
# Transforming the Experience of Chemotherapy for Cancer Patients

CORPORATE PRESENTATION

# Forward Looking Statements

Statements in this presentation 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 and/or trials anticipated; whether results obtained in preclinical and nonclinical studies and clinical trials will be indicative of results obtained in future clinical trials; whether preliminary or interim results from a clinical trial such as the interim data referenced in this release will be indicative of the final results of the 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 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; whether the coronavirus pandemic will have an impact 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.

# Aileron: Leading a Paradigm Shift in Chemoprotection for Cancer Patients

## ALRN-6924

- First-in-Class MDM2/MDMX dual inhibitor
- Protect patients from multiple chemotherapy-induced side effects

### PROOF-OF-CONCEPT PHASE 1B UNDERWAY

- ALRN-6924 + Topotecan in SCLC
- Dose Optimization & Schedule Optimization
- Positive Interim Data — Q2 2020

### UPCOMING 2020 MILESTONES

- Final Dose Optimization Data – Q4
- Preliminary Schedule Optimization Data — Q4
- Initiate Healthy Volunteer Study — Q3

*Inform expansion into other cancer types & chemotherapies*

### POTENTIAL TO TRANSFORM PATIENT EXPERIENCE

- Remove fear & burden of chemotherapy-induced side effects
- Better tolerate chemotherapy
- Complete chemotherapy w/o dose delays or dose reductions

## LONG-TERM VISION

**Chemoprotection for patients with p53-mutated cancers regardless of cancer type or chemotherapy**

## 50% OF CANCER PATIENTS

**Have p53-mutated cancer**

# We want to enable patients to fight cancer without the fear and burden of chemotherapy-induced side effects

**MILLIONS OF PATIENTS**

Need chemotherapy to fight cancer

**SIDE EFFECTS**

Impact all patients undergoing chemotherapy

**UNSELECTIVE**

Chemotherapy can't distinguish between cancer cells and healthy cells, causing side effects

## TODAY'S SUPPORTIVE CARE APPROACH

- Multiple drugs; none addresses >1 toxicity
- Often ineffective; associated with harmful toxicities
- No options for some side effects (like hair loss)

**Resignation: side effects accepted**

## AILERON'S MISSION AND POTENTIAL

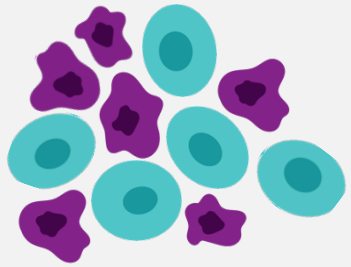
- One medicine to protect multiple cell types, safely and effectively
- Improved quality of life and better tolerance for chemotherapy, without dose reductions or delays

**Proactive prevention**

# Basic principles to successfully protect against chemotherapy-induced side effects

**CURRENT PARADIGM:**

**Chemotherapy targets both healthy cells and cancer cells that are cycling (undergoing cell division process)**



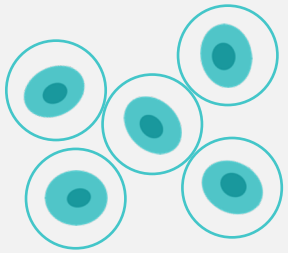
Both healthy cells and cancer cells are destroyed by chemotherapy

