Aileron Therapeutics Announces Interim Data from Phase 1b Chemoprotection Trial of ALRN-6924 in Patients with p53-Mutated Non-Small Cell Lung Cancer (NSCLC) and Confirms Development Path for ALRN-6924 Focused on p53-Mutated Breast Cancer

June 29, 2022

- Patients on ALRN-6924 were able to stay on treatment longer, completing more of the first 4 cycles of carboplatin/pemetrexed (93% of cycles on ALRN-6924 versus 78% on placebo); this imbalance between treatment arms may have introduced a bias against ALRN-6924 on the composite primary endpoint
    - Evaluating cycles 1-6, the imbalance increases further (79% of cycles on ALRN-6924 versus 57% on placebo)
- Interim finding on the trial's composite primary endpoint, which was the proportion of treatment cycles free of Grade ≥3 neutropenia, anemia, thrombocytopenia, blood transfusions, use of growth factors, dose reductions/delays in the first 4 cycles, demonstrated 56% of cycles on ALRN-6924 versus 50% of cycles on placebo
- 25 of the total 83 cycles completed across both treatment arms showed Grade ≥3 hematologic toxicities (30%); only 3 patients experienced Grade 4 hematologic toxicities in 6 of 83 cycles
- Aileron plans to stop further enrollment in the NSCLC trial, and to apply key learnings from the NSCLC data to strengthen the Phase 1b breast cancer trial in accordance with clinical and regulatory precedents
- Aileron to host webcast today at 8:00 am ET

BOSTON, June 29, 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 interim data from its Phase 1b chemoprotection trial of patients with advanced p53-mutated NSCLC undergoing treatment with first-line carboplatin plus pemetrexed with or without immune checkpoint inhibitors. Aileron plans to stop further enrollment in the NSCLC trial and to apply key learnings from the interim analysis to strengthen the Phase 1b breast cancer trial in accordance with clinical and regulatory precedents.

The interim analysis consisted of the first 20 patients randomized to ALRN-6924 0.3 mg/kg plus carboplatin/pemetrexed (n=11) or placebo plus carboplatin/pemetrexed (n=9).[1,2] ALRN-6924-treated patients were able to stay on chemotherapy treatment longer, completing 93% of the first 4 cycles of carboplatin/pemetrexed administered compared to 78% on placebo.[2,3] This imbalance of completed cycles between the treatment arms may have introduced a bias against ALRN-6924 on the composite primary endpoint. The imbalance increases further when looking at percentages of patients completing 6 cycles of treatment (79% on ALRN-6924 versus 57% on placebo). This is reflected in the progression free survival, which was 4.6 months in the ALRN-6924 arm versus 3.2 months in the placebo arm. The composite primary endpoint consisted of the proportion of treatment cycles free of Grade ≥3 neutropenia, Grade ≥3 thrombocytopenia, Grade ≥3 anemia, blood transfusions, and the use of growth factors, as well as dose reductions or dose delays within the first 4 cycles of treatment. ALRN-6924-treated patients demonstrated 56% of cycles free from these Grade ≥3 hematologic toxicities and related events compared to 50% on placebo.

"We remain passionate about advancing ALRN-6924 for patients with p53-mutated cancer, and these interim NSCLC findings have significantly helped to clarify our development path toward that goal. We are very encouraged by the finding that ALRN-6924-treated patients were able to complete more cycles of chemotherapy in the NSCLC trial, but unfortunately it also appears that this may have worked against us given the nature of the exploratory composite primary endpoint. The more cycles patients completed the more opportunity they had to experience toxicities. This introduced an imbalance of toxicities between the active and placebo arms and, may have resulted in a bias against ALRN-6924 on the composite primary endpoint," said Manuel Aivado, M.D., Ph.D., President and CEO of Aileron.

While the ALRN-6924 0.3 mg/kg dose previously demonstrated protection against topotecan-induced hematologic toxicities in Aileron's small cell lung cancer trial, Aileron believes that a higher dose level could provide more durable cell cycle arrest and, thus more chemoprotection against certain chemotherapies, including carboplatin/pemetrexed. This is supported by the recently generated data from the company's healthy volunteer study. In that study, serum MIC-1 levels were measured as an indicator of the duration of effect of ALRN-6924, including the duration of cell cycle arrest. Increasing dose levels of ALRN-6924 elicited more durable p53 activation, which correlates with cell cycle arrest in the bone marrow. Cell cycle arrest is a basis for protecting cells from chemotherapy.

