AILERON

Corporate Presentation

Canaccord 2019 Healthcare Conferenc

Manuel Aivado, MD, PhD
CEO and President

August 7, 2019

Legal Matters

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Aileron's New 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

Don Dougherty, MBA, CFA, CPA
Chief Financial Officer

CCGrowth, Essex Investment
Management, Putnam Investments, KPMG

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 US alone**

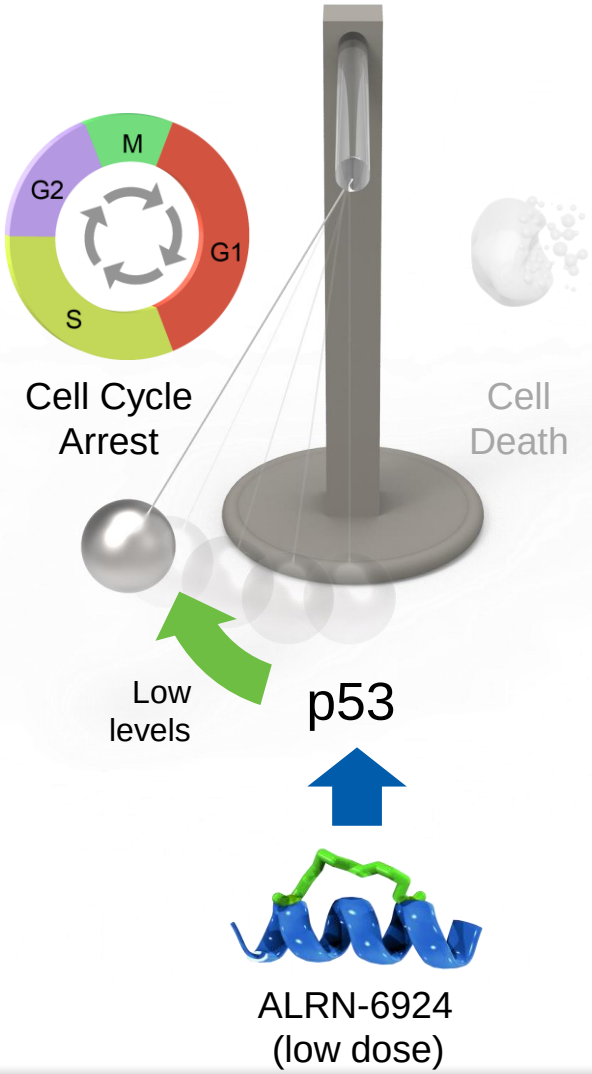
ALRN-6924 for myelopreservation

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 ≈130,000 patients in US alone**

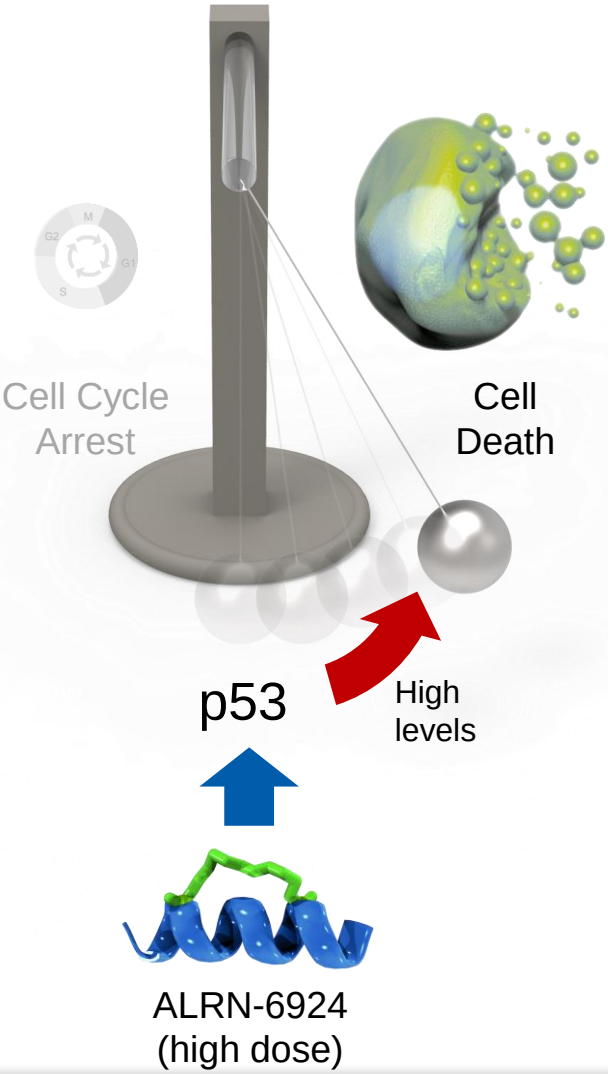
*Zehir et al, "Mutational landscape …" Nat Med. 2017; ‡ Lane et al, "Drugging the p53 pathway …" Nature Reviews Drug Discovery 2014

