AILERON

Corporate Presentation

H.C. Wainwright 2019 Healthcare Conference

Manuel Aivado, MD, PhD
CEO and President

September 9, 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

Aileron Therapeutics: Developing ALRN-6924 as a Pipeline-in-a-Product

ALRN-6924 for MDM2-amplified cancers

p53-wildtype cancers	In combination with CDK4/6-inhibitor (palbociclib) MDM2 amplification found in up to **4%** of all cancers*	**Potential medical need ≈39,000 patients in the US alone**

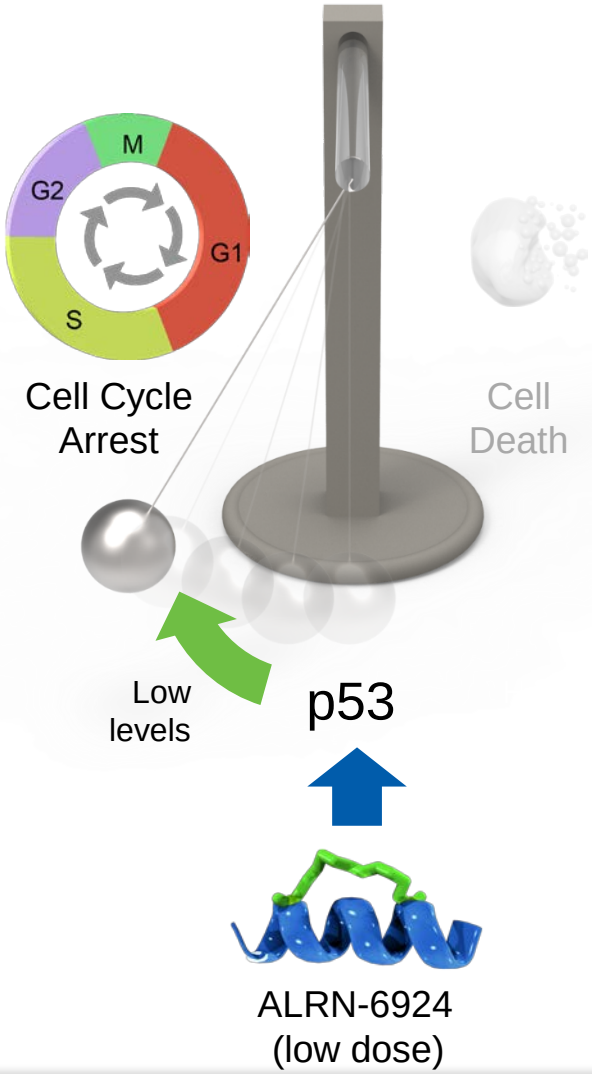
ALRN-6924 for myelopreservation

p53-mutant cancers	Protecting normal cells from chemotherapy during treatment of p53-mutated cancers P53 mutations found in ≈**50%** of all cancer patients‡	**Potential medical need in over 300,000 patients in the US alone**

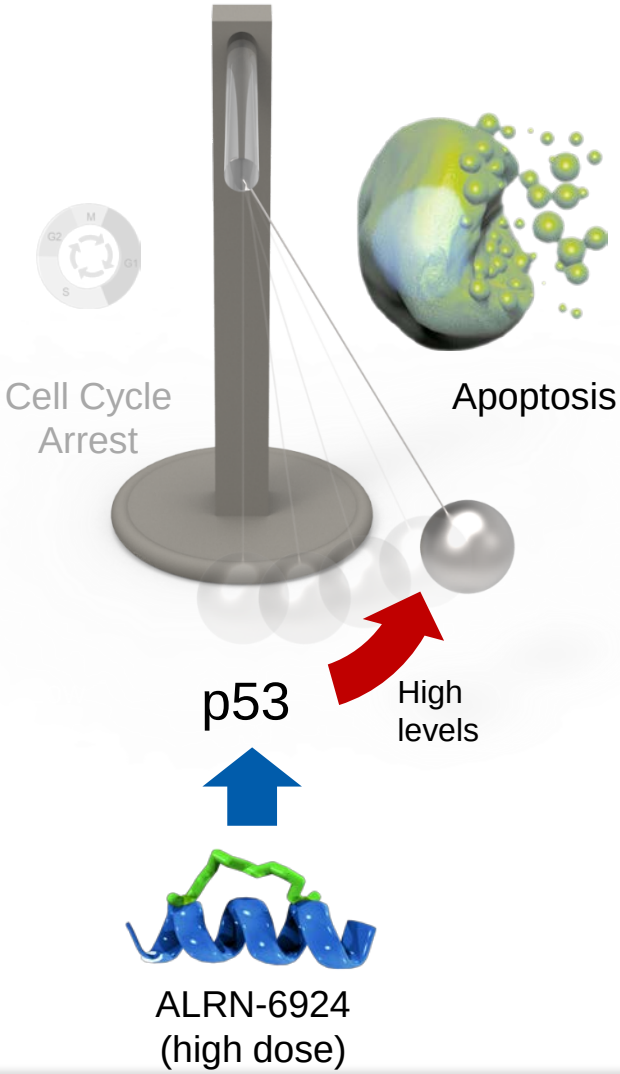
*Zehir et al, "Mutational landscape …" Nat Med. 2017; ‡ Lane et al, "Drugging the p53 pathway …" Nature Reviews Drug Discovery 2014

