Aileron Therapeutics Presents Data at AACR-NCI-EORTC International Conference Demonstrating ALRN-6924's Activity as Radioprotective Agent in Preclinical Models of Acute Radiation-Induced Toxicity

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-- Aileron is currently developing ALRN-6924 as a novel, selective chemoprotective agent for patients with p53-mutated cancer undergoing chemotherapy --

-- Preclinical data demonstrated ALRN-6924's activation of p21-induced cell cycle arrest in murine bone marrow cells and epithelial mucosa cells in the gastrointestinal (GI) tract --

-- New preclinical findings support further study of ALRN-6924 as a potential radioprotective agent --

BOSTON, Oct. 07, 2021 (GLOBE NEWSWIRE) -- Aileron Therapeutics (Nasdaq: ALRN), a chemoprotection oncology company focused on fundamentally transforming the experience of chemotherapy for cancer patients, today presented new preclinical data at the AACR-NCI-EORTC International Conference on Molecular Targets and Cancer Therapeutics 2021 on ALRN-6924, currently in development as a novel, selective chemoprotective agent. The new data demonstrated ALRN-6924's activity as a radioprotective agent in preclinical mouse models of acute radiation-induced toxicity, leveraging the same mechanism of action – p53 activation and subsequent p21 upregulation as well as p21-induced cell cycle arrest – that has clinically shown protection against chemotherapy-induced toxicities.

"Like chemotherapy, ionizing radiation is associated with serious, often dangerous side effects, as both chemotherapy and radiation destroy normal, healthy cells," said Manuel Aivado, M.D., Ph.D. "While preliminary, these new preclinical data suggest that ALRN-6924's mechanism of action, which has demonstrated protection against chemotherapy-induced toxicities of the bone marrow, may also protect against radiation-induced toxicities. Furthermore, these preclinical studies provide our first evidence of ALRN-6924-mediated activation of p21 in epithelial mucosa cells in the GI tract, protecting irradiated mice from body weight loss, and the potential of ALRN-6924 to protect multiple tissues beyond the bone marrow from both chemotherapy and radiation-induced toxicities."

Dr. Aivado continued, "Developing ALRN-6924 as a selective chemoprotective agent in p53-mutated cancers continues to be our chief priority. Nonetheless, these encouraging preclinical data signal a potential future secondary application of ALRN-6924 complementing our ongoing chemoprotection program, and we look forward to conducting more research to further explore that possibility."

Aileron is currently developing ALRN-6924, a first-in-class MDM2/MDMX dual inhibitor, to selectively protect healthy cells in patients with cancers that harbor p53 mutations to reduce or eliminate chemotherapy-induced side effects while preserving chemotherapy's attack on cancer cells. ALRN-6924 is designed to activate p53 in normal cells, which in turn upregulates p21, which pauses cell cycle in normal, healthy, proliferating cells but not in p53-mutated cancer cells.

In the AACR-NCI-EORTC poster titled, "The Investigational Chemoprotection Drug ALRN-6924, a Dual Inhibitor of MDMX and MDM2, Shows Potential for Radioprotection" (Poster #P211), Aileron presented the results of preclinical studies designed to evaluate whether p53 activation with ALRN-6924 may protect healthy, proliferating cells in normal tissues from radiation-induced cellular toxicity.

In a non-lethal radiation exposure model, mice were exposed to a single dose of abdominally targeted radiation at 15 Gy following one or more doses/schedules of ALRN-6924 or placebo and then monitored for body weight. Aileron evaluated serum levels of macrophage inhibitory cytokine-1 (MIC-1), a biomarker of p53 activation, as well as biomarkers of p53-mediated cell cycle arrest (p21), and of apoptosis (cleaved poly-ADP-ribose polymerases, or cPARP) in mouse bone marrow and GI tract tissue. Repeated doses of ALRN-6924 administered every eight hours yielded sustained MIC-1 elevation, which correlated with increased p21 positivity in the bone marrow and intestine, while treatment-dependent changes in cPARP expression were minimal. Additionally, mice treated with ALRN-6924 had less radiation-induced body-weight loss than untreated mice. Mice receiving one or more doses of ALRN-6924 eight hours prior to irradiation had an average of 4% body weight loss, while placebo-treated mice had 10% to 15% body weight loss five days after irradiation. The poster will be archived on the Scientific Publications page of Aileron's website at: https://www.aileronrx.com/science/scientific-publications.

Aileron is currently conducting a Phase 1b randomized, double-blind, placebo-controlled study of ARLN-6924 as a chemoprotective agent in the

United States and Europe. The study is enrolling patients with advanced p53-mutated non-small cell lung cancer undergoing treatment with first-line carboplatin plus pemetrexed with or without immunotherapy. The company is pursuing a clinical development strategy designed to advance its vision to bring selective chemoprotection to all patients with p53-mutated cancer regardless of type of cancer or chemotherapy.

About Aileron Therapeutics

Aileron is a clinical stage chemoprotection oncology company focused on fundamentally transforming the experience of chemotherapy for cancer patients. ALRN-6924, our first-in-class MDM2/MDMX dual inhibitor, is designed to activate p53, which in turn upregulates p21, a known inhibitor of the cell replication cycle. ALRN-6924 is the only reported chemoprotective agent in clinical development to employ a biomarker strategy, in which we exclusively focus on treating patients with p53-mutated cancers. Our targeted strategy is designed to selectively protect multiple healthy cell types throughout the body from chemotherapy while ensuring we do not protect cancer cells. As a result, healthy cells are spared from chemotherapeutic destruction while chemotherapy continues to kill cancer cells. By reducing or eliminating multiple chemotherapy-induced side effects, ALRN-6924 may improve patients' quality of life and help them better tolerate chemotherapy. Enhanced tolerability may result in fewer dose reductions or delays of chemotherapy and the potential for improved efficacy.

Nearly 1 million patients in the U.S., across all cancer types, are diagnosed annually with p53-mutated cancer. Our vision is to bring selective chemoprotection to patients with p53-mutated cancers regardless of type of cancer or chemotherapy. Visit us at aileronrx.com to learn more.

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 potential of ALRN-6924 as a chemoprotective agent or a radioprotective agent and 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 anticipated or with respect to the matters anticipated; whether initial findings or results of clinical trials will be indicative of final results of those trials or results obtained in future clinical trials, including trials in different indications or with different chemotherapies; whether ALRN-6924 will advance through the clinical trial process on a timely basis, or at all; whether the results of such trials will be accepted by and warrant submission for approval from the United States Food and Drug Administration or equivalent foreign regulatory agencies; whether ALRN-6924 will receive approval from regulatory agencies on a timely basis or at all; whether, if ALRN-6924 obtains approval, it will be successfully distributed and marketed; uncertainties as to the impact the coronavirus pandemic may have on the timing of our clinical development, clinical supply and our operations; and other factors discussed in the "Risk Factors" section of Aileron's annual report on Form 10-Q for the quarter ended June 30, 2021, filed on August 11, 2021, 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.

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