# Alkermes Announces Initiation of Study 217 for ALKS 5461 for Treatment of Major Depressive Disorder

June 12, 2017

*— Phase 3b Study Designed to Further Evaluate ALKS 5461's Potential Benefits on Mood Domains Regulated by Endogenous Opioid Modulation —*

*— Company Reiterates Plans to Submit New Drug Application to FDA by Year-End 2017 —*

DUBLIN--(BUSINESS WIRE)--Jun. 12, 2017-- Alkermes plc (NASDAQ: ALKS) today announced the initiation of study 217, a phase 3b trial of ALKS 5461, a once-daily, oral investigational medicine with a novel mechanism of action for the adjunctive treatment of major depressive disorder (MDD). The study will evaluate the efficacy and safety of ALKS 5461 in patients suffering from MDD who have had an inadequate response to commonly prescribed drugs for depression, including selective serotonin reuptake inhibitors (SSRIs) or serotonin-norepinephrine reuptake inhibitors (SNRIs). In addition to the traditional Montgomery–Åsberg Depression Rating Scale (MADRS) for assessing improvement in depression symptoms, study 217 will include scales to further evaluate ALKS 5461's potential benefits on mood and associated behavioral domains known to be regulated by endogenous opioid modulation. The company also reiterated plans to submit a New Drug Application (NDA) for ALKS 5461 for the adjunctive treatment of MDD to the U.S. Food and Drug Administration (FDA) by year-end 2017.

"Opioid modulation represents a new mechanism for the treatment of depression that may provide benefits beyond those observed with traditional antidepressants. Along with the clinical community, we are looking forward to further exploring ALKS 5461's potential in regulating domains such as social connection, resilience and anhedonia. Study 217 includes scales and endpoints to help elucidate ALKS 5461's potential effects on these specific mood domains where opioid modulation may yield singular benefit," stated Elliot Ehrich, M.D., Executive Vice President, Research and Development of Alkermes. "In parallel, we plan to meet with the FDA in July for our scheduled pre-NDA meeting and are preparing our New Drug Application for ALKS 5461 for the adjunctive treatment of MDD."

Study 217 is a phase 3b, multinational, randomized, double-blind, placebo-controlled clinical trial that will evaluate the efficacy, safety and tolerability of ALKS 5461 as adjunctive treatment in patients with MDD. The 11-week, 2-stage study will randomize up to 325 patients and incorporates design features informed by the FORWARD pivotal program to help ensure rigorous patient selection, monitoring and evaluation. The primary objective of the study is to assess ALKS 5461's ability to improve depressive symptoms, as measured by MADRS-6 and MADRS-10. Specific scales to evaluate additional potential benefits of ALKS 5461 included in study 217 are the Connor-Davidson Resilience Scale (CD-RISC), Snaith-Hamilton Pleasure Scale (SHAPS), Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form, Brief Pain Inventory-Short Form (BPI-SF), and the Clinical Global Impression-Severity (CGI-S) and Clinical Global Impression-Improvement (CGI-I) scales.

**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 the adjunctive treatment of 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 plc**
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 and commercial potential of ALKS 5461, and the development and regulatory plans and timelines, including the timing of submission of the NDA, for 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 expressed or implied 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 under the heading "Risk Factors" in the company's Annual Report on Form 10-K for the year ended Dec. 31, 2016 and Quarterly Report on Form 10-Q for the quarter ended Mar. 31, 2017 and in 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 hereof. Except as required by law, the company disclaims any intention or responsibility for updating or revising any forward-looking statements contained in this press release.

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

[1] Kessler RC et al (2005) *Archives of General Psychiatry*, Jun; 62 (6), pp. 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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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