**PARADIGM SHIFT**

**AILERON PARADIGM:**

**Temporarily pause cell cycling in healthy cells, shielding them**

**No interruption of cycling in cancer cells, leaving them fully susceptible to chemotherapy**



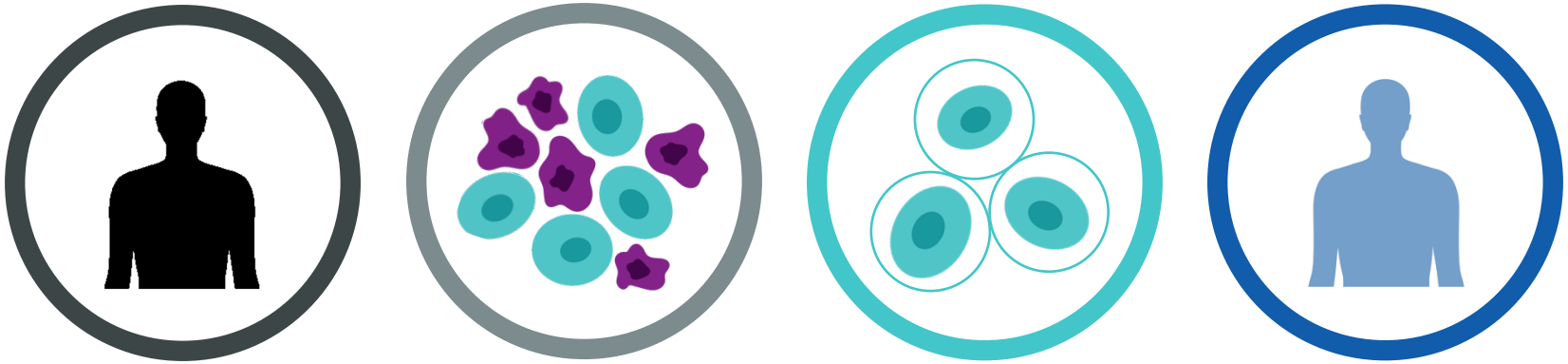
Healthy cells are not destroyed

Cancer cells are destroyed

**A COUNTERINTUITIVE APPROACH:**

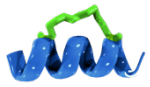
Treat healthy cells, not cancer cells

# ALRN-6924 activates p53 to pause the cell cycle in healthy cells, but not cancer cells



**Patient receives ALRN-6924 before chemotherapy** → **ALRN-6924 activates p53 in healthy cells** → **Activated p53 pauses cell cycling in healthy cells** → **Patient administered chemotherapy**

