AILERON

Corporate Presentation

December, 2019

Legal Matters

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Aileron's Executive Team

Manuel Aivado, MD, PhD
President and CEO

Taiho Oncology, GlaxoSmithKline,
Beth Israel / Harvard Medical School

Vojo Vukovic, MD, PhD
Chief Medical Officer

Taiho Oncology, Synta,
Pfizer, Ilex Oncology

Allen Annis, PhD
SVP, Research

Schering-Plough,
NeoGenesis Pharmaceuticals

Kathryn Gregory, MBA
Chief Business Officer

Avillion, Seneb BioSciences, Purdue
Pharma, Shire, PhaseBio, Teva

Rick Wanstall, MBA
VP, Finance and Operations

Moderna, Stream Global Services,
Coopers and Lybrand

Aileron Therapeutics:
Focus on Clinical Development of ALRN-6924

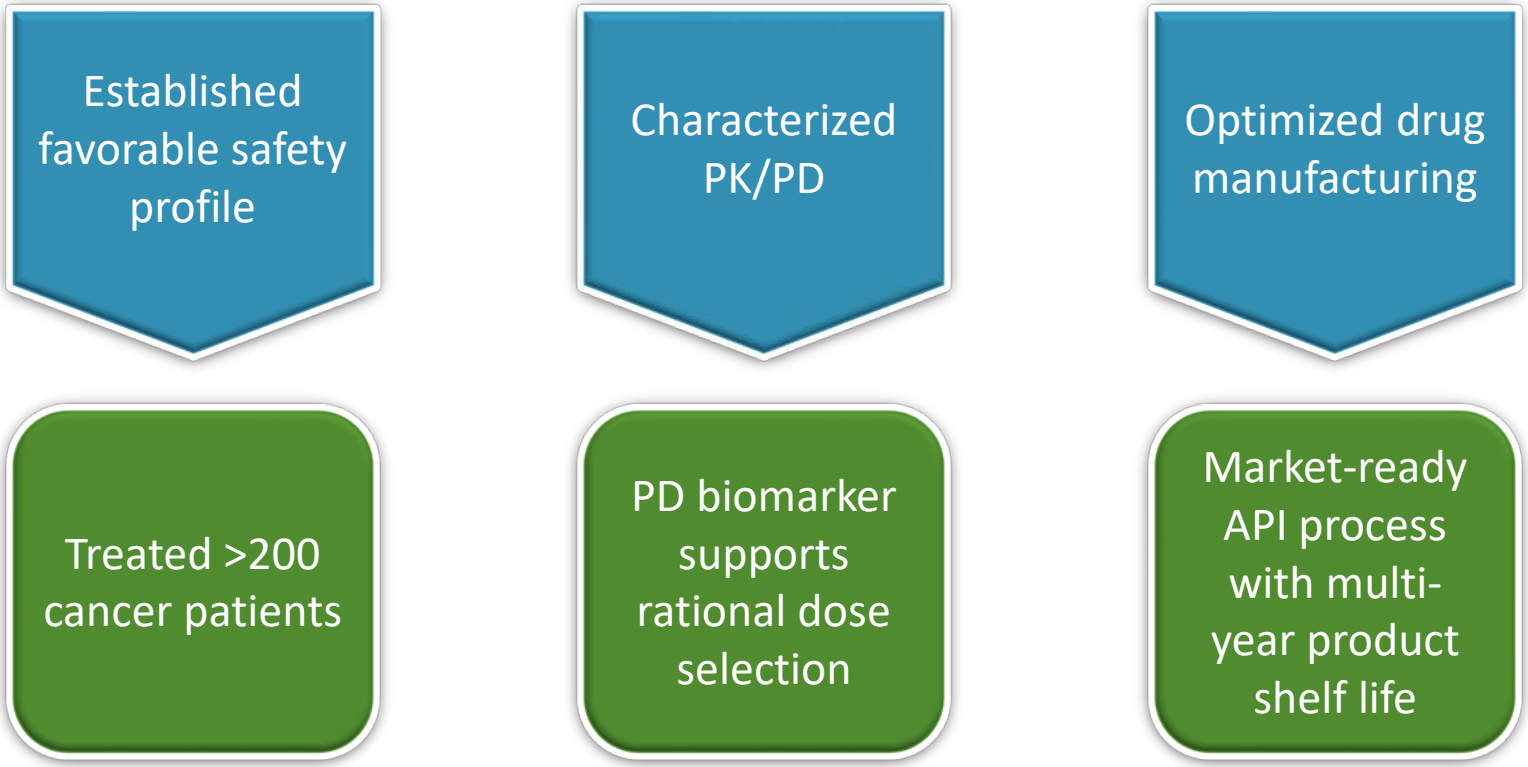
Ongoing and Planned Trials

Programs	ALRN-6924	Preclinical	Phase 1	Phase 2	Milestone
Myelopreservation **Protecting normal cells from chemotherapy**	**Prior to chemotherapy**				**Started enrollment Sept 2019** **Phase 1b results 2Q-2020**
MDM2-amplified cancers	+ Palbociclib				Final results 2Q-2020
Investigator-sponsored	+ Paclitaxel in Breast Cancer				
	+/- Ara-C Pediatric Cancers				

Past Trials

- ✓ Phase 1 First in Human
- ✓ Phase 1/1b in AML and MDS
- ✓ Phase 2a in Peripheral T-cell Lymphoma

ALRN-6924 is at a Mature Stage of Clinical Development



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Protecting Normal Healthy Cells from Chemotherapy-induced Toxicities

→

Improving Patient Outcomes

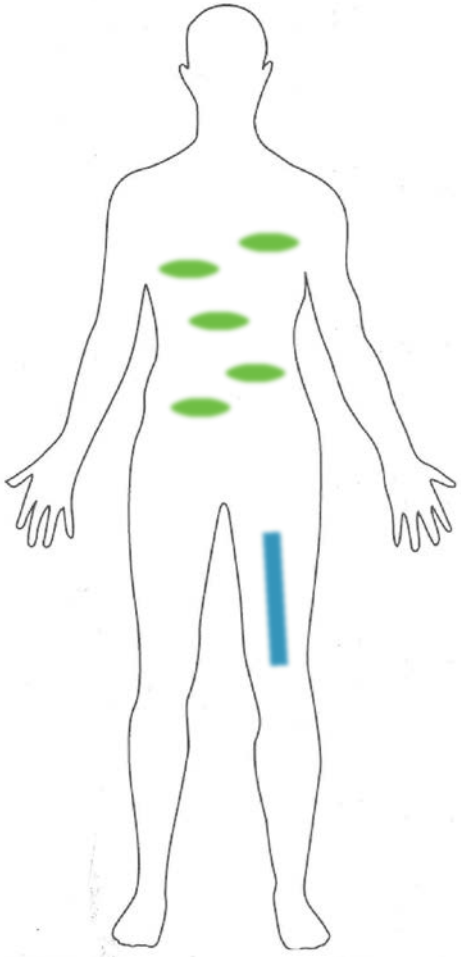
Chemotherapy Damages ***Proliferating Cells*** – Regardless if Cancer Cells or Normal Cells

