



Alkermes Initiates Clinical Evaluation of Novel Immuno-Oncology Drug Candidate ALKS 4230 in Combination With PD-1 Inhibitor Pembrolizumab

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-- Ongoing Phase 1 Study Expanded to Assess Safety and Anti-Tumor Activity of ALKS 4230 With Pembrolizumab in Patients With Advanced Solid Tumors --

DUBLIN, Sept. 10, 2018 /PRNewswire/ -- [Alkermes plc](#) (Nasdaq: ALKS) today announced that it has expanded its ongoing phase 1 study for ALKS 4230, the company's immuno-oncology drug candidate, to evaluate its safety and anti-tumor activity when administered in combination with the FDA-approved PD-1 inhibitor KEYTRUDA® (pembrolizumab) in patients with advanced solid tumors. ALKS 4230 is an engineered fusion protein designed to preferentially bind and signal through the intermediate affinity interleukin-2 (IL-2) receptor complex, thereby selectively activating and increasing the number of immunostimulatory tumor-killing immune cells while avoiding the expansion of immunosuppressive cells that interfere with anti-tumor response. Pembrolizumab is an anti-PD-1 therapy that works by increasing the ability of the body's immune system to help detect and fight tumor cells.

"The emergence of therapeutics targeting the PD-1 pathway has revolutionized the field of oncology, yet there remains significant opportunity to improve the clinical benefit of checkpoint inhibitors for the treatment of solid tumors. There is strong scientific rationale supporting the combination of PD-1 pathway inhibition with cytokine therapy such as ALKS 4230 to activate the body's own immune system to fight cancer, and the potential synergies of ALKS 4230 and pembrolizumab on anti-tumor activity may expand treatment options for patients in a variety of tumor settings," said Craig Hopkinson, M.D., Chief Medical Officer and Senior Vice President of Medicines Development and Medical Affairs at Alkermes. "We've accelerated clinical evaluation of ALKS 4230 in combination with pembrolizumab based on data from our ongoing monotherapy dose-escalation stage of the phase 1 study, where ALKS 4230 demonstrated dose-dependent pharmacodynamic effects on circulating natural killer cells and CD8+ T cells, and minimal and non-dose dependent effects on immunosuppressive regulatory T cells. These data validate our design rationale for ALKS 4230, and we look forward to sharing initial data from our dose-escalation cohorts at a medical meeting later this year."

Evaluation of the safety and anti-tumor activity of ALKS 4230 in combination with pembrolizumab will be assessed in certain PD-1 approved tumor types in both refractory and treatment naïve patients, including non-small cell lung cancer (NSCLC), head and neck squamous cell carcinoma, gastric cancer, urothelial carcinoma and microsatellite instability-high cancers. Melanoma and renal cell carcinoma will also be evaluated in the cohort of treatment naïve patients. The combination of ALKS 4230 and pembrolizumab will also be assessed in certain PD-1 unapproved tumor types, including colorectal cancer, triple-negative breast cancer, ovarian carcinoma, soft tissue sarcomas, and patients with metastatic NSCLC whose tumors express low or undetectable PD-L1 (tumor proportion score <1%).

About the Phase 1 Study

The Alkermes-sponsored phase 1 study for ALKS 4230 includes three distinct stages: the ongoing monotherapy dose-escalation stage, the planned monotherapy dose-expansion stage and the newly initiated combination therapy stage with pembrolizumab. The dose-escalation stage is designed to determine a maximum tolerated dose of ALKS 4230 in a monotherapy setting and to identify the optimal dose range of ALKS 4230 based on measures of immunological-pharmacodynamic effects. Upon completion of the dose-escalation stage, the company expects to initiate the monotherapy dose-expansion stage in up to 42 patients with renal cell carcinoma or melanoma. The newly initiated combination therapy stage of the phase 1 study will assess the safety profile and anti-tumor activity of ALKS 4230 with pembrolizumab in up to 148 patients with select advanced solid tumors. This combination therapy stage will be run independent of, and concurrently with, the monotherapy dose-escalation and dose-expansion stages of the trial.

Anti-tumor response and duration of response assessments in the dose-expansion and combination stages of the phase 1 study will be based on investigator-assessed, immune-related response (irRC) criteria and independent, central, blinded radiographic review per Response Evaluation Criteria in Solid Tumors (RECIST 1.1) criteria.

About ALKS 4230

ALKS 4230 is an engineered fusion protein designed to preferentially bind and signal through the intermediate affinity interleukin-2 (IL-2) receptor complex, thereby selectively activating and increasing the number of immunostimulatory tumor-killing immune cells while avoiding the expansion of immunosuppressive cells that interfere with anti-tumor response. The selectivity of ALKS 4230 is designed to leverage the proven anti-tumor effects while overcoming limitations of existing IL-2 therapy, which activates both immunosuppressive and tumor-killing immune cells.

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 potential therapeutic and commercial value of ALKS 4230; and the clinical development plans for ALKS 4230, including the timing of expected presentation of initial data from the monotherapy dose-escalation stage of


the phase 1 study and details of the planned monotherapy dose-expansion stage of the phase 1 study and the newly initiated combination therapy stage of the phase 1 study. 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 are subject to a variety of risks and uncertainties, many of which are beyond the company's control, which could cause actual results to differ materially from those expressed or implied in the forward-looking statements. These risks and uncertainties include, among others, whether preclinical and early clinical results for ALKS 4230 will be predictive of future clinical study results; whether ALKS 4230 could be shown to be unsafe or ineffective; whether future clinical trials or future stages of ongoing clinical trials for ALKS 4230 will be initiated or completed on time or at all; changes in the cost, scope and duration of development activities for ALKS 4230; 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.

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