IV administration;
1-hour infusion

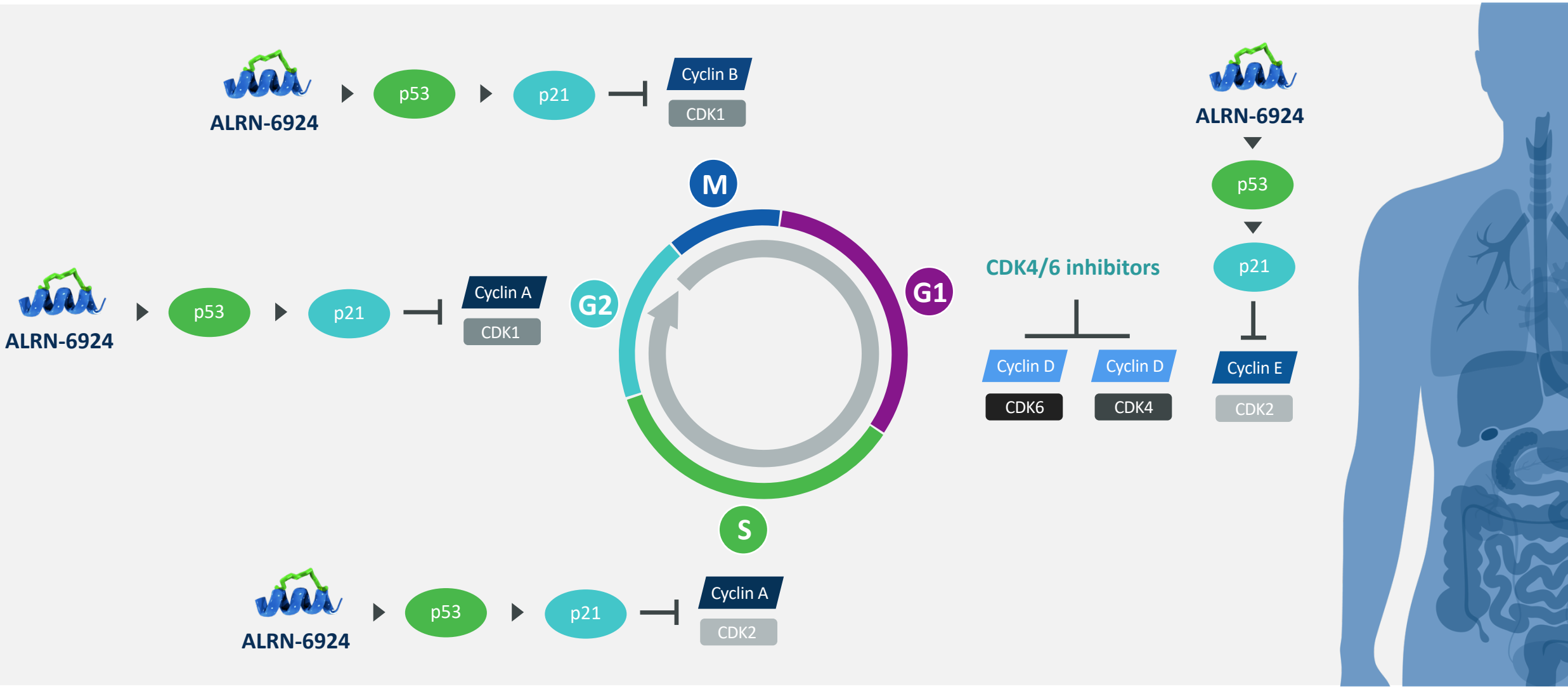


**ALRN-6924**

First-in-class MDM2/MDMX dual inhibitor designed to selectively and temporarily activate normal p53 in healthy cells, creating a window of protection for healthy cells during chemotherapy.

ALRN-6924 cannot work in p53-mutated cancer cells because p53 has lost its function in those cells. Chemotherapy's attack on cancer cells is uninterrupted.

# ALRN-6924 is capable of inducing cell cycle arrest in all cell cycle phases



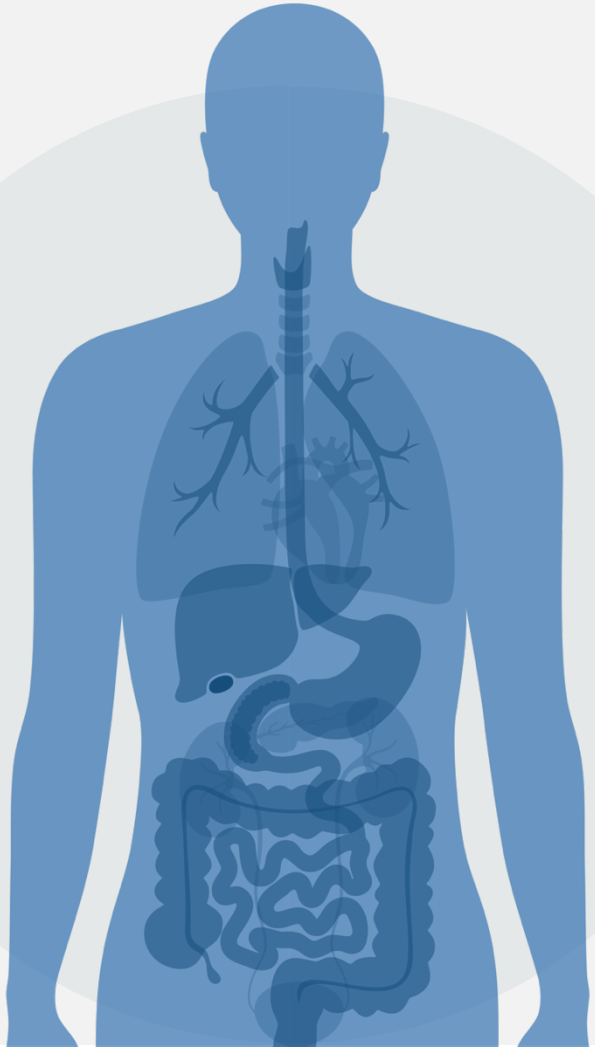
# ALRN-6924: A systemic therapeutic approach to a systemic issue

