# Aileron Therapeutics Initiates Enrollment in Schedule Optimization Part of Phase 1b/2 Study of ALRN-6924 as a Chemoprotection Agent in Small Cell Lung Cancer (SCLC) Patients Being Treated with Topotecan

June 29, 2020

*-- Novel approach leverages the ability of intracellular p53 protein to induce cell cycle arrest in healthy cells to prevent severe toxicities driven by chemotherapy's off-target effects --*

*– In p53-mutant cancers, ALRN-6924 is designed to shield healthy cells from chemotherapy while preserving cancer cells' susceptibility to chemotherapy –*

*– p53 mutations occur in approximately 50% of all cancer patients; potential for ALRN-6924 to transform treatment paradigm for cancer patients undergoing chemotherapy --*

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*-- Company plans to report topline data from the schedule optimization and final data from the dose optimization parts of Phase 1b/2 study in Q4 2020 –*

WATERTOWN, Mass., June 29, 2020 (GLOBE NEWSWIRE) -- Aileron Therapeutics (NASDAQ:ALRN), a biotechnology company advancing a novel chemoprotective therapy for cancer patients, announced today that it has enrolled the first patient in the open-label Phase 1b schedule optimization part of its ongoing Phase 1b/2 clinical trial, evaluating ALRN-6924's potential to protect patients against chemotherapy-induced toxicities. Patients in this open-label trial have p53-mutated extensive disease small cell lung cancer (SCLC) and are being treated with second-line topotecan following administration of ALRN-6924. The schedule optimization part of the trial is intended to determine whether ALRN-6924 given six hours before topotecan further enhances the protective effect of ALRN-6924 against severe hematological adverse events observed when ALRN-6924 was given 24 hours before topotecan in the dose optimization part of the trial, as reported by Aileron earlier this month.

"Following our recent announcement of positive interim data from the Phase 1b dose optimization part of this ongoing Phase 1b/2 study, we are pleased to reach another key milestone in our advancement of ALRN-6924 to potentially transform the treatment paradigm for cancer patients undergoing chemotherapy," said Manuel Aivado, M.D., Ph.D., President & CEO of Aileron Therapeutics.

Dr. Aivado explained, "Chemotherapy remains a critical cornerstone treatment for millions of cancer patients. Unfortunately, in the process of killing cancer cells, chemotherapy inadvertently harms healthy cells, too. This leads to a multitude of common, damaging, severe toxicities. We treat healthy cells ahead of chemotherapy to prevent those toxicities, importantly, without interrupting chemotherapy's potent onslaught against cancer cells. ALRN-6924 could dramatically improve patients' quality of life by improving their tolerance to chemotherapy."

ALRN-6924's novel mechanism of action leverages the innate ability of intracellular p53 protein to induce cell cycle arrest in healthy cells to prevent toxicities driven by chemotherapy's off-target effects in bone marrow and potentially other tissues and organs. In patients with p53-mutant cancers, which represent approximately 50% of all cancer patients, ALRN-6924 is designed to shield healthy cells from chemotherapy while preserving the susceptibility of cancer cells to chemotherapy.

**About the Phase 1b/2 Study**

The ongoing Phase 1b/2 study is designed to identify an optimal dose and schedule of ALRN-6924 administration to reduce chemotherapy toxicities such as severe anemia, thrombocytopenia, and neutropenia caused by topotecan in patients with small cell lung cancer. There are two parts to the Phase 1b study: (i) dose optimization and (ii) schedule optimization.

i. **In the dose optimization part**, which enrolled 18 patients, ALRN-6924 was administered at three dose levels (0.3, 0.6, and 1.2 mg/kg) 24 hours before each dose of topotecan on days 1 through 5 of every 21-day treatment cycle. An expansion cohort of the dose optimization part of the trial at the 0.3 mg/kg dose level is ongoing.

