



## Alkermes Announces Positive Preliminary Topline Results From Phase 3 Antipsychotic Efficacy Study of ALKS 3831 for Treatment of Schizophrenia

June 29, 2017

—Once-Daily, Oral Product Candidate Demonstrated Antipsychotic Efficacy Statistically Superior to Placebo and Similar to Olanzapine in ENLIGHTEN-1 Study —

— Management to Hold Conference Call Today at 4:30 p.m. ET —

DUBLIN--(BUSINESS WIRE)--Jun. 29, 2017-- [Alkermes plc](#) (NASDAQ: ALKS) today announced positive preliminary topline results from ENLIGHTEN-1, the first of two key phase 3 studies in the ENLIGHTEN clinical development program for ALKS 3831, an investigational, novel, once-daily, oral atypical antipsychotic drug candidate for the treatment of schizophrenia. ENLIGHTEN-1 was a multinational, double-blind, randomized, phase 3 study that evaluated the antipsychotic efficacy, safety and tolerability of ALKS 3831 compared to placebo over four weeks in 403 patients experiencing an acute exacerbation of schizophrenia. The study also included a comparator arm of olanzapine, an established atypical antipsychotic agent with proven efficacy. The study met the prespecified primary endpoint, with ALKS 3831 demonstrating statistically significant reductions from baseline in Positive and Negative Syndrome Scale (PANSS) scores compared to placebo ( $p < 0.001$ ). Data from the study also showed that olanzapine achieved similar improvements from baseline PANSS scores, compared to placebo ( $p = 0.004$ ). The study also met its key secondary endpoint of improvement on the Clinical Global Impression – Severity (CGI-S) scale for ALKS 3831 versus placebo ( $p = 0.002$ ). ALKS 3831 is designed to provide the strong antipsychotic efficacy of olanzapine and a differentiated safety profile with favorable weight and metabolic properties.

“The positive results of ENLIGHTEN-1 provide clear evidence of the safety, tolerability and antipsychotic efficacy of ALKS 3831 in a large, randomized registration trial,” said Elliot Ehrich, M.D., Executive Vice President of Research and Development at Alkermes. “The results of this phase 3 study also provide additional evidence of the antipsychotic properties of ALKS 3831 relative to olanzapine, an agent well known to clinicians. We look forward to completing our analysis of this large study and presenting the data at a future medical meeting.”

“Many physicians recognize the powerful efficacy profile of olanzapine, but are hesitant to prescribe it given the severe weight gain and metabolic side effects commonly associated with its use,” said Christoph Correll, M.D., Professor of Psychiatry and Molecular Medicine at Hofstra Northwell School of Medicine. “A new antipsychotic with robust efficacy and a favorable weight and metabolic profile compared to olanzapine would be a welcome addition to the schizophrenia treatment landscape. This study confirms a key element of this profile, with a clear demonstration of efficacy in a large, well-conducted clinical trial.”

Overall, 91% of patients who received ALKS 3831 completed the study, compared to 89% of patients who received olanzapine and 83% of patients who received placebo. The most common adverse events for both the ALKS 3831 and olanzapine treatment groups were weight gain, somnolence and dry mouth.

Alkermes will present comprehensive data from the ENLIGHTEN-1 study at an upcoming medical meeting and submit the results for publication in a peer-reviewed journal. ENLIGHTEN-2, a six-month phase 3 study evaluating the weight gain profile of olanzapine compared to ALKS 3831, is ongoing with data expected in 2018.

### **About the ENLIGHTEN-1 Study**

ENLIGHTEN-1 was a multinational, double-blind, randomized, phase 3 study that evaluated the antipsychotic efficacy, safety and tolerability of ALKS 3831 compared to placebo over four weeks in patients experiencing an acute exacerbation of schizophrenia. The study also included a comparator arm of olanzapine, an established atypical antipsychotic agent with proven efficacy but also metabolic liabilities, including significant weight gain.<sup>1</sup> The trial included adult patients who met the *Diagnostic and Statistical Manual of Mental Disorders – Fifth Edition* criteria for schizophrenia, and had a PANSS score of 80 or higher at study baseline.

A total of 403 patients were randomized in a 1:1:1 manner to receive once-daily, oral tablets of ALKS 3831, olanzapine or placebo for four weeks. Patients randomized to the ALKS 3831 treatment group received a bilayer fixed-dose tablet of 10 mg samidorphan co-formulated with either 10 or 20 mg of olanzapine. Patients randomized to the olanzapine treatment group received either 10 or 20 mg of olanzapine. The primary efficacy endpoint of the study was the mean change from baseline at Week 4 in PANSS total score for ALKS 3831 compared to placebo, using a Mixed Model with Repeated Measurements (MMRM) model. The key secondary endpoint of the study was change from baseline in the CGI-S score at Week 4.

All participants who completed the double-blind portion of the study were eligible to continue in an open-label, long-term safety study and receive ALKS 3831 for an additional 12 months. The objective of the extension phase of the study is to assess the long-term safety, tolerability and durability of effect of ALKS 3831.

### **Conference Call**

Alkermes will host a conference call today, June 29, 2017, at 4:30 p.m. ET (9:30 p.m. BST), to discuss these topline results. The conference call may be accessed by dialing +1 888 424 8151 for U.S. callers and +1 847 585 4422 for international callers. The conference call ID number is 6037988. The conference call will also be webcast on the Investors section of Alkermes' website at [www.alkermes.com](http://www.alkermes.com). The webcast will be archived on the Investors section of the Alkermes website for at least 90 days.

### **About the ENLIGHTEN Clinical Development Program**

The ENLIGHTEN clinical development program for ALKS 3831 is comprised of two key studies: a study evaluating the antipsychotic efficacy of ALKS 3831 compared to placebo over four weeks and a study assessing weight gain with ALKS 3831 compared to olanzapine in patients with schizophrenia

over six months. The program also includes supportive studies to evaluate the pharmacokinetic and metabolic profile of ALKS 3831, the effect on body weight of ALKS 3831 in young adult patients early in their illness, and long-term safety.

#### **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, 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<sup>®</sup>, has one of the highest incidences and greatest amounts of weight gain among the widely prescribed products in this class of drugs.<sup>1</sup> ALKS 3831 is designed to provide the strong antipsychotic efficacy of olanzapine and a differentiated safety profile with favorable weight and metabolic properties.

#### **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,<sup>2</sup> with men and women affected equally.

#### **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](http://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 timing of receipt and reporting of the phase 1 metabolic and ENLIGHTEN-2 study results; and 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 expressed or implied 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 the ENLIGHTEN-2 study for ALKS 3831 will be 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 and uncertainties 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 Report on Form 10-Q for the quarter ended Mar. 31, 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](http://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.

ZYPREXA<sup>®</sup> is a registered trademark of Eli Lilly & Company.

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

<sup>2</sup>National Institutes of Health. *Schizophrenia*. Accessed on June 29, 2017 from <http://report.nih.gov/NIHfactsheets/ViewFactSheet.aspx?csid=67&key=S#S>.



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