Cells proliferating are:
cancer cells and
normal cells such as bone marrow cells

Proliferating Cell

Chemotherapy

Cell Death



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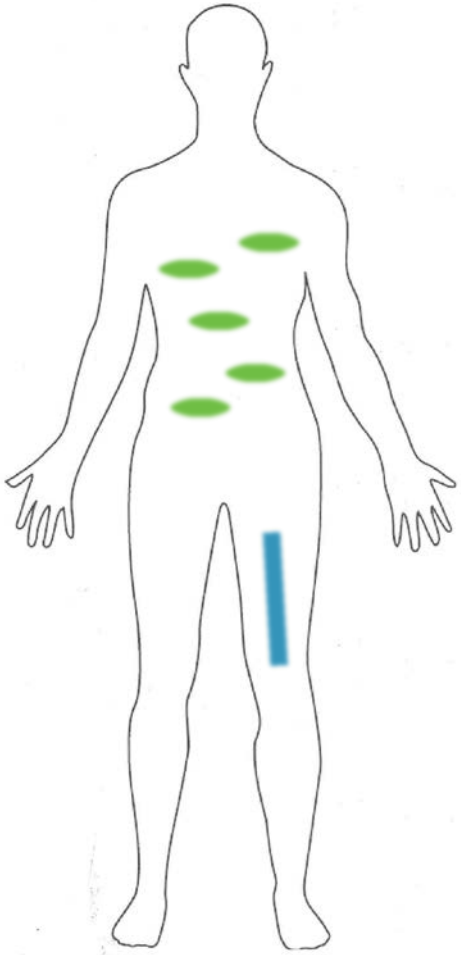
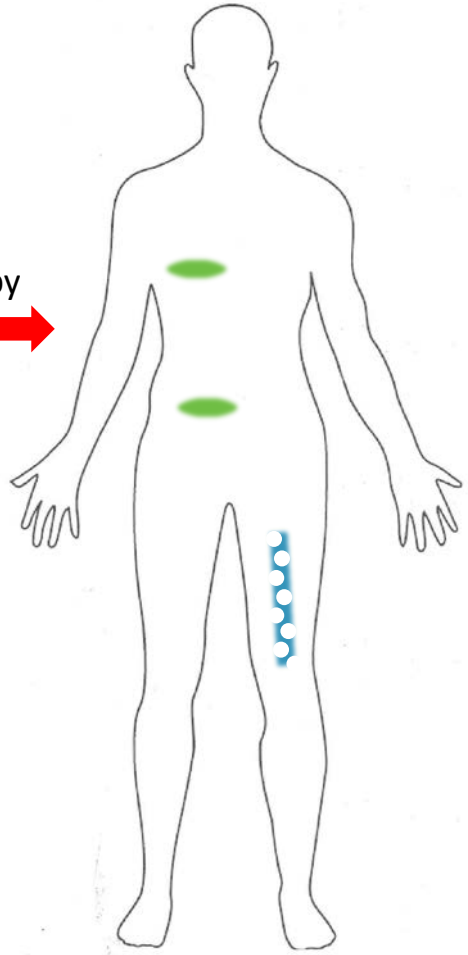
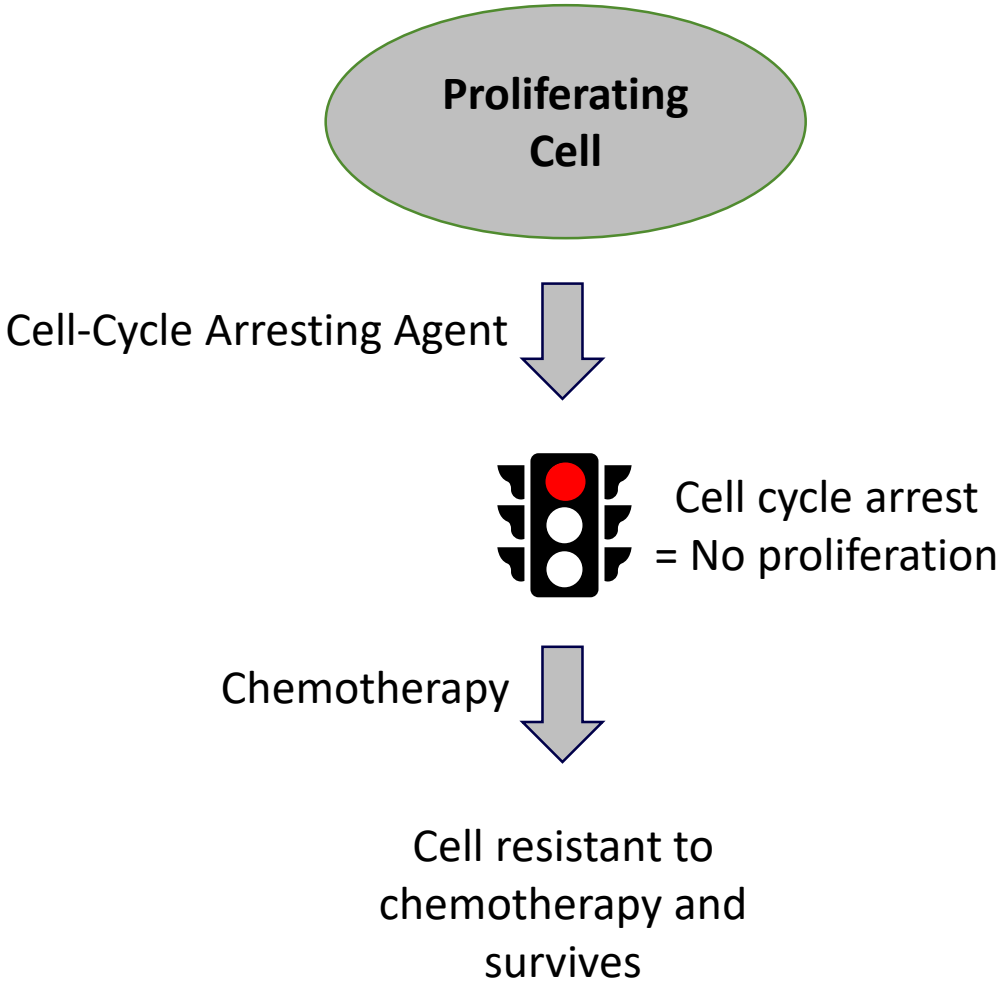


