Aileron Therapeutics Announces Late-Breaking Oral Presentation of Non-Clinical Data Demonstrating ALRN-6924 Protected Human Hair Follicles and Their Stem Cells from Chemotherapy-Induced Damage at Upcoming Society for Investigative Dermatology 2022 Annual Meeting

May 10, 2022

- Taxanes, such as paclitaxel and docetaxel, cause severe and often permanent chemotherapy-induced hair loss (alopecia)
- New non-clinical data demonstrate proof of principle that ALRN-6924 can temporarily arrest the cell cycle in human scalp hair follicles and their stem cells
- ALRN-6924-induced cell cycle arrest protected hair follicles from paclitaxel-induced toxicity and irreversible stem cell damage
- Aileron's precision medicine-based approach is designed to selectively protect normal, healthy cells from chemotherapy while ensuring cancer cells cannot be protected from chemotherapy's attack
- Aileron's ongoing non-small cell lung cancer (NSCLC) clinical trial and upcoming breast cancer clinical trial will evaluate ALRN-6924's protection against chemotherapy-induced bone marrow toxicities and other side effects, including alopecia

BOSTON, May 10, 2022 (GLOBE NEWSWIRE) -- Aileron Therapeutics (Nasdaq: ALRN), a chemoprotection oncology company that aspires to make chemotherapy safer and thereby more effective to save more patients' lives, today announced a late-breaking oral presentation at the upcoming Society for Investigative Dermatology (SID) Annual Meeting, which will be held May 18 – 21, 2022 in Portland, Oregon. The presentation will highlight new non-clinical data developed in collaboration with Professor Ralf Paus, M.D., DSc, FRSB and his colleagues at the Dr. Phillip Frost Department of Dermatology & Cutaneous Surgery at the University of Miami Miller School of Medicine. This collaboration has generated promising *ex vivo* data demonstrating that ALRN-6924 protected human hair follicles and their stem cells from chemotherapy-induced acute and permanent damage. Details of the presentation are as follows:

Title:	ALRN-6924, a dual inhibitor of MDMX and MDM2, protects human scalp hair follicles and their epithelial stem cells from paclitaxel-induced toxicity (LB1018)
Presenter:	Jennifer Gherardini, Ph.D.; Paus Laboratory, University of Miami Miller School of Medicine
Date:	Thursday, May 19th
Time:	8:45 AM - 11:15 AM PT
Session:	Late-Breaking Abstract Concurrent Session

"Chemotherapy-induced toxicities range from severe and life-threatening to those that impact and diminish patients' quality of life, sometimes long after chemotherapy has been completed. These toxicities occur because chemotherapy destroys normal, healthy cells while simultaneously destroying cancer cells," said Manuel Aivado, M.D., Ph.D., President and Chief Executive Officer at Aileron. "Previously, we showed chemoprotection against severe bone marrow toxicities in small cell lung cancer patients receiving topotecan and demonstrated in healthy volunteers the mechanism of action – cell cycle arrest – underlying this chemoprotection benefit. We are excited to now present new data that may suggest ALRN-6924's ability to also protect against chemotherapy-induced hair loss, another devastating chemotherapy-induced side effect for millions of cancer patients."

Dr. Paus commented, "These results got us quite excited as they directly follow in the footsteps of our prior work that showed arresting the cell cycle can have a strong protective effect against taxane-induced hair follicle damage. Until our research with ALRN-6924, we had not come across a cell cycle arrest-inducing drug that is in clinical testing for protection of normal cells without protecting cancer cells. Thus, ALRN-6924 invites a very promising and completely novel selective protection approach. In addition, we found that ALRN-6924 may exert some additional benefits that could reduce the risk of long-term damage of human hair follicle stem cells by taxanes."

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 cells but not in p53-mutated cancer cells. The company's vision is to bring chemoprotection to all patients with p53-mutated cancer regardless of the type of cancer or chemotherapy.

About the Findings

Taxanes, such as paclitaxel and docetaxel, are known to cause severe and often permanent chemotherapy-induced alopecia. Over 90% of patients treated with this chemotherapy class experience alopecia, and approximately 10% (paclitaxel) to 25% (docetaxel) of patients experience permanent alopecia. Dr. Paus and his team previously demonstrated that paclitaxel damages human scalp hair follicles by inducing massive mitotic defects and apoptosis in hair matrix keratinocytes as well as bulge stem cell DNA damage, and that pharmacological induction of transient cell cycle arrest can protect hair follicles and stem cells (Purba et al. EMBO Molecular Medicine 2019). Aileron previously conducted *in vitro* studies showing that ALRN-6924 protected human fibroblasts in cell culture from multiple chemotherapies, but not p53-mutant breast cancer cells.

In the new non-clinical findings to be presented at the SID meeting, when organ-cultured anagen (i.e., active growth phase) scalp hair follicles from two human donors were pre-treated with ALRN-6924 or vehicle (i.e., placebo), followed by paclitaxel or vehicle, ALRN-6924 significantly increased the number of p21-positive hair matrix keratinocytes and bulge stem cells compared to vehicle or paclitaxel alone, confirming cell cycle arrest *ex vivo*. Further, pretreatment of paclitaxel-treated human hair follicles with ALRN-6924, led to a reduction in the number of melanin clumps, a marker of hair follicle cytotoxicity and dystrophy, as well as a reduction in apoptosis, pathological mitosis, and DNA damage. Aileron believes that these findings support clinical investigation of ALRN-6924 to prevent both acute and permanent chemotherapy-induced alopecia, in addition to its ongoing evaluation of ALRN-6924 to protect against chemotherapy-induced bone marrow and other toxicities.

About Aileron's Clinical Trials of ALRN-6924

Aileron is on track to initiate a Phase 1b randomized, controlled trial of ALRN-6924 in patients with p53-mutated ER+/HER2- neoadjuvant breast cancer in 2Q 2022. The planned breast cancer trial will evaluate ALRN-6924's protection against chemotherapy-induced bone marrow toxicities, as well as other toxicities, including alopecia, in patients with p53-mutated ER+/HER2- breast cancer treated with a doxorubicin plus cyclophosphamide and docetaxel chemotherapy regimen.

The company is currently enrolling patients in a Phase 1b randomized, double-blind, placebo-controlled trial evaluating ALRN-6924's protection against chemotherapy-induced bone marrow and other toxicities in patients with advanced p53-mutated non-small cell lung cancer undergoing treatment with first-line carboplatin plus pemetrexed with or without immunotherapy. While patients in this trial are monitored for alopecia, historically, only a small percentage of patients treated with carboplatin plus pemetrexed experience acute alopecia. Aileron is on track to report interim results on the first 20 patients enrolled in the NSCLC trial in June 2022 and topline results on 60 patients in 4Q 2022.

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, including its ability to prevent both acute and permanent chemotherapy-induced alopecia, 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 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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