ALRN-6924 can induce two distinct p53-effects: Cell-Cycle Arrest or Cell Death

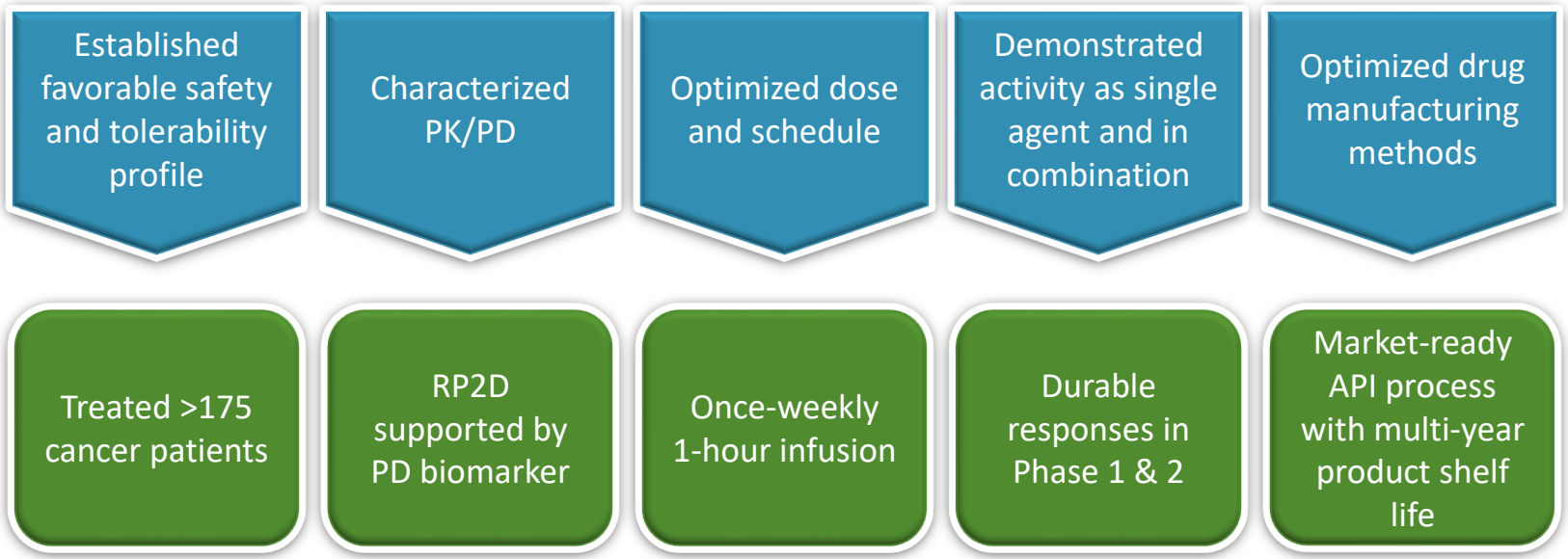
Applied in Myelopreservation Trial



Applied in MDM2-Amplification Trial

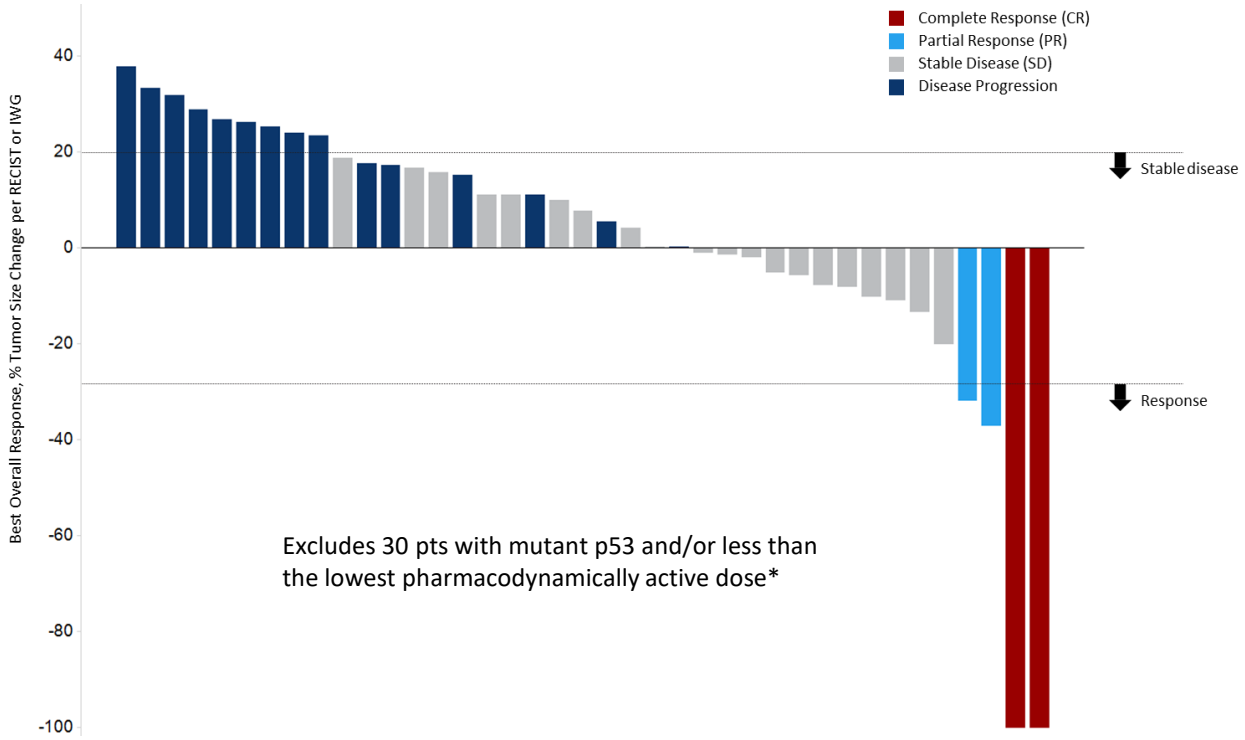


ALRN-6924 Clinical Development Accomplishments



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
ALRN-6924	71	28x	**0%**	**3%**
AMG 232	39	32x	33%	21%
DS-3032b	103	22x	19%	12%
HDM201	107	28x	24%	23%
RO6839921	41	8x	15%	20%
RG7388	95	16x	33%	21%
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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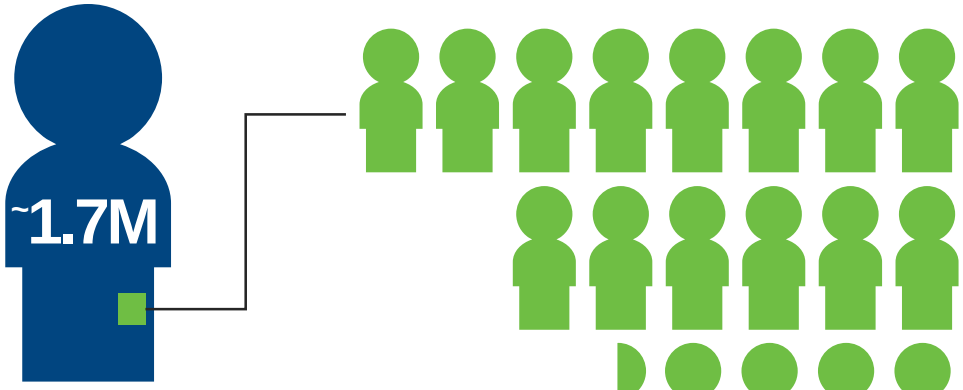
ALRN-6924 against MDM2-amplified Cancers