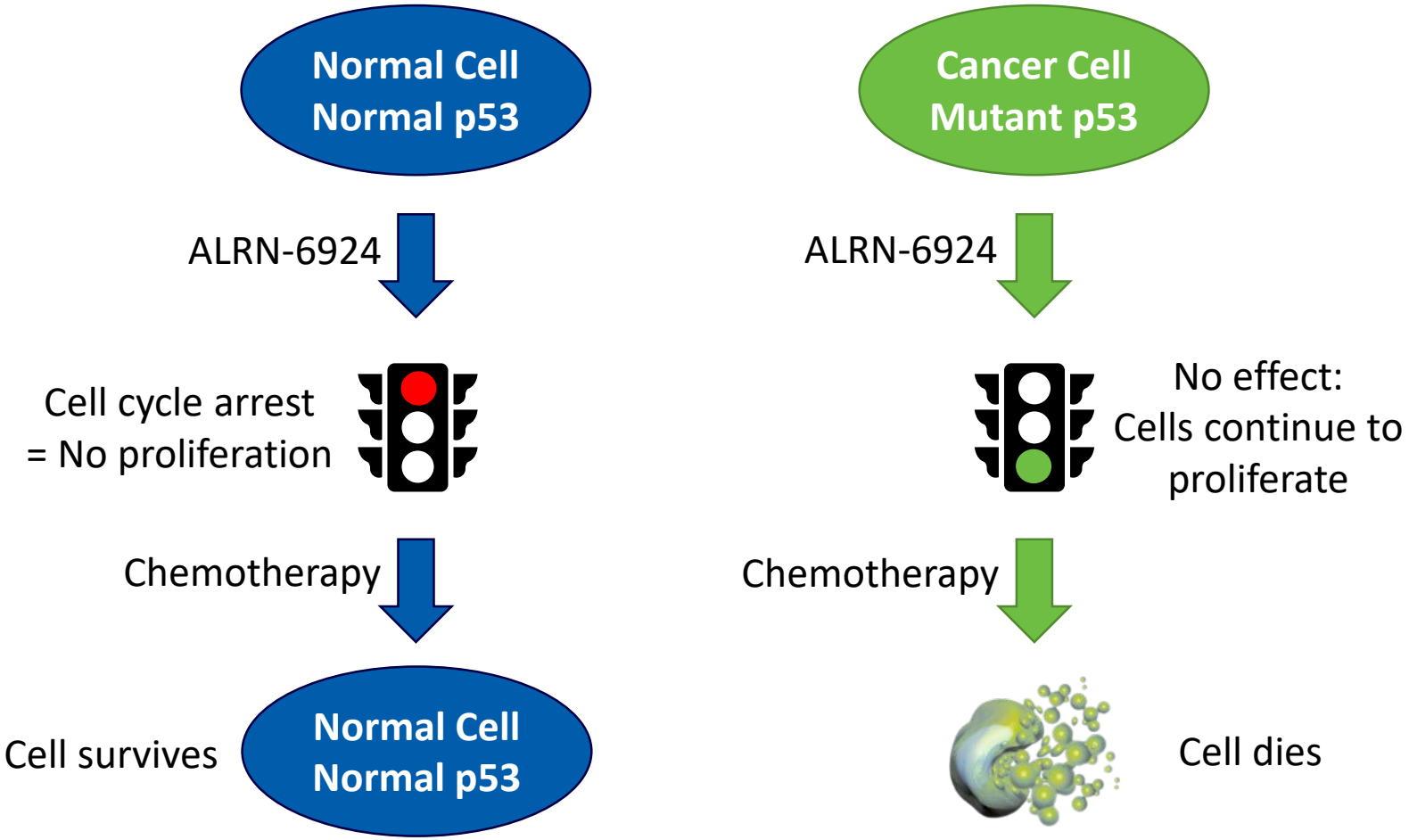
Chemotherapy



Proliferating Cells Can Be Protected From Chemotherapeutic Toxicity By ***Cell Cycle Arrest***

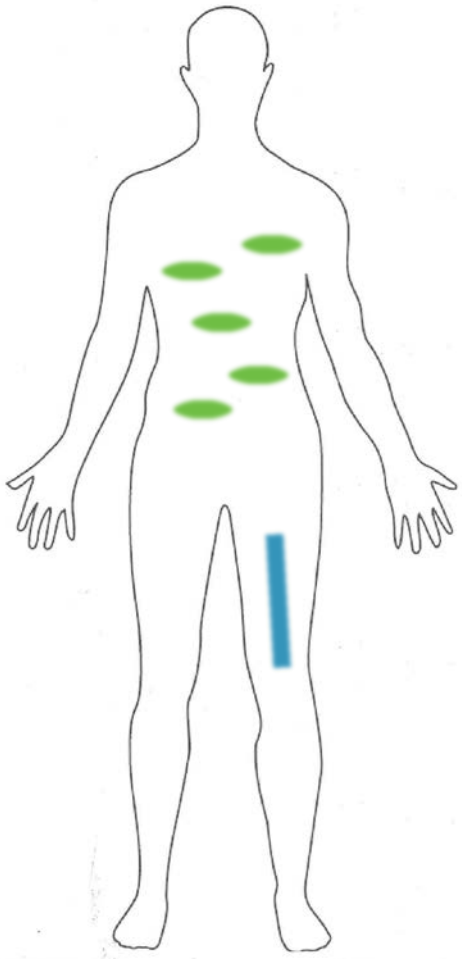


p53 Mutation is Biomarker for ALRN-6924 to Distinguish Between Cancer Cells and Normal Cells



ALRN-6924 Selectively Protects Normal Tissues with Normal p53 to Prevent Chemotherapeutic Toxicity

Cells proliferating are:
cancer cells and
normal cells such as bone marrow cells



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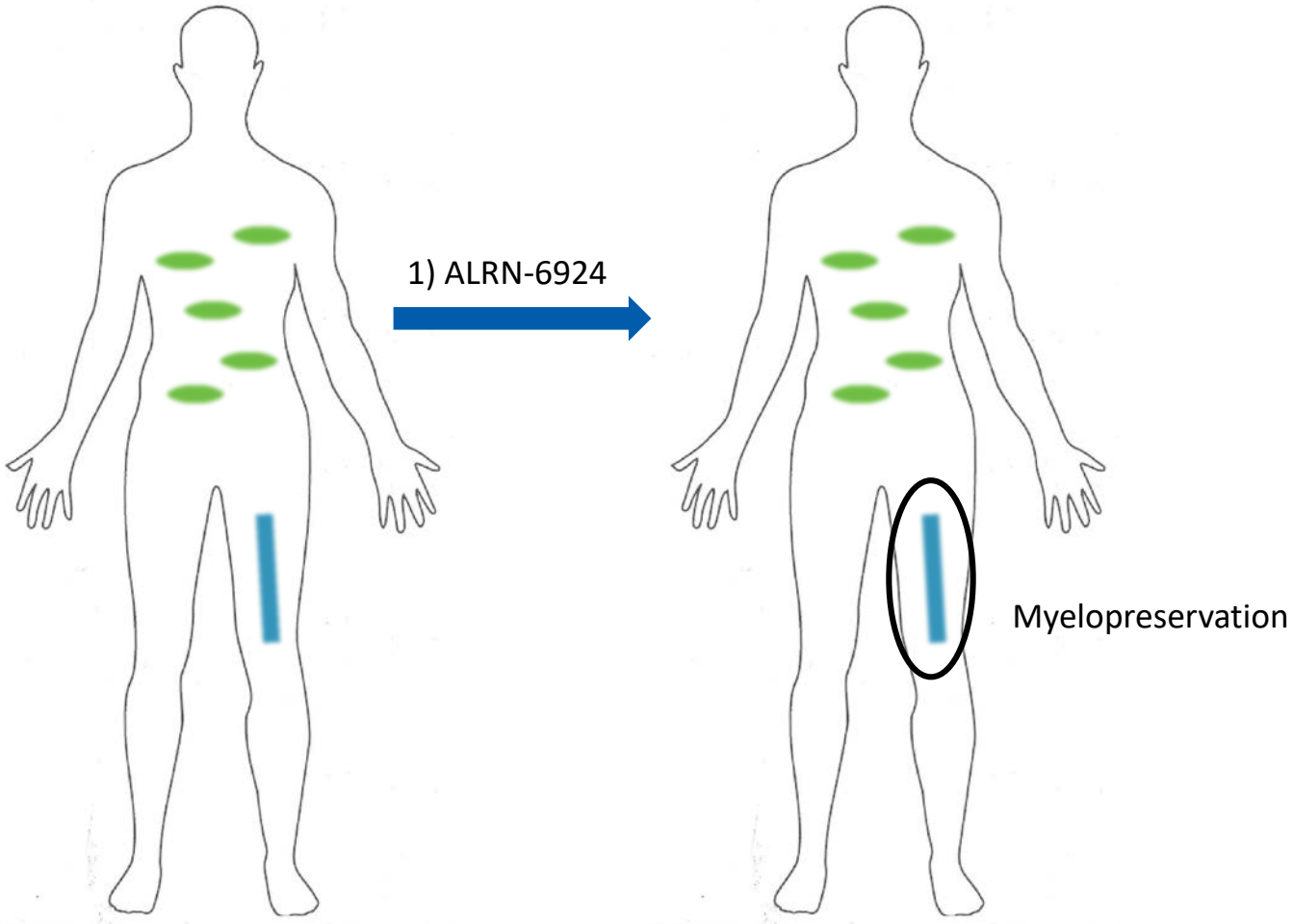

