Aileron Therapeutics Presents New Clinical Data at ESMO Virtual Congress 2021 Supporting ALRN-6924's Best-in-Class Potential as a Chemoprotective Agent

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- Final results from completed Phase 1b trial in patients with small cell lung cancer (SCLC) receiving second-line topotecan demonstrated ALRN-6924's ability to reduce neutropenia, thrombocytopenia and anemia caused by chemotherapy, as well as the need for transfusions
- Preliminary results from ongoing Phase 1 pharmacology study in healthy volunteers confirmed ALRN-6924's optimal dose (0.3 mg/kg), its mechanism of action, and demonstrated time to onset, duration and magnitude of its pharmacodynamic effects
- These new data will inform the design of anticipated future clinical studies to investigate ALRN-6924 as a chemoprotective agent in other p53-mutated cancers and with other types of chemotherapy
- A precision medicine-based chemoprotective agent, ALRN-6924 is designed to selectively activate p53 in normal cells, thereby upregulating p21, which pauses cell cycle in normal cells but not in p53-mutated cancer cells

BOSTON, Sept. 16, 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 clinical data at the European Society of Medical Oncology (ESMO) Virtual Congress 2021 supporting ALRN-6924's best-in-class potential as a chemoprotective agent. The company presented final results from its completed Phase 1b trial of ALRN-6924 in patients with small cell lung cancer (SCLC) receiving second-line topotecan treatment, which demonstrated ALRN-6924's 'triple-play efficacy' for the reduction of neutropenia, thrombocytopenia and anemia, as well as a reduction of platelet and red blood cell transfusions, as compared to historical controls. Aileron today also presented preliminary results from its ongoing Phase 1 pharmacology study of ALRN-6924, which confirmed 0.3 mg/kg as the optimal dose for ALRN-6924 and confirmed its novel p53 biomarker-driven mechanism of action, as well as its pharmacodynamic effects, including time to onset, magnitude and duration.

Aileron is developing ALRN-6924 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, a first-in-class MDM2/MDMX dual inhibitor, 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.

"We are pleased to present final results from our completed Phase 1b trial of ALRN-6924 in patients with SCLC being treated with topotecan and preliminary results from our ongoing Phase 1 pharmacology study in healthy volunteers. The data presented at ESMO further strengthen our belief in ALRN-6924's best-in-class potential in the emerging chemoprotection space," said Manuel Aivado, M.D., Ph.D., President and CEO of Aileron. "With our precision medicine strategy, our vision is to bring the first selective chemoprotective agent to all patients with p53-mutated cancer while ensuring no interruption of chemotherapy. We believe chemoprotection during chemotherapy, ultimately, should be as compulsory as anesthesia during surgery."

ALRN-6924 Phase 1b SCLC Trial Final Results

Aileron conducted a Phase 1b open-label clinical trial to evaluate ALRN-6924 as a chemoprotective agent against bone marrow-related, chemotherapy-induced toxicities in patients with SCLC undergoing treatment with topotecan. The company reported the final results from this trial in a poster presentation at ESMO titled, "A Phase 1b Study of the Dual MDMX/MDM2 Inhibitor, ALRN-6924, for the Prevention of Chemotherapy-induced Myelosuppression" (Abstract/Poster #: 1654P).

A total of 39 patients were enrolled in the trial, 38 of whom were evaluable per the trial protocol. Topotecan (1.5 mg/ m^2) was administered on days 1 through 5 of every 21-day treatment cycle. 32 patients (31 evaluable) were treated with ALRN-6924 at 24 hours before each dose of topotecan at the following dose levels: 0.2 mg/kg (N=4), 0.3 mg/kg (N=16), 0.6 mg/kg (N=6; 5 evaluable) and 1.2 mg/kg (N=6). 7 patients were treated with 0.3 mg/kg of ALRN-6924 at 6 hours before each dose of topotecan.

In the Phase 1b SCLC trial, toxicities were evaluated using the National Cancer Institute's (NCI) Common Terminology Criteria for Adverse Events (CTCAE). Per the trial protocol, patients were not permitted to receive prophylactic G-CSF treatment in cycle 1. The median number of completed topotecan treatment cycles across all cohorts was 3. 13% of patients required topotecan dose reduction. No patients reported NCI CTCAE Grade ≥3

events of nausea, vomiting, diarrhea; 5% had Grade 3 fatigue.

