# Alkermes Presents New Data on Nemvaleukin Alfa at 2021 American Society of Clinical Oncology Annual Meeting

June 4, 2021

**- Updated Data From ARTISTRY Clinical Program Highlight Anti-Tumor Activity as Monotherapy and in Combination With Pembrolizumab -**

**- Data Support Advancement of Regulatory Strategy in Cancers With High Unmet Need -**

**- Company to Host Investor Webcast Today at 4:00 p.m. ET -**

DUBLIN, June 4, 2021 /PRNewswire/ -- Alkermes plc (Nasdaq: ALKS) today announced new data from its ARTISTRY clinical development program for nemvaleukin alfa (nemvaleukin), Alkermes' novel, investigational engineered interleukin-2 (IL-2) variant immunotherapy. The data are being presented at the 2021 American Society of Clinical Oncology (ASCO) Annual Meeting, taking place virtually June 4-8, 2021, and in an investor webcast presentation hosted by the company.

The presentations include updated efficacy and safety data from ARTISTRY-1, an ongoing phase 1/2 study investigating intravenous (IV) nemvaleukin, which showed anti-tumor activity of IV nemvaleukin monotherapy in checkpoint inhibitor (CPI)-experienced melanoma and renal cell carcinoma (RCC) patients, and anti-tumor activity of IV nemvaleukin in combination with pembrolizumab in a range of difficult-to-treat tumors, including in CPI-unapproved tumor types, and in CPI-approved tumor types among both CPI treatment-naïve and pretreated patients. Durable and deepening responses have been observed with IV nemvaleukin, as monotherapy or in combination with pembrolizumab, in platinum-resistant ovarian cancer (PROC) and mucosal melanoma. Treatment-related adverse events (AEs) were mostly transient and manageable and the maximum tolerated dose had not yet been reached.

Alkermes' presentations also include data from ARTISTRY-2, an ongoing phase 1/2 study evaluating subcutaneous (SC) nemvaleukin. Findings include a pharmacodynamic response and safety profile that support the recommended phase 2 dose (RP2D), and encouraging early signs of anti-tumor activity in PROC.

"Intravenous nemvaleukin's observed single-agent activity in melanoma and renal cell carcinoma, and combination activity in both PD-1/L1 unapproved and approved tumor types, support its potential to be a treatment option for a range of difficult-to-treat cancers," said Valentina Boni, M.D., Ph.D., Lead Investigator, ARTISTRY-1 and Medical Oncologist Principal Investigator START Madrid at Centro Integral Oncológico Clara Campal. "In the ARTISTRY-1 trial, the durable and deepening responses observed in PROC and mucosal melanoma are particularly encouraging as these patients have limited treatment options."

"ARTISTRY-1 and ARTISTRY-2 have yielded important clinical data that will guide and serve as the foundation for future clinical evaluation of nemvaleukin. As the data have evolved, we have seen new objective responses in a range of tumors, and improvements upon certain previously reported responses, which provide additional support for nemvaleukin's potential utility," said Craig Hopkinson, M.D., Chief Medical Officer and Executive Vice President of Research & Development at Alkermes. "We are proud to participate in the important dialogue at this year's Annual Meeting of the American Society of Clinical Oncology and are committed to the development of medicines that seek to improve treatment outcomes for people affected by cancer, particularly cancers for which there are limited or no treatment options currently available."

Data highlights from the ASCO poster presentations and the company's investor presentation include:

**ARTISTRY-1, IV Nemvaleukin Monotherapy Cohort**
The ARTISTRY-1 monotherapy cohort included CPI-experienced patients with melanoma and renal cell carcinoma. Data are as of March 19, 2021 unless otherwise noted:

- Melanoma monotherapy cohort: Among 30 total evaluable patients, 24 continued on study, including 13 patients who rolled over to a combination cohort evaluating nemvaleukin in combination with pembrolizumab.
  - Metastatic mucosal melanoma: 2 out of 6 patients achieved a partial response (PR) (one unconfirmed). The patient with the confirmed PR demonstrated a durable, deepening response and had been on treatment for 74 weeks.
  - Cutaneous melanoma: 2 out of 18 evaluable patients achieved a PR (one unconfirmed, one awaiting confirmation), as of May 3, 2021.
  - Stable disease (SD) was observed in 21 patients.
- RCC monotherapy cohort: Among 20 evaluable patients, 12 continued on study, including 6 who rolled over to a combination cohort.
  - 2 patients achieved a PR (one awaiting confirmation as of May 3, 2021) and SD was observed in 10 patients.

**ARTISTRY-1, IV Nemvaleukin in Combination with Pembrolizumab**
The combination cohorts in ARTISTRY-1 included: patients with PD-1/L1 unapproved tumor types; patients with PD-1/L1 approved tumor types (PD-1/L1 pretreated and PD-1/L1 treatment naïve); patients in tumor-specific cohorts; and patients who rolled over from monotherapy cohorts. Data are as of May 3, 2021:

- Among the total 100 evaluable patients in the combination cohorts, 19 objective responses were observed.