## Aileron Proof-of-Concept Focus

**Severe Anemia**
**(weakness, fatigue)**
Red blood cells

**Severe Thrombocytopenia**
**(excessive bleeding)**
Platelets

**Severe Neutropenia**
**(serious infection, fever, sepsis)**
White blood cells



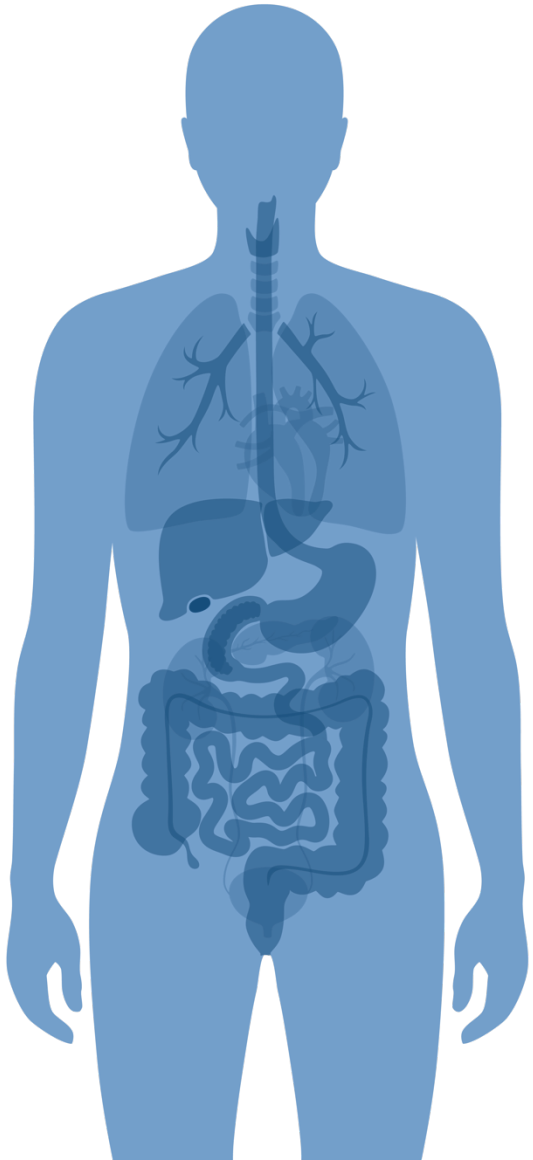
## Potential Other Benefits

**Alopecia (Hair Loss)**
Hair follicle cells

**Stomatitis (Mouth Sores)**
Cells lining the oral cavity

**Vomiting, diarrhea, bloating**
Cells lining the stomach and intestines

# Chemotherapy-Induced Bone Marrow Toxicities: Insufficient Current Standard of Care



**SEVERE ANEMIA**

**Standard of Care:** "EPOs" (e.g., Aranesp®/Epogen®); Blood transfusions

**Safety Concerns:**

- EPOs: promote tumor growth and thrombo-embolic events (black box warning ⚠)
- Transfusions: risk of infection; limited supply

