Alkermes Presents New Data From Psychiatry Portfolio at Virtual 2021 Congress of the Schizophrenia International Research Society

April 20, 2021

- New Exploratory Analyses Presented From ENLIGHTEN-2 Study of LYBALVI™ in Patients With Schizophrenia -

DUBLIN, April 20, 2021 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today announced the presentation of new research from its psychiatry portfolio at the 2021 Congress of the Schizophrenia International Research Society (SIRS), taking place virtually April 17-21, 2021.

The company's presentations included new exploratory analyses from the phase 3 ENLIGHTEN-2 study of olanzapine/samidorphan (LYBALVI™), formerly referred to as ALKS 3831, including:

- Results from prespecified subgroup analyses evaluating olanzapine/samidorphan's effect on weight gain across several patient subgroups, including those known to be at higher risk for weight gain with olanzapine, based on sex, race, age and baseline body mass index (BMI).
- New findings from post hoc analyses assessing the effects of olanzapine/samidorphan compared to olanzapine across multiple cardiometabolic risk factors, including blood pressure, BMI and metabolic syndrome.

In addition, the company presented data from an exploratory analysis within the phase 3b ALPINE (Aripiprazole Lauroxil and Paliperidone palmitate: INitiation Effectiveness) study for ARISTADA® (aripiprazole lauroxil), evaluating the relationship between baseline handwriting kinematics and treatment response. Results suggest that handwriting kinematic measures may serve as a biomarker for anticipating response to antipsychotic treatment.

"Alkermes is committed to advancing research in mental health and we were pleased to present new data from our psychiatry portfolio at this year's SIRS congress," said Craig Hopkinson, M.D., Executive Vice President, Research & Development and Chief Medical Officer at Alkermes. "In particular, results from new exploratory analyses from our phase 3 ENLIGHTEN-2 study provide valuable insight into LYBALVI's potential clinical utility. We are excited to share this data with the clinical community as part of our ongoing commitment to developing new treatment options for people living with serious mental illness."

The full list of Alkermes' presentations at SIRS includes:

LYBALVI

- **Oral Presentation:** Olanzapine/Samidorphan Mitigates Weight Gain Across Subgroups of Patients Known to Be at Increased Risk for Weight Gain With Olanzapine Treatment
- **Poster #S2:** Reduced Risk Across Multiple Cardiometabolic Risk Factors With OLZ/SAM Compared With Olanzapine: Results From a 24-Week Phase 3 Study
- **Poster #S16:** Long-Term Safety of Olanzapine and Samidorphan Combination in Patients With Schizophrenia: Pooled Analyses From Phase 2 and 3 Studies
- **Poster #M22:** Long-Term Weight and Metabolic Effects of Olanzapine and Samidorphan Combination in Patients With Schizophrenia: Pooled Analyses From Phase 3 Studies
- **Poster #T17:** Long-Term Antipsychotic Efficacy of Olanzapine and Samidorphan Combination in Patients With Schizophrenia: Pooled Analyses From Phase 3 Studies
- **Poster #T92:** In Vivo Characterization of the Opioid Receptor Binding Profiles of Samidorphan and Naltrexone in Rats: Comparisons at Clinically Relevant Concentrations

ARISTADA

- **Poster #T19:** Handwriting Kinematics in Schizophrenia Patients Treated with Long-Acting Injectable Atypical Antipsychotics: Results from the ALPINE Study

For more information, please visit the SIRS website at: www.schizophreniaresearchsociety.org.

About olanzapine/samidorphan (LYBALVI™)
LYBALVI is an investigational, novel, once-daily, oral atypical antipsychotic drug candidate for the treatment of adults with schizophrenia and for the treatment of adults with bipolar I disorder. LYBALVI is composed of samidorphan, a novel, new molecular entity, co-formulated with the established antipsychotic agent, olanzapine, in a single bilayer tablet.

About ARISTADA®
ARISTADA is an injectable atypical antipsychotic approved in four doses and three dosing durations for the treatment of schizophrenia (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®
ARISTADA INITIO, in combination with a single 30 mg dose of oral aripiprazole, can be used to initiate onto any dose of ARISTADA. The first ARISTADA dose may be administered on the same day as the ARISTADA INITIO regimen or up to 10 days thereafter.

INDICATION and IMPORTANT SAFETY INFORMATION for ARISTADA INITIO® (aripiprazole lauroxil) and ARISTADA® (aripiprazole lauroxil) extended-release injectable suspension, for intramuscular use

INDICATION

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

ARISTADA is indicated for the treatment of schizophrenia in adults.

IMPORTANT SAFETY INFORMATION

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: May cause extrapyramidal and/or withdrawal symptoms in neonates with third trimester exposure. 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. 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 Alkermes

Alkermes plc is a fully-integrated, global biopharmaceutical company developing innovative medicines in the fields of neuroscience and oncology. The company has a portfolio of proprietary commercial products focused on addiction and schizophrenia, and a pipeline of product candidates in development for schizophrenia, bipolar I disorder, neurodegenerative disorders, and cancer. Headquartered in Dublin, Ireland, Alkermes plc has an R&D center in Waltham, Massachusetts; a research and manufacturing facility in Athlone, Ireland; and a manufacturing facility in Wilmington, 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 LYBALVI and results from exploratory analyses from the ENLIGHTEN-2 study for LYBALVI and the ALPINE study for ARISTADA. 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 the results of the company's clinical development activities, including exploratory analyses, are predictive of real-world results or of results in subsequent clinical trials or analyses; whether the data contained in the company's new drug application for LYBALVI will meet the regulatory requirements for approval by the FDA; potential changes in the cost, scope or timelines for LYBALVI development or regulatory activities, including changes relating to the COVID-19 pandemic; and those risks described in the Alkermes plc Annual Report on Form 10-K for the year ended Dec. 31, 2020 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. The information contained in this press release is provided by the company as of the date hereof, and, except as required by law, the company disclaims any intention or responsibility for updating or revising any forward-looking information contained in this press release.

ARISTADA® and ARISTADA INITIO® are registered trademarks of Alkermes Pharma Ireland Limited; LYBALVI ™is a trademark of Alkermes Pharma Ireland Limited.

Alkermes Contacts:
For Investors: Sandy Coombs +1 781 609 6377
For Media: Marisa Borgasano +1 781 609 6659

View original content to download multimedia:http://www.prnewswire.com/news-releases/alkermes-presents-new-data-from-psychiatry-portfolio-at-virtual-2021-congress-of-the-schizophrenia-international-research-society-301272600.html

SOURCE Alkermes plc