically Dependent on Opioids: LYBALVI can precipitate opioid withdrawal in patients who are dependent on opioids, which can lead to an opioid withdrawal syndrome, sometimes requiring hospitalization. LYBALVI is contraindicated in patients who are using opioids or undergoing acute opioid withdrawal. Prior to initiating LYBALVI, there should be at least a 7-day opioid-free interval from last use of short-acting opioids, and at least a 14-day opioid-free interval from the last use of long-acting opioids. Explain the risks associated with precipitated withdrawal and the importance of giving an accurate account of last opioid use to patients and caregivers.

Vulnerability to Life-Threatening Opioid Overdose: Attempting to overcome opioid blockade with high or repeated doses of exogenous opioids could lead to life-threatening or fatal opioid intoxication, particularly if LYBALVI therapy is interrupted or discontinued, subjecting the patient to high levels of unopposed opioid agonist as the samidorphan blockade wanes. Inform patients of the potential consequences of trying to overcome the opioid blockade and the serious risks of taking opioids concurrently with LYBALVI or while transitioning off LYBALVI. In emergency situations, if a LYBALVI-treated patient requires opioid treatment as part of anesthesia or analgesia, discontinue LYBALVI. Opioids should be administered by properly trained individual(s) and patient should be continuously monitored in a setting equipped and staffed for cardiopulmonary resuscitation. Patients with a history of chronic opioid use prior to treatment with LYBALVI may have decreased opioid tolerance if LYBALVI therapy is interrupted or discontinued. Advise patients that this decreased tolerance may increase the risk of opioid overdose if opioids are resumed at the previously tolerated dosage.

Neuroleptic Malignant Syndrome, a potentially fatal reaction. Signs and symptoms include hyperpyrexia, muscle rigidity, delirium, autonomic instability, elevated creatine phosphokinase, myoglobinuria (and/or rhabdomyolysis), and acute renal failure. Manage with immediate discontinuation, intensive symptomatic treatment, and close monitoring.

Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS), a potentially fatal condition reported with exposure to olanzapine, a component of LYBALVI. Symptoms include a cutaneous reaction (such as rash or exfoliative dermatitis), eosinophilia, fever, and/or lymphadenopathy with systemic complications such as hepatitis, nephritis, pneumonitis, myocarditis, and/or pericarditis. Discontinue if DRESS is suspected.

Metabolic Changes, including hyperglycemia, diabetes mellitus, dyslipidemia, and weight gain. Hyperglycemia, in some cases extreme and associated with ketoacidosis or hyperosmolar coma or death, has been reported in patients treated with atypical antipsychotics. Any patient treated with LYBALVI should be monitored for symptoms of hyperglycemia including polydipsia, polyuria, polyphagia, and weakness. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients required anti-diabetic treatment despite discontinuation of the suspect drug. Measure weight and assess fasting glucose and lipids when initiating LYBALVI and monitor periodically.

Tardive Dyskinesia (TD): Risk of developing TD (a syndrome of potentially irreversible, involuntary, dyskinetic movements) and the likelihood it will become irreversible increases with the duration of treatment and the cumulative dose. The syndrome can develop after a relatively brief treatment period, even at low doses, or after discontinuation. Given these considerations, LYBALVI should be prescribed in a manner that is most likely to reduce the risk of tardive dyskinesia. If signs and symptoms of TD appear, drug discontinuation should be considered.

Orthostatic Hypotension and Syncope: Monitor orthostatic vital signs in patients who are vulnerable to hypotension, patients with known cardiovascular disease, and patients with cerebrovascular disease.

Falls: LYBALVI may cause somnolence, postural hypotension, and motor and sensory instability, which may lead to falls, and consequently, fractures or other injuries. Assess patients for risk when using LYBALVI.

Leukopenia, Neutropenia, and Agranulocytosis (including fatal cases): Perform complete blood counts in patients with a history of a clinically significant low white blood cell (WBC) count or history of leukopenia or neutropenia. Discontinue LYBALVI if clinically significant decline in WBC occurs in the absence of other causative factors.

Dysphagia: Use LYBALVI with caution in patients at risk for aspiration.

Seizures: Use LYBALVI with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: Because LYBALVI may cause somnolence, and may impair judgment, thinking, or motor skills, caution patients about operating hazardous machinery, including motor vehicles, until they are certain that LYBALVI does not affect them adversely.

