



Alkermes Receives FDA Complete Response Letter Related to ALKS 3831 Manufacturing Records Review

November 17, 2020

-- No Clinical Efficacy or Safety Issues Raised and No Further Studies Required by FDA to Support Approval --

-- Company Plans to Engage With FDA Toward Expeditious Resolution of Outstanding Items --

-- Investor Conference Call Scheduled for Today at 8:00 a.m. ET --

DUBLIN, Nov. 17, 2020 /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 3831 (olanzapine/samidorphan) for the treatment of adults with schizophrenia and adults with bipolar I disorder. Following a remote review of manufacturing records, FDA stated that resolution of certain conditions related to the tablet coating process at the company's Wilmington, OH facility is required before ALKS 3831 may be approved. The CRL did not identify or raise any concerns about the clinical or non-clinical data in the NDA and the FDA has not asked Alkermes to complete any new clinical trials to support approval of the application.

The observations noted in the CRL were specific to certain development batches of ALKS 3831. The company believes this issue has since been resolved and that sufficient data is available to address these observations. Alkermes is preparing those data for submission and plans to work closely with the Agency to resolve these items in a timely manner and complete labeling discussions for the application.

Consistent with FDA's August 2020 Guidance for Industry related to manufacturing inspections during the COVID-19 global pandemic, the Agency did not conduct an on-site Pre-Approval Inspection (PAI) at the company's Wilmington, OH manufacturing facility during its review of the NDA, and instead conducted a remote review of records under section 704(a)(4) of the Federal Food, Drug, and Cosmetic Act. FDA confirmed receipt of the requested records provided by Alkermes on Sept. 11, 2020 and, since that date, no report or feedback from this records review was provided to Alkermes until receipt of the CRL.

"We will continue to work closely with the Agency in an expeditious manner to support approval of ALKS 3831 for the treatment of schizophrenia and bipolar I disorder and believe we have a clear path to resolution. Importantly, there were no clinical issues identified in the CRL pertaining to ALKS 3831's efficacy or safety, and no new studies were requested for approval of the application," said Craig Hopkinson, M.D., Chief Medical Officer and Executive Vice President of Research & Development at Alkermes.

The NDA submission for ALKS 3831 was based on data from 27 clinical studies, including 18 studies evaluating ALKS 3831 and nine studies evaluating samidorphan alone, and pharmacokinetic bridging data comparing ALKS 3831 and ZYPREXA[®]. Throughout the clinical development program, ALKS 3831 demonstrated a consistent antipsychotic efficacy, safety, and tolerability profile in patients with schizophrenia.

In October 2020, the Psychopharmacologic Drugs Advisory Committee and the Drug Safety and Risk Management Advisory Committee appointed by the FDA jointly voted that samidorphan meaningfully mitigates olanzapine-associated weight gain (16 yes, 1 no) and that the safety profile of ALKS 3831 has been adequately characterized (13 yes, 3 no, 1 abstention). The committees also jointly voted that labeling is sufficient to mitigate the risks related to the opioid antagonist action of samidorphan (11 yes, 6 no).

Conference Call

Alkermes will host a conference call for analysts and investors on Tuesday, Nov. 17, 2020, at 8:00 a.m. ET (1:00 p.m. GMT). The webcast player may be accessed on the Investors section of Alkermes' website at www.alkermes.com. To participate in the question and answer session, please dial in to the conference call, which may be accessed by dialing +1 877-407-2988 for U.S. callers and +1 201-389-0923 for international callers. In addition, a replay of the conference call may be accessed by visiting Alkermes' website or by dialing +1 877-660-6853 for U.S. callers and +1 201-612-7415 for international callers, using replay access code 13713465. The conference call replay will be available from 11:00 a.m. ET (4:00 p.m. GMT) on Tuesday, Nov. 17, 2020 through Tuesday, Nov. 24, 2020.

