# Alkermes Announces Positive Results from Phase 2 Clinical Study of ALKS 5461 for Major Depressive Disorder

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*–– Significantly Improved Depression Scores in 142-Patient Study Testing Novel Mechanism of Action for Once-Daily, Oral Medication ––*

*–– Company Plans to Initiate Pivotal Development Program ––*

*–– Data to be Presented at NCDEU Conference in May ––*

DUBLIN--(BUSINESS WIRE)--Apr. 17, 2013-- Alkermes plc (NASDAQ: ALKS) today announced positive preliminary topline results from a phase 2 study of ALKS 5461, its novel drug compound for major depressive disorder (MDD) in patients who have an inadequate response to standard therapies for clinical depression. ALKS 5461 reflects a new approach to the treatment of MDD based on modulation of opioid receptors in the brain and is designed as a non-addictive, oral, once-daily medicine. Data from the study showed that ALKS 5461 significantly reduced depressive symptoms across a range of standard measures including the study's primary outcome measure, the Hamilton Depression Rating Scale (HAM-D17) (p=0.026), the Montgomery–Åsberg Depression Rating Scale (MADRS) (p=0.004) and the Clinical Global Impression – Severity Scale (CGI-S) (p=0.035). ALKS 5461 was generally well tolerated. Based on these results, as well as the positive phase 1/2 results previously reported, Alkermes plans to request a meeting with the U.S. Food and Drug Administration (FDA) and advance ALKS 5461 into a pivotal development program. Data from this phase 2 study will be presented at the 53rd Annual New Clinical Drug Evaluation Unit (NCDEU) Meeting in Hollywood, Fla., May 28-31, 2013.

"The improvements in depressive symptoms observed in patients treated with ALKS 5461 in this study were clinically meaningful and among the most robust I have seen in a phase 2 study for depression in the past two decades. This promising candidate could provide a valuable new treatment approach for this serious and chronic disease," stated Maurizio Fava, M.D., Director of the Depression Clinical and Research Program at Massachusetts General Hospital and Slater Family Professor of Psychiatry at Harvard Medical School. "There is significant unmet medical need for novel treatments with new mechanisms of action for depression, as many patients do not adequately respond to existing pharmacological therapies."

The phase 2, randomized, double-blind, multicenter, placebo-controlled study assessed the efficacy and safety of two doses of ALKS 5461 when administered once daily for four weeks as adjunctive treatment in 142 patients with MDD who had an inadequate response to a stable dose of either a selective serotonin reuptake inhibitor (SSRI) or a serotonin-norepinephrine reuptake inhibitor (SNRI). Patients received one of two dosing regimens of oral ALKS 5461 or placebo for a treatment period of four weeks. The study utilized a sequential parallel comparison design, a design developed ten years ago by Drs. Fava and Schoenfeld at Massachusetts General Hospital and now widely utilized in clinical trials. The primary endpoint of the study was the change from baseline in depressive symptoms over a four-week treatment period, as measured by the HAM-D17. Secondary endpoints included additional analyses of patient responses based on HAM-D17, MADRS and CGI-S scores.

"ALKS 5461 has the potential to be a novel therapy with a unique mechanism of action for depression and validates our expertise with opioid modulators," stated Elliot Ehrich, M.D., Chief Medical Officer of Alkermes. "Based on the strength of these data, as well as the positive results seen in the prior clinical study, we will move forward rapidly to meet with the FDA and initiate a pivotal development program with a goal of bringing this important new medication to patients with MDD."

**About ALKS 5461**

ALKS 5461 is the combination of ALKS 33 and buprenorphine and is designed to be a non-addictive opioid modulator. ALKS 33 is an oral opioid modulator that builds on Alkermes' scientific expertise in opioid biology and pharmacology, as well as the company's clinical and commercial knowledge in the field of addiction and central nervous system disorders.

**About MDD**

According to the *DSM-IV-TR*® (*Diagnostic and Statistical Manual of Mental Disorders*, *Fourth Edition, Text Revision*), 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 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, including, but not limited to statements concerning: the therapeutic value of ALKS 5461; the clinical development of ALKS 5461, including

the results of meetings with regulatory authorities and the product's clinical development timeline; and the timing of the company's planned presentation of phase 2 data of ALKS 5461. 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 5461 will be predictive of future clinical study results; whether the company will initiate a pivotal development program for ALKS 5461; whether future clinical trials for ALKS 5461 will be completed on time or at all; potential changes in cost, scope and duration of the ALKS 5461 clinical development program; whether ALKS 5461 could be shown ineffective or unsafe during clinical studies, and whether the company will not be permitted by regulatory authorities to undertake new or additional clinical studies for ALKS 5461; and those risks described in the Alkermes plc Annual Report on Form 10-K for the year ended March 31, 2012, and in other filings made by the company with the U.S. Securities and Exchange Commission (SEC), which are available at 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-IV-TR*® 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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Alkermes
For Investors:
Rebecca Peterson, +1 781-609-6378
or
For Media:
Jennifer Snyder, +1 781-609-6166