**SEVERE NEUTROPENIA**

**Standard of Care:** G-CSF (e.g. Neulasta® /Neupogen®)

**Safety Concerns:**

- Can promote tumor growth and cause bone pain

**SEVERE THROMBOCYTOPENIA**

**Standard of Care:** No drugs used as standard of care – instead platelet transfusions

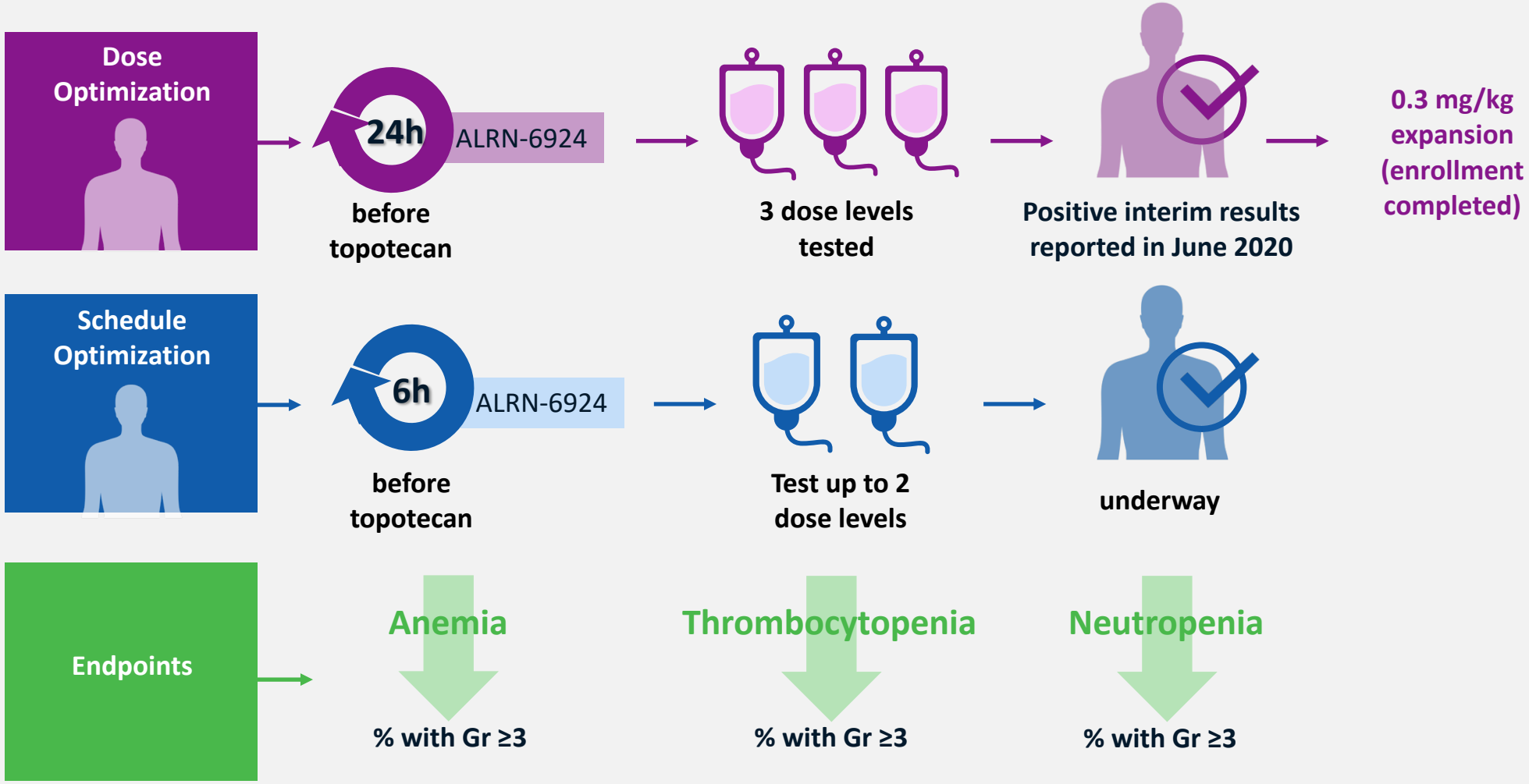
**Safety Concerns:**

- Effects limited to 2-5 days maximum
- Patients can become transfusion-refractory
- Transfusion-related risk of infection; limited supply

