Alkermes Presents New Data on ALKS 4230 at Society for Immunotherapy of Cancer's (SITC) 33rd Annual Meeting

November 6, 2018

-- Initial Clinical Data From Ongoing Monotherapy Dose-Escalation Stage of Phase 1 Study to be Presented --

DUBLIN, Nov. 6, 2018 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today announced the presentation of three abstracts at the Society for Immunotherapy of Cancer's (SITC) 33rd Annual Meeting in Washington, D.C., Nov. 9-11, 2018. Initial clinical data from the ongoing monotherapy dose-escalation stage of the phase 1 study for ALKS 4230, the company's immuno-oncology drug candidate, will be presented for the first time. ALKS 4230 is a novel, engineered fusion protein designed to selectively activate tumor-killing immune cells while avoiding the expansion of immunosuppressive cells by preferentially binding to the intermediate-affinity interleukin-2 (IL-2) receptor complex.

"The selectivity of ALKS 4230 is designed to leverage the proven anti-tumor effects of existing IL-2 therapy while overcoming its limitations. These initial data from our phase 1 study demonstrate the unique mechanism of ALKS 4230, with 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," said Craig Hopkinson, M.D., Chief Medical Officer and Senior Vice President of Medicines Development and Medical Affairs at Alkermes. "Based on these data from our initial monotherapy dose-escalation cohorts, we've accelerated the development program to include evaluation of ALKS 4230 in combination with the PD-1 inhibitor pembrolizumab (KEYTRUDA®). As we continue to pursue the optimal dose of ALKS 4230 in the monotherapy setting, we are also eager to explore other regimens that may provide greater dosing flexibility for patients, and plan to initiate a study for subcutaneous dosing in early 2019."

Details of the poster presentations at SITC are as follows:

- Abstract Poster #P423: "Safety, Pharmacokinetics and Pharmacodynamic Effects of ALKS 4230 in Patients With Advanced Solid Tumors From the Ongoing Dose Escalation Portion of a First-in-Human (FIH) Study," will be presented by Ulka N. Vaishampayan, M.D., Barbara Ann Karmanos Cancer Institute
  - ALKS 4230 was assessed in 24 patients with refractory solid tumors at doses ranging from 0.1 µg/kg/day to 3 µg/kg/day as part of the ongoing phase 1 study.
  - Treatment with ALKS 4230 resulted in a dose-dependent increase in circulating natural killer (NK) cells and $CD8^+$ T cells with a near 4-fold and 2-fold expansion, respectively, at 3 µg/kg/day, and minimal, non-dose-dependent change in regulatory T (T_{reg}) cells.
  - Fever and chills were the most common treatment-related adverse events (AEs) for ALKS 4230.
  - These data support the rationale for assessing ALKS 4230 at the 3 µg/kg/day dose in combination with pembrolizumab, as well as for continued dose escalation in the monotherapy setting.
- Abstract Poster #P425: "Pharmacokinetics and Pharmacodynamic Effects of ALKS 4230, an Investigational Immunotherapeutic Agent, in Cynomolgus Monkeys After Intravenous and Subcutaneous Administration," will be presented by Lei Sun, Ph.D., Alkermes, Inc.
  - Data from two non-human primate studies demonstrated that subcutaneous administration of ALKS 4230 can achieve similar total systemic exposure of ALKS 4230 compared to intravenous administration, yet with less frequent dosing and a lower C_{max}, leading to similar expansion of total $CD8^+$ T cell and NK cell populations.
  - These data support further clinical evaluation of subcutaneous administration of ALKS 4230 as an alternative to intravenous dosing.
- Abstract Poster #P123: "Peripheral Blood Lymphocyte Responses in Patients With Renal Cell Carcinoma Treated With High-Dose Interleukin-2," will be presented by Wenxin Xu, M.D., Beth Israel Deaconess Medical Center
  - Consistent with the known biological activities of IL-2, administration of high-dose IL-2 resulted in an approximate 2-fold expansion of circulating cytotoxic effector $CD8^+$ T cells and NK cells and an approximate 4-fold expansion of circulating T_{reg} cells.
  - These data provide quantitative measures of the expansion of cytotoxic effectors such as $CD8^+$ T cells and NK cells relative to T_{reg} cells for high-dose IL-2, and may be useful in the future for evaluating possible differences in immune response to newer formulations of IL-2.

Posters will be on display both Friday, Nov. 9 and Saturday, Nov. 10 beginning at 8:00 a.m. ET in Hall E of the Walter E. Washington Convention Center. For more information, including a complete list of abstracts, please visit the SITC website at https://www.sitcancer.org/2018/.

About the Phase 1 Study for ALKS 4230

The phase 1 study for ALKS 4230 includes three distinct stages: the ongoing monotherapy dose-escalation stage, the planned monotherapy dose-expansion stage and the recently 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, Alkermes expects to initiate the monotherapy dose-expansion stage in patients with renal cell carcinoma or melanoma. The combination therapy stage of the phase 1 study will assess the safety profile and anti-tumor activity of ALKS 4230 with pembrolizumab in 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 criteria(irRC) and independent, central, blinded radiographic review per Response Evaluation Criteria in Solid Tumors (RECIST 1.1) criteria.

About ALKS 4230

ALKS 4230 is a novel, engineered fusion protein designed to selectively activate tumor-killing immune cells while avoiding the expansion of immunosuppressive cells by preferentially binding to the intermediate-affinity interleukin-2 (IL-2) receptor complex. The selectivity of ALKS 4230 is designed to leverage the proven anti-tumor effects of existing IL-2 therapy while overcoming its limitations.

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 clinical development plans for ALKS 4230, including the timing of the expected presentation of, and other details concerning, the initial data from the monotherapy dose-escalation stage of the phase 1 study, and the expected timing and details of the planned monotherapy dose-expansion stage of the phase 1 study, the newly initiated combination therapy stage of the phase 1 study and the planned subcutaneous dosing 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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