Alkermes Receives Refusal to File Letter From FDA for ALKS 5461

April 2, 2018

-- Conference Call Scheduled for Today at 8:30 a.m. ET --

DUBLIN, April 2, 2018 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today announced that it received a Refusal to File letter from the U.S. Food and Drug Administration (FDA) regarding its New Drug Application (NDA) 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.

Upon its preliminary review, the FDA has taken the position that it is unable to complete a substantive review of the regulatory package, based on insufficient evidence of overall effectiveness for the proposed indication, and that additional well-controlled clinical trials are needed prior to the resubmission of the NDA for ALKS 5461. In addition, FDA has requested the conduct of a bioavailability study to generate additional bridging data between ALKS 5461 and the reference listed drug, buprenorphine.

Alkermes strongly disagrees with the FDA's conclusions and plans to appeal the FDA's decision. The company intends to seek immediate guidance, including requesting a Type A meeting with the FDA, to determine appropriate next steps and what additional information may be required to resubmit the NDA.

"We are extremely disappointed with this decision and the implications for patients in the U.S. suffering from major depressive disorder, a serious disease where there is a clear and urgent need for new treatment options for patients and their families," said Richard Pops, Chief Executive Officer of Alkermes. "We strongly believe that the clinical development program, including data from more than 1,500 patients with MDD, provides substantial evidence of ALKS 5461's consistent antidepressant activity and a favorable benefit-risk profile."

Alkermes is evaluating the impact of this update on its previously-issued financial guidance for 2018; any update will be provided in its first quarter 2018 financial results disclosures.

Conference Call Information

Alkermes will host a conference call at 8:30 a.m. ET (1:30 p.m. BST) on Monday, April 2, 2018, to discuss this update. The conference call may be accessed by visiting Alkermes' website or 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. In addition, a replay of the conference call will be available from 11:00 a.m. ET (4:00 p.m. BST) on Monday, April 2, 2018, through 5:00 p.m. ET (10:00 p.m. BST) on Monday, April 9, 2018, 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 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 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 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, 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 expressed or implied in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: the timing, occurrence and outcome of the Type A meeting to discuss the refusal to file letter from the FDA; whether filing over protest is a viable path; whether discussions with the FDA will impact the likelihood of acceptance, and if accepted, approval, of the NDA for ALKS 5461 by the FDA; if approved, whether ALKS 5461 will be commercialized successfully; 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 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 April 1, 2018 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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View original content with multimedia:http://www.prnewswire.com/news-releases/alkermes-receives-refusal-to-file-letter-from-fda-for-alks-5461-300622455.html

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