- Out of the 14 evaluable patients with ovarian cancer enrolled in the PD-1/L1 unapproved cohort, there was 1 complete response (CR), 3 PRs (one unconfirmed) and 6 had SD. As of the data cut, 3 of the 4 patients with objective responses had been on treatment for more than a year and continued on therapy.
- Out of the 4 evaluable patients with cervical cancer enrolled in the PD-1/L1 approved cohort, 2 achieved a PR (one awaiting confirmation). As of the data cut, 3 out of the 4 evaluable patients continued on therapy.
- Objective responses were also observed in patients with the following cancers: esophageal, bladder, Hodgkin's lymphoma, breast, RCC, mucosal melanoma, colorectal, gastric, pancreatic, head and neck, small cell and non-small cell lung.

As of March 19, 2021, treatment-related AEs across the monotherapy and combination cohorts were consistent with expectations based on nemvaleukin's mechanism of action and were mostly transient and manageable at the IV RP2D of 6 µg/kg. Pyrexia, chills and nausea were the most commonly reported AEs. Transient and asymptomatic neutropenia/neutrophil count decrease were the most commonly reported events of grade ≥3. Nemvaleukin, whether as monotherapy or in combination with pembrolizumab, demonstrated no additive toxicity to that established with pembrolizumab alone.

**ARTISTRY-2, SC Nemvaleukin Study**
The dose-escalation stage of ARTISTRY-2 evaluated the safety and tolerability of ascending doses of SC nemvaleukin administered once weekly (q7d) or once-every-three-weeks (q21d) as lead-in monotherapy for six weeks, followed by combination with pembrolizumab. The ongoing efficacy-expansion stage of ARTISTRY-2 is examining the safety and efficacy of SC nemvaleukin administered at the RP2D in combination with pembrolizumab in select solid tumors. Data are as of March 19, 2021 unless otherwise noted:

- SC 3 mg q7d nemvaleukin was selected as the RP2D for the efficacy expansion stage following its demonstration of pharmacodynamic effects on Natural Killer (NK) cells and CD8+ T cells, with minimal expansion of regulatory T cells ($T_{regs}$), and a safety and tolerability profile largely consistent with the anticipated pharmacological effect and that observed with IV nemvaleukin.
- Phase 2 expansion cohorts at the RP2D recently opened for enrollment. As of May 3, 2021, one confirmed PR had been observed in a patient with PROC, with a 53% reduction in target lesion and a normalization of CA-125 levels.

The safety profile of SC nemvaleukin was largely consistent with that reported for IV nemvaleukin. The most common AEs were pyrexia, fatigue, chills and injection site reactions. Three dose-limiting toxicities were reported, all in the highest doses evaluated in each dosing regimen (declared as the maximum tolerated dose). No additive toxicity was observed with the addition of pembrolizumab to the SC treatment regimen.

Data from both presentations are available on the ASCO website at https://meetinglibrary.asco.org/.

**Abstract:** 2513
**Title**: ARTISTRY-1: Nemvaleukin Alfa Monotherapy and in Combination With Pembrolizumab in Patients With Advanced Solid Tumors
**Presenter**: Valentina Boni, M.D., Ph.D., Medical Oncologist and Principal Investigator, START Madrid at Centro Integral Oncológico Clara Campal, Madrid, Spain
**Presentation Date/Time**: The on-demand poster discussion session will take place on June 4, 2021 at 9:00 a.m. ET

**Abstract:** 2552
**Title**: Selection of the Recommended Phase 2 Dose (RP2D) for Subcutaneous Nemvaleukin Alfa: ARTISTRY-2
**Presenter**: Omid Hamid, M.D., Chief of Research and Immunotherapy, The Angeles Clinic and Research Institute
**Presentation Date**: The poster presentation will be available on-demand to attendees beginning June 4, 2021

**Conference Call and Webcast**
Alkermes will host a webcast presentation and conference call with accompanying slides for analysts and investors on Friday, June 4, 2021, at 4:00 p.m. ET (9:00 p.m. BST) to discuss the latest data from the ARTISTRY-1 and ARTISTRY-2 clinical trials. The webcast will feature ARTISTRY clinical program investigators, Valentina Boni, M.D., Ph.D., Medical Oncologist and Principal Investigator, START Madrid at Centro Integral Oncológico Clara Campal; and Omid Hamid, M.D., Chief of Research and Immunotherapy, The Angeles Clinic and Research Institute, 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. A replay of the webcast will be archived on the company's website for 30 days following the presentation.

**About Nemvaleukin Alfa ("nemvaleukin")**
Nemvaleukin 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 nemvaleukin 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 nemvaleukin alfa as a potential immunotherapy for cancer. The ARTISTRY program is comprised of multiple clinical trials evaluating intravenous and subcutaneous dosing of nemvaleukin, both as a monotherapy and in combination with the anti-PD-1 therapy KEYTRUDA® (pembrolizumab) in patients with advanced solid tumors. Ongoing trials include: ARTISTRY-1, ARTISTRY-2, ARTISTRY-3 and ARTISTRY-6.

**About Alkermes plc**
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, schizophrenia and bipolar I disorder, and a pipeline of product candidates in development for 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.

**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 and utility of nemvaleukin, whether as monotherapy or in combination, as an immunotherapy for patients with advanced solid tumors and difficult-to-treat cancers. 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 nemvaleukin could be shown to be unsafe or ineffective; whether preclinical results and data from ongoing clinical studies for nemvaleukin 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 nemvaleukin 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 nemvaleukin, 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, 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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