# ALRN-6924 Proof-of-Concept Clinical Development Program

**Ongoing Ph1b Study of ALRN-6924 in Small Cell Lung Cancer Patients Receiving Topotecan**

Protocol consists of open-label Ph1b, and randomized, controlled Phase 2



# ALRN-6924 Phase 1b Study

# Dose Optimization: Positive Interim Results

REPORTED JUNE 2020

# Demographics and Key Baseline Characteristics

| | | 0.3 mg/kg N (%) N=6 | 0.6 mg/kg N (%) N=5 | 1.2 mg/kg N (%) N=6 | Total N (%) N=17 |
|---|---|---|---|---|---|
| **AGE** | Median | 69.5 | 67 | 58 | 65 |
| | Mean | 66 | 64.4 | 59.5 | 63.2 |
| **GENDER** | Male | 6 (100) | 2 (40) | 4 (67) | 12 (71) |
| **ECOG PS** | 0 | 6 (100) | 2 (40) | 3 (50) | 11 (65) |
| | 1 | - | 3 (60) | 3 (50) | 6 (35) |
| **BASELINE LDH** | ≥ULN | 2 (33) | 3 (60) | 2 (33) | 7 (41) |
| **TIME SINCE PREVIOUS THERAPY** | <60 days | 3 (50) | 1 (20) | 5 (83) | 9 (53) |
| **STAGE AT INITIAL TUMOR DIAGNOSIS** | Extensive Disease | 6 (100) | 5 (100) | 6 (100) | 17 (100) |
| **P53 MUTATION STATUS** | Mutated | 6 (100) | 5 (100) | 6 (100) | 17 (100) |

*Data cutoff for interim analysis of the dose optimization part of the trial 5/13/2020; 3 patients on-going*

# Study Drug Exposure

| | 0.3 mg/kg N=6 | 0.6 mg/kg N=5 | 1.2 mg/kg N=6 | Total N=17 |
|---|---|---|---|---|
| **DURATION OF EXPOSURE (DAYS)** | | | | |
| Mean (SD) | 49 | 41 | 61 | 51 |
| Median (Min, Max) | 31 (6, 103) | 27 (6, 90) | 42 (27, 157) | 28 (6, 157) |
| **NUMBER OF CYCLES COMPLETED** | | | | |
| Mean (SD) | 2.8 | 2 | 3.3 | 2.8 |
| Median (Min, Max) | 2 (1, 5) | 1 (1, 4) | 2.5 (1, 8) | 2 (1, 8) |
| **TOPOTECAN DOSE REDUCTIONS** | | | | |
| Patients with any dose reductions (N, %) | - | - | 1 (17) | 1 (6) |
| **ALRN-6924 DOSE REDUCTIONS** | | | | |
| Patients with any dose reductions (N, %) | - | - | - | - |

*Data cutoff for interim analysis of the dose optimization part of the trial 5/13/2020; 3 patients on-going*

# Historical Data for Topotecan Hematological Toxicity in Small Cell Lung Cancer

| Trial | Phase | N* | Cycles median | Hematological Toxicity Grade ≥3 | | | | Comments |
|---|---|---|---|---|---|---|---|---|
| | | | | Neutropenia (%) | Febrile N-penia (%) | Thrombo-cytopenia (%) | Anemia (%) | |
| **Hematological toxicity reported by laboratory values** | | | | | | | | |
| Hart et al. ASCO 2019 | 2 | 28 | 3 | 86 | 17 | 70 | 63 | Chemosensitive population not reported<br>GCSF not prophylactic in C1<br>Transfusions: Plt 31%, RBC 41% |
| **Hematological toxicity reported as AEs** | | | | | | | | |
| Pawel et al. JCO 2014 | 3 | 213 | 5 | 54 | 3 | 54 | 31 | Chemosensitive population 55%<br>RBC transfusions 53%<br>Mandatory prophylactic growth factors |
| Eckardt et al. JCO 2007 | 3 | 151 | 4 | 88 | 5 | 43 | 31 | Chemosensitive population 100%<br>RBC transfusions 43%,<br>GCSF 16% |
| Jotte et al. JCO 2011 | 2 | 26 | 2 | 78 | 9 | 61 | 30 | Chemosensitive population 100%<br>Growth factors as necessary<br>Worst toxicities in cycle #1 |
| Inoue et al. JCO 2008 | 2 | 30 | 2 | 87 | 3 | 40 | 30 | Chemosensitive population 63%<br>GCSF not prophylactic |

*Data cutoff for interim analysis of the dose optimization part of the trial 5/13/2020; 3 patients on-going*

