Alkermes Announces Positive Results of Phase 2 Clinical Trial of ALKS 3831 in Schizophrenia

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— Once-Daily, Oral Product Candidate Showed Efficacy Equivalent to Olanzapine With Clinically Meaningful and Statistically Significant Lower Weight Gain in 300-Patient Study —

— Company Plans to Initiate Pivotal Development Program in 2015 —

DUBLIN--(BUSINESS WIRE)--Jan. 7, 2015-- Alkermes plc (NASDAQ: ALKS) today announced positive topline results from the 12-week, randomized, double-blind, active-controlled, dose-ranging stage of a phase 2 study of ALKS 3831, an investigational, novel, oral atypical antipsychotic drug candidate designed to be a broad-spectrum treatment for schizophrenia. ALKS 3831 is composed of samidorphan, a novel, potent mu-opioid antagonist, in combination with the established antipsychotic drug, olanzapine. Data from the 300-patient study showed that ALKS 3831 achieved the study's primary efficacy endpoint, demonstrating equivalence to olanzapine in reduction from baseline in Positive and Negative Syndrome Scale (PANSS) total scores at Week 12. ALKS 3831 also met the principal pre-specified secondary endpoint of the study, demonstrating a 37% lower mean weight gain compared to olanzapine at Week 12 in the full study population ($p=0.006$), and a 51% lower mean weight gain compared to olanzapine at Week 12 in a pre-specified subset of patients who gained weight in the one-week olanzapine lead-in ($p<0.001$). ALKS 3831 was generally well tolerated in the study. The most common adverse events in the ALKS 3831 treatment groups relative to olanzapine were somnolence, sedation and dizziness. Based on the positive results from this phase 2 study, Alkermes plans to request an End-of-Phase 2 meeting with the U.S. Food and Drug Administration (FDA) and advance ALKS 3831 into a pivotal development program in 2015.

"Olanzapine is considered one of the most efficacious atypical antipsychotics, yet it has one of the highest incidences and greatest amounts of weight gain among the widely prescribed products in this class of drugs, severely limiting its clinical use," said Peter Weiden, M.D., Professor of Psychiatry at the University of Illinois Medical Center. "This study showed very promising results for ALKS 3831 in addressing the major drawback of weight gain in patients treated with olanzapine, and it offers the potential for widening the therapeutic use of an olanzapine agent to meet the needs of patients."

All patients enrolled in the study received olanzapine alone for a one-week period prior to randomization to treatment with olanzapine or one of three different doses of ALKS 3831 (olanzapine + 5 mg, 10 mg or 20 mg samidorphan) for a period of 12 weeks. The one-week lead-in period enabled the determination of early weight gain on olanzapine alone. These data were used to balance treatment groups upon randomization and enabled the pre-specification of two analysis groups for the key secondary endpoints related to weight. The first group comprised all patients in the study ("full study population"), and the second was comprised of those patients showing any early weight gain in the one-week lead-in period ("early weight gain population"). Of the 300 patients randomized in the full analysis set, 195 patients (65%) comprised the early weight gain population.

Data from the full study population comparing all doses of ALKS 3831 to olanzapine showed that the study met its primary endpoint, with treatment with ALKS 3831 resulting in PANSS score reductions comparable to olanzapine (mean difference ALKS 3831 vs. olanzapine: 0.6 points, 95% confidence interval (CI): -1.2 – 2.5).

The principal secondary endpoint of the study was the overall percentage change from baseline in body weight of the combined ALKS 3831 treatment groups compared to olanzapine alone at Week 12. Data from the phase 2 study showed:

- In the full study population, treatment with ALKS 3831 demonstrated a 37% lower mean weight gain from baseline, compared to olanzapine alone ($p=0.006$).
- In the early weight gain population, treatment with ALKS 3831 demonstrated a 51% lower mean weight gain from baseline, compared to olanzapine alone ($p<0.001$).
- Weight gain observed in the olanzapine-only arm was consistent with that reported in the olanzapine label.

Additional analyses focused on those patients with weight gain of at least 5%, 7% and 10% of their baseline body weight at Week 12. Although the study was not powered for statistical significance on these endpoints, the results showed ALKS 3831's effect in attenuating significant weight gain in these clinically significant cohorts, compared to olanzapine alone.

- Across the full study population, the risk of weight gain of at least 10% of baseline body weight with olanzapine was 2.7 times that of ALKS 3831 ((95% CI 1.1 – 6.7), $p=0.023$).
- In the early weight gain population, the risk of weight gain of at least 10% of baseline body weight with olanzapine was 4.1 times that of ALKS 3831 ((95% CI 1.4 – 12.3), $p=0.008$).

The phase 2 study met the objective of providing clear information relating to dose response of samidorphan and dose selection for the phase 3 program.

"The unequivocal results of the first 12 weeks of this study confirm and advance the results seen in earlier studies and suggest that ALKS 3831 has the potential to be a meaningful new treatment option for patients suffering with schizophrenia," said Elliot Ehrich, M.D., Chief Medical Officer of Alkermes. "ALKS 3831 is designed to offer the efficacy benefits of olanzapine while attenuating the significant weight gain frequently associated with its use."

