Aileron Therapeutics Presents Results from Phase 1 Study in Healthy Volunteers Demonstrating ALRN-6924 Induced Cell Cycle Arrest in Bone Marrow Stem Cells and Hair Follicles at EORTC-NCI-AACR International Conference

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- p53-mediated cell cycle arrest results demonstrate potential of ALRN-6924 to prevent chemotherapy-induced neutropenia, thrombocytopenia, and anemia, as well as chemotherapy-induced alopecia (hair loss)
- Study showed greater degree and longer duration of effect for ALRN-6924 at higher doses, supporting dose selection of 1.2 mg/kg for ongoing ALRN-6924 breast cancer trial
- 3-minute IV bolus and 1-hour IV infusion demonstrated similar safety profiles, pharmacokinetics, and pharmacodynamics, providing rationale for future development of a simplified bolus administration

BOSTON, Oct. 26, 2022 (GLOBE NEWSWIRE) -- Aileron Therapeutics (Nasdaq: ALRN), a chemoprotection oncology company focused on fundamentally transforming the experience of chemotherapy for cancer patients, today presented detailed results from its completed Phase 1 study of ALRN-6924 in healthy volunteers at the EORTC-NCI-AACR International Conference on Molecular Targets and Cancer Therapeutics 2022 taking place in Barcelona October 26 – 28, 2022. The poster titled, *"ALRN-6924 Induces Cell Cycle Arrest in Bone Marrow Stem Cells and Hair Follicles with Dose-Dependent Degree and Duration of Effects after a Single Infusion in Healthy Volunteers"* (Poster #136) is also available in the Scientific Resources section of Aileron's website linked here.

ALRN-6924 is a first-in-class MDM2/MDMX dual inhibitor that is currently in development as a novel, selective chemoprotective agent for patients with p53-mutated cancer. The findings presented at the EORTC-NCI-AACR conference, which showed that ALRN-6924 induced p53-mediated cell cycle arrest in bone marrow stem cells and hair follicles, demonstrate the potential of ALRN-6924 to prevent chemotherapy-induced neutropenia, thrombocytopenia, and anemia, as well as chemotherapy-induced alopecia.

"While we previewed some of these new findings from our now completed Phase 1 study of ALRN-6924 in healthy volunteers earlier this year, we're pleased to present the comprehensive results at an international scientific conference," said Manuel Aivado, M.D., Ph.D., President and Chief Executive Officer at Aileron. "These results contribute to the substantial body of scientific evidence that we believe has reliably and reproducibly demonstrated ALRN-6924's potential as a biomarker-driven chemoprotective agent, driving us to work diligently to address the significant impact chemotherapy-induced toxicities have on cancer patients' treatment experience and outcomes."

ALRN-6924 is designed to activate p53, which in turn upregulates p21, a known inhibitor of the cell replication cycle, thereby inducing cell cycle arrest to protect normal, healthy cells from chemotherapy-induced damage. The Phase 1 study in healthy volunteers was conducted to evaluate the safety, tolerability, pharmacokinetics (PK), and pharmacodynamics (PD) of ALRN-6924. Aileron previously presented data from the study showing that a 0.3 mg/kg and 0.6 mg/kg 1-hour intravenous (IV) ALRN-6924 infusion was well tolerated, and transiently upregulated p21 in human bone marrow cells with minimal signal for apoptosis (n=37; Voors-Pette et al., ESMO 2021).

In the new findings presented today, cell cycle arrest was directly measured in the bone marrow and hair follicles of an additional 41 females. ALRN-6924 was administered as a single 1-hour IV infusion or 3-minute bolus injection at 0.3, 0.6, or 0.9 mg/kg to cohorts of 3 to 9 subjects and compared to placebo. Plasma and serum samples were obtained to determine PK and levels of macrophage inhibitory cytokine-1 (MIC-1), a biomarker of p53 activation. Bone marrow was sampled 12 hours post-dose to directly measure cell cycle arrest by flow cytometry in CD34+, lineage-negative bone marrow stem cells. Occipital scalp skin was sampled by a 2 mm punch biopsy for p21 immunohistochemistry in hair follicles.

In addition to the cell cycle arrest findings, ALRN-6924 continued to demonstrate a favorable tolerability profile, with subjects experiencing only mild, transient adverse events (AEs), with nausea/vomiting as the most frequent related AE. The degree and duration of serum MIC-1 elevation was dose-dependent, indicating more durable p53 activation at higher ALRN-6924 doses. At 12 hours post-dose, the proportion of cycling bone marrow stem cells was significantly reduced at all dose levels. Blinded pathology review suggested ALRN-6924-dependent p21 induction in anagen-phase hair follicles. Safety profiles, PK and PD were similar for both the 3-minute bolus and 1-hour infusion, providing rationale for future development of ALRN-6924 bolus administration.

"These findings are particularly compelling as they support our selection of the 1.2 mg/kg dose for our ongoing Phase 1b trial in patients with

p53-mutated breast cancer, as well as our evaluation of protection against both chemotherapy-induced neutropenia and alopecia in that trial," said Allen Annis, Ph.D., Senior Vice President, Research at Aileron. "Beyond informing the dose and schedule for our current trial evaluating ALRN-6924 in breast cancer patients being treated with docetaxel, doxorubicin and cyclophosphamide, or TAC, these results suggest this dosing regimen can be uniformly applied when developing ALRN-6924 as a chemoprotective agent with other chemotherapies and for patients with other p53-mutated cancer indications."

About Aileron Therapeutics

Aileron is a clinical stage chemoprotection oncology company that aspires to make chemotherapy safer and thereby more effective to save more patients' lives. 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 without protecting 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.

Our vision is to bring chemoprotection to all patients with p53-mutated cancers, which represent approximately 50% of cancer patients, 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 and 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 anticipated or with respect to the matters anticipated; whether initial 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; 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 or in which territories or indications ALRN-6924 may receive approval; whether, if ALRN-6924 obtains approval, it will be successfully distributed and marketed; what 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-K for the year ended December 31, 2021, filed on March 28, 2022, and quarterly report on Form 10-Q for the quarter ended June 30, 2022, filed on August 15, 2022, 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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