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

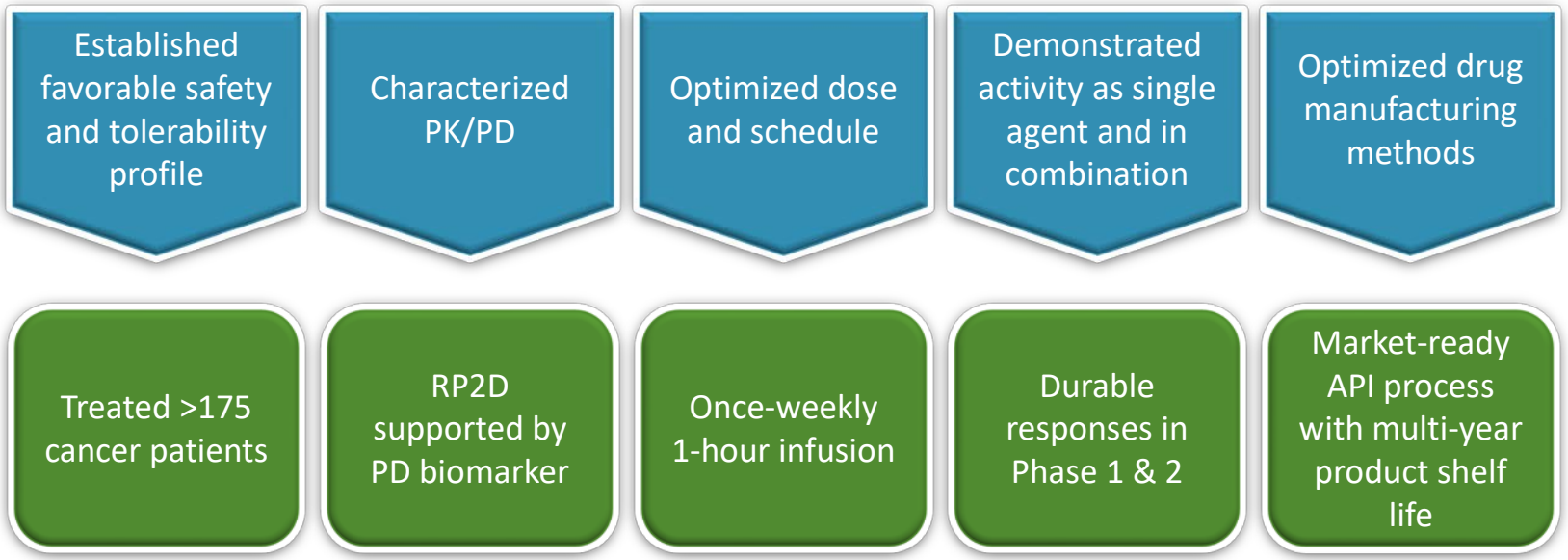
Applied in Myelopreservation Trial



Applied in MDM2-Amplification Trial

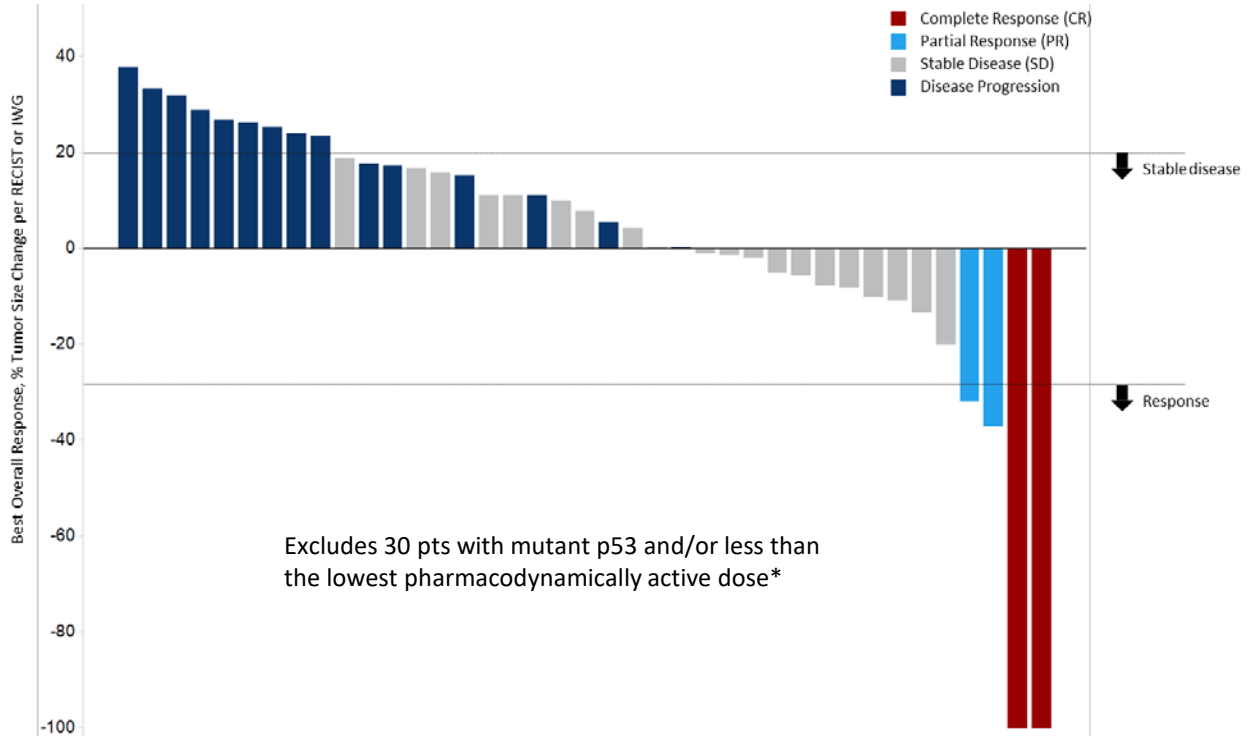


ALRN-6924 Clinical Development Accomplishments



ALRN-6924 Phase 1: Compelling Single-agent Activity

Oral ASCO Presentation, Selected for "Best of ASCO 2017"



- 71 pts monotherapy dose-escalation
- 2 CRs (Merkel and PTCL), 2 PRs (liposarcoma and CRC), 11/20 SDs w/ shrinkage
- Durable responses >2 years
- Activity in MDM2↑ liposarcoma patient and T-cell-related malignancies

** <0.8 mg/kg per dose (Recommended Phase 2 Dose = 3.1 mg/kg per dose)*

ALRN-6924: Best in Class Hematological Safety Profile in First-In-Human Phase 1

First-in-Human Phase 1 Trials	# Patients	Dose Range	Thrombocytopenia Grade ≥ 3	Neutropenia Grade ≥ 3
AILERON **ALRN-6924***	71	28x	**0%**	**3%**
AMGEN AMG 232	39	32x	33%	21%
Daiichi-Sankyo DS-3032b	103	22x	19%	12%
NOVARTIS HDM201	107	28x	24%	23%
Roche RO6839921	41	8x	15%	20%
Roche RG7388	95	16x	33%	21%
MERCK INVENTING FOR LIFE MK-8242	47	8x	15%	19%

ALRN-6924, a Dual MDMX and MDM2 Inhibitor

Ongoing and Planned Trials

Programs	ALRN-6924	Preclinical	Phase 1	Phase 2	Milestone
MDM2-amplified cancers	+ Palbociclib	Interim Data ≥15 patients ESMO 2019			**Present results on ≈35 pts 2Q2020**
Myelopreservation Protecting normal cells from chemotherapy	Prior to chemotherapy	Planned start Sept 2019			**Present results on 30-40 pts 2Q2020**
Investigator Sponsored	+ Paclitaxel in Breast Cancer				
	+/- Ara-C Pediatric Cancers				

