UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 29, 2022

Aileron Therapeutics, Inc.
(Exact Name of Company as Specified in Charter)

Delaware	**001-38130**	**13-4196017**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

285 Summer Street, Unit 101 **Boston, MA**	**02210**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 995-0900

Not applicable
(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol	Name of each exchange on which registered
Common Stock, $0.001 par value per share	**ALRN**	**Nasdaq Capital Market**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 8.01 Other Items.

On June 29, 2022, Aileron Therapeutics, Inc. ("Aileron" or the "Company") announced interim data from its Phase 1b randomized, double-blind, placebo-controlled clinical trial evaluating ALRN-6924 as a chemoprotective agent in patients with p53-mutated non-small cell lung cancer, or NSCLC, undergoing treatment with first-line carboplatin plus pemetrexed with or without immune checkpoint inhibitors, and announced plans to stop further enrollment in the NSCLC trial. Aileron plans to apply key learnings from the interim analysis to strengthen its Phase 1b clinical trial to evaluate ALRN-6924 as a chemoprotective agent in patients with p53-mutated ER+/HER2- neoadjuvant breast cancer undergoing treatment with doxorubicin plus cyclophosphamide and docetaxel.

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.

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.

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 breast cancer trial and will not further enroll additional patients in the ongoing 0.3 mg/kg and 0.6 mg/kg dose cohorts.

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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.

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%)

Forward-Looking Statements

Statements in this Current Report on Form 8-K 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

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.

described in other filings that Aileron may make with the Securities and Exchange Commission. Any forward-looking statements contained in this Current Report on Form 8-K 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.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Aileron Therapeutics, Inc.

Date: June 29, 2022

By: /s/ Manuel Aivado
Manuel Aivado, M.D., Ph.D.
President and Chief Executive Officer