Alkermes Announces Positive Results From Study of ALKS 5461 for Treatment of Major Depressive Disorder

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— Safety and Tolerability Profile of ALKS 5461 Confirmed in FORWARD-1 Study, a Supportive Study in the FORWARD Phase 3 Pivotal Program —

— Dosing Regimen Confirmed; Efficacy Data Showed Statistically Significant Improvements in Depression Scores Beginning at Week One and Continuing Through Eight-Week Treatment Period —

DUBLIN--(BUSINESS WIRE)--Jan. 6, 2015-- Alkermes plc (NASDAQ: ALKS) today announced topline results from FORWARD-1, one of a series of supportive clinical studies in the comprehensive FORWARD phase 3 pivotal program for ALKS 5461, a once-daily, oral investigational medicine with a novel mechanism of action for the adjunctive treatment of major depressive disorder (MDD). The FORWARD-1 study was designed to evaluate the safety and tolerability of two titration schedules of ALKS 5461. In addition, the study assessed the efficacy of ALKS 5461 over an eight-week period, compared to baseline, in patients with MDD.

Data from the 66-patient study showed that ALKS 5461 was generally well tolerated in both of the two titration schedules evaluated – one-week and two-week dose escalation schedules. The most common adverse events in the study were nausea, constipation and dry mouth. These findings were consistent with the safety and tolerability profile seen in the 142-patient phase 2 study completed in 2013. Additionally, the exploratory efficacy analyses showed that ALKS 5461 significantly reduced depressive symptoms from baseline starting at Week One and continued to the end of the treatment period at Week Eight in patients who received either of the two titration schedules. The observed changes from baseline were clinically meaningful and statistically significant ($p<0.001$). These data support the one-week titration schedule being utilized in the core phase 3 efficacy studies in the FORWARD program.

“This successful study achieved multiple objectives and provided further confirmation of the tolerability and antidepressive effects of ALKS 5461 in patients failing to achieve adequate clinical response to standard therapy,” stated Elliot Ehrich, M.D., Chief Medical Officer of Alkermes. “Over the first four weeks of the study, ALKS 5461 showed significant efficacy and rapid onset of action consistent with the findings from our large phase 2 study. In addition, for the first time, we evaluated ALKS 5461 for an additional four-week period, for a total of eight weeks, and showed continuing improvement in depression scores. Furthermore, data from the study confirmed the rationale of the one-week titration schedule that we are deploying in our three core phase 3 efficacy studies in the FORWARD program.”

Data from the randomized, double-blind, parallel-arm study showed that both titration schedules of ALKS 5461 were generally well tolerated, and there were no serious adverse events reported in the study. The most common adverse events in the study were nausea, constipation and dry mouth. Alkermes will present comprehensive safety and efficacy data from the phase 3 study at an upcoming medical meeting and submit the results for publication in a peer-reviewed journal.

FORWARD-1 Study Design

The FORWARD-1 study evaluated the safety, tolerability and efficacy of two titration schedules of ALKS 5461 administered once daily as adjunctive treatment in 66 patients with MDD who had an inadequate response to commonly prescribed drugs for depression, including selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs). Patients were assigned to either a one-week or two-week titration schedule of oral ALKS 5461, for a total treatment period of eight weeks. The primary objective of the study was to evaluate the safety and tolerability of the two titration schedules for ALKS 5461. Efficacy endpoints, including the change in Montgomery–Åsberg Depression Rating Scale (MADRS) total score from baseline and the Clinical Global Impression–Severity Scale (CGI-S) score at Week Eight, were assessed in exploratory analyses. All participants in the double-blind portion of the study were eligible to continue in an open-label phase and receive ALKS 5461 for an additional 12 months. The objective of the extension phase of the study is to assess the safety and long-term durability of effect of ALKS 5461.

About the Phase 3 FORWARD Clinical Program

The FORWARD (**F**ocused **O**n **R**esults **W**ith **A** **R**ethinking of **D**epression) pivotal program for ALKS 5461 includes three core phase 3 efficacy studies, as well as nine supportive studies to evaluate the long-term safety, dosing, pharmacokinetic profile and human abuse liability of ALKS 5461. The three core efficacy studies utilize state-of-the-art methodologies to reduce the impact of clinically meaningful placebo response and are expected to randomize a total of approximately 1,500 patients with MDD who have had an inadequate response to standard therapies. The primary efficacy endpoint for the three core efficacy studies is the change from baseline in Montgomery–Åsberg Depression Rating Scale (MADRS) scores. Alkermes expects to use safety and efficacy data from the FORWARD program as the basis for a New Drug Application (NDA) to be submitted to the U.S. Food and Drug Administration (FDA), pending study results.

Further information about the FORWARD studies can be found at www.clinicaltrials.gov.

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 MDD

According to the *DSM-5*® (*Diagnostic and Statistical Manual of Mental Disorders*, *Fifth Edition*), major depressive disorder (MDD) is a condition in

which patients exhibit depressive symptoms, such as a depressed mood or a loss of interest or pleasure in daily activities consistently for at least a two-week period, and demonstrate impaired social, occupational, educational or other important functioning. An estimated 16.1 million people in the U.S. suffer from MDD in a given year,[1,2] the majority of whom may not adequately respond to initial antidepressant therapy.[3]

About Alkermes

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, tolerability, development plans and commercial potential of ALKS 5461. 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 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 5461 will be predictive of future clinical study results; whether future clinical trials for ALKS 5461 will be completed on time or at all; potential changes in cost, scope and duration of the FORWARD pivotal program for ALKS 5461; whether ALKS 5461 could be shown ineffective or unsafe during clinical studies; and those risks described in the Alkermes plc Transition Report 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.

DSM-5® is a registered trademark of the American Psychiatric Association.

[1] Kessler RC, Chiu WT, Demler O, Walters EE. Prevalence, severity, and comorbidity of twelve-month DSM-IV disorders in the National Comorbidity Survey Replication (NCS-R). *Archives of General Psychiatry*, 2005 Jun; 62 (6): 617-27.

[2] U.S. Census.

[3] Rush AJ et al (2007) *Am J. Psychiatry* 163:11, pp. 1905-1917 (STAR*D Study).

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