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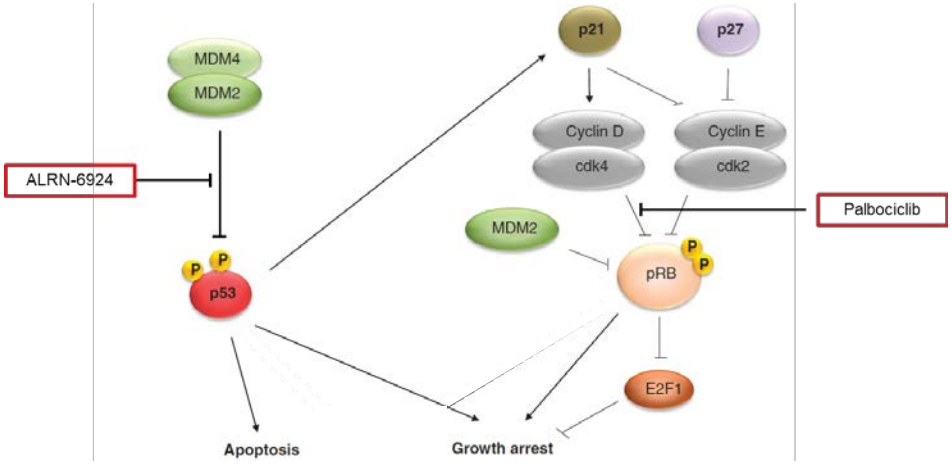
ALRN-6924 against MDM2-amplified Cancers

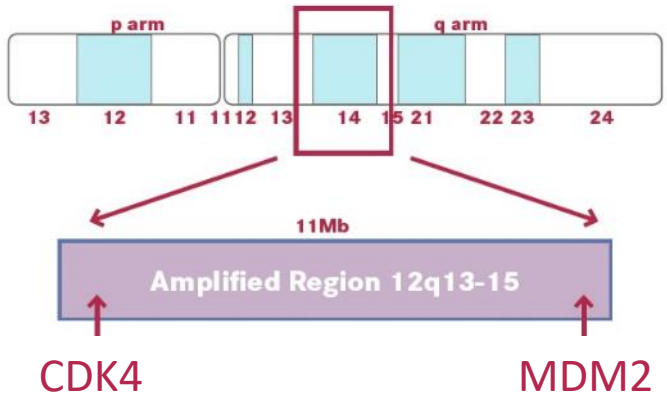
ALRN-6924 + Palbociclib Trial in Collaboration with Pfizer: Biomarker-driven, Tumor-agnostic Patient Selection



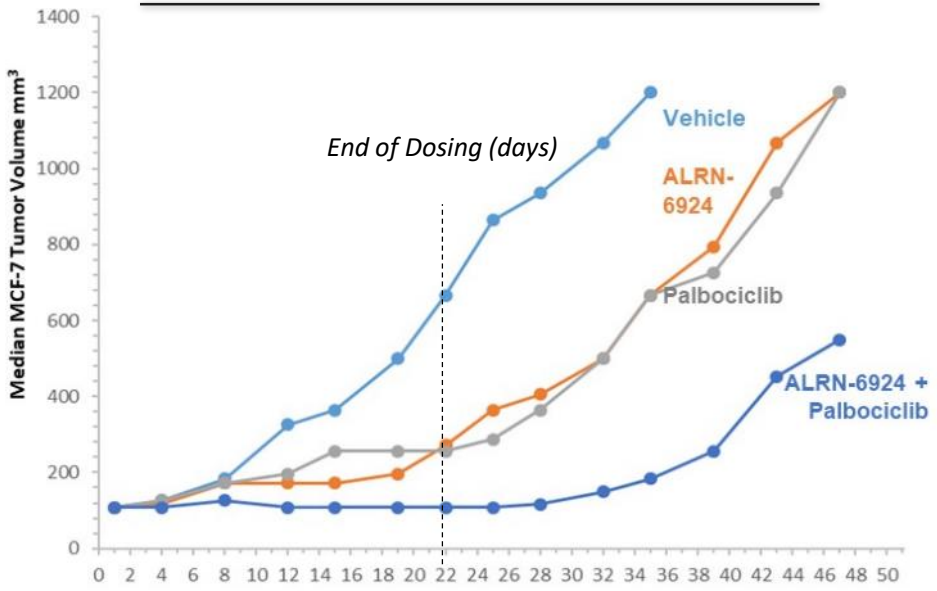
MDM2 amplification is found in up to **4% of all cancers.‡**

Most frequently found in sarcomas, breast, lung cancer, glioblastoma, etc.

CDK4 and MDM2 are often co-amplified



CDK4 plus MDM2 inhibition was synergistic*



‡Zehir et al, "Mutational landscape of metastatic cancer revealed from prospective clinical sequencing of 10,000 patients." Nat Med. 2017 * Annis SACBS 2018

ALRN-6924 in MDM2-amplified Cancers: Palbociclib Phase 2a Combination Trial Ongoing

Strategy	Phase 2a N=25 (mostly sarcoma pts); enrolling additional 10 pts to include a broader set of cancer types Objectives: Safety and Signal of activity
Diagnostic assay	Use existing standard gene tests such as 'Foundation One' to test for biomarkers: p53-wildtype and MDM2-amplification
Dosing	ALRN-6924 IV on Days 1, 8, 15 every 28 days Palbociclib orally on Days 1-21 every 28 days
Endpoints	PFS, OS, Durable ORR
Data Presentations	Interim results for ≥15 sarcoma pts will be presented as a poster at ESMO on Sep 28, 2019. Expect to present results on all pts 2Q 2020.