All patients who completed this 12-week, double-blind portion of the phase 2 study were eligible to continue in an extension phase and receive one of the three doses of ALKS 3831 for an additional 12 weeks. This 12-week extension is currently ongoing and data to date indicate the durability of ALKS 3831's effect on weight. Complete results from the 12-week extension stage are expected in the second quarter of 2015.

Data from the study showed that ALKS 3831 was generally well tolerated, and the safety profile of ALKS 3831 was similar to that reported with oral olanzapine, with the exception of significantly lower weight gain. The most common adverse events in the ALKS 3831 treatment groups relative to olanzapine were somnolence, sedation and dizziness. Discontinuations due to adverse events were low and similar to olanzapine. Alkermes will present comprehensive safety and efficacy data from the phase 2 study at an upcoming medical meeting and submit the results for publication in a peer-reviewed journal.

Phase 2 Study Design

This phase 2, randomized, multicenter, double-blind, active-controlled, dose-ranging study was designed to assess the efficacy, safety and tolerability of ALKS 3831, as well as evaluate the impact of ALKS 3831 on weight and other metabolic factors in comparison to olanzapine alone in adult patients with stable schizophrenia. A total of 309 patients were randomized in the study, and the 300 patients who had at least one post baseline PANSS assessment were included in the full study population. In the study, following a one-week oral lead-in of olanzapine, patients were randomly assigned to treatment with olanzapine or one of three different doses of ALKS 3831 (olanzapine + 5 mg, 10 mg or 20 mg samidorphan) for a period of 12 weeks.

The primary efficacy endpoint of the study was the change from baseline at Week 12 in PANSS total score, to assess equivalence of ALKS 3831 to olanzapine using a Mixed-Effect Model Repeated Measure (MMRM) model. Secondary endpoints evaluated the effects of ALKS 3831 on weight gain and other metabolic factors. All participants who completed the 12-week, double-blind portion of the study are eligible to continue in an extension portion and receive ALKS 3831 for an additional 12 weeks. The objective of the 12-week extension period is to assess the safety and long-term durability of effect of ALKS 3831 on PANSS total score reductions and attenuation of weight gain. Alkermes expects to provide topline results from the 12-week extension in the second quarter of 2015.

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. ALKS 3831 is designed to attenuate olanzapine-induced metabolic side effects, including weight gain, in patients with schizophrenia and to have utility in the treatment of schizophrenia in patients with alcohol use.

The ALKS 3831 comprehensive phase 2 clinical program is comprised of two separate studies, including this study focused on the attenuation of weight gain associated with olanzapine. Weight gain is a common and clinically relevant metabolic side effect of atypical antipsychotic medications, and olanzapine has one of the highest incidences and greatest amounts of weight gain among the widely prescribed products in this class of drugs.[1] The second phase 2 study, initiated in June 2014, is investigating the potential utility of ALKS 3831 for the large number of patients with schizophrenia whose disease is exacerbated by alcohol use – a group representing over one-third of patients with schizophrenia.[2]

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,[3] with men and women affected equally. Worldwide, it is estimated that one person in every 100 develops schizophrenia, which is one of the most serious types of mental illness.

About Alkermes plc

Alkermes plc is a fully integrated, global biopharmaceutical company that applies its scientific expertise and proprietary technologies to develop innovative medicines that improve patient outcomes. The company has a diversified portfolio of more than 20 commercial drug products and a substantial clinical pipeline of product candidates that address central nervous system (CNS) disorders such as addiction, schizophrenia and depression. Headquartered in Dublin, Ireland, Alkermes plc has an R&D center in Waltham, Massachusetts; a research and manufacturing facility in Athlone, Ireland; and manufacturing facilities in Gainesville, Georgia and 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 value, development plans and commercial potential of ALKS 3831. 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 projected or suggested in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: whether preclinical and clinical results for ALKS 3831 will be predictive of future clinical study results; whether ongoing or future clinical trials for ALKS 3831 will be initiated or completed on time or at all; potential changes in cost, scope and duration of the ALKS 3831 clinical development program; whether ALKS 3831 could be shown ineffective or unsafe during clinical studies; and those risks described in the Alkermes plc Transition Report on Form 10-K for the fiscal period ended December 31, 2013, 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.

[1]Komossa K, Rummel-Kluge C, Hunger H, Schmid F, Schwarz S, Duggan L, Kissling W, Leucht S. Olanzapine versus other atypical antipsychotics for schizophrenia. *Cochrane Database of Systematic Reviews*. 2010, Issue 3. Art. No.: CD006654.

[2]Regier D, Farmer M, Rae D, Locke B, Keith S, Judd L, Goodwin F. Comorbidity of Mental Disorders With Alcohol and Other Drug Abuse. *JAMA*. 1990, 264: 2511-2518.

[3]National Institutes of Health. Accessed on Jan. 6, 2015 from http://report.nih.gov/NIHfactsheets/ViewFactSheet.aspx?csid=67&key=S#S.

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