Alkermes Announces New Data From ALKS 4230 Clinical Development Program at Society for Immunotherapy of Cancer's (SITC) 34th Annual Meeting

November 8, 2019

–Preliminary Safety and Efficacy Data From ARTISTRY-1 Show Signs of Clinical Benefit and Tolerability of ALKS 4230 as Monotherapy and in Combination With Pembrolizumab–

–Posters and a Corporate Presentation Related to the ALKS 4230 Program Posted to Company Website–

DUBLIN, Nov. 8, 2019 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today presented new data from the company's ARTISTRY clinical development program related to ALKS 4230 at the Society for Immunotherapy of Cancer's (SITC) 34th Annual Meeting in National Harbor, MD. ALKS 4230 is an investigational, engineered fusion protein designed to selectively expand tumor-killing immune cells while avoiding the IL-2-induced activation of immunosuppressive cells by preferentially binding to the intermediate-affinity interleukin-2 (IL-2) receptor complex. The company presented preliminary clinical data from ARTISTRY-1, the ongoing phase 1/2 study investigating ALKS 4230 administered intravenously, as well as study design details and preliminary safety data from ARTISTRY-2, the ongoing phase 1/2 study investigating ALKS 4230 administered subcutaneously. Both studies are evaluating ALKS 4230 as a monotherapy and in combination with pembrolizumab (KEYTRUDA®). The posters presented by the company at SITC and a corporate presentation related to the ALKS 4230 program are available on the Investors section of www.alkermes.com.

"The early signs of clinical efficacy and safety that we have seen so far with ALKS 4230 as both monotherapy and in combination with pembrolizumab are encouraging, and have been observed in multiple solid tumor types, including in PD-(L)1 inhibitor unapproved indications," said Craig Hopkinson, M.D., Chief Medical Officer and Senior Vice President of Medicines Development and Medical Affairs at Alkermes. "In addition to the preliminary data from ARTISTRY-1, we are making progress in ARTISTRY-2 and are now enrolling the next set of cohorts that will evaluate once-weekly and once-every-three-week dosing regimens. We look forward to presenting data from ARTISTRY-2 at a future medical meeting."

"Despite the introduction of immunotherapies and other innovations in the field of oncology, there remains a high unmet need for new treatments, as many patients are not eligible to receive certain medications such as checkpoint inhibitors, or don't respond well to such medications," said Ulka N. Vaishampayan, M.D., Professor of Oncology at Wayne State University and Director of the Phase I Program at the Karmanos Cancer Institute. "The emerging data from the ARTISTRY clinical program are encouraging, with ALKS 4230 demonstrating initial signs of clinical benefit and a safety profile that is generally consistent with what is expected with cytokine therapy. Importantly, no evidence of vascular leak syndrome, which is the most significant limitation to currently available IL-2 therapy, has been observed as of October 31st."

The following preliminary safety and efficacy findings from the ARTISTRY-1 monotherapy and combination therapy cohorts are as of Aug. 2, 2019, unless otherwise noted:

Data presented from the ongoing monotherapy dose-escalation stage of ARTISTRY-1 included five completed cohorts, spanning a dose range of 0.1 µg/kg/day to 6 µg/kg/day:

- A total of 36 patients with refractory advanced solid tumors were treated.
- Consistent with earlier non-clinical findings, treatment with ALKS 4230 selectively expanded natural killer (NK) and $CD8^+$ T cells and had negligible, non-dose-dependent effects on regulatory T cells (T_{regs}).
- ALKS 4230 3 µg/kg/day dose was selected for initial evaluation in combination with pembrolizumab, based on the cell expansion and tolerability profile seen at this dose.
- ALKS 4230 6 µg/kg/day dose was identified as the monotherapy recommended phase 2 dose (RP2D) for intravenous administration. Data from this dose demonstrated our targeted tolerability profile, along with the targeted lymphocyte cell expansion without corresponding IL-2-induced T_{reg} activation.
- At doses of 3 µg/kg/day and 6 µg/kg/day of ALKS 4230, 8 of 14 patients with evaluable initial scans had stable disease.
    - This includes one patient in the 6 µg/kg/day group with heavily pretreated pancreatic adenocarcinoma who received monotherapy ALKS 4230 for 10 months, with stable disease maintained for approximately 6 months. Following progressive disease, this patient rolled over to combination therapy with pembrolizumab for 4.5 months.
- The most frequently reported adverse events (AEs), regardless of relationship to ALKS 4230, were fever and chills, which are anticipated effects of cytokine administration. No Grade 4 or 5 treatment-related AEs were reported, and no signs of vascular leak syndrome were observed at any dose.
- The maximum tolerated dose of monotherapy intravenous ALKS 4230 has not been determined and dose escalation is ongoing.

Data presented from the combination stage of ARTISTRY-1 focused on the cohort of PD-(L)1 inhibitor unapproved tumor types and one monotherapy rollover patient. These patients received the ALKS 4230 3 µg/kg/day dose in combination with pembrolizumab:

- 26 patients (n=1 monotherapy rollover, n=25 PD-(L)1 inhibitor unapproved tumor types) were treated in the cohort.
- 12 of the 18 patients with evaluable scans achieved stable disease or better, including:

- One patient with ovarian cancer had a confirmed partial response at Cycle 6 and demonstrated complete normalization of her CA-125 (tumor marker) levels at Cycle 4, which continued in the normal range: 282 U/mL (screening) to 12.6 U/mL (Cycle 10). As of Oct. 31, 2019, this patient remains on therapy.
- One patient with triple negative breast cancer showed a >50% reduction in target lesion size at Cycle 8. As is common with checkpoint inhibitor treatment, small new lesions developed for this patient at Cycle 2. The decrease in her target lesions and in these small new lesions qualified her for an immune-partial response (iPR) based on iRECIST (Response Evaluation Criteria in Solid Tumors) criteria. As of Oct. 31, 2019, this patient remains on therapy.

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In addition to data from ARTISTRY-1, the company also presented a trials-in-progress poster on ARTISTRY-2. The study's initial dose escalation cohort (n=7) has been completed at the once-weekly 0.3 mg subcutaneous dose of ALKS 4230. Initial signals of tolerability were observed, and no patient discontinued treatment due to AEs.

As of Oct. 31, 2019, 6 of 7 patients from the first cohort remained on therapy. Enrollment in the next two dose escalation cohorts, to evaluate ALKS 4230 0.6 mg once-weekly and ALKS 4230 1.0 mg once-every-three-weeks, is ongoing. The company plans to present data from ARTISTRY-2 at a future medical meeting.

About ALKS 4230

ALKS 4230 is a 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 IL-2-induced 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, a recently initiated 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 of ALKS 4230 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 plc

Alkermes plc is a fully integrated, global biopharmaceutical company developing innovative medicines for the treatment of central nervous system (CNS) diseases and oncology. The company has a diversified commercial product portfolio and a substantial clinical pipeline of product candidates for diseases that include schizophrenia, depression, addiction, multiple sclerosis 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 design hypothesis and potential therapeutic value of ALKS 4230, including in combination with pembrolizumab; clinical development plans for ALKS 4230, including details of the ongoing ARTISTRY-1 and ARTISTRY-2 phase 1/2 studies and the company's plans for presentation of data relating to the ARTISTRY development program. 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 preliminary, interim or final data from preclinical and early clinical studies of ALKS 4230, 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 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, 2018 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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