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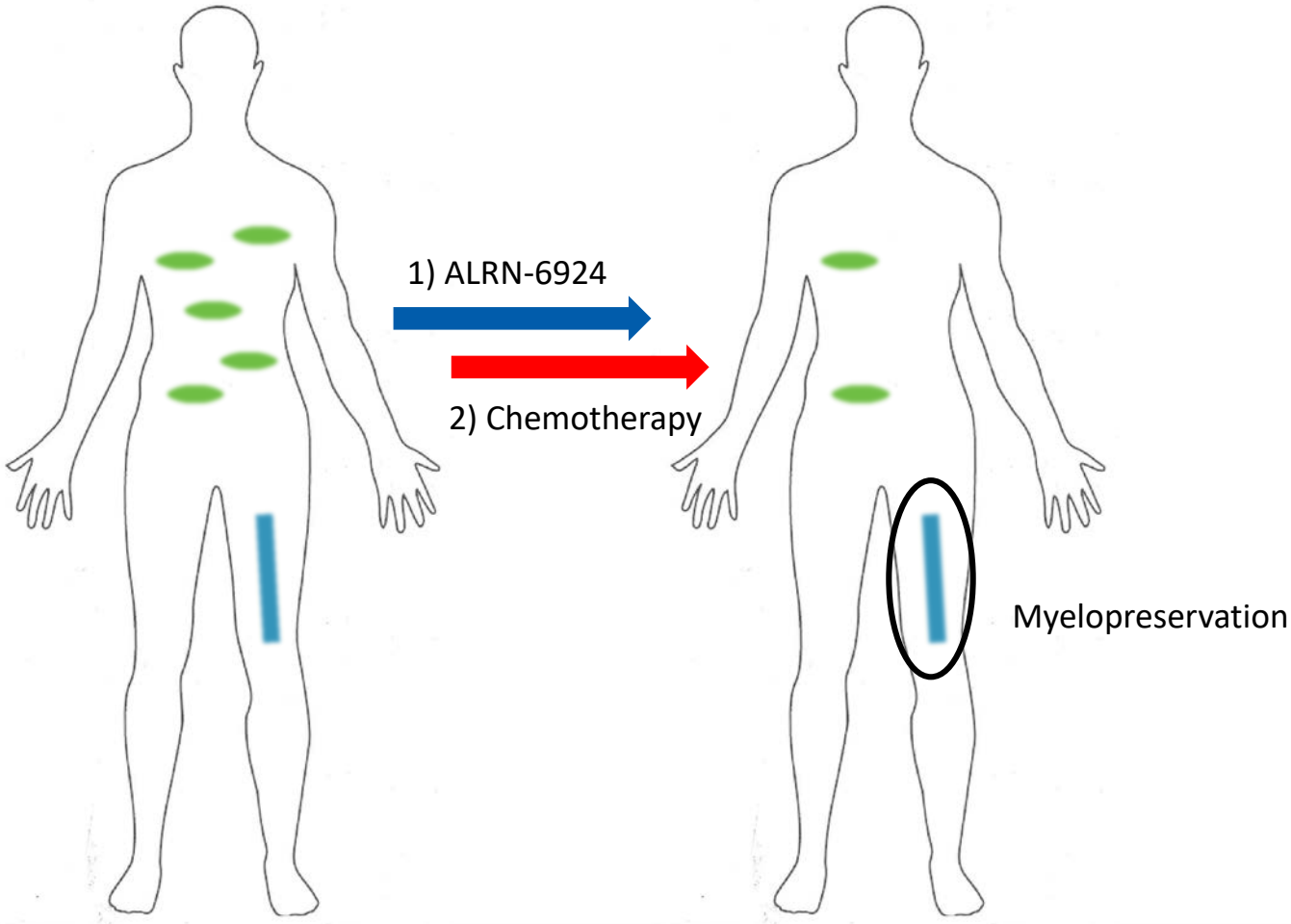
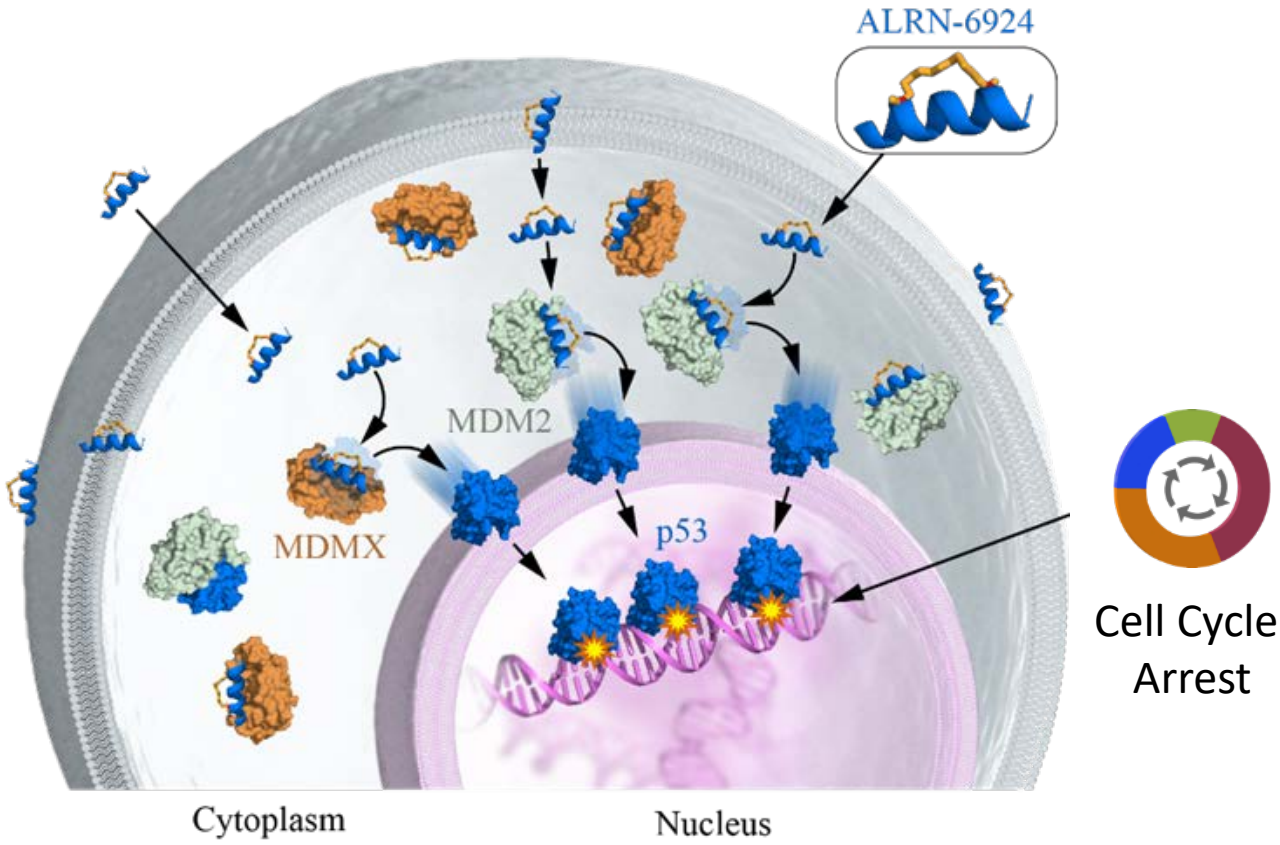


