



Alkermes Announces Publication of Preclinical Data for ALKS 4230 in the Journal for ImmunoTherapy of Cancer

April 22, 2020

- In Preclinical Model, ALKS 4230 Exhibited Improved Anti-tumor Efficacy and Lower Toxicity Relative to Recombinant Human IL-2 -

DUBLIN, April 22, 2020 /PRNewswire/ -- [Alkermes plc](#) (Nasdaq: ALKS) today announced the publication of preclinical data demonstrating the selectivity and anti-tumor efficacy of its investigational, immunotherapy candidate, ALKS 4230, in the [Journal for ImmunoTherapy of Cancer](#) (JITC). 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.

The manuscript, titled "[ALKS 4230: a novel engineered IL-2 fusion protein with an improved cellular selectivity profile for cancer immunotherapy](#)," provides an in-depth explanation of the design of ALKS 4230 and includes data from multiple assays that demonstrated that ALKS 4230 selectively activated the intermediate-affinity IL-2 receptor as intended. Additionally, data from a mouse B6F10 lung metastasis model demonstrated that treatment with ALKS 4230 achieved a maximum of 100% inhibition of tumor growth with one of the doses tested, as compared to treatment with recombinant human IL-2 (rhIL-2), which achieved a maximum of 70% inhibition of tumor growth with one of the doses tested. In this model, equivalent anti-tumor activity of ALKS 4230 was observed whether it was administered intravenously or subcutaneously.

"Targeting the IL-2 pathway has shown significant efficacy in renal cell carcinoma and melanoma, however the broader and more prevalent use of this approach in treating cancer has been limited by the toxicity profile and side effects associated with currently available IL-2-based therapy," said Marc Ernstoff, M.D., Roswell Park Comprehensive Cancer Center, and publication co-author. "These preclinical data demonstrated that ALKS 4230 selectively activated and expanded cancer-fighting cells in mice with less toxicity than conventional high-dose IL-2 therapy. These data support further clinical evaluation of ALKS 4230 as a potential novel cytokine-based cancer immunotherapy."

Key findings published in the manuscript include the following:

- ALKS 4230 demonstrated a similar potency to rhIL-2 in activating mouse CD8⁺ T cells and Natural Killer (NK) cells. However, ALKS 4230 was ~ 1000 times less potent than rhIL-2 in activating regulatory T cells (T_{regs}), which are known to suppress cancer-fighting immune mechanisms.
- ALKS 4230 treatment of peripheral blood mononuclear cells (PBMCs) from patients with melanoma or renal cell carcinoma resulted in the selective expansion of CD8⁺ T cells and NK cells with negligible effects on T_{reg} expansion.
- ALKS 4230 showed superior anti-tumor efficacy to rhIL-2 in a mouse B6F10 lung metastasis model and the ability to achieve equivalent anti-tumor efficacy when administered either intravenously or subcutaneously.
- In mice, ALKS 4230 treatment induced markedly lower levels of cytokines typically associated with cytokine release syndrome, compared to rhIL-2.

"We leveraged our therapeutic development expertise and protein engineering capabilities to create ALKS 4230, a stable fusion protein. It is designed to minimize toxicity without compromising the proven anti-cancer effects of IL-2-based therapies," said Heather Losey, Ph.D., Director, Program Lead in Immuno-Oncology at Alkermes, and corresponding author of the publication. "We are encouraged by ALKS 4230's preclinical profile, as discussed in this important peer-reviewed publication, including its selectivity for immune effector cells, pharmacokinetics and preclinical efficacy. We look forward to progressing the ARTISTRY clinical development program and seeing how the data mature for this novel, investigational immunotherapy."

ALKS 4230 is currently being studied in both monotherapy and combination settings as part of the Alkermes-sponsored ARTISTRY clinical development program.

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](#) is an ongoing phase 1/2 study in which ALKS 4230 is administered as an intravenous infusion daily for five consecutive days. ARTISTRY-1 has three distinct stages: an ongoing monotherapy dose-escalation stage, an ongoing monotherapy expansion stage, and an ongoing combination therapy stage with the PD-1 inhibitor KEYTRUDA[®] (pembrolizumab) in patients with select advanced solid tumors.

[ARTISTRY-2](#) is an ongoing phase 1/2 study in which ALKS 4230 is administered subcutaneously as monotherapy and in combination with pembrolizumab in patients with advanced solid tumors. ARTISTRY-2 is designed to explore the safety, tolerability and efficacy of ALKS 4230 administered subcutaneously and assess once-weekly and once-every-three-week dosing schedules.

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 and commercial value of ALKS 4230 as a cancer immunotherapy; and clinical development plans for ALKS 4230, including details of the ongoing ARTISTRY-1 and ARTISTRY-2 phase 1/2 studies. 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 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 ALKS 4230, as a monotherapy or in combination, could be shown to be unsafe or ineffective; 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 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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Alkermes Contacts:

For Investors: Sandy Coombs, +1 781 609 6377

For Media: Sourojit Bhowmick, Ph.D., +1 781 609 6397



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