



Alkermes to Present Data on Depression and Schizophrenia Portfolios at Upcoming American Society of Clinical Psychopharmacology Annual Meeting

May 23, 2018

-- Long-Term Safety and Clinical Evaluation of Abuse Potential of ALKS 5461 to be Highlighted --

DUBLIN, May 23, 2018 /PRNewswire/ -- [Alkermes plc](#) (Nasdaq: ALKS) today announced that new clinical data will be presented at the American Society of Clinical Psychopharmacology (ASCP) Annual Meeting in Miami, May 29 – June 1, 2018. The poster presentations will highlight data from the company's depression and schizophrenia portfolios, including ALKS 5461, ARISTADA® (aripiprazole lauroxil extended-release injectable suspension) and ALKS 3831.

Depression

Clinical data for ALKS 5461 will be presented, including long-term safety, tolerability and durability of antidepressant effect over a 52-week treatment period in patients with major depressive disorder (MDD). In addition, data from a human abuse potential study conducted in healthy, nondependent opioid users will be presented. In the study, ALKS 5461, a combination of buprenorphine with the mu-opioid receptor antagonist samidorphan, posed a low risk of abuse.

Wednesday, May 30, 2018, 11:15 a.m. – 1:00 p.m. ET

- Poster #W41: "Clinical Evaluation of Abuse Potential of ALKS 5461," will be presented by Sanjay Mathew, M.D., Baylor College of Medicine
- Poster #W31: "ALKS 5461 for Adjunctive Treatment of Major Depressive Disorder: Results From Analyses of U.S. Patients From Three Placebo-Controlled Trials," will be presented by Maurizio Fava, M.D., Massachusetts General Hospital
- Poster #W34: "Long-Term Efficacy, Safety, and Tolerability of Adjunctive ALKS 5461 in Patients With Major Depressive Disorder," will be presented by Michael E. Thase, M.D., Perelman School of Medicine at the University of Pennsylvania

Friday, June 1, 2018, 9:00 a.m. ET

- Oral Presentation: "Optimizing Signal Detection in Antidepressant Clinical Trials: Role of Blinding and Masking," will be presented by William Martin, Ph.D., Alkermes, Inc. during the panel "Optimizing Signal Detection in Psychiatric Clinical Trials"

Schizophrenia

Alkermes will present data related to ARISTADA, including results from a two-year safety study in patients with schizophrenia, and results from a pharmacokinetic and safety study evaluating Aripiprazole Lauroxil NanoCrystal® Dispersion (AL_{NCD}), a novel, investigational product designed for initiation onto ARISTADA. The company will also present results from a phase 2 study of ALKS 3831 in patients with schizophrenia and co-occurring alcohol use disorder.

Wednesday, May 30, 2018, 11:15 a.m. – 1:00 p.m. ET

- Poster #W50: "Long-Term Outcomes With Aripiprazole Lauroxil for the Treatment of Schizophrenia: A Two-Year, Phase 3, Multicenter Extension Study," will be presented by John Lauriello, M.D., University of Missouri

Thursday, May 31, 2018, 12:30 p.m. – 2:00 p.m. ET

- Poster #T52: "Aripiprazole Lauroxil NanoCrystal® Dispersion: A Potential One-Day Initiation Regimen for Long-Acting Aripiprazole Lauroxil," will be presented by David Walling, Ph.D., CNS Network, LLC
- Poster #T53: "A Phase 2, Randomized, Double-Blind Study of ALKS 3831 in Schizophrenia and Co-Occurring Alcohol Use Disorder," will be presented by Bernard Silverman, M.D., Alkermes, Inc.

"Our focused innovation and scientific expertise have put us at the forefront of advancing potential new treatments for central nervous system diseases, and we are pleased to share data on our depression and schizophrenia programs at this important medical meeting," stated Craig Hopkinson, M.D., Chief Medical Officer and Senior Vice President of Medicines Development and Medical Affairs at Alkermes. "We're also excited to present long-term data on ALKS 5461, including safety, tolerability and durability of antidepressant effect for up to 52 weeks in patients with major depressive disorder. We believe ALKS 5461, if approved, could be an important new treatment option for people living with MDD and these data underscore the important safety and efficacy profile of this potential medicine."

For more information, please visit the ASCP website at <http://ascpmeeting.org/>.

About ALKS 5461

ALKS 5461 is a proprietary, investigational, once-daily oral medicine that acts as an opioid system modulator and represents a novel mechanism of action for the adjunctive treatment of major depressive disorder (MDD) in patients with an inadequate response to standard antidepressant therapies. ALKS 5461 is a fixed-dose combination of buprenorphine, a partial mu-opioid receptor agonist and kappa-opioid receptor antagonist, and

samidorphan, a mu-opioid receptor antagonist.

About ALKS 3831

ALKS 3831 is an investigational, novel, once-daily, oral atypical antipsychotic drug candidate for the treatment of schizophrenia. ALKS 3831 is composed of samidorphan, a novel, new molecular entity co-formulated with the established antipsychotic agent, olanzapine, in a single bilayer tablet.

Weight gain is a common and clinically relevant metabolic side effect of atypical antipsychotic medications, and olanzapine, commercially available as ZYPREXA[®], has one of the highest incidences and greatest amounts of weight gain among the widely prescribed products in this class of drugs.¹ ALKS 3831 is designed to provide the strong antipsychotic efficacy of olanzapine and a differentiated safety profile with favorable weight and metabolic properties.

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. Oral aripiprazole should be administered for 21 consecutive days in conjunction with the first injection of ARISTADA. A New Drug Application (NDA) for Aripiprazole Lauroxil NanoCrystal[®] Dispersion (AL_{NCD}), an investigational product designed for initiation onto ARISTADA, is under review by the U.S. Food and Drug Administration (FDA). If approved, administration of AL_{NCD} in conjunction with a single oral dose of 30 mg aripiprazole will provide an alternative to the three weeks of concomitant oral aripiprazole with the first dose of ARISTADA.

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 $<1000/\text{mm}^3$) 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 ($\geq 5\%$ 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 plc

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 therapeutic, clinical and commercial value of our marketed products and development candidates. 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 clinical results for the company's marketed products and development candidates will be predictive of future clinical study results or commercial success; whether ALKS 5461 and AL_{NCD} will be approved by the FDA in a timely manner or at all; and if approved, whether ALKS 5461 and AL_{NCD} will be commercialized successfully; 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, 2017 and Quarterly Report on Form 10-Q for the quarter ended Mar. 31, 2018 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.

ARISTADA® and NanoCrystal® are registered trademarks of Alkermes Pharma Ireland Limited.

ZYPREXA® is a registered trademark of Eli Lilly & Company.

¹ Komossa, K. et al. Olanzapine versus other atypical antipsychotics for schizophrenia. Cochrane Database of Systematic Reviews. 2010, Issue 3. Art. No.: CD006654.

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