Patients Switched to Alkermes' ARISTADA® Showed Significant Improvement in Schizophrenia Symptoms After Inadequate Response or Intolerance to INVEGA SUSTENNA®

September 18, 2017

— Data Presented at 30th Annual Psych Congress —

DUBLIN--(BUSINESS WIRE)--Sep. 18, 2017-- Alkermes plc (NASDAQ: ALKS) today announced positive topline results from a phase 4 clinical study of ARISTADA® (aripiprazole lauroxil) extended-release injectable suspension for the treatment of schizophrenia. Data from the open-label prospective study showed that switching to treatment with ARISTADA led to statistically significant and clinically meaningful improvement in schizophrenia symptoms at the end of the six-month study in patients who had experienced inadequate response or intolerance to INVEGA SUSTENNA® (paliperidone palmitate). Results from the study were presented at the 30th Annual Psych Congress (Psych Congress) in New Orleans.

"These data further add to the substantial body of evidence supporting the differentiated efficacy and safety profile of ARISTADA in the treatment of this chronic and debilitating disease," said Elliot Ehrich, M.D., Executive Vice President, Research and Development of Alkermes. "Driven by scientific and economic outcomes data, the recognition of the benefits of long-acting atypical antipsychotics continues to grow within the medical community. Alkermes remains committed to innovating in this disease area where there remains significant unmet medical need and suffering."

"The results from this study highlight the potential clinical benefits of switching to ARISTADA for patients who experience inadequate response or intolerance to INVEGA SUSTENNA, a medicine widely recognized in the clinical community as a powerful antipsychotic agent," stated Steven Potkin, M.D., Professor Emeritus of Psychiatry and Human Behavior at the University of California, Irvine. "Patients and their healthcare providers need options with different pharmacology when choosing a treatment regimen, and these data further support the use of ARISTADA in the treatment of schizophrenia."

Data from the phase 4 study showed that treatment with a flexible dose regimen of ARISTADA 441 mg, 662 mg or 882 mg monthly, or 882 mg every six weeks resulted in significant improvement in schizophrenia symptoms at six months, as measured by the Brief Psychiatric Rating Scale (BPRS) and the Clinical Global Impressions-Severity (CGI-S) scale. The mean BPRS total score decreased from 37.6 to 32.7 ($p=0.002$), and the mean CGI-S score decreased from 3.9 to 3.4 ($p<0.001$) between baseline and the six-month endpoint. Thirty-four patients (68%) completed the six-month study. The most commonly reported adverse events in the study were psychotic disorders, anxiety and suicidal ideation.

"These important data underscore the unique attributes of ARISTADA in the market. With a strong efficacy and safety profile, along with an unmatched range of doses and durations, ARISTADA has the potential to become a market leader in the growing long-acting atypical antipsychotic class," said Richard Pops, Chief Executive Officer of Alkermes. "We continue to make progress with the ARISTADA launch and look forward to helping patients living with schizophrenia manage their disease with additional flexibility."

A poster on the data, titled, "Switching Patients With Schizophrenia From Paliperidone Palmitate to Aripiprazole Lauroxil: A 6-month Prospective Open-Label Study," was presented at Psych Congress on Sept. 17 and 18, 2017. For more information, please visit the Psych Congress website at http://www.psychcongress.com/psychcongress/.

Study Design

The six-month, open-label, single-arm phase 4 study was designed to assess the efficacy, safety and tolerability of ARISTADA (441 mg, 662 mg, or 882 mg monthly; or 882 mg every six weeks) in 50 symptomatic, clinically stable patients with schizophrenia who had an inadequate response or intolerance to INVEGA SUSTENNA. Efficacy was evaluated in the study based on BPRS and CGI-S scores from commencement of treatment with ARISTADA through the end of the treatment period. Safety and tolerability were evaluated based on reported adverse events.

Patients enrolled in the study had received at least three consecutive doses of INVEGA SUSTENNA prior to screening, with nearly half of the patients entering the study having received the highest dose of INVEGA SUSTENNA 234 mg. The primary reason for discontinuation of INVEGA SUSTENNA was insufficient control of positive symptoms (n=33, 66%). Eight patients (16%) switched due to breakthrough negative symptoms, and nine patients (18%) switched due to intolerance to INVEGA SUSTENNA.

About Schizophrenia

Schizophrenia is a chronic, severe and disabling brain disorder. The disease is marked by positive symptoms (hallucinations and delusions) and negative symptoms (depression, blunted emotions and social withdrawal), as well as by disorganized thinking. An estimated 2.4 million American adults have schizophrenia,[1] with men and women affected equally.

About ARISTADA®

ARISTADA is an injectable atypical antipsychotic with one-month, six-week and two-month dosing options for the treatment of schizophrenia. Oral aripiprazole should be administered for 21 consecutive days in conjunction with the first injection of ARISTADA. Once in the body, ARISTADA converts to aripiprazole.

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

INDICATION

ARISTADA is indicated for the treatment of schizophrenia.

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 is 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 is not approved for the treatment of patients with dementia-related psychosis.

Neuroleptic Malignant Syndrome (NMS): A potentially fatal symptom complex sometimes referred to as NMS may occur with administration of antipsychotic drugs, including 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 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 ARISTADA 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 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. Patients with a history of clinically significant low white blood cell count (WBC)/absolute neutrophil count (ANC) and history of drug-induced leukopenia/neutropenia should have frequent complete blood count (CBC) during the first few months of receiving ARISTADA. Consider discontinuation of ARISTADA at the first sign of a clinically significant decline in WBC count in the absence of other causative factors. Monitor patients with clinically significant neutropenia for fever or other symptoms or signs of infection and treat promptly if such symptoms or signs occur. Discontinue ARISTADA in patients with severe neutropenia (absolute neutrophil count <1000/mm^3) and follow their WBC until recovery.

Seizures: ARISTADA should be used with caution in patients with a history of seizures or with conditions that lower the seizure threshold.

Potential for Cognitive and Motor Impairment: ARISTADA may impair judgment, thinking, or motor skills. Patients should be cautioned about operating hazardous machinery, including automobiles, until they are certain 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: Decreasing the ARISTADA dosage is recommended in patients taking strong CYP3A4 inhibitors and/or strong CYP2D6 inhibitors for longer than 2 weeks. Increasing the ARISTADA dosage from 441 mg to 662 mg is recommended in patients taking CYP3A4 inducers for longer than 2 weeks. No ARISTADA dosage changes are recommended for patients taking CYP450 modulators for less than 2 weeks.

Most Commonly Observed Adverse Reaction: 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: 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 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 and any potential adverse effects on the infant from ARISTADA or from the underlying maternal condition.

Please see FULL PRESCRIBING INFORMATION, including **Boxed Warning**, for ARISTADA.

About Alkermes

Alkermes plc is a fully integrated, global biopharmaceutical company developing innovative medicines for the treatment of central nervous system (CNS) diseases. The company has a diversified commercial product portfolio and a substantial clinical pipeline of product candidates for chronic diseases that include schizophrenia, depression, addiction and multiple sclerosis. 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 and commercial value of ARISTADA for the treatment of schizophrenia. 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 whether results of ARISTADA's development activities are predictive of real-world results and those described under the heading "Risk Factors" in the company's Annual Report on Form 10-K for the year ended Dec. 31, 2016 and Quarterly Reports on Form 10-Q for the quarters ended March 31, 2017 and June 30, 2017 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]National Institutes of Health. *Schizophrenia*. Accessed on Sept. 15, 2017 from https://report.nih.gov/nihfactsheets/ViewFactSheet.aspx?csid=67.

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