MDM2-amplified Sarcoma – an Unmet Medical Need

- Annual incidence*: US ≈2500; EU ≈2500, Asia ≈10,000
- Largest subtype of MDM2-amplified sarcomas: liposarcoma (40%)
  - Median OS[#] for metastatic liposarcoma patients barely > 1 year
- No curative therapy for metastatic sarcoma
  - Immune-checkpoint inhibitor therapies have very limited activity
- Available therapies:

	Doxorubicin (1st line)	Trabectidin (2nd line)	Eribulin (3rd line)
Median PFS	4.6 months	4.2 months	2.9 months
Median OS	12.8 months	13.7 months	15.6 months

*https://emedicine.medscape.com/article/1102007-overview#a6 [#]Lancet Oncol. 2014, 15(4):415-23; JCO 2016, 34:786-93; JCO 2017, 35:3433-39

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Myelopreservation

for Chemotherapy-induced Toxicities

Aileron Therapeutics: Developing ALRN-6924 as a Pipeline-in-a-Product

ALRN-6924 for MDM2-amplified cancers

p53-wildtype cancers

In combination with CDK4/6-inhibitor (palbociclib)

MDM2 amplification found in up to **4%** of all cancers*

Potential medical need ≈39,000 patients in US alone

ALRN-6924 for myelopreservation

p53-mutant cancers

Protecting normal cells from chemotherapy during treatment of p53-mutated cancers

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

Potential medical need in over 300,000 patients in the US alone

*Zehir et al, "Mutational landscape …" Nat Med. 2017; ‡ Lane et al, "Drugging the p53 pathway …" Nature Reviews Drug Discovery 2014

Chemotherapies Cause Significant Toxicities

Patients Suffering

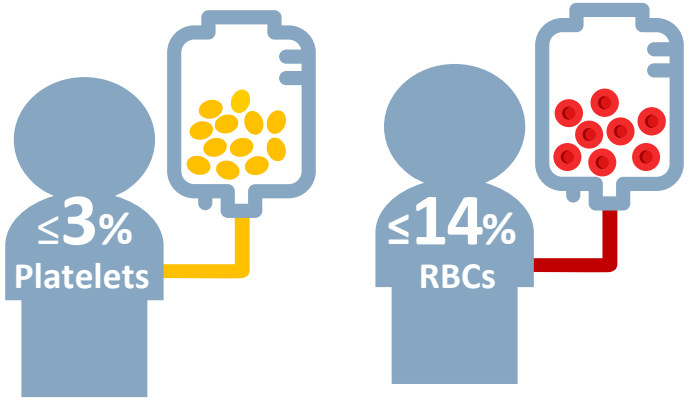
Unintended effects of chemotherapy on normal cells

