Alkermes Announces Positive Topline Results From FORWARD-5 Pivotal Phase 3 Study of ALKS 5461 for Major Depressive Disorder

October 20, 2016

— Once-Daily ALKS 5461 Significantly Improved Depression Scores in Patients With Inadequate Response to Standard Antidepressant Therapies —

— Company to Request Meeting with FDA to Discuss Next Steps for Potential Regulatory Submission —

— Management to Hold Conference Call Today at 5:00 p.m. EDT —

DUBLIN--(BUSINESS WIRE)--Oct. 20, 2016-- Alkermes plc (NASDAQ: ALKS) today announced positive topline results from FORWARD-5, the third phase 3 efficacy study to read out from the FORWARD 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) in patients with an inadequate response to standard antidepressant therapies. The study met its prespecified primary endpoint showing treatment with ALKS 5461 significantly reduced symptoms of depression in patients with MDD compared to placebo. ALKS 5461 was generally well tolerated. The most common adverse events observed for ALKS 5461 were nausea, dizziness and fatigue. Based on these results, along with the substantial data collected to date on the efficacy and safety of ALKS 5461 for the treatment of MDD, the company plans to request a meeting with the U.S. Food and Drug Administration's (FDA) Division of Psychiatric Products to discuss the filing strategy for this Fast Track designated medicine.

"We designed ALKS 5461 to have a novel mechanism of action for the treatment of MDD, a serious disease where new therapeutic options are highly sought after as millions of patients in the U.S. do not respond to standard courses of antidepressant therapy," said Elliot Ehrich, M.D., Chief Medical Officer of Alkermes. "With the successful completion of the FORWARD-5 study and data from more than 1,500 patients to date, we have established a strong foundation of evidence of ALKS 5461's clinical utility in the adjunctive treatment of major depressive disorder. With these data now in hand, we will move forward rapidly to meet with the FDA to determine the appropriate next steps toward a regulatory submission for ALKS 5461, with a goal of bringing this important new medication to patients with MDD."

"ALKS 5461 embodies our dedication to developing novel and safe CNS medicines that address compelling unmet needs faced by large numbers of patients," said Richard Pops, Chief Executive Officer of Alkermes. "Major depressive disorder affects millions of people and their families, and represents one of the greatest burdens of suffering and cost of any disease today. New drug development in the field is challenging and we are excited to advance ALKS 5461 in this important indication."

In the study, ALKS 5461 2mg/2mg met the prespecified primary endpoint of significantly reducing depression scores compared to placebo, as measured by 6-item Montgomery–Åsberg Depression Rating Scale (MADRS-6) scores (p=0.018). ALKS 5461 2mg/2mg also demonstrated statistically significant reductions in 10-item MADRS (MADRS-10) scores compared to placebo (p=0.026). The 1mg/1mg dose of ALKS 5461 showed improvement in depressive symptoms in the study, but did not separate significantly from placebo.

The most commonly reported adverse events for ALKS 5461 in the FORWARD-5 study were nausea, dizziness and fatigue. These findings are consistent with those observed in previously reported studies of ALKS 5461. Alkermes will present comprehensive data from FORWARD-5 at an upcoming medical meeting and submit the results for publication in a peer-reviewed journal.

About the FORWARD-5 Study
FORWARD-5 was a phase 3, randomized, double-blind, multicenter, placebo-controlled, sequential parallel comparison design (SPCD) study that evaluated the safety, tolerability and efficacy of two dose levels of ALKS 5461 (2mg/2mg and 1mg/1mg) as adjunctive treatment in 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). The study randomized 407 subjects.

The study was conducted in two sequential stages: Stage 1 was 5 weeks in duration, Stage 2 was 6 weeks. In Stage 1, the average change from baseline depression scores was calculated for weeks 3 through 5. For Stage 2, the average change was calculated for weeks 3 through 6. The results of Stages 1 and 2 were then averaged. Depression scores were assessed using the 6-item Montgomery–Åsberg Depression Rating Scale (MADRS-6) and MADRS-10. MADRS-6, a subscale of the MADRS-10 assessment tool for depression, focuses on the core symptoms of depression.

About the 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 additional supportive studies to evaluate the long-term safety, dosing, pharmacokinetic profile and human abuse potential of ALKS 5461. FORWARD-5 is the third phase 3 efficacy study to read out from the FORWARD program. Results from FORWARD-3 and FORWARD-4 were announced in January 2016 and detailed data were presented at the American Society of Clinical Psychopharmacology (ASCP) in June 2016.

Conference Call
Alkermes will host a conference call on Thursday, Oct. 20, 2016 at 5:00 p.m. EDT (10:00 p.m. BST). The conference call may be accessed by dialing +1 888 424 8151 for U.S. callers and +1 847 585 4422 for international callers. The conference call ID number is 6037988. The conference call will also be webcast on the Investors section of Alkermes' website at www.alkermes.com. In addition, a replay of the conference call will be available from 8:00 p.m. EDT on Thursday, Oct. 20, 2016 (1:00 a.m. BST, Friday, Oct. 21), through 5:00 p.m. EDT (10:00 p.m. BST) on Thursday, Oct. 27, 2016, and may be accessed by visiting Alkermes' website or by dialing +1 888 843 7419 for U.S. callers and +1 630 652 3042 for international callers. The replay access code is 6037988.

About ALKS 5461
ALKS 5461 is a proprietary, investigational, once-daily oral medicine that acts as a balanced neuromodulator in the brain and represents a novel

mechanism of action for treating MDD. ALKS 5461 consists of samidorphan and buprenorphine, and is designed to rebalance brain function that is dysregulated in the state of depression. 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 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 17 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 developing innovative medicines for the treatment of central nervous system (CNS) diseases. The company has a diversified commercial product portfolio and a substantial clinical pipeline of product candidates for chronic diseases that include schizophrenia, depression, addiction and multiple sclerosis. Headquartered in Dublin, Ireland, Alkermes plc has an R&D center in Waltham, Massachusetts; a research and manufacturing facility in Athlone, Ireland; and a manufacturing facility in 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 and regulatory plans, and commercial potential 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 and commercial potential of 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; whether the preclinical and clinical results of ALKS 5461 will meet the regulatory requirements for approval; whether regulatory submissions may occur or be submitted in a timely manner; and those risks and uncertainties described in Item 1A under the heading "Risk Factors" in the company's Annual Report on Form 10-K for the fiscal year ended Dec. 31, 2015, and in any 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. Existing and prospective investors are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date they are made. 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).

View source version on businesswire.com: http://www.businesswire.com/news/home/20161020006475/en/

Source: Alkermes plc

Alkermes plc
For Investors:
Eva Stroynowski, +1 781-609-6823
or
Sandy Coombs, +1 781-609-6377
or
For Media:
Jennifer Snyder, +1 781-609-6166