# Alkermes Presents Positive Clinical Data of ALKS 5461 at 52nd Annual New Clinical Drug Evaluation Unit Meeting

May 29, 2012

PHOENIX & DUBLIN--(BUSINESS WIRE)--May. 29, 2012-- Alkermes plc (NASDAQ: ALKS) today presented positive results from the phase 1/2 study of ALKS 5461, a novel drug compound for major depressive disorder (MDD) in patients who have an inadequate response to standard therapies for clinical depression, in an oral session at the 52nd Annual New Clinical Drug Evaluation Unit (NCDEU) Meeting in Phoenix.

In the phase 1/2 clinical study, ALKS 5461 was shown to significantly reduce depressive symptoms, as measured by the Hamilton Depression Rating Scale (HAM-D17; a standard, clinician-assessed measure of depression severity), in patients with MDD who received ALKS 5461 for the seven-day treatment period. In addition, data from the study showed that ALKS 5461 was generally well tolerated. ALKS 5461 is the combination of buprenorphine and ALKS 33, a proprietary opioid modulator.

"We are delighted to present these results to experts in the mental health community at the NCDEU meeting showing that ALKS 5461 offers potential as a novel treatment for patients with MDD who have inadequate response to antidepressant therapy. Our study showed a rapid onset of action and clinically meaningful reduction in depressive symptoms after only seven days of treatment with ALKS 5461, which is very encouraging and prompted us to accelerate initiation of our phase 2 study," stated Elliot Ehrich, M.D., Chief Medical Officer of Alkermes. "ALKS 5461, one of several product candidates in our advancing clinical pipeline, is an excellent example of how Alkermes is leveraging our unique understanding of opioid biology and pharmacology to develop medications that address unmet medical needs for central nervous system disorders."

Based on the positive results of the phase 1/2 study, a phase 2 study of ALKS 5461 was initiated in January 2012 to further evaluate the utility of ALKS 5461 in treating MDD. The phase 2 trial is a randomized, double-blind, multicenter, placebo-controlled study that will evaluate the efficacy and safety of ALKS 5461 when administered once daily for four weeks in approximately 130 patients with MDD who have inadequate response to antidepressant therapy. Data from the study are expected in the first half of calendar 2013.

**Study Design and Results**

This phase 1/2 multicenter, randomized, double-blind, placebo-controlled, parallel-group study was designed to evaluate the safety and tolerability and explore the efficacy of ALKS 5461 compared to placebo in 32 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).

Two dose ratios of the ALKS 5461 components, buprenorphine and ALKS 33, were evaluated (8:1 and 1:1). Patients received one of these two sublingual dosing regimens of ALKS 5461 or placebo for seven days. In both dosing cohorts, patients administered ALKS 5461 demonstrated greater reductions from baseline in depressive symptoms, as measured by the HAM-D17, compared to those administered placebo. In the 1:1 dosing cohort, where full blockade of the mu agonist effects of buprenorphine were achieved, these differences in depressive severity were statistically significant as measured by the HAM-D17 ($p=0.032$). ALKS 5461 was generally well tolerated in both dosing cohorts.

**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. ALKS 5461 is also in clinical development for the treatment of cocaine dependence, which is being funded through a grant from the National Institute on Drug Abuse (NIDA).

**About MDD**

According to the *DSM-IV-TR*® (*Diagnostic and Statistical Manual of Mental Disorders*, *Fourth Edition, Text Revision*), a person who suffers from major depressive disorder (MDD) must 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 New Clinical Drug Evaluation Unit (NCDEU)**

NCDEU is a scientific meeting that focuses on the latest developments in psychopharmacologic clinical research and related methodology. The meeting brings together over 1,200 academic and industry investigators, research pharmacists, nurses, social workers, psychologists and other clinicians. NCDEU focuses on timely issues in psychiatric clinical research and includes presentations and information from the American Society of Clinical Psychopharmacology (ASCP) and its federal partners, the National Institute of Mental Health (NIMH), National Institute on Drug Abuse (NIDA), National Institute on Alcohol Abuse and Alcoholism (NIAAA), the Food and Drug Administration (FDA) and the European Medicines Agency (EMA). For more information, visit http://www.ncdeumeeting.org.

**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 and manufacturing facilities in Athlone, Ireland; Gainesville, Georgia; and Wilmington, Ohio. For more information, please visit Alkermes' website at 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, including, but not limited to: statements concerning the planned future development of ALKS 5461, including the expected timing of the phase 2 study; and the therapeutic value 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 early 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; whether there will occur 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 the company may not be permitted by regulatory authorities to undertake new or additional clinical studies for ALKS 5461; and those risks described in the company's recent Annual Report on Form 10-K, subsequent Quarterly Reports on Form 10-Q, recent Current Reports on Form 8-K and in other filings made by the company with the SEC, which are available at the SEC's website at http://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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