Alkermes Announces Initiation of ALKS 5461 Pivotal Clinical Program for Treatment of Major Depressive Disorder

March 6, 2014

— FORWARD Phase 3 Studies Designed to Provide Basis for New Drug Application —

DUBLIN--(BUSINESS WIRE)--Mar. 6, 2014-- Alkermes plc (NASDAQ: ALKS) today announced the initiation of the pivotal clinical development 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 comprehensive pivotal program, named FORWARD (**F**ocused **O**n **R**esults **W**ith **A** **R**ethinking of **D**epression), includes a total of 12 studies, including three core phase 3 efficacy studies and nine supportive studies. The first FORWARD study, evaluating the onset of clinical effect, safety and tolerability of ALKS 5461 in approximately 60 patients with MDD, has begun, and the three core efficacy studies are expected to begin in mid 2014.

The FORWARD pivotal program will evaluate the safety and efficacy 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). Alkermes expects to use safety and efficacy data from the FORWARD studies as the basis for a New Drug Application (NDA) to be submitted to the U.S. Food and Drug Administration (FDA), pending study results.

“With a novel mechanism of action and Fast Track designation from the FDA, ALKS 5461 is designed to offer a new treatment option for the millions of people with MDD with urgent unmet medical needs,” stated Elliot Ehrich, M.D., Chief Medical Officer of Alkermes. “The comprehensive FORWARD program incorporates state-of-the-art design elements for depression trials and will be conducted in collaboration with leading clinical investigators.”

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 will include 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.

About the Phase 2 Study Results for ALKS 5461

In April 2013, Alkermes announced positive data from a phase 2 randomized, double-blind, multicenter, placebo-controlled study of ALKS 5461 in 142 patients with MDD who had an inadequate response to a stable dose of either an SSRI or an SNRI. Data from the study showed that ALKS 5461 was generally well tolerated and significantly reduced depressive symptoms across a range of standard measures, including the Hamilton Depression Rating Scale (HAM-D17) (p=0.026), MADRS (p=0.004) and the Clinical Global Impression – Severity Scale (CGI-S) (p=0.035).

About ALKS 5461

ALKS 5461 is a proprietary investigational oral medicine for the treatment of MDD. ALKS 5461 has a novel mechanism of action in the treatment of depressive symptoms based on modulation of 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 FDA granted Fast Track status for ALKS 5461 for the adjunctive treatment of MDD in patients with an inadequate response to standard 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, 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: clinical trials of the company's products may be unsuccessful or not initiated or conducted in a timely manner; its products may not show sufficient therapeutic effects or acceptable safety profiles; adverse decisions by regulatory authorities; existing clinical and preclinical data with respect to its products may not be indicative of future clinical or commercial results; the company's inability to manufacture successfully its products; 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 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).

Source: Alkermes plc

Alkermes
For Investors:
Rebecca Peterson, +1 781 609 6378
or
For Media:
Jennifer Snyder, +1 781 609 6166