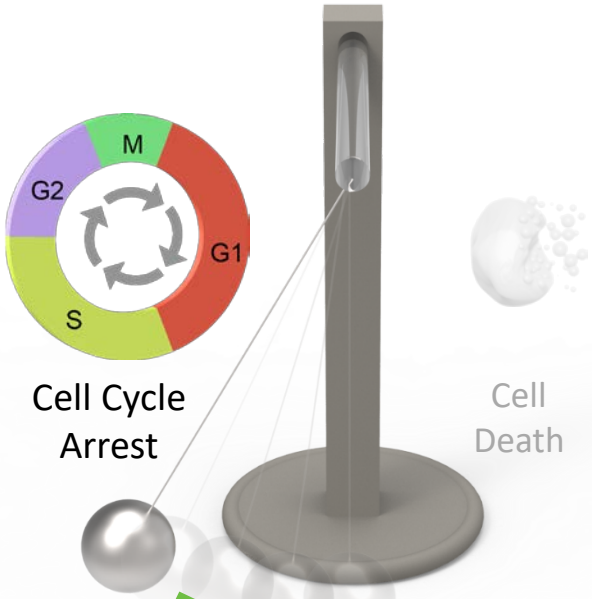
ALRN-6924 is a Cell-permeating Peptide Drug that Selectively Inhibits MDM2 and MDMX



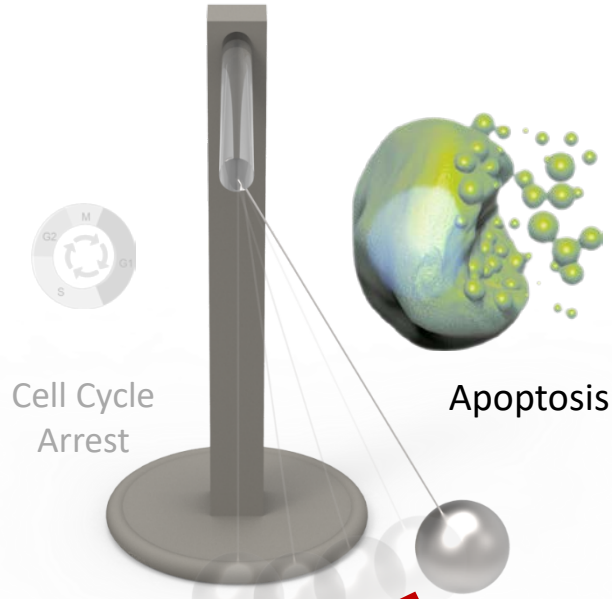
ALRN-6924 is a decoy that mimics p53 and selectively binds to MDMX + MDM2, releasing and reactivating p53 to induce cell cycle arrest

ALRN-6924 Can Induce Two Distinct p53-effects: Cell-Cycle Arrest or Cell Death

Applied in Myelopreservation Trial



Applied in MDM2-Amplification Trial



Patients Receiving 1st Line Chemotherapy (US & EU5)

≈85% of ovarian cancer patients

≈80% of pancreatic cancer patients

≈80% of lung cancer patients

≈75% of gastric cancer patients

≈65% of CRC patients

≈60% of breast cancer patients

≈1.3 M Chemotherapy Patients†

≈25% of prostate cancer patients

≈20% of bladder cancer patients

P53 mutations found in ≈50% of all cancer patients‡

Potential market opportunity for ALRN-6924
≈675,000 patients in the US and EU5 alone

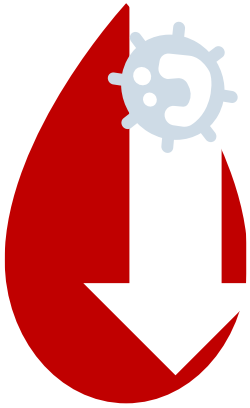
Source: Kantar Reports; ClearView Analysis. †Incident 1L chemotherapy patients/yr in U.S. and EU5; ‡ Lane et al, Nature Reviews Drug Discovery 2014

Chemotherapies Cause Significant Toxicities

Patients Suffering

Unintended effects of chemotherapy on normal cells

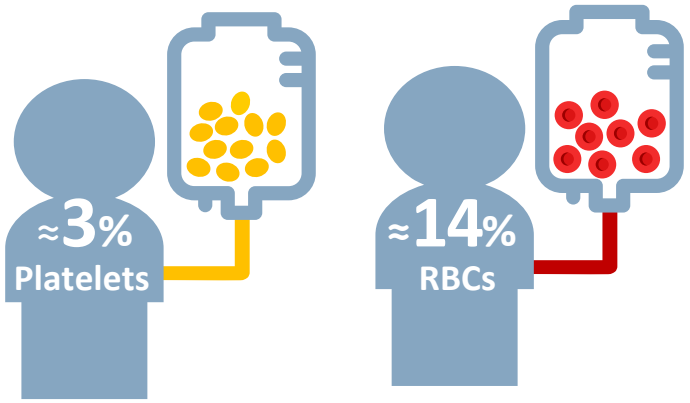
Severe Neutropenia



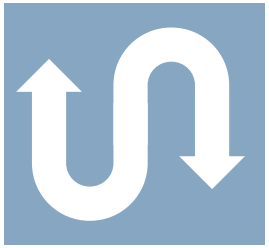
40-70%

Incidence in lung, breast and colorectal cancer patients[1-3]