While chemoprotection effects were observed across all ALRN-6924 dose levels studied in the Phase 1b SCLC trial, the 0.3 mg/kg ALRN 6924 dose level given 24 hours prior to topotecan demonstrated the most robust chemoprotection results. None of the patients treated at the 0.3 mg/kg 24 hour ALRN-6924 dose level had a related serious adverse event (SAE). One patient (6%) at the 0.3 mg/kg 24 hour ALRN-6924 dose level required a red blood cell transfusion and a platelet transfusion. In the topotecan plus placebo arm of a recent third-party randomized Phase 2 trial in SCLC patients receiving topotecan (N=28), 41% and 31% of SCLC patients received red blood cell and platelet transfusions, respectively (Hart et al., ASCO 2019).

Summary of Final Key Efficacy Findings from ALRN-6924 Phase 1b SCLC Trial

ALRN-6924 (given 24h prior to chemotherapy) Phase 1b Trial Bone Marrow-Related Key Toxicity Findings Adverse Events (AEs)* NCI CTCAE ≥ Grade 3			**Third Party Randomized Phase 2 Trial in SCLC Historical Control‡**
Toxicity	ALRN-6924 0.3 mg/kg + Topotecan N (%) N=16	ALRN-6924 (All Dose Levels) Topotecan N (%) N=39	Placebo + Topotecan N (%) N=28
All AEs	14 (88)	35 (90)	27 (96)
Neutropenia	13 (81)	34 (87)	24 (86)
Thrombocytopenia	7 (44)	18 (46)	20 (70)
Anemia	3 (19)	6 (15)	18 (63)
Febrile Neutropenia	0	1 (3)	5 (17) †
Fatigue	1 (6)	2 (5)	2 (7)
Nausea	0	0	1 (4)
Neutropenia Grade 4	5 (31)**	14 (36)**	21 (76)

*AEs based on laboratory values, as applicable
**For cycle 1
‡ Hart et al. ASCO 2019
† Febrile neutropenia assessed in 29 patients

Dr. Vojislav Vukovic, M.D., Ph.D., Chief Medical Officer at Aileron, commented, “The final results from the Phase 1b SCLC we are presenting at ESMO are fully consistent with the interim, proof-of-concept data we presented from this trial last year demonstrating ALRN-6924’s ability to protect this very sick patient population against severe and life-threatening bone marrow-related side effects associated with a highly toxic chemotherapy. With the Phase 1b SCLC trial successfully completed, we look forward to continuing our ongoing Phase 1b randomized, double-blind, placebo-controlled trial of ALRN-6924 in patients with advanced non-small cell lung cancer treated with first-line carboplatin plus pemetrexed.”

ALRN-6924 Phase 1 Pharmacology Study Initial Results

Aileron is conducting a multi-part Phase 1 pharmacology study in healthy volunteers to evaluate the pharmacokinetics and pharmacodynamics of ALRN-6924. In a poster presentation at ESMO titled, “A Phase 1 Study of the Dual MDMX/MDM2 Inhibitor, ALRN 6924, in Healthy Volunteers” (Abstract/Poster #: 1791P), Aileron presented the findings from Parts 1 and 2 of the study. The objectives of these first two parts were to determine a dose of ALRN-6924 that initiated p53-mediated transcriptional regulation and yielded transient cell cycle arrest via p21 induction in human bone marrow while minimizing the signal for apoptosis (Part 1), and to determine the time to onset, magnitude, and duration of bone marrow pharmacodynamic effects (Part 2). The study is ongoing, and Aileron anticipates presenting additional findings at a later date.

Aileron reported results for a total of 37 subjects (females and males aged 18-65) enrolled and evaluated in Parts 1 and 2 of the study. In Part 1, a total of 14 subjects (6 placebo, 4 each at 0.3 and 0.6 mg/kg of ALRN-6924) received one intravenous infusion of ALRN-6924, and bone marrow samples were obtained 8 hours post-infusion. Immunohistochemistry analysis showed that both dose levels yielded robust induction of p21, a p53-regulated mediator of cell cycle arrest, in bone marrow cells, with minimal evidence of apoptosis compared to placebo. In Part 2, 23 subjects allocated to 8 groups received one 0.3 mg/kg infusion of ALRN-6924. Bone marrow samples were obtained at 4, 8, 12, 16, 20, 24, 36, and 48 hours post-infusion. The 0.3 mg/kg dose demonstrated favorable tolerability, with subjects experiencing only mild, transient adverse events. Robust p21 induction was observed in bone marrow cells, with peak expression observed between 4 hours and 16 hours following ALRN-6924 administration.

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 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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