Aileron Therapeutics Announces Proof-of-Concept Clinical Data from Ongoing ALRN-6924 Phase 1b Trial Presented in Late-Breaking Presentation at the EORTC-NCI-AACR Annual Symposium

October 24, 2020

- First and only chemoprotective therapy in clinical development that utilizes a biomarker strategy designed to protect patients with p53-mutated cancers from chemotherapy-induced toxicities and side effects
- Treatment with ALRN-6924 prior to topotecan administration resulted in a protective effect against severe chemotherapy-induced bone marrow toxicities in patients with p53-mutated small cell lung cancer (SCLC)
- Robust and clinically meaningful protection against toxicities observed with 0.3 mg/kg dose of ALRN-6924
- Aileron to host conference call and webcast on Monday, October 26, 2020 at 8:30 a.m. ET to discuss the data and its clinical development strategy to expand chemoprotection to multiple p53-mutated cancers and chemotherapies

Data Highlights

As of August 31, 2020, the data cut-off for this data presentation, a total of 26 adult patients were enrolled in the dose optimization part of the ALRN-6924 Phase 1b trial, evaluating treatment with ALRN-6924 given 24 hours prior to chemotherapy. 18 patients were enrolled across three ALRN-6924 dose levels (1.2 mg/kg, 0.6 mg/kg and 0.3 mg/kg) and an additional eight (8) patients were enrolled in a 0.3 mg/kg expansion cohort. 25 of these patients were evaluable per the trial protocol. ALRN-6924 was administered 24 hours before each dose of topotecan. Topotecan (1.5 mg/m²) was administered on days 1 through 5 of every 21-day treatment cycle. In the trial, toxicities were evaluated using the National Cancer Institute’s (NCI) Common Terminology Criteria for Adverse Events (CTCAE). Per the Phase 1b trial protocol, patients were not permitted to receive prophylactic G-CSF treatment in cycle 1.
Across all ALRN-6924 dose levels, Grade 3/4 anemia, Grade 3/4 thrombocytopenia and Grade 4 neutropenia (defined as <500/µL) were limited to 24%, 36% and 48% of patients, respectively. In the topotecan plus placebo arm of a recent third-party randomized Phase 2 trial in SCLC patients receiving topotecan (n=28), Grade 3/4 anemia, Grade 3/4 thrombocytopenia and Grade 4 neutropenia were reported in 63%, 70% and 76% of patients, respectively (Hart et al., ASCO 2019). In the ALRN-6924 trial, while chemoprotection effects were observed across all ALRN-6924 dose levels, the 0.3 mg/kg dose level showed the most robust chemoprotection results, with Grade 3/4 anemia, Grade 3/4 thrombocytopenia and Grade 4 neutropenia limited to 21%, 36% and 43% of patients, respectively. Additionally, none of the patients on ALRN-6924 experienced febrile neutropenia. In the topotecan plus placebo arm of the recent third-party randomized Phase 2 trial in SCLC patients receiving topotecan (n=29), febrile neutropenia was observed in 17% of patients (Hart et al., ASCO 2019). None of the patients treated at the 0.3 mg/kg ALRN-6924 dose level had hematological serious adverse events (SAEs) and only one patient (7%) received one red blood cell transfusion and one platelet transfusion. In the topotecan plus placebo arm of the recent third-party randomized Phase 2 trial, 41% and 31% of SCLC patients received red blood cell and platelet transfusions, respectively (Hart et al., ASCO 2019). At the 0.3 mg/kg ALRN-6924 dose level, no patients required erythropoiesis-stimulating agents, and seven patients (50%) required G-CSF treatment.

**Finding followed EORTC-NCI-AACR Symposium Late-Breaking Abstract submission.

### ALRN-6924 (given 24h prior to chemotherapy) Phase 1b Trial

<table>
<thead>
<tr>
<th>Toxicity</th>
<th>ALRN-6924 0.3 mg/kg + Topotecan N (%)</th>
<th>ALRN-6924 (All Dose Levels) Topotecan N (%)</th>
<th>Placebo + Topotecan N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All AEs</td>
<td>13 (93)</td>
<td>24 (96)</td>
<td>27 (96)</td>
</tr>
<tr>
<td>Anemia</td>
<td>3 (21)</td>
<td>6 (24)</td>
<td>17 (61)</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>5 (36)</td>
<td>9 (36)</td>
<td>16 (57)</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>11 (79)</td>
<td>22 (88)</td>
<td>24 (86)</td>
</tr>
<tr>
<td>Febrile Neutropenia</td>
<td>0</td>
<td>0</td>
<td>5 (17)†</td>
</tr>
<tr>
<td>Neutropenia Grade 4</td>
<td>6 (43)**</td>
<td>12 (48)**</td>
<td>21 (76)</td>
</tr>
</tbody>
</table>

*AEs based on laboratory values, as applicable

**For cycle 1 and for all treatment cycles

‡ Hart et al. ASCO 2019

† Febrile neutropenia reported for 29 patients

“Chemotherapy-induced toxicities historically have been viewed by the medical community as an unfortunate yet unavoidable reality associated with effective chemotherapeutics. With therapeutic advancements like ALRN-6924, I believe there is a potential to dramatically evolve that mindset,” said Bojan Zaric, M.D., Ph.D., Head of Clinical Research, Head of Lung Cancer Clinic, Institute for Pulmonary Diseases of Vojvodina, Serbia, and Principal Investigator of the ALRN-6924 Phase 1b trial.