Transfusions[4]



Other Frequent Side Effects



- **Mucositis**
- **Neurotoxicity**
- **Diarrhea**
- **Hair loss**
- **Nausea**
- **Vomiting**

Toxicities Impact Efficacy

- **Toxicities cause dose delays and dose reductions of chemotherapy, which can reduce efficacy**
- **Toxicities prevent administration of chemotherapies that are known to be more effective, e.g. FOLFIRINOX for metastatic pancreatic cancer**

[1]NEJM 2002 346(2):92-8. [2]Eloxatin PI [3]JCO (2010) 28(1):77-82 [4]Arch Intern Med. (2008) 168(21):2377–2381

Current Therapies for Chemotherapy-related Toxicities Are Inadequate

Inefficient

Treat one problem at a time rather than prevent multiple toxicities

- E.g. G-CSF improves neutrophil counts, but has no effects on other bone marrow toxicities

Deficient

No effective treatment available for certain side effects

- E.g. mucositis, neurotoxicity, severe diarrhea, hair loss, thrombocytopenia

Risky

Due to intrinsic side effects

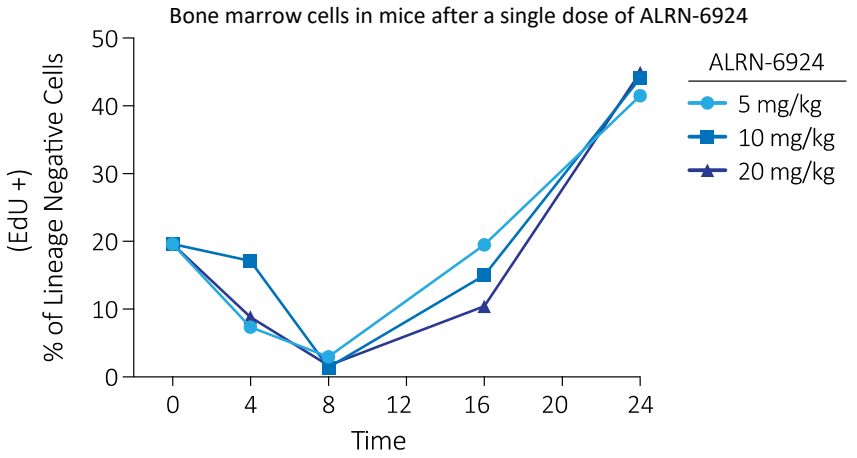
- Erythropoietin increases risk of thromboembolic events
- G-CSF and erythropoietin can promote cancer growth

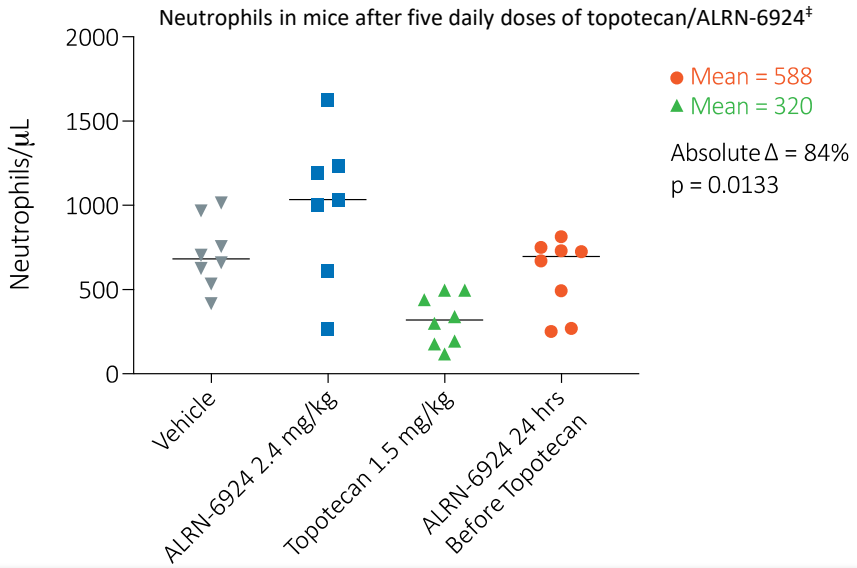
Aileron Nonclinical Research Supports the Use of ALRN-6924 as a Myelopreservation Agent

- **ALRN-6924 induces cell cycle arrest:** As established for other p53-activating agents and mechanisms, ALRN-6924 exhibits dose-dependent switching from growth arrest to apoptosis
- **Correlated serum biomarker with cell cycle arrest:** Low doses of ALRN-6924 cause cell cycle arrest in mouse bone marrow without inducing apoptosis, and the arrest correlates with the same MIC-1 biomarker we follow in patients to project the dose and timing of bone marrow arrest in human
- **ALRN-6924 protects against topotecan-induced neutropenia in mouse**, and does not diminish (but modestly enhances) topotecan's efficacy in p53-mutant cancer models
- **Beyond myelopreservation for topotecan:** Preliminary results also support ALRN-6924 myelopreservation for carboplatin/paclitaxel and potentially protection against topotecan-induced gastrointestinal toxicity in mouse
- **Nonclinical ALRN-6924 results presented** at the AACR-NCI-EORTC Conference, October 29, 2019

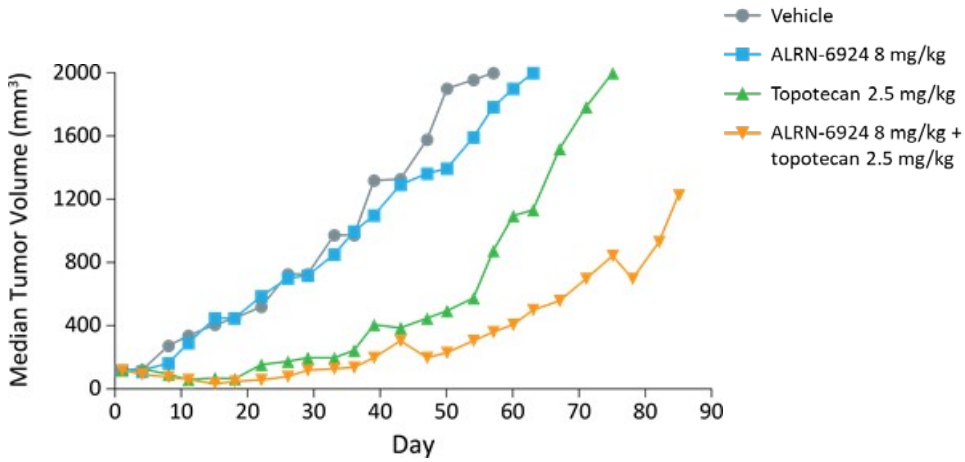
ALRN-6924 Is an Effective Myelopreservation Agent in Preclinical Studies

