Alkermes Presents New Clinical Data on ALKS 4230 in Mini Oral Presentation at 2020 European Society for Medical Oncology (ESMO) Virtual Congress

September 18, 2020

- Data Provide Evidence of Clinical Benefit and Tolerability of ALKS 4230 as Monotherapy in Melanoma and in Combination With Pembrolizumab in Multiple Tumor Types -

- Monotherapy Melanoma Cohort Expanded Based on Achievement of Protocol-Defined Response Criteria -

- Company to Host Investor Webcast at 8:30 a.m. ET on Friday, Sept. 18, 2020 -

DUBLIN, Sept. 18, 2020 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today presented new clinical data from ARTISTRY-1, an ongoing phase 1/2 study evaluating Alkermes' investigational engineered interleukin-2 (IL-2) variant immunotherapy, ALKS 4230, administered intravenously as monotherapy and in combination with the PD-1 inhibitor pembrolizumab (KEYTRUDA®) in patients with refractory solid tumors. Data from the ongoing ARTISTRY-1 study showed encouraging single-agent activity of ALKS 4230 in melanoma and durable responses in multiple tumor types in combination with pembrolizumab. The most frequently observed treatment-emergent adverse events (AEs) in both the monotherapy and combination cohorts were transient fever and chills, consistent with anticipated effects of immunotherapy. These data are being presented in a mini oral presentation at the 2020 European Society for Medical Oncology (ESMO) Virtual Congress, held Sept. 18-21. The company also announced today the expansion of the ARTISTRY-1 monotherapy melanoma cohort based on achievement of protocol-defined efficacy response criteria.

"New treatment options are needed to improve clinical outcomes in many cancer types. Current immunotherapies are not an option for all cancer types and only a portion of eligible patients respond to them," said Ulka N. Vaishampayan, M.D., Lead Investigator and Professor, Internal Medicine, Division of Hematology/Oncology, University of Michigan. "The monotherapy anti-tumor efficacy and the durable responses in the combination cohorts in multiple tumor types, including heavily pretreated platinum-resistant ovarian cancer, triple-negative breast cancer and esophageal cancer, provide additional insights into ALKS 4230's potential as a treatment option for patients with advanced tumors that may not respond to the current standard of care."

Data highlights include:

ALKS 4230 Monotherapy
The monotherapy expansion stage of ARTISTRY-1 is evaluating the recommended phase 2 dose of ALKS 4230 (6 µg/kg/day) administered intravenously in patients with refractory melanoma or refractory renal cell carcinoma (RCC). A total of 15 patients across both monotherapy cohorts were treated, with responses observed in melanoma. *(Data as of July 24, 2020 unless otherwise noted.)*

- Melanoma cohort
  - Of the 5 evaluable melanoma patients (≥1 scan), one had a confirmed partial response (PR) and two had stable disease on at least two consecutive scans.
  - The PR was achieved in a patient with metastatic urethral melanoma by week 20 of treatment, and a deepening of response was observed through week 39 of treatment. This patient's serum lactate dehydrogenase (LDH) levels, a known marker for treatment response in melanoma, normalized at week 5 of treatment and remained within the normal range throughout the treatment period. As of July 27, 2020, the patient had experienced a total tumor shrinkage of 39% and was continuing monotherapy treatment.
  - Since the July 24, 2020 data cut, one additional melanoma patient achieved a PR, awaiting a confirmatory scan. As of Sept. 1, 2020, this additional patient had experienced a total tumor shrinkage of 39% and was continuing monotherapy treatment.
  - With the observance of two PRs among the first 6 evaluable patients in the monotherapy melanoma cohort, the protocol-defined response criteria for expansion of this cohort was achieved, and the cohort will now enroll up to 20 additional patients for a total of up to 41 patients.

