# Alkermes Initiates Phase 2 Study Designed to Evaluate Clinical and Immunologic Activity of ALKS 4230 on Tumor Microenvironment in Patients with Advanced Solid Tumors

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DUBLIN, Aug. 19, 2020 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today announced the initiation of ARTISTRY-3, a new phase 2 study to evaluate the clinical and immunologic effects of ALKS 4230 monotherapy on the tumor microenvironment of a variety of advanced, malignant solid tumors. ALKS 4230, a novel cytokine, is an investigational, engineered fusion protein designed to selectively expand tumor-killing immune cells while avoiding the interleukin-2 (IL-2)-induced activation of immunosuppressive cells by preferentially binding to the intermediate-affinity IL-2 receptor complex.

"Early clinical data from our ARTISTRY program showed that ALKS 4230 selectively expanded cancer-fighting immune cells in the periphery, with negligible effects on regulatory T cells (Tregs)," said Craig Hopkinson, M.D., Chief Medical Officer and Executive Vice President of Research & Development at Alkermes. "Data from the ARTISTRY-3 clinical trial will provide a deeper understanding of the effects of ALKS 4230 on immunologic activity in the tumor microenvironment across a variety of tumor types. Findings from this trial may help us answer important mechanistic questions and identify the tumor types for which ALKS 4230 could offer the most clinical benefit, thereby helping to inform a potential registration strategy."

This single-center, open-label study will evaluate treatment-emergent changes in the tumor microenvironment and peripheral blood immunophenotypes, as well as the safety, tolerability, and pharmacokinetic profile of ALKS 4230 (6µg/kg) dosed intravenously, as lead-in monotherapy followed by combination with the anti-PD-1 therapy KEYTRUDA® (pembrolizumab), in patients with select advanced malignant solid tumors. Paired tumor biopsies will be collected pre–treatment and following the monotherapy and combination phases to evaluate the effects of ALKS 4230 on the immune cell repertoire, including changes in density and ratio of immune cells, within the tumor microenvironment. The study will also assess clinical anti-tumor activity (overall response rate and duration of response) of ALKS 4230 as one of its secondary objectives.

ARTISTRY-3 is the fourth clinical trial evaluating ALKS 4230 as a novel immuno-oncology candidate. ARTISTRY-1 and ARTISTRY-2 are ongoing, phase 1/2 studies evaluating ALKS 4230 as a monotherapy and in combination with pembrolizumab. ARTISTRY-1 and ARTISTRY-2 are evaluating intravenous and subcutaneous administration of ALKS 4230, respectively. ION-01 is an ongoing, phase 2 multi-site trial, designed to estimate the response rate to ALKS 4230 in combination with pembrolizumab in patients with advanced or recurrent head and neck squamous cell cancer who did not achieve complete remission with an anti-PD-(L)1 antibody treatment.

**About ALKS 4230**

ALKS 4230 is an investigational, novel, engineered fusion protein comprised of modified interleukin-2 (IL-2) and the high affinity IL-2 alpha receptor chain, designed to selectively expand tumor-killing immune cells while avoiding the activation of immunosuppressive cells by preferentially binding to the intermediate-affinity IL-2 receptor complex. The selectivity of ALKS 4230 is designed to leverage the proven anti-tumor effects of existing IL-2 therapy while mitigating certain limitations.

**About the ARTISTRY Clinical Development Program**

ARTISTRY is an Alkermes-sponsored clinical development program evaluating ALKS 4230 in patients with advanced solid tumors.

ARTISTRY-1 and ARTISTRY-2 are phase 1/2 studies evaluating the safety, tolerability, efficacy and pharmacokinetic and pharmacodynamic effects of ALKS 4230 in patients with refractory advanced solid tumors, in both monotherapy and combination settings with the PD-1 inhibitor KEYTRUDA® (pembrolizumab). In ARTISTRY-1, ALKS 4230 is administered as an intravenous infusion daily for five consecutive days. In ARTISTRY-2, ALKS 4230 is administered subcutaneously and is being evaluated with once-weekly and once-every-three-week dosing schedules.

ARTISTRY-3 will evaluate the clinical and immunologic activity of intravenous ALKS 4230 monotherapy on tumor microenvironment in advanced solid tumor patients.

**About Alkermes**

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.

**Alkermes 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 value of ALKS 4230 as a cancer immunotherapy when used as monotherapy or in combination; and the clinical trial design for, and potential findings from, the ARTISTRY-3 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 they are necessarily subject to a high degree of uncertainty and risk. Actual 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 ALKS 4230, as a monotherapy or in combination, could be shown to be unsafe or ineffective; whether preclinical and preliminary, interim or final clinical results for ALKS 4230—whether as a monotherapy or in combination with pembrolizumab—will be predictive of future data from the same studies, results of future clinical studies or real-world results; whether future clinical trials or future stages of ongoing clinical trials for ALKS 4230, as a monotherapy or in combination, will be initiated or completed on time or at all; changes in the cost, scope and duration of, and clinical trial operations for, development activities for ALKS 4230, including changes relating to the novel coronavirus (COVID-19); 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.

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