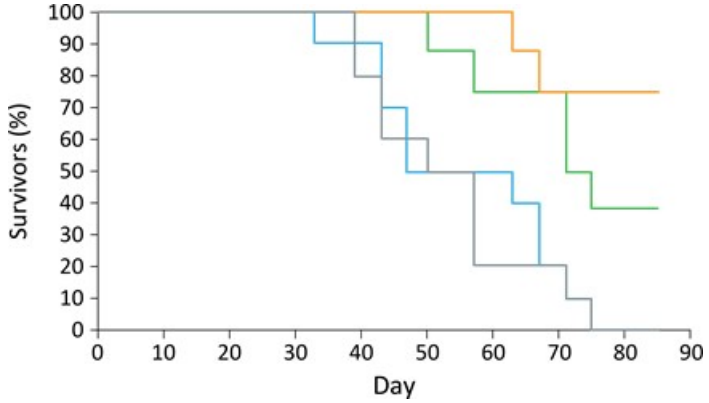
ALRN-6924 induces cell cycle arrest in bone marrow to protect against topotecan-induced DNA damage[1]





ALRN-6924 does not diminish, and moderately enhances, topotecan's activity against p53-mutant cancer[1]





C57BL/6 mice bearing H211 small cell lung cancer xenograft tumors after five daily doses of topotecan/ALRN-6924‡

‡ Mice dosed with topotecan on days 1-5 preceded by ALRN-6924 by 24 hrs; [1] Carvajal et al, AACR-NCI-EORTC 2019

Cell Cycle Arrest is Proven Approach to Achieve Myelopreservation

- G1-Therapeutics (NASDAQ: GTHX) has demonstrated that trilaciclib-induced cell cycle arrest achieves myelopreservation in Rb1-deficient cancer patient populations
  - GTHX has established a regulatory pathway for myelopreservation with FDA agreement to utilize Phase 2 data[1] for filing
  - About 9% of all cancers are Rb1-deficient[3]

- Aileron Therapeutics (NASDAQ: ALRN) has preclinically demonstrated that ALRN-6924 induces cell cycle arrest, which led to myelopreservation in p53-mutant cancer xenograft models
  - Approximately 50% of all cancers harbor p53-mutations[2]
  - p53-mutations represent biomarker that can be tested using standard gene tests such as 'Foundation One'

[1] G1TX 2Q-2019 Quarterly report, SEC.gov; [2] Lane et al, "Drugging the p53 pathway…" Nature Reviews Drug Discovery 2014 [3] Foundation Medicine "Insights" Database

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Clinical Development Plan for ALRN-6924 as a Myelopreservative Agent

ALRN-6924's Ph1b/2 Trial in Myelopreservation

Strategy	Patients with advanced, p53-mutated SCLC receiving 2nd line topotecan Phase 1b, N=40 pts, parallel group dose-optimization Phase 2*, N=80 pts, randomized, controlled, open-label
Diagnostic assay	Use existing standard gene tests such as 'Foundation One' to test for p53-mutation
Dosing	ALRN-6924 on Days 0-4 every 21 days, Topotecan on Days 1-5 every 21 days
Endpoints	Reduction of Gr ≥3 neutropenia (1ºEP) Reduction of Febrile Neutropenia Reduction of Gr ≥3 Anemia Reduction of Gr ≥3 Thrombocytopenia **Primary Endpoint Read-Out 12 Days After Treatment Start**
Data Presentations	Expected to present results on all pts (≈30-40) from phase 1b 2Q2020

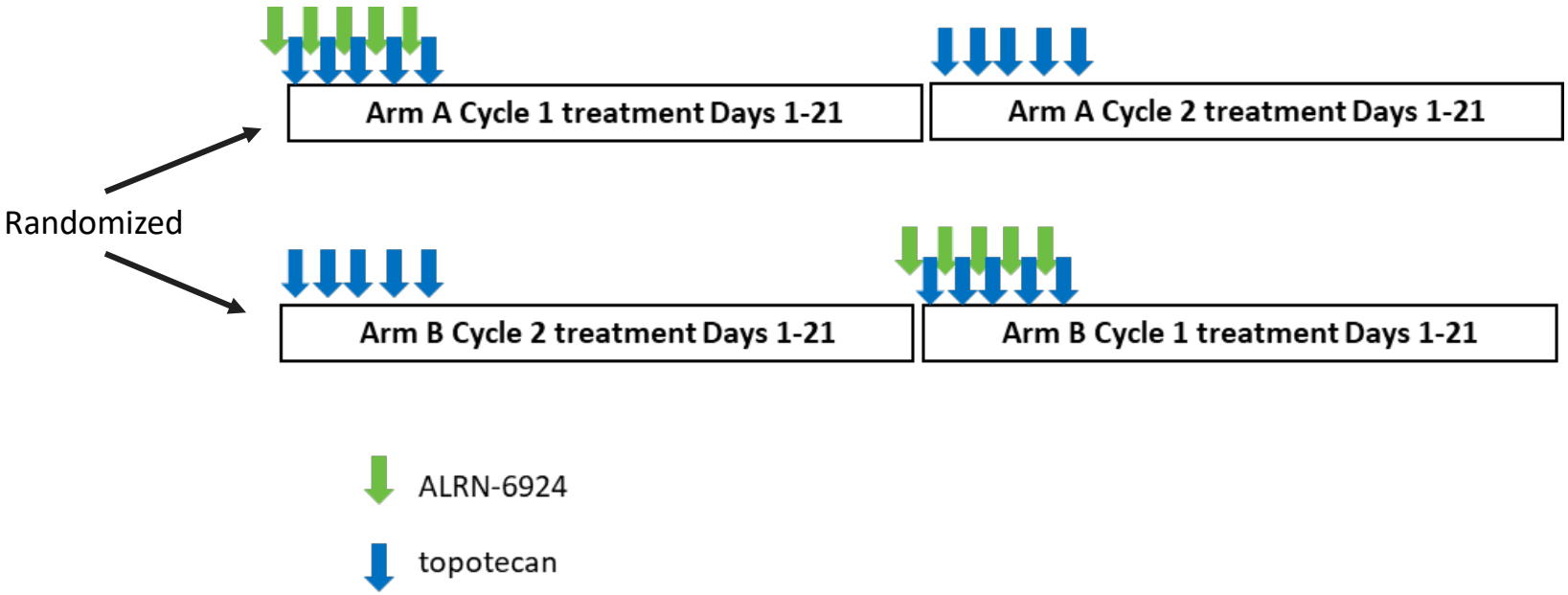
* Definitive N of patients remains subject to clinical and regulatory considerations as well as funding

