Alkermes Announces Initiation of FORWARD-3 and FORWARD-4 Efficacy Studies in Pivotal Program for ALKS 5461 for Treatment of Major Depressive Disorder

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DUBLIN, Ireland--(BUSINESS WIRE)--Jun. 10, 2014-- Alkermes plc (NASDAQ: ALKS) today announced the initiation of FORWARD-3 and FORWARD-4, two of the three planned phase 3 core efficacy studies in the pivotal clinical 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). These studies will evaluate the efficacy and safety of ALKS 5461 in patients suffering from MDD who have had an inadequate response to commonly prescribed drugs, including selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs). Approximately two-thirds of patients who are diagnosed with MDD do not adequately respond to initial antidepressant therapy.[1]

"FORWARD-3 and FORWARD-4 incorporate features from our previous successful studies of ALKS 5461, including state-of-the-art design elements to reduce the impact of placebo response in depression trials," stated Elliot Ehrich, M.D., Chief Medical Officer of Alkermes. "With these study initiations, four of the 12 studies from the FORWARD program are now underway since the launch of the pivotal program in March."

FORWARD-3 and FORWARD-4 are both phase 3, multinational, randomized, double-blind, placebo-controlled studies designed to evaluate the efficacy and safety of ALKS 5461 as adjunctive treatment in patients with MDD. The two studies combined are expected to randomize approximately 1,000 patients and incorporate sophisticated design features to ensure rigorous patient selection, monitoring and evaluation. Data from these two core efficacy studies are expected in 2016. FORWARD-5, the third core efficacy trial, is expected to initiate in mid 2014.

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

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 will 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 will be 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.

About ALKS 5461

ALKS 5461 is a proprietary investigational oral medicine for the treatment of major depressive disorder (MDD). ALKS 5461 is designed to modulate the opioid system in the brain, employing a balanced combination of agonist and antagonist components that act on opioid receptors, and includes a novel opioid modulator, samidorphan, discovered by Alkermes. Samidorphan was formerly referred to as ALKS 33. 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,[2,3] the majority of whom may not adequately respond to initial antidepressant therapy.[1]

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, 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 publicly updating or revising any forward-looking information contained in this press release.

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

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

[2] U.S. Census.

[3] 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.

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