   Aileron announced positive interim findings from this part of the trial in June 2020. ALRN-6924 demonstrated a protective effect against severe chemotherapy-induced anemia and thrombocytopenia across all dose levels as compared to historical

controls. In addition, patients treated with 0.3 mg/kg ALRN-6924 met the protocol-defined criteria for reduction of NCI CTC Grade 3/4 neutropenia to ≤50% in the first treatment cycle triggering the expansion cohort in up to eight patients.

ii. **In the schedule optimization part**, ALRN-6924 is being administered at two dose levels (0.3 and 0.6 mg/kg) 6 hours before each dose of topotecan on days 1 through 5 of every 21-day treatment cycle. Aileron expects to enroll approximately 20 patients in this part of the study.

"We were highly encouraged by the strong chemoprotective effect of ALRN-6924 seen in the dose optimization part of this study as previously reported, as it reinforces our belief that ALRN-6924 can selectively induce cell cycle arrest to protect cancer patients from the toxic side effects of chemotherapy," said Vojo Vukovic, M.D., Ph.D., Chief Medical Officer of Aileron. "The schedule optimization part of the trial is intended to inform whether ALRN-6924 given six hours before topotecan can further enhance the protective effects we have observed when giving our drug 24 hours before topotecan."

**Phase 1b/2 Trial - Next Steps**

While enrollment in the 6-hour dosing schedule is underway, Aileron is continuing to enroll patients in the expansion cohort of its 0.3mg/kg dose level using the 24-hour schedule.

As previously reported, the company plans to report topline data from the schedule optimization and final data from the dose optimization parts of the trial in the fourth quarter of 2020. Aileron expects that these results will enable the company to determine a recommended ALRN-6924 dose and schedule for subsequent trials.

Aileron is carefully monitoring the effect of the coronavirus pandemic on its clinical trial sites and the healthcare system, which may impact the future timing of the trial and the company's planned data announcements.

**About ALRN-6924**
ALRN-6924 is a first-in-class dual MDM2/MDMX inhibitor that is currently being evaluated in a Phase 1b/2 clinical trial as a chemoprotective agent to protect against chemotherapy-related toxicities.

**About Aileron**
Aileron is a clinical-stage biopharmaceutical company advancing a proprietary platform of cell-permeating alpha-helical peptides. The stabilized helical structure of our peptides allows the design of cell-permeating therapeutic agents with large molecular surfaces for optimal target binding properties, resulting in drug candidates like ALRN-6924. Our current focus is to improve the standard of care for patients with cancer by developing safe and effective therapies that leverage our proprietary peptide platform. For more information, visit www.aileronrx.com, and for more information about our clinical trials please visit www.clinicaltrials.gov.

**Forward-Looking Statements**
Statements in this press release about Aileron's future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. These statements include, but are not limited to, statements about the Company's strategy and clinical development plans. The words "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "plan," "potential," "predict," "project," "should," "target," "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including whether Aileron's cash resources will be sufficient to fund its continuing operations for the periods and/or trials anticipated; whether results obtained in preclinical and nonclinical studies and clinical trials will be indicative of results obtained in future clinical trials; whether preliminary or interim results from a clinical trial will be indicative of the final results of the trial; whether Aileron's product candidates will advance through the clinical trial process on a timely basis, or at all; whether the results of such trials will warrant submission for approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; whether Aileron's product candidates will receive approval from regulatory agencies on a timely basis or at all; whether, if product candidates obtain approval, they will be successfully distributed and marketed; whether the coronavirus pandemic will have an impact on the timing of our clinical development, clinical supply and our operations; and other factors discussed in the "Risk Factors" section of Aileron's quarterly report on Form 10-Q for the period ended March 31, 2020, filed on May 11, 2020, and risks described in other filings that Aileron may make with the Securities and Exchange Commission. Any forward-looking statements contained in this press release speak only as of the date hereof, and Aileron specifically disclaims any obligation to update any forward-looking statement, whether because of new information, future events or otherwise.

**Investor Contacts:**
Aileron Therapeutics
Richard Wanstall, SVP Chief Financial Officer
617-995-0900
rwanstall@aileronrx.com

Hans C. Vitzthum
LifeSci Advisors, LLC.
617-430-7578
hans@lifesciadvisors.com


Source: Aileron Therapeutics, Inc.