Dr. Aivado continued, “By stopping the NSCLC trial, we plan to fully focus our resources on our Phase 1b breast cancer trial to continue our development of ALRN-6924 to protect p53-mutated cancer patients from chemotherapy-induced side effects. Neoadjuvant chemotherapy for breast cancer is associated with frequent severe neutropenia in cycle 1, and we believe this offers a well-established endpoint, which has been used to secure FDA approval of multiple supportive care drugs. This endpoint also obviates any potential imbalance in the number of cycles completed on ALRN-6924 versus placebo. The breast cancer trial also gives us the ability to evaluate protection against alopecia, which occurs in more than 90% of breast cancer patients on neoadjuvant chemotherapy compared to less than 10% of patients receiving carboplatin/pemetrexed.”

The learnings from the NSCLC interim analysis create an opportunity for Aileron to take several steps to strengthen the Phase 1b breast cancer trial, including revising the primary endpoint to duration of severe neutropenia in cycle 1 and changing the chemotherapy regimen to a simultaneous administration of doxorubicin plus cyclophosphamide and docetaxel, referred to as TAC. Additionally, the company plans to modify the dosing strategy for the trial and will not further enroll additional patients in the ongoing 0.3 mg/kg and 0.6 mg/kg dose cohorts.

Additional NSCLC Trial highlights (Cycles 1-6)

- Of the 83 cycles of carboplatin/pemetrexed administered, Grade ≥3 hematologic toxicities were observed in 25 cycles (30%): 18 cycles with 28 instances[4] of hematologic toxicities on ALRN-6924, and 7 cycles with 10 instances of hematologic toxicities on placebo.
- One patient receiving ALRN-6924 accounted for 15 of the total 28 Grade ≥3 hematologic instances observed on that arm, or 53%.
- Grade 4 events[5] were infrequent, occurring in 1 patient on ALRN-6924 and 2 patients on placebo.
- 5 of 11 patients treated with ALRN-6924 completed 6 planned cycles (45%) versus 1 out of 9 placebo patients (11%).
- Frequency of patients experiencing Grade ≥3 hematologic events:

Treatment (n of patients)	Patients with grade≥3 neutropenia n (%)	Patients with grade ≥3 thrombocytopenia n (%)	Patients with grade ≥3 anemia n (%)
ALRN-6924 (n=11)	5 (45%)	5 (45%)	1 (9%)
Placebo (n=9)	2 (22%)	4 (44%)	2 (22%)

Investor Webcast Details

Aileron will host a conference call and webcast today at 8:00 am ET to discuss these data and the company’s planned strategic prioritization of its breast cancer trial. The conference call can be accessed by dialing 844-838-0770 (United States) or 213-320-2558 (International) with the conference code 3218779. A live webcast may be accessed using the link here, or by visiting the “Events and Presentations” page in the investors section of the Aileron website at www.aileronrx.com. After the live webcast, the event will be archived on the Company’s website for approximately 30 days after the call.

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, the Company’s strategy and the Company’s 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 interim results of clinical trials will be indicative of final results of those trials; whether preclinical or clinical results will be indicative of 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 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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[1] One patient was randomized to the placebo arm, but treatment was initiated with ALRN-6924 due to a dispensing error, and the decision was made to maintain that patient on ALRN-6924.

[2] The composite primary endpoint was designed to evaluate the first 4 cycles of chemotherapy, which is standard of care for patients receiving checkpoint inhibitors (CPI). Given that none of the 20 patients in the interim analysis received a CPI, the interim analysis also included results for all 6 cycles of chemotherapy, which is standard of care for patients not receiving CPI.

[3] As of the interim analysis data cut-off of June 16, 2022, 3 patients on each arm included in this interim analysis remained on treatment.

[4] An 'instance' is defined as the occurrence of each individual hematologic toxicity. For example, the occurrence of Grade ≥3 neutropenia, thrombocytopenia and anemia in a given cycle is counted as three instances.

[5] An 'event' is defined as the occurrence of one or more Grade ≥3 hematologic toxicities in a given cycle. For example, the occurrence of neutropenia, thrombocytopenia and anemia in the same cycle are considered one event.