About Schizophrenia

Schizophrenia is a serious brain disorder marked by positive symptoms (hallucinations and delusions, disorganized speech and thoughts, and agitated or repeated movements) and negative symptoms (depression, blunted emotions and social withdrawal).¹ An estimated 2.4 million American adults have schizophrenia,² with men and women affected equally.

About Bipolar I Disorder

Bipolar disorder is a brain disorder that causes shifts in a person's mood, energy and ability to function. Individuals with this brain disorder may experience debilitating mood shifts from extreme highs (mania) to extreme lows (depression). Bipolar I disorder is characterized by the occurrence of at least one manic episode, with or without the occurrence of a major depressive episode, and affects approximately one percent of the adult population in the United States in any given year.³

About ALKS 3831 (olanzapine/samidorphan)

ALKS 3831 is an investigational, novel, once-daily, oral atypical antipsychotic drug candidate for the treatment of adults with schizophrenia and for the treatment of adults with bipolar I disorder. ALKS 3831 is composed of samidorphan, a novel, new molecular entity, co-formulated with the established antipsychotic agent, olanzapine, in a single bilayer tablet.

About Alkermes plc

Alkermes plc is a fully integrated, global biopharmaceutical company developing innovative medicines in the fields of neuroscience and oncology. The company has a portfolio of proprietary commercial products focused on addiction and schizophrenia, and a pipeline of product candidates in development for schizophrenia, bipolar I disorder, neurodegenerative disorders and cancer. 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 potential therapeutic and commercial value of ALKS 3831 for the treatment of adults with schizophrenia and the treatment of adults with bipolar I disorder; the company's expectations regarding next steps for the NDA for ALKS 3831, including its plans to engage with the FDA to resolve any outstanding FDA requests; and the company's belief in its ability to expeditiously complete labeling discussions with the FDA and resolve any outstanding items required by the FDA to support approval of the NDA for ALKS 3831. The company cautions 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 be able to sufficiently resolve all FDA requests to meet the FDA's requirements for approval in a timely manner or at all; whether data from the company's manufacturing processes may be interpreted by the FDA in different ways than the company interprets it; potential changes in the cost, scope and duration of the ALKS 3831 development and regulatory program following receipt of the FDA's CRL; whether the FDA will approve the NDA for ALKS 3831 in a timely manner or at all; if approved, whether the FDA will impose conditions on the marketing of ALKS 3831, such as a risk evaluation and mitigation strategy; whether future clinical trials for ALKS 3831, if any, will be completed on time or at all; unanticipated impacts of the COVID-19 pandemic on the operations of the company and on the operations of the regulatory agencies involved in the review and potential approval of ALKS 3831; whether ALKS 3831 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, 2019, the company's Quarterly Report on Form 10-Q for the quarter ended June 30, 2020 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.

ZYPREXA® is a registered trademark of Eli Lilly & Company.

¹American Psychiatric Association. Schizophrenia Spectrum and Other Psychiatric Disorders. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington, DC: American Psychiatric Publishing; 2013.

² National Institutes of Health. *Schizophrenia*. Accessed on Nov. 16, 2020 from [https://archives.nih.gov/asites/report/09-09-2019/report.nih.gov/nihfactsheets/Pdfs/Schizophrenia\(NIMH\).pdf](https://archives.nih.gov/asites/report/09-09-2019/report.nih.gov/nihfactsheets/Pdfs/Schizophrenia(NIMH).pdf).

³ Merikangas et al. Lifetime and 12-Month Prevalence of Bipolar Spectrum Disorder in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*, 2007 May; 64(5): 543-552. <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1931566/>

Alkermes Contacts:

For Investors: Sandy Coombs, +1 781 609 6377
For Media: Eva Stroynowski, +1 781 609 6823



C View original content to download multimedia: <http://www.prnewswire.com/news-releases/alkermes-receives-fda-complete-response-letter-related-to-alks-3831-manufacturing-records-review-301174254.html>

SOURCE Alkermes plc