Expansion of the Ph1b/Ph2 Protocol: “On/Off” Cohort

SCLC

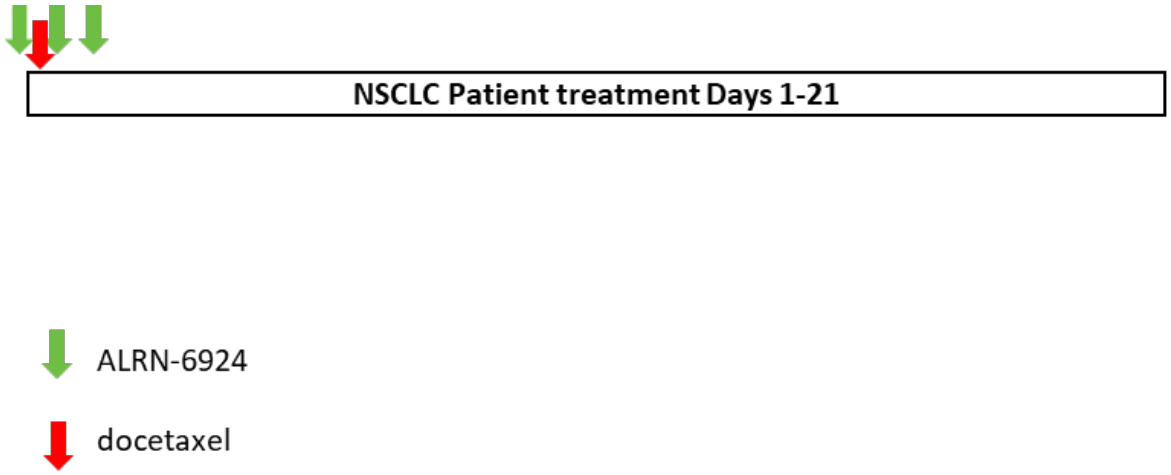
On/Off cohort consists of 2 randomized cohorts, each with 10 patients, total of N=20. Each patient will be treated with topotecan monotherapy and with the combination of topotecan + ALRN-6924, therefore **each patient will serve as their own control**.

Objective: Achieve robust clinical POC.



Expansion of the Ph1b/Ph2 Protocol: NSCLC Cohort

NSCLC	New Ph1b cohort (N=20) of advanced NSCLC patients who receive treatment with docetaxel with the recommended phase 2 dose of ALRN-6924. Objective: Develop a tumor-type agnostic, chemotherapy-agnostic myelopreservation product.



ALRN-6924 Myelopreservation Opportunity: Summary

Clinical Development	Commercial
Precision medicine - theoretically addresses ≥**50% of all cancers** who require chemotherapy	**Large market potential –** approx. **700,000 patients** annually in the US and EU5 alone
p53 biomarker available via standard gene tests	**Unmet need** for prevention of chemotherapeutic toxicities
Regulatory pathway[1] for FDA registration; potential for Breakthrough Therapy Designation	**Plan to develop** ALRN-6924 as **tumor type-agnostic and chemotherapy-agnostic drug**
Potential to improve efficacy of chemotherapy by avoiding dose delays & dose reductions of chemo	**IP - Composition of Matter to 2033** (before extensions)

[1] Pathway based on G1TX - FDA agreement noted in their 2Q-2019 Quarterly report, SEC.gov

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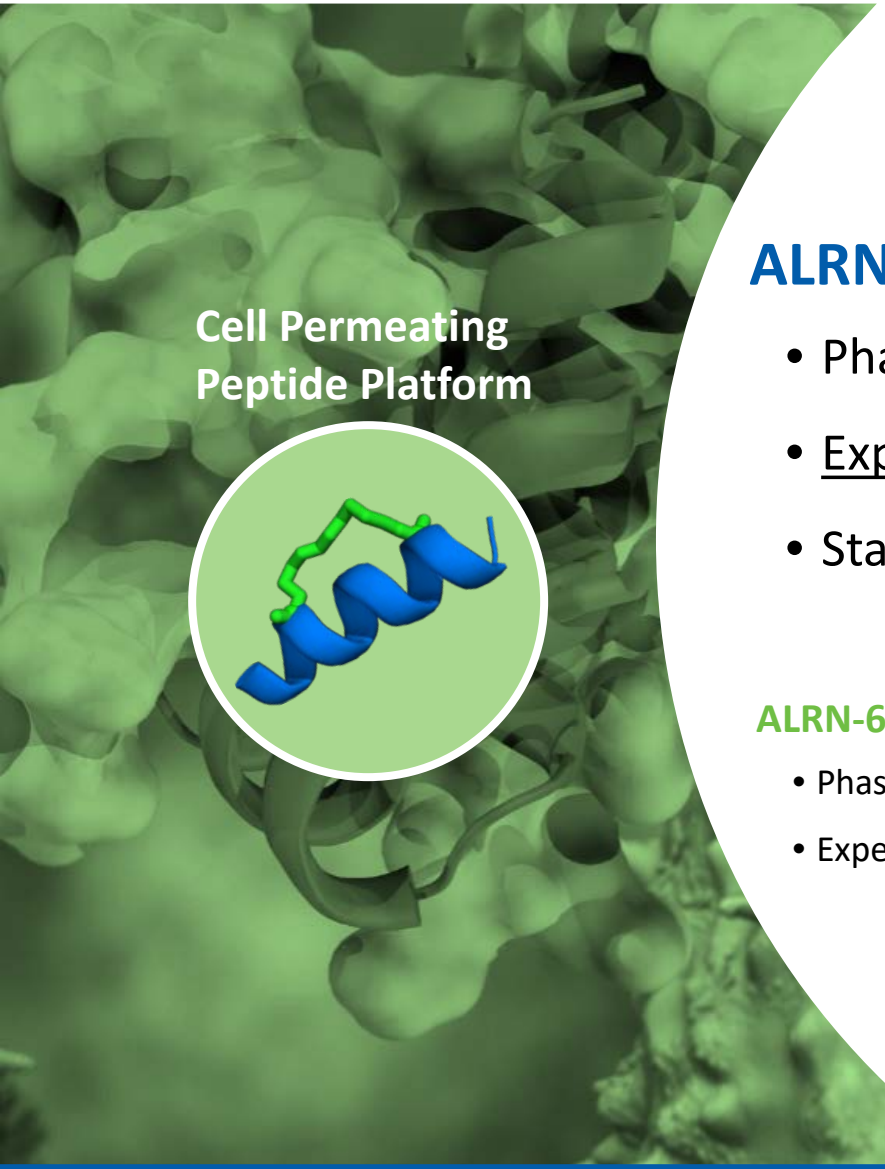
Corporate Development

Financial Summary

- As of September 30, 2019, $24.6M in cash and equivalents
- Current expected cash runway into the fourth quarter, 2020
- 27.8M shares outstanding; additional warrants to purchase 12.9M shares

Value Creation Opportunities



ALRN-6924 for Myelopreservation

- Phase 1b/2 started September 2019
- Expect to present Ph1b results in 2Q2020
- Start of On/Off cohort and NSCLC cohort 2Q2020

ALRN-6924 Against MDM2-amplified cancers

- Phase 2a combination with palbociclib ongoing
- Expect to present Ph2a results in 2Q2020

Intellectual Property & Strategic Alliances

- Composition of matter for ALRN-6924 expires 2033 (w/o ext.)
- Aileron owns exclusive patent rights to ALRN-6924 worldwide

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Thank You

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