# Key side effects when adding ALRN-6924 to topotecan relative to historical controls

| Topotecan + ALRN-6924 in SCLC patients (Phase 1b interim results) | | | | | Topotecan ± Trilaciclib in SCLC patients‡ | |
|---|---|---|---|---|---|---|
| | Topotecan 1.5 mg/m² + ALRN-6924 | | | | Topotecan 1.5 mg/m² + Placebo | Topotecan 1.5 mg/m² + Trilaciclib |
| | 0.3 mg/kg | 0.6 mg/kg | 1.2 mg/kg | Total | | |
| | N (%) N=6 | N (%) N=5 | N (%) N=6 | N (%) N=17 | N (%) N=28 | N (%) N=32 |
| **All AEs* (NCI CTC Grade ≥3)** | 5 (83) | 5 (100) | 6 (100) | 16 (94) | 27 (96) | 28 (88) |
| **Neutropenia** | 4 (67) | 5 (100) | 6 (100) | 15 (88) | 24 (86) | 22 (69) |
| **Thrombocytopenia** | 2 (33) | 2 (40) | 2 (33) | 6 (35) | 20 (70) | 22 (68) |
| **Anemia** | 1 (17) | 2 (40) | 1 (17) | 4 (24) | 18 (63) | 10 (39) |
| **Fatigue** | - | - | - | - | 2 (7) | 3 (9) |
| **Nausea** | - | - | - | - | 1 (4) | 0 (0) |
| **Neutropenia NCI CTC Grade 4**** | 2 (33) | 5 (100) | 1 (17) | 8 (47) | 21 (76) | 13 (41) |

*AEs based on laboratory values, as applicable
** in the first treatment cycle

‡ Hart et al. ASCO 2019 – G1 Therapeutics; Phase 2 Clinical Trial

*Data cutoff for interim analysis of the dose optimization part of the trial 5/13/2020; 3 patients on-going*

# Other results support chemoprotection signal with ALRN-6924 treatment

**SAEs**

| SAE | 0.3 mg/kg N (%) N=6 | 0.6 mg/kg N (%) N=5 | 1.2 mg/kg N (%) N=6 | Total* N (%) N=17 |
|---|---|---|---|---|
| NEUTROPENIA | - | 1 (20) | 2 (33) | 3 (18) |
| LEUKOPENIA | - | - | 2 (33) | 2 (12) |
| THROMBOCYTOPENIA | - | - | 2 (33) | 2 (12) |
| ANEMIA | - | - | 2 (33) | 2 (12) |
| FEBRILE NEUTROPENIA | - | - | - | - |

**Transfusions**

| | 0.3 mg/kg N=6 | 0.6 mg/kg N=5 | 1.2 mg/kg N=6 | Total N=17 |
|---|---|---|---|---|
| RBC transfusions (% of patients, N of transfusions) | - | 3 (60) | 3 (50)* | 6 (35) |
| Platelet transfusions (% of patients, N of transfusions) | - | 2 (40) | 1 (17) | 3 (18) |

*One patient received multiple RBC transfusions with Hb NCI CTC Grade 2

**Performance Status**

| | 0.3 mg/kg N=6 | 0.6 mg/kg N=5 | 1.2 mg/kg N=6 | Total N=17 |
|---|---|---|---|---|
| ECOG PS at baseline (Mean, Median) | 0, 0 | 0.5, 0.5 | 0.5, 0.5 | 0.3, 0 |
| ECOG final PS (Mean, Median) | 0, 0 | 1, 1 | 0.5, 0.7 | 0.6, 0 |

*Data cutoff for interim analysis of the dose optimization part of the trial 5/13/2020; 3 patients on-going*