Body Temperature Dysregulation: Use LYBALVI with caution in patients who may experience conditions that increase core body temperature (e.g., strenuous exercise, extreme heat, dehydration, or concomitant use with anticholinergics).

Anticholinergic (Antimuscarinic) Effects: Olanzapine, a component of LYBALVI, was associated with constipation, dry mouth, and tachycardia. Use LYBALVI with caution with other anticholinergic medications and in patients with urinary retention, prostatic hypertrophy, constipation, paralytic ileus or related conditions. In postmarketing experience, the risk for severe adverse reactions (including fatalities) was increased with concomitant use of anticholinergic medications.

Hyperprolactinemia: LYBALVI elevates prolactin levels. Galactorrhea, amenorrhea, gynecomastia, and impotence have been reported in patients receiving prolactin-elevating compounds.

Risks Associated with Combination Treatment with Lithium or Valproate: If LYBALVI is administered with lithium or valproate, refer to the lithium or valproate Prescribing Information for a description of the risks for these products.

Interference with Laboratory Tests for Opioid Detection: LYBALVI may cause false positive results with urinary immunoassay methods for detecting opioids. Use an alternative analytical technique (e.g., chromatographic methods) to confirm positive opioid urine drug screen results.

Most Common Adverse Reactions observed in clinical trials were:

- *Schizophrenia (LYBALVI):* weight increased, somnolence, dry mouth, and headache
- *Bipolar I Disorder, Manic or Mixed Episodes (olanzapine):* somnolence, dry mouth, dizziness, asthenia, constipation, dyspepsia, increased appetite, and tremor
- *Bipolar I Disorder, Manic or Mixed Episodes, adjunct to lithium or valproate (olanzapine):* dry mouth, weight gain, increased appetite, dizziness, back pain, constipation, speech disorder, increased salivation, amnesia, paresthesia

Concomitant Medication: LYBALVI is contraindicated in patients who are using opioids or undergoing acute opioid withdrawal. Concomitant use of LYBALVI is not recommended with strong CYP3A4 inducers, levodopa and dopamine agonists. Reduce dosage of LYBALVI when using with strong CYP1A2 inhibitors. Increase dosage of LYBALVI with CYP1A2 inducers. Use caution with diazepam, alcohol, other CNS acting drugs, or in patients receiving anticholinergic (antimuscarinic) medications. Monitor blood pressure and reduce dosage of antihypertensive drug in accordance with its approved product labeling.

Pregnancy: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure. Advise patients to notify their healthcare provider if they become pregnant or intend to become pregnant during treatment with LYBALVI. Inform patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to LYBALVI during pregnancy.

Renal Impairment: LYBALVI is not recommended for patients with end-stage renal disease (eGFR of <15 mL/minute/1.73 m^2).

Please see full Prescribing Information, including Boxed Warning, for LYBALVI.

About ARISTADA® (aripiprazole lauroxil) Extended-Release Injectable Suspension, for Intramuscular Use

ARISTADA® is indicated for the treatment of schizophrenia in adults. ARISTADA is in injectable atypical antipsychotic approved in four dose strengths and three dosing durations for the treatment of schizophrenia in adults (441 mg, 662 mg or 882 mg monthly, 882 mg once every six weeks and 1064 mg once every two months). Once in the body, ARISTADA converts to aripiprazole.

About ARISTADA INITIO® (aripiprazole lauroxil) Extended-Release Injectable Suspension, for Intramuscular Use

ARISTADA INITIO®, in combination with oral aripiprazole, is indicated for the initiation of ARISTADA when used for the treatment of schizophrenia in adults.

IMPORTANT SAFETY INFORMATION for ARISTADA INITIO® (aripiprazole lauroxil) and ARISTADA® (aripiprazole lauroxil)

Boxed Warning: INCREASED MORTALITY IN ELDERLY PATIENTS WITH DEMENTIA-RELATED PSYCHOSIS

Elderly patients with dementia-related psychosis treated with antipsychotic drugs are at an increased risk of death. ARISTADA INITIO and ARISTADA are not approved for the treatment of patients with dementia-related psychosis.

Contraindication: Known hypersensitivity reaction to aripiprazole. Reactions have ranged from pruritus/urticaria to anaphylaxis.

