Aileron Therapeutics Announces Oral Presentation of Non-Clinical Data Demonstrating ALRN-6924 Protected Human Hair Follicles and Their Stem Cells from Chemotherapy-Induced Damage at the European Society for Dermatological Research Annual Meeting 2022

September 30, 2022

- New ex vivo data demonstrates protection against cyclophosphamide-induced damage to hair follicles and their stem cells
- Encore presentation of data presented at Society for Investigative Dermatology in May 2022 shows:
    - ALRN-6924 temporarily arrested the cell cycle in human scalp hair follicles and their stem cells
    - Ex vivo data demonstrated protection against taxane-induced damage to hair follicles and their stem cells
- Nearly all breast cancer patients receiving neoadjuvant or adjuvant chemotherapy, including cyclophosphamide and taxanes, such as docetaxel, experience alopecia (hair loss)
- Aileron is evaluating ALRN-6924 as a novel chemoprotective agent to prevent chemotherapy-induced bone marrow toxicities and alopecia in its ongoing Phase 1b breast cancer trial

BOSTON, Sept. 30, 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 an oral presentation at the European Society for Dermatological Research (ESDR) Annual Meeting, taking place September 28 – October 1, 2022 in Amsterdam.

This presentation includes non-clinical data initially presented at the Society for Investigative Dermatology in May 2022 as well as 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.

Details of the presentation are as follows:

Title:	Temporary cell cycle arrest in human scalp hair follicles and their epithelial stem cells by ALRN-6924: A novel strategy to selectively protect p53-wildtype cells against paclitaxel-induced alopecia [Abstract 549]
Presenter:	Dr. Ralf Paus; Paus Laboratory, University of Miami Miller School of Medicine
Date:	Saturday, October 1, 2022
Time:	12:40 – 12:50 p.m. (local time)
Session:	Concurrent session #9: Photobiology and Pigmentation

"Until one is confronted personally with the loss of hair due to chemotherapy, I think it's difficult to truly understand just how difficult this side effect can be for patients. It is yet another burden layered on top of their already-daunting fight against cancer," said Dr. Paus. "Cold caps, the only FDA-approved treatment for chemotherapy-induced alopecia, are unavailable in many institutions, can cause additional discomfort, and – while often quite useful – are of unpredictable efficacy in a given individual patient. One also cannot help wondering whether scalp micro-metastases might profit from scalp cooling."

Dr. Paus continued, "Based on our hair follicle and scalp skin organ culture work with ALRN-6924, testing two of the most hair loss-inducing chemotherapies, paclitaxel and cyclophosphamide, we're very encouraged by the potential this drug may hold to prevent alopecia in cancer patients, including for protecting the hair follicle's sensitive stem cell compartment from permanent damage. We're particularly excited by ALRN-6924's highly innovative design, which selectively protects normal cells from the destructive effects of chemotherapy, but – in contrast to any other currently available alopecia-protective strategy – crucially, not the cancer cells."

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. The company is conducting a Phase 1b clinical trial of ALRN-6924 in patients with p53-mutated breast cancer undergoing either neoadjuvant or adjuvant treatment with docetaxel, doxorubicin and cyclophosphamide, also known as TAC. Aileron's vision is to bring chemoprotection to all patients with p53-mutated

cancer regardless of the type of cancer or chemotherapy.

Manuel Aivado, M.D., Ph.D., President and Chief Executive Officer at Aileron, commented, “We’re excited about the results generated by Dr. Paus and his colleagues, particularly given their significant and widely recognized expertise in chemotherapy-induced alopecia. We have amassed a body of strong scientific evidence, including the data being presented at the ESDR meeting, which demonstrate ALRN-6924’s cell cycle arrest mechanism and support its potential to protect against chemotherapy-induced bone marrow toxicities and other toxicities, including alopecia. Collectively, these nonclinical and clinical data have informed the design of our breast cancer trial. We look forward to our anticipated data readouts from that trial later this year and into 2023.”

About the Paus et al. 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. Cyclophosphamide is also known to cause alopecia: it is commonly co-administered with doxorubicin (Adriamycin) chemotherapy in the “AC” combination, with greater than 90% of patients experiencing hair loss.

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 non-clinical findings presented at the ESDR and SID meetings, when organ-cultured anagen (i.e., active growth phase) scalp hair follicles from 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. In new data presented at the ESDR meeting, these assays also yielded positive findings for 4-HC (4-hydroperoxy cyclophosphamide), the active metabolite of cyclophosphamide that is formed in vivo and commonly used for in vitro studies. Aileron believes that these findings support clinical investigation of ALRN-6924’s ability to prevent both acute and permanent chemotherapy-induced alopecia, in addition to its ongoing evaluation of ALRN-6924’s ability to protect against chemotherapy-induced bone marrow and other toxicities.

About Aileron’s Breast Cancer Clinical Trial

Aileron is underway with a Phase 1b, open-label, single-arm, multicenter trial designed to evaluate the safety, tolerability and chemoprotective effect of ALRN-6924 in up to 24 patients with p53-mutated breast cancer undergoing either neoadjuvant or adjuvant treatment with docetaxel, doxorubicin and cyclophosphamide, also known as TAC. The primary endpoints are duration and incidence of severe neutropenia (Grade 4) in cycle 1. Secondary endpoints include the chemoprotective effect of ALRN-6924 on chemotherapy-induced alopecia, as well as other hematologic and non-hematologic toxicities. Planned readouts from the breast cancer trial include data from initial patients in the trial in the fourth quarter of 2022; an interim analysis on 12 patients in the second quarter of 2023; and topline results from 20 patients in the third quarter of 2023.

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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