Alkermes Receives Complete Response Letter From U.S. Food and Drug Administration for ALKS 5461 New Drug Application

February 1, 2019

DUBLIN, Feb. 1, 2019 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today announced that it received a Complete Response Letter (CRL) from the U.S. Food and Drug Administration (FDA) regarding its New Drug Application (NDA) for ALKS 5461 for the adjunctive treatment of major depressive disorder (MDD).

The CRL states that the FDA is unable to approve the ALKS 5461 NDA in its present form and is requesting additional clinical data to provide substantial evidence of effectiveness of ALKS 5461 for the adjunctive treatment of MDD. Alkermes plans to meet with the FDA to discuss the contents of the CRL and potential next steps for ALKS 5461. This interaction with the Agency will inform whether there is a viable path forward for the ALKS 5461 program.

The NDA submission for ALKS 5461 was based on results from a clinical efficacy and safety package with data from more than 30 clinical trials and more than 1,500 patients with MDD. Throughout the clinical development program, ALKS 5461 demonstrated a consistent profile of antidepressant activity, safety and tolerability in the adjunctive treatment of MDD.

About ALKS 5461

ALKS 5461 is a proprietary, investigational, once-daily oral medicine that acts as an opioid system modulator and represents a novel mechanism of action for the adjunctive treatment of major depressive disorder (MDD) in patients with an inadequate response to standard antidepressant therapies. ALKS 5461 is a fixed-dose combination of buprenorphine, a partial mu-opioid receptor agonist and kappa-opioid receptor antagonist, and samidorphan, a mu-opioid receptor antagonist.

About Major Depressive Disorder (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 16.2 million people in the U.S. suffered from MDD in 2016,[1] the majority of whom may not adequately respond to initial antidepressant therapy.[2]

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 company's plans to meet with the FDA to discuss the contents of the CRL and potential next steps 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 the company will continue to pursue FDA approval of ALKS 5461; whether the company will generate sufficient additional clinical data to meet the FDA's requirements for approval; if approved, whether the FDA will impose conditions on the marketing of ALKS 5461, such as a risk evaluation and mitigation strategy; whether future clinical trials for ALKS 5461, if any, will be completed on time or at all; changes in cost, scope and duration of the ALKS 5461 clinical development program; whether ALKS 5461 could be shown ineffective or unsafe during additional clinical studies; 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, 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] National Institutes of Mental Health: Major Depression. Accessed on Feb. 1, 2019 from https://www.nimh.nih.gov/health/statistics/major-depression.shtml.

[2] Rush AJ et al (2007) *Am J. Psychiatry,* 163:11, pp. 1905-1917 (STAR*D Study).

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