Dr. Zaric continued, “These Phase 1b data provide early yet important insights into ALRN-6924’s unique activity among chemoprotective agents in development, as well as potential advantages over the current standard of care therapies to address bone marrow toxicities. The findings suggest a strong potential for ALRN-6924 to protect patients undergoing chemotherapy against severe anemia, thrombocytopenia and neutropenia.”

Enrollment in the dose optimization part of the Phase 1b trial (ALRN-6924 administered 24 hours before topotecan) is complete, and monitoring is ongoing with four of the evaluable patients continuing treatment past the data cut-off date.

### Upcoming Milestones

Aileron continues to enroll patients in a schedule optimization part of the Phase 1b trial intended to determine whether ALRN-6924 given six hours prior to topotecan (“6h-schedule part”) could be an alternative dosing schedule that could provide patients and healthcare providers with additional flexibility of when to administer ALRN-6924 before topotecan. The company expects to report final data from the Phase 1b trial, including data from the 6h-schedule part, in the first quarter of 2021.

In addition, in the fourth quarter of 2020, Aileron plans to initiate a clinical study of ALRN-6924 in healthy volunteers to characterize the time to onset, and the magnitude and duration of cell cycle arrest in human bone marrow relative to ALRN-6924 administration. Subject to the results of the healthy volunteer study and the final data from the Phase 1b trial, Aileron expects to initiate a non-small cell lung cancer program beginning with a Phase 1b trial in the fourth quarter of 2021 and a development program in a gastrointestinal cancer indication at a later point in time. Aileron does not currently plan to conduct additional development of ALRN-6924 in patients with SCLC.

“We designed a robust Phase 1b trial to enable us to evaluate multiple dose levels and schedules of ALRN-6924,” said Dr. Vukovic. “We anticipate garnering additional insights from the alternative six-hour dosing schedule part of the Phase 1b SCLC trial and the healthy volunteer study that could provide a strong foundation for regulatory discussions around a registration program for ALRN-6924 in non-small cell lung cancer patients who are...
receiving platinum-based chemotherapy.”

Conference Call and Webcast
Aileron will host a conference call and webcast on Monday, Oct. 26, 2020 at 8:30 a.m. ET to discuss the Phase 1b data and the company’s clinical development strategy to expand its chemoprotection research to multiple p53-mutated cancers and chemotherapies. To access the conference call, investors are invited to dial 877-705-6003 (domestic) or +1 201-493-6725 (international). The conference ID number is 13712133. A live audio webcast can be accessed by visiting the investor relations section of Aileron’s website at https://investors.aileronrx.com/events-presentations. The webcast will be archived on Aileron’s site for one year.

How ALRN-6924 Is Designed to Protect Healthy Cells from Chemotherapy
ALRN-6924 is being developed by Aileron as a novel chemoprotective medicine to selectively protect healthy cells in patients with cancers that harbor p53 mutations to reduce or eliminate chemotherapy-induced side effects.

Chemotherapy preferentially acts on cells that are cycling or undergoing the process of cell division. In cancer cells, the cell cycle is unchecked, which leads to uncontrolled cell proliferation, a hallmark of cancer. Certain types of healthy cells also naturally need to cycle, such as bone marrow cells, hair follicle cells, skin cells, and cells lining the oral cavity and the gastrointestinal tract. As a result, chemotherapy targets and kills both cycling healthy cells and cycling cancer cells. This, in turn, can lead to a spectrum of chemoprotection-induced side effects, from unpleasant to life-threatening and fatal.

ALRN-6924, an investigational first-in-class MDM2/MDMX dual inhibitor, is administered prior to chemotherapy to patients with p53-mutant cancers. ALRN-6924 is designed to activate normal p53 protein in patients’ healthy cells, temporarily and reversibly pausing cell cycling to selectively shield the patients’ healthy cells from chemotherapy. The protection is limited to healthy cells, as ALRN-6924 cannot work in p53-mutated cancer cells given that p53 has lost its function in those cells. Therefore, cancer cells continue to cycle uninterrupted and remain fully susceptible to destruction by chemotherapy.

About Aileron Therapeutics
At Aileron, we are focused on transforming the experience of chemotherapy for cancer patients, enabling them to fight cancer without the fear or burden of chemotherapy-induced side effects. ALRN-6924, our first-in-class MDM2/MDMX dual inhibitor activating p53, is the only reported therapeutic agent in clinical development to employ a biomarker strategy, in which we exclusively focus on treating patients with p53-mutated cancers. With this unique, targeted strategy, ALRN-6924 is designed to protect multiple healthy cell types throughout the body from chemotherapy while chemotherapy continues to destroy cancer cells.

In addition to potentially reducing or eliminating multiple side effects, ALRN-6924 may also improve patients’ quality of life and help them better tolerate chemotherapy, potentially allowing patients to complete their treatment without dose reductions or delays. Our long-term vision is to bring chemoprotection to patients with p53-mutated cancers – approximately 50% of cancer patients – regardless of cancer type 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 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; whether the Company will obtain sufficient cash resources to conduct its planned clinical trials; whether results obtained in clinical trials will be indicative of results obtained in future clinical trials; whether third party data would be indicative of the data that would be obtained in a randomized, head-to-head clinical trial; whether Aileron’s product candidates 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 Aileron’s product candidates will receive approval from regulatory agencies on a timely basis or at all; whether, if product candidates obtain approval, they 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 quarterly report on Form 10-Q for the period ended June 30, 2020, filed on August 5, 2020, 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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