Cerebrovascular Adverse Reactions, Including Stroke: Increased incidence of cerebrovascular adverse reactions (e.g., stroke, transient ischemic attack), including fatalities, have been reported in placebo-controlled trials of elderly patients with dementia-related psychosis treated with risperidone, aripiprazole, and olanzapine. ARISTADA INITIO and ARISTADA are not approved for the treatment of patients with dementia-related psychosis.

Potential for Dosing and Medication Errors: Medication errors, including substitution and dispensing errors, between ARISTADA INITIO and ARISTADA could occur. ARISTADA INITIO is intended for single administration in contrast to ARISTADA which is administered monthly, every 6 weeks, or every 8 weeks. Do not substitute ARISTADA INITIO for ARISTADA because of differing pharmacokinetic profiles.

Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex may occur with administration of antipsychotic drugs, including ARISTADA INITIO and ARISTADA. Clinical manifestations of NMS include hyperpyrexia, muscle rigidity, altered mental status, and evidence of autonomic instability (irregular pulse or blood pressure, tachycardia, diaphoresis, and cardiac dysrhythmia). Additional signs may include elevated creatine phosphokinase, myoglobinuria (rhabdomyolysis), and acute renal failure. The management of NMS should include: 1) immediate discontinuation of antipsychotic drugs and other drugs not essential to concurrent therapy; 2) intensive symptomatic treatment and medical monitoring; and 3) treatment of any concomitant serious medical problems for which specific treatments are available.

Tardive Dyskinesia (TD): The risk of developing TD (a syndrome of abnormal, involuntary movements) and the potential for it to become irreversible are believed to increase as the duration of treatment and the total cumulative dose of antipsychotic increase. The syndrome can develop, although much less commonly, after relatively brief treatment periods at low doses. Prescribing antipsychotics should be consistent with the need to minimize TD. Discontinue ARISTADA if clinically appropriate. TD may remit, partially or completely, if antipsychotic treatment is withdrawn.

Metabolic Changes: Atypical antipsychotic drugs have been associated with metabolic changes that include:

- **Hyperglycemia/Diabetes Mellitus:** Hyperglycemia, in some cases extreme and associated with ketoacidosis, coma, or death, has been reported in patients treated with atypical antipsychotics. There have been reports of hyperglycemia in patients treated with oral aripiprazole. Patients with diabetes should be regularly monitored for worsening of glucose control; those with risk factors for diabetes should undergo baseline and periodic fasting blood glucose testing. Any patient treated with atypical antipsychotics should be monitored for symptoms of hyperglycemia, including polydipsia, polyuria, polyphagia, and weakness. Patients who develop symptoms of hyperglycemia should also undergo fasting blood glucose testing. In some cases, hyperglycemia has resolved when the atypical antipsychotic was discontinued; however, some patients require continuation of antidiabetic treatment despite discontinuation of the suspect drug.
- **Dyslipidemia:** Undesirable alterations in lipids have been observed in patients treated with atypical antipsychotics.
- **Weight Gain:** Weight gain has been observed with atypical antipsychotic use. Clinical monitoring of weight is recommended.

Pathological Gambling and Other Compulsive Behaviors: Compulsive or uncontrollable urges to gamble have been reported with use of aripiprazole. Other compulsive urges less frequently reported include sexual urges, shopping, binge eating and other impulsive or compulsive behaviors which may result in harm for the patient and others if not recognized. Closely monitor patients and consider dose reduction or stopping aripiprazole if a patient develops such urges.

Orthostatic Hypotension: Aripiprazole may cause orthostatic hypotension which can be associated with dizziness, lightheadedness, and tachycardia. Monitor heart rate and blood pressure, and warn patients with known cardiovascular or cerebrovascular disease and risk of dehydration and syncope.

Falls: Antipsychotics including ARISTADA INITIO and ARISTADA may cause somnolence, postural hypotension or motor and sensory instability which may lead to falls and subsequent injury. Upon initiating treatment and recurrently, complete fall risk assessments as appropriate.

Leukopenia, Neutropenia, and Agranulocytosis: Leukopenia, neutropenia and agranulocytosis have been reported with antipsychotics. Monitor complete blood count in patients with pre-existing low white blood cell count (WBC)/absolute neutrophil count or history of drug-induced leukopenia/neutropenia. Discontinue ARISTADA INITIO and/or ARISTADA at the first sign of a clinically significant decline in WBC and in severely neutropenic patients.