Severe Neutropenia

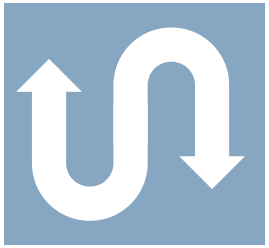
40-70%

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

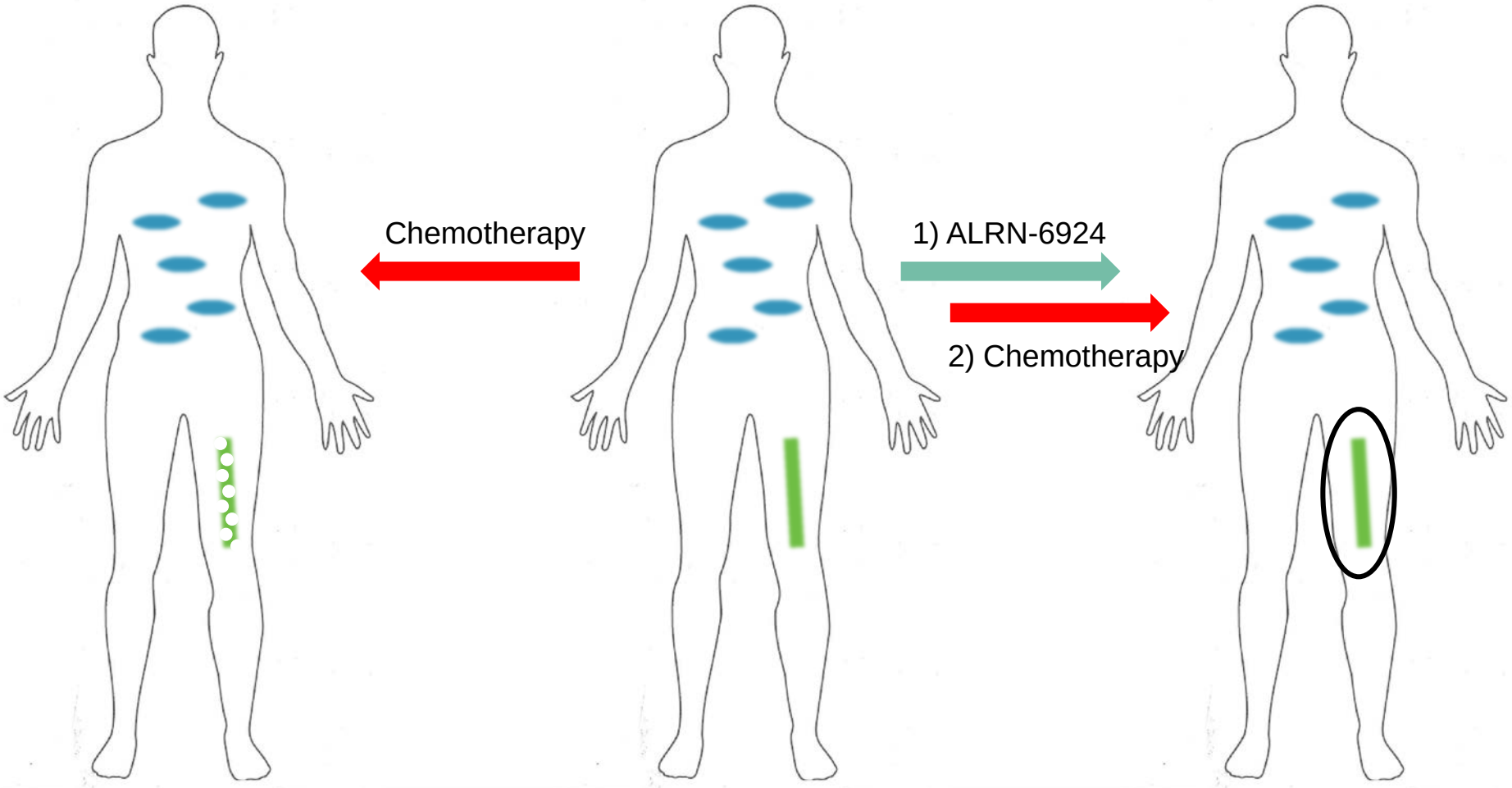
- Erythropoietin increases risk of thromboembolic events
- G-CSF and erythropoietin can promote cancer growth

ALRN-6924 as a Myelopreservation Agent Against Chemotherapeutic Toxicities in p53-mutant Cancers

Chemotherapy can damage both p53-mutant tumors and p53-wild-type bone marrow

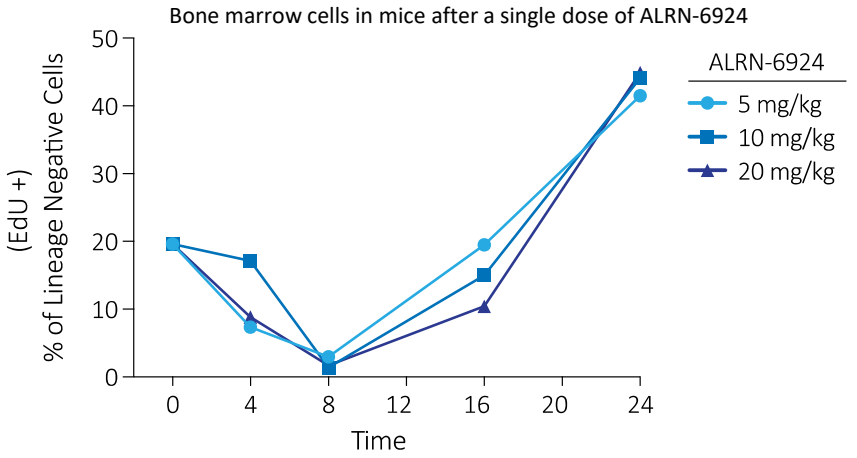
Patient with p53-mutant tumors, p53-wild-type bone marrow