ALKS 4230 in Combination with Pembrolizumab
Data presented at ESMO from the combination stage of ARTISTRY-1 included data from patients in the PD-1/L1-approved, PD-1/L1-unapproved and monotherapy rollover cohorts (n=67 total). Patients representing more than 10 tumor types received ALKS 4230 3 µg/kg/day in combination with pembrolizumab. Responses were observed across multiple tumor types. *(Data as of Aug. 7, 2020.)*

- Refractory ovarian cancer
  - Of the 13 evaluable patients (≥1 scan) with progressive, refractory ovarian cancer, 9 demonstrated stable disease on their first scan. Six of these 9 patients received a second scan by the data cutoff date, and 5 had stable disease or better. All 5 of these ovarian cancer patients were heavily pretreated and platinum-resistant, and each experienced tumor burden reduction with the combination of ALKS 4230 and pembrolizumab. Of these 5 patients:
    - One patient with platinum-resistant ovarian cancer achieved a complete response (CR) by week 45 of treatment, and a deepening of response was observed through week 81 of treatment. As of the data cut,

this patient had a durable, confirmed CR and had remained on treatment for more than 18 months.
    - Two other patients with platinum-resistant ovarian cancer achieved PRs, one confirmed and one unconfirmed. As of the data cut, the patient with the confirmed PR demonstrated a deepening of response and had remained on treatment for more than 5 months.

- Other tumor types
    - Additional PRs were achieved in multiple other tumor types across the PD-1/L1 approved and unapproved cohorts, including one patient with triple-negative breast cancer and two patients with esophageal cancer (one of which is awaiting confirmation). As of the data cut, these three patients had sustained PRs and continued on treatment.

Safety and Tolerability
(Data as of July 24, 2020 unless otherwise noted.)

- The safety profile of ALKS 4230 in combination with pembrolizumab was generally consistent with the monotherapy profile. Based on the data available, ALKS 4230 in combination with pembrolizumab did not demonstrate any additive toxicity to that already established with pembrolizumab alone.
- The most frequently observed treatment-emergent AEs in both the monotherapy and combination groups were transient fever and chills, all grade 1 or 2 in severity, which are consistent with anticipated effects of cytokine therapy. One patient in the monotherapy cohort had a grade 3 transient hypotension that was managed with fluids. There were no reports of vascular leak syndrome, which is a known AE associated with high-dose IL-2 treatment.
- There were no deaths due to treatment-related AEs in the monotherapy cohorts. One death of a pancreatic cancer patient in the combination cohort, which occurred after the data cutoff, was due to inanition (starvation) and assessed as related to both study drugs.

"The data presented at ESMO include early evidence of ALKS 4230's single-agent activity and its potential to deliver clinical benefit in multiple tumor types as a combination therapy," said Craig Hopkinson, M.D., Chief Medical Officer and Executive Vice President of Research & Development at Alkermes. "We're seeing increased momentum in enrollment trends across the broader ARTISTRY clinical development program, and we look forward to presenting our accumulating data for ALKS 4230 at future medical meetings."

The mini oral presentation (#1027) titled, "ALKS 4230 Monotherapy and in Combination With Pembrolizumab in Patients With Refractory Solid Tumors (ARTISTRY-1)," is available on the ESMO website at www.esmo.org/meetings/esmo-virtual-congress-2020.

Conference Call and Webcast
Alkermes will host a webcast presentation and conference call with accompanying slides for analysts and investors on Friday, Sept. 18, 2020, at 8:30 a.m. ET (1:30 p.m. BST) to discuss the latest data from the ARTISTRY-1 clinical trial. The webcast will feature the lead study investigator, Dr. Ulka N. Vaishampayan, Professor of Internal Medicine, Division of Hematology/Oncology, at the University of Michigan, and members of Alkermes' management team. The webcast player may be accessed on the Investors section of Alkermes' website at www.alkermes.com. To participate in the question and answer session, please also dial in to the conference call, which may be accessed by dialing +1 877-407-2988 for U.S. callers and +1 201-389-0923 for international callers. In addition, a replay of the conference call may be accessed by visiting Alkermes' website or by dialing +1 877-660-6853 for U.S. callers and +1 201-612-7415 for international callers, using replay access code 13708824. The conference call replay will be available from 11:30 a.m. ET (4:30 p.m. BST) on Friday, Sept. 18, 2020 through Friday, Sept. 25, 2020.

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 pembrolizumab (KEYTRUDA®). 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 is a phase 2 study evaluating the clinical and immunologic effects of ALKS 4230 monotherapy administered intravenously on the tumor microenvironment of a variety of advanced, malignant solid tumors.

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 across multiple tumor types; and the status of and plans for the clinical development of

ALKS 4230, including enrollment trends across the ARTISTRY clinical development program, details of the ongoing ARTISTRY 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 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 results and data from ongoing clinical studies for ALKS 4230—whether as a monotherapy or in combination—will be predictive of future or final results from such 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 impact of the novel coronavirus (COVID-19) pandemic; 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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