Alkermes Announces Achievement of Milestones for CNS Medicines in Proprietary Product and Pipeline Portfolio

December 16, 2015

— Pivotal Programs Initiated for ALKS 3831 for Schizophrenia and ALKS 8700 for Multiple Sclerosis —

— Positive Data Announced From Supportive Study in FORWARD Pivotal Program for ALKS 5461 in Major Depressive Disorder —

— New Patent Issued for ARISTADA™, Extending Protection Into 2033 —

DUBLIN--(BUSINESS WIRE)--Dec. 16, 2015-- Alkermes plc (NASDAQ: ALKS) today announced new developments and milestones related to its proprietary product and late-stage pipeline portfolio of medicines for the treatment of central nervous system (CNS) diseases. The company has initiated pivotal clinical development programs for two of its pipeline candidates: ALKS 3831, a novel, oral atypical antipsychotic drug candidate designed to be a broad-spectrum treatment for schizophrenia, and ALKS 8700, a novel, oral monomethyl fumarate (MMF) drug candidate for the treatment of multiple sclerosis (MS).

Alkermes also announced positive topline results from a recently-completed human abuse potential study of ALKS 5461, a once-daily, oral investigational medicine with a novel mechanism of action for the adjunctive treatment of major depressive disorder. Additionally, the company announced a newly issued patent expiring in 2033 that extends patent coverage for ARISTADA™ (aripiprazole lauroxil) extended-release injectable suspension for the treatment of schizophrenia.

“As we near the end of 2015, Alkermes is aggressively executing on our strategy to build a leading biopharmaceutical company for CNS innovation, characterized by one of the most exciting late-stage CNS pipelines in the industry,” said Richard Pops, Chief Executive Officer of Alkermes. “This is a particularly productive time in the company's history, and looking ahead to 2016, we expect significant value-creating milestones as we continue to advance our late-stage pipeline and grow our commercial products, ARISTADA and VIVITROL.”

“We are pleased with the rapid progress of our late-stage pipeline, with ALKS 5461 nearing completion of its pivotal phase 3 program, and ALKS 3831 and ALKS 8700 entering registration trials,” said Elliot Ehrich, M.D., Chief Medical Officer of Alkermes. “We have successfully hit the key milestones we set out to achieve in 2015 and look forward to data from the core efficacy studies of ALKS 5461 in early 2016.”

Highlights of Milestone Achievements

- **ENLIGHTEN pivotal program initiated for ALKS 3831**: The ENLIGHTEN pivotal program for ALKS 3831 is comprised of two key studies. ENLIGHTEN-1, a multicenter, randomized, double-blind phase 3 study to evaluate the antipsychotic efficacy of ALKS 3831 compared to placebo over four weeks in approximately 390 patients experiencing acute exacerbation of schizophrenia, is now underway and enrolling patients. The study will also include an olanzapine comparator arm. ENLIGHTEN-2, a phase 3 study assessing weight gain with ALKS 3831 compared to olanzapine in patients with schizophrenia over six months, is expected to initiate in Q1 2016. The program will also include supportive studies to evaluate the pharmacokinetic and metabolic profile of ALKS 3831, as well as long-term safety. Alkermes expects to use safety and efficacy data from the ENLIGHTEN pivotal program to serve as the basis for a New Drug Application (NDA) to be submitted to the U.S. Food and Drug Administration (FDA), pending study results.
- **EVOLVE pivotal program initiated for ALKS 8700**: EVOLVE-1, a two-year, multicenter, open-label study to assess the safety of ALKS 8700 in approximately 600 patients with MS, is now underway and enrolling patients. This is the first study to initiate from the EVOLVE (**E**ndea**vo**ring to Advance Treatment for Patients **Li**v**i**ng with Multip**l**e Sclerosis) pivotal program of ALKS 8700 for the treatment of MS. Alkermes plans to include data from EVOLVE-1, as well as pharmacokinetic bridging data from studies comparing ALKS 8700 and TECFIDERA®, to support registration of ALKS 8700, based on feedback from the FDA. In addition, Alkermes intends to initiate EVOLVE-2, a randomized, head-to-head study comparing the gastrointestinal tolerability of ALKS 8700 and TECFIDERA in up to 420 patients with MS, in mid-2016. Alkermes plans to submit the NDA for ALKS 8700 to the FDA in 2018.
- **Positive topline results announced from human abuse potential study of ALKS 5461**: In the study, all doses of ALKS 5461 tested met the trial’s primary endpoint and demonstrated a statistically significant and meaningful reduction in abuse potential compared to buprenorphine ($p<0.001$). Further, no difference was observed in overall drug liking for ALKS 5461 compared to placebo. Data from this study is expected to support the comprehensive data package for ALKS 5461 to be submitted as part of the NDA to the FDA. The three core efficacy studies for ALKS 5461 remain on track to read out in 2016, with data from the first two studies expected in Q1 2016, and data from the third study anticipated in mid-2016.
- **New patent issued for ARISTADA**: The United States Patent and Trademark Office (USPTO) has issued U.S. Patent No. 9,193,685 covering ARISTADA. The patent covers drug compositions that confer long-term stability. This patent adds to the robust, existing patent estate for ARISTADA and is expected to extend protection to October 2033.