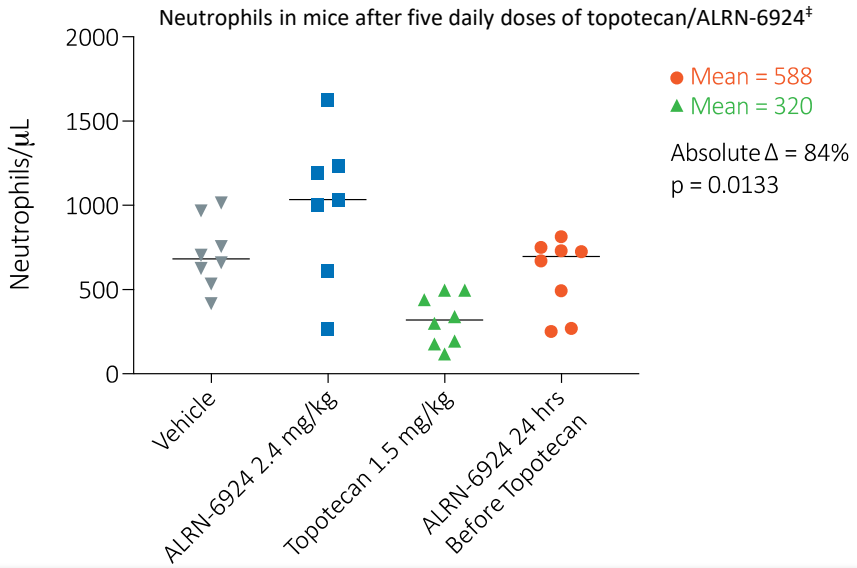
Pre-treatment with ALRN-6924 preserves p53-wild-type bone marrow to prevent toxicity



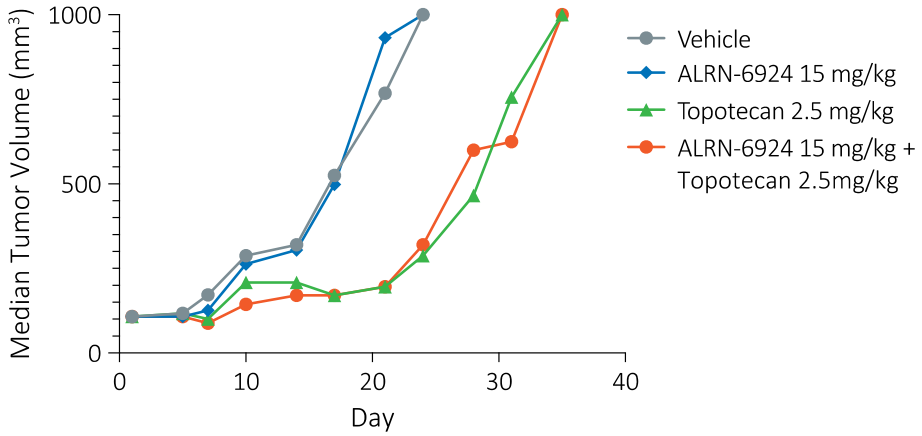
ALRN-6924 Is an Effective Myelopreservation Agent in Preclinical Studies

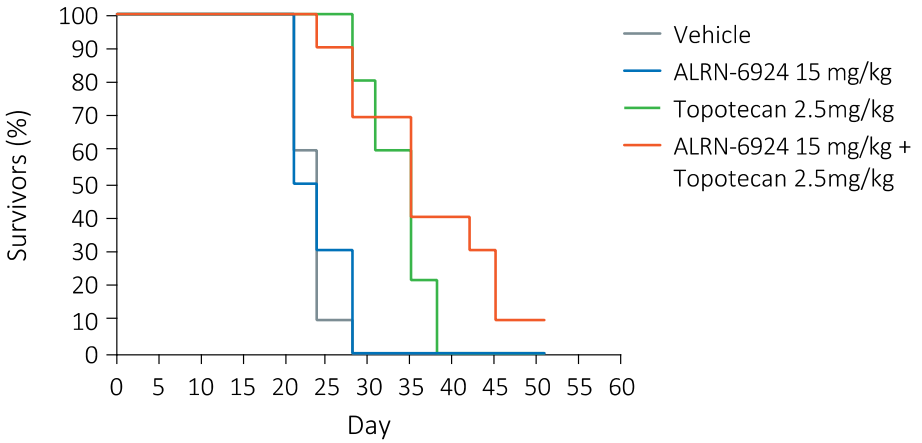
ALRN-6924 induces cell cycle arrest in bone marrow to protect against topotecan-induced DNA damage[1]





ALRN-6924 does not diminish topotecan's activity against p53-mutant mouse cancer[1]





C57BL/6 mice bearing syngeneic MC38 colon cancer 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] Data on file

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

ALRN-6924 Clinical Development Plan in Myelopreservation

Strategy	Patients with advanced p53 mutated SCLC receiving 2nd line treatment with 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 data and funding

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[1]

≈25% of prostate cancer patients

≈20% of bladder cancer patients

Potential market opportunity for ALRN-6924
≈675,000 patients with p53-mutant cancer in the US and EU5 alone

Source: Kantar Reports; ClearView Analysis. [1]Incident cancer patients receiving first-line chemotherapy per year in U.S. and EU5.