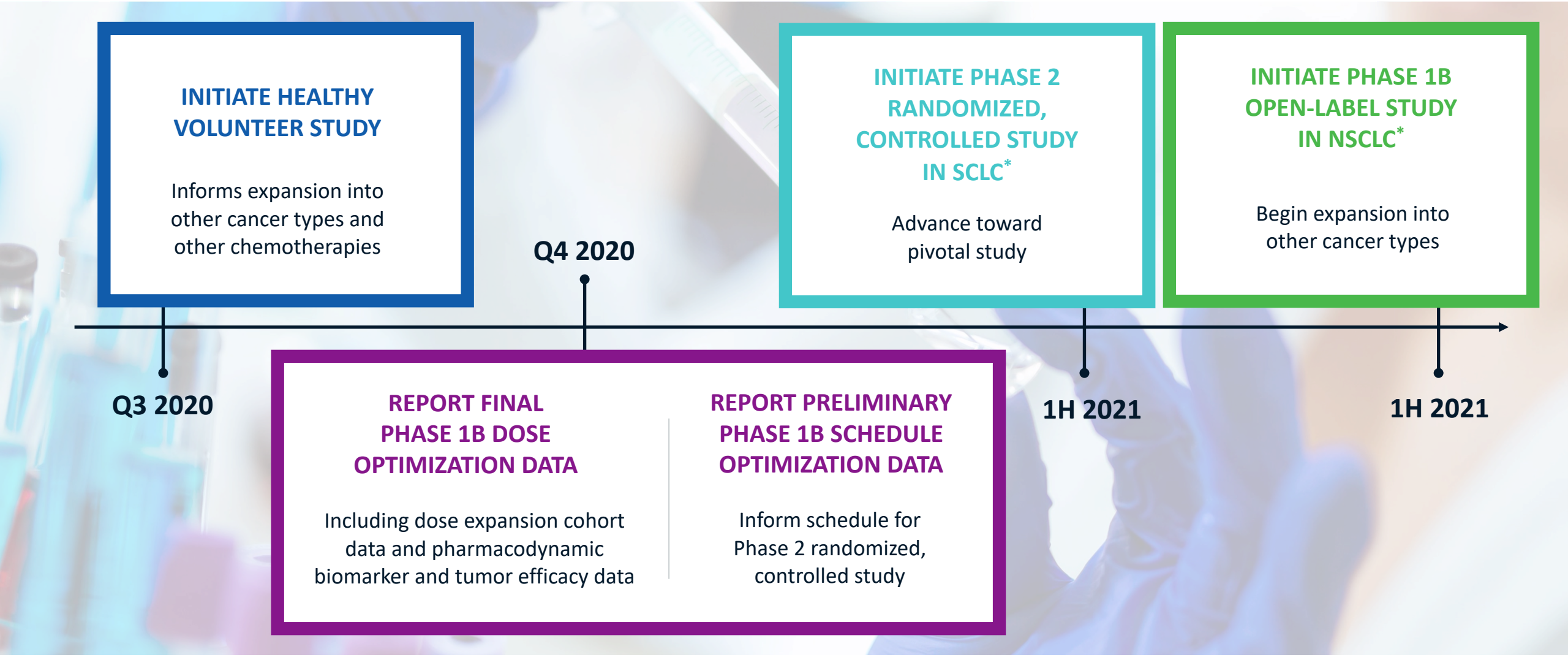
# Summary of Interim Clinical Results

Clinically meaningful protection against severe anemia and thrombocytopenia; promising protection against severe neutropenia

0.3 mg/kg dose level achieved most robust and consistent chemoprotection effects, including absence of febrile neutropenia, blood transfusions, severe nausea, vomiting, diarrhea, or fatigue

Enrollment completed into expansion cohort of the 0.3 mg/kg dose level at -24 hour schedule

# Multiple Key Value Drivers in next 6 – 12 months




* Conduct of future trials dependent on funding and results from ongoing dose- and schedule-optimization trial as well as subject to the impact of the Covid-19 pandemic

# Key Financial Highlights

| Q2 2020 | |
|---|---|
| **Cash, Cash Equivalents and Investments**<br>*Expected to support operations into Q4 2021* | **$19MM** |
| **Common Shares Outstanding** | **39MM** |
| **Common Warrants ($2.01)** | **13MM** |

# Strategic Execution to Advance Broad Long-Term Vision

- Validated scientific foundation and proven MOA to pause cell cycle and protect healthy cells in patients with p53-mutated cancers
- Initial clinical results demonstrated ability to protect against severe anemia and thrombocytopenia
- Planned clinical studies to assess expanded protective effects to other chemotherapies, cancers, and additional chemotherapy-induced toxicities

**LONG-TERM VISION**

- Provide chemoprotection for patients with p53-mutated cancers – 50% of cancer patients – regardless of cancer type or chemotherapeutic drug


# Transforming the Experience of Chemotherapy for Cancer Patients

NASDAQ: ALRN

WWW.AILERONRX.COM