About ALKS 3831

ALKS 3831 is a proprietary, investigational medicine designed as a broad-spectrum antipsychotic for the treatment of schizophrenia. ALKS 3831 is composed of samidorphan, a novel, potent mu-opioid antagonist, in combination with the established antipsychotic drug, olanzapine.

About ALKS 8700

ALKS 8700 is an oral, novel and proprietary monomethyl fumarate (MMF) drug candidate in development for the treatment of multiple sclerosis (MS). ALKS 8700 is designed to rapidly and efficiently convert to MMF in the body and to offer differentiated features as compared to the currently marketed dimethyl fumarate, TECFIDERA®.

About ALKS 5461

ALKS 5461 is a proprietary, oral investigational medicine for the treatment of major depressive disorder (MDD). ALKS 5461 acts as a balanced neuromodulator in the brain and represents a new approach with a novel mechanism of action for treating MDD. In October 2013, the U.S. Food and Drug Administration (FDA) granted Fast Track status for ALKS 5461 for the adjunctive treatment of MDD in patients with an inadequate response to standard antidepressant therapies.

About ARISTADA™

ARISTADA is an injectable atypical antipsychotic with one-month and six-week dosing options for the treatment of schizophrenia. ARISTADA is administered by a healthcare professional. 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. There is no known treatment for established TD, although the syndrome 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.

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.

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 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 in patients treated with ARISTADA) was akathisia.

Injection-Site Reactions: Injection-site reactions were reported by 4%, 5%, and 2% of patients treated with 441 mg ARISTADA, 882 mg ARISTADA, 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 nature, timing and likelihood of success of clinical development activities for, and the therapeutic value of, ALKS 3831, ALKS 8700 and ALKS 5461; the number of patients to be enrolled in the phase 3 studies for ALKS 3831 and ALKS 8700; the adequacy of the ENLIGHTEN and EVOLVE pivotal programs for ALKS 3831 and ALKS 8700, respectively, to serve as the basis for NDAs for each such product; the timing of regulatory submissions to the FDA; and whether U.S. Patent No. 9,193,685 covering ARISTADA will adequately protect the pharmaceutical composition against competition until October 2033. You are cautioned 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 preclinical and early clinical results for our clinical candidates will be predictive of future clinical study results; whether ongoing or future clinical trials for our clinical candidates will be initiated or completed on time or at all; changes in the cost, scope and duration of the ALKS 3831 and ALKS 8700 clinical trials; whether our clinical candidates could be shown ineffective or unsafe during clinical studies and whether, in such instances, Alkermes may not be permitted by regulatory authorities to undertake new or additional clinical studies of our clinical candidates; whether regulatory submissions for our clinical candidates will be submitted on time or at all; whether adverse decisions by regulatory authorities in respect of our clinical candidates will occur; whether the validity of U.S. Patent No. 9,193,685 will be challenged by one or more third parties and upheld; and those risks described in the Alkermes plc Quarterly Report on Form 10-Q for the period ended Sept. 30, 2015 and Annual Report on Form 10-K for the fiscal year ended Dec. 31, 2014, and in other 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.

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