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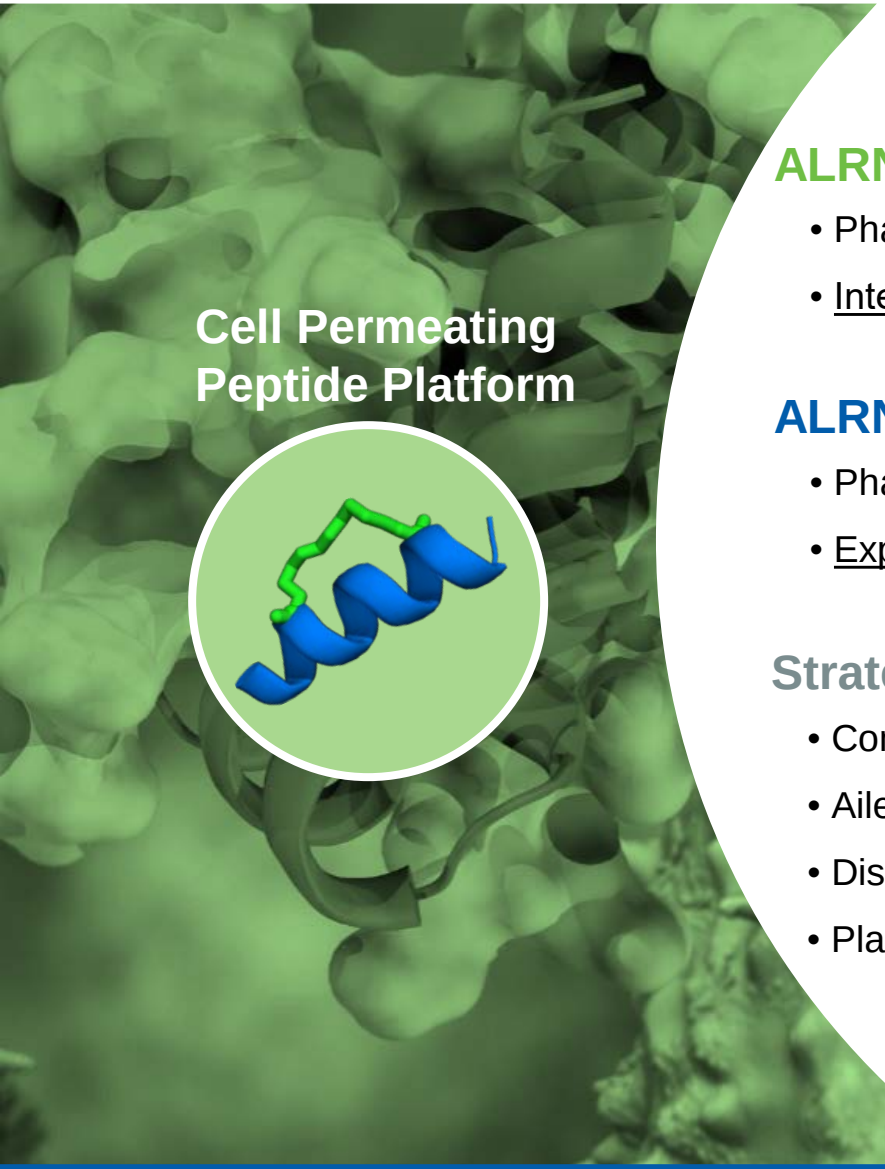
Corporate Development

Financial Summary

- As of June 30, 2019, $31.5M 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 against MDM2-amplified cancers

- Phase 2a combination with Pfizer's palbociclib ongoing
- Interim data (≥15 pts) ESMO 2019, data on ≈35 pts in 2Q2020

ALRN-6924 for Myelopreservation

- Phase 1b/2 planned start September 2019
- Expect to present results on 30-40 pts from Ph1b 2Q2020

Strategic alliances & out-licensing opportunities

- Composition of matter for ALRN-6924 expires 2033 (w/o ext.)
- Aileron owns exclusive patent rights to ALRN-6924 worldwide
- Discovery programs: HIF1/2-α inhibitor, dual Bcl-2/Mcl-1 inhibitor
- Platform expansion programs: PROTACs

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Thank You

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