# Alkermes Reports on Outcome of FDA Advisory Committee Meeting on ALKS 5461 for the Adjunctive Treatment of Major Depressive Disorder

November 1, 2018

DUBLIN, Nov. 1, 2018 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today announced that the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee, appointed by the U.S. Food and Drug Administration (FDA), met to review the company's New Drug Application (NDA) for ALKS 5461. The committee jointly voted that the benefit-risk profile was not adequate to support approval (Vote: 2 Yes/ 21 No). ALKS 5461 is 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.

"We were disappointed and surprised by the FDA's characterization of the safety and efficacy data for ALKS 5461 and the resulting outcome of the Advisory Committee vote, particularly for the patients, their families and treatment providers who need and deserve access to novel therapies that work differently than currently available antidepressants," said Richard Pops, Chief Executive Officer of Alkermes. "We remain steadfast in our commitment to make a meaningful difference in the lives of people suffering with serious mental health conditions, and will continue to work with the FDA as it completes its review of the ALKS 5461 regulatory submission."

Advisory committees provide the FDA with independent expert advice and recommendations on the safety and efficacy of potential new medicines. The advisory committee's recommendation, while not binding, will be considered by the FDA in its review of the NDA that Alkermes has submitted for ALKS 5461. The FDA has set a Prescription Drug User Fee Act (PDUFA) target action date for the ALKS 5461 NDA of Jan. 31, 2019.

The NDA submission for ALKS 5461 is 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 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: review and potential approval by the FDA of the ALKS 5461 NDA and the anticipated timing of such review and approval; and the potential therapeutic and commercial 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 expressed or implied in the forward-looking statements due to various risks and uncertainties. These risks and uncertainties include, among others: whether the preclinical and clinical results of ALKS 5461 studies will meet the regulatory requirements for approval by the FDA; whether the FDA's bases for the Refusal to File letter for the ALKS 5461 NDA, later rescinded by the FDA, or other bases will cause the FDA to require more data or information prior to approval of ALKS 5461; whether ALKS 5461 will be approved by the FDA in a timely manner or at all; whether 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; 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.

[1] National Institutes of Mental Health: Major Depression. Accessed on Nov. 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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