Seizures: Use with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: ARISTADA INITIO and ARISTADA may impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are certain therapy with ARISTADA INITIO and/or ARISTADA does not affect them adversely.

Body Temperature Regulation: Disruption of the body's ability to reduce core body temperature has been attributed to antipsychotic agents. Advise patients regarding appropriate care in avoiding overheating and dehydration. Appropriate care is advised for patients who may exercise strenuously, may be exposed to extreme heat, receive concomitant medication with anticholinergic activity, or are subject to dehydration.

Dysphagia: Esophageal dysmotility and aspiration have been associated with antipsychotic drug use; use caution in patients at risk for aspiration pneumonia.

Concomitant Medication: ARISTADA INITIO is only available at a single strength as a single-dose pre-filled syringe, so dosage adjustments are not possible. Avoid use in patients who are known CYP2D6 poor metabolizers or taking strong CYP3A4 inhibitors, strong CYP2D6 inhibitors, or strong CYP3A4 inducers, antihypertensive drugs or benzodiazepines.

Depending on the ARISTADA dose, adjustments may be recommended if patients are 1) known as CYP2D6 poor metabolizers and/or 2) taking strong CYP3A4 inhibitors, strong CYP2D6 inhibitors, or strong CYP3A4 inducers for greater than 2 weeks. Avoid use of ARISTADA 662 mg, 882 mg, or 1064 mg for patients taking both strong CYP3A4 inhibitors and strong CYP2D6 inhibitors. (See Table 4 in the ARISTADA full Prescribing Information.)

Commonly Observed Adverse Reactions: In pharmacokinetic studies the safety profile of ARISTADA INITIO was generally consistent with that observed for ARISTADA**.** The most common adverse reaction (≥5% incidence and at least twice the rate of placebo reported by patients treated with ARISTADA 441 mg and 882 mg monthly) was akathisia.

Injection Site Reactions: In pharmacokinetic studies evaluating ARISTADA INITIO, the incidences of injection site reactions with ARISTADA INITIO were similar to the incidence observed with ARISTADA. Injection site reactions were reported by 4%, 5%, and 2% of patients treated with 441 mg ARISTADA (monthly), 882 mg ARISTADA (monthly), and placebo, respectively. Most of these were injection site pain and associated with the first injection and decreased with each subsequent injection. Other injection site reactions (induration, swelling, and redness) occurred at less than 1%.

Dystonia: Symptoms of dystonia, prolonged abnormal contractions of muscle groups, may occur in susceptible individuals during the first days of treatment and at low doses.

Pregnancy/Nursing: Neonates exposed to antipsychotic drugs, including ARISTADA INITIO and ARISTADA, during the third trimester of pregnancy are at risk for extrapyramidal and/or withdrawal symptoms. Advise patients to notify their healthcare provider of a known or suspected pregnancy. Inform patients that there is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ARISTADA INITIO and/or ARISTADA during pregnancy. Aripiprazole is present in human breast milk. Aripiprazole exposure during pregnancy and/or the postpartum period may decrease milk supply. Monitor the breastfed infant for dehydration and lack of appropriate weight gain. The benefits of breastfeeding should be considered along with the mother's clinical need for ARISTADA INITIO and/or ARISTADA and any potential adverse effects on the infant from ARISTADA INITIO and/or ARISTADA or from the underlying maternal condition.

Please see full Prescribing Information, including Boxed Warning, for ARISTADA INITIO and ARISTADA.

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. LUMRYZ is not currently approved by regulatory authorities for the treatment of idiopathic hypersomnia (IH).

IMPORTANT SAFETY INFORMATION for LUMRYZ (sodium oxybate)

Boxed 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 for LUMRYZ.

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.[1] Targeting the orexin system may address excessive daytime sleepiness across hypersomnolence disorders,

whether or not orexin deficiency is the underlying cause of disease.[2]

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 has established a leadership position in orexin biology and is advancing a portfolio of investigational orexin 2 receptor agonists for narcolepsy, idiopathic hypersomnia and other psychiatric and neurological disorders, including attention-deficit hyperactivity disorder (ADHD), major depressive disorder (MDD) 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.

[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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