Potential Market Opportunity in MDM2-amplified Cancers



2018 Incidence of cancer patients in USA*

69K
Up to 4% of cancers have amplified MDM2‡

52K
Est. 75% identified with standard gene tests

39K
75% of patients with wildtype p53‡

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

Among MDM2-amplified Cancers: Liposarcoma (LPS) – an Unmet Medical Need

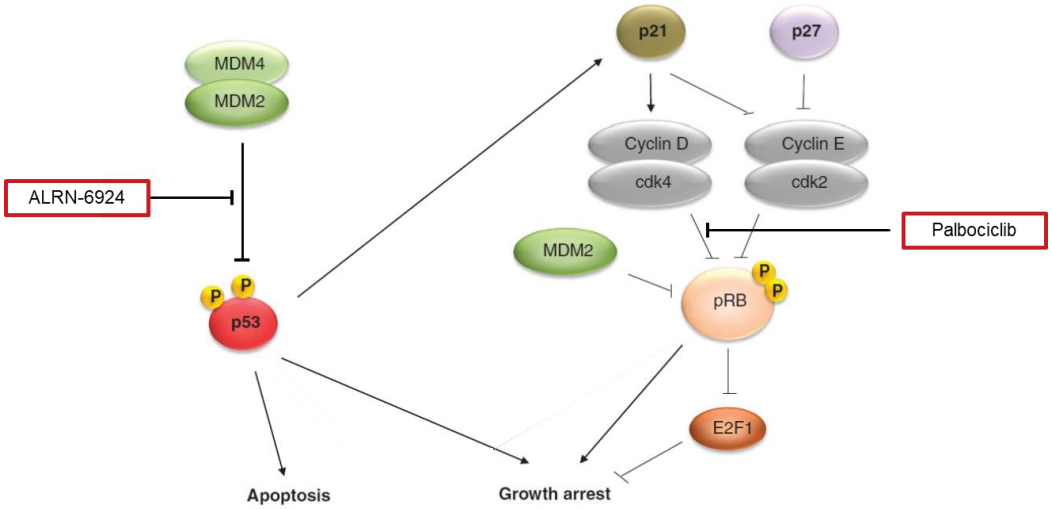
- Annual incidence*: US ≈1000; EU ≈1000, Asia ≈4000
- Median OS# for metastatic LPS patients only 1 year
- No curative therapy for metastatic LPS
  - Immune-checkpoint inhibitor therapies have not worked
- Available therapies:

	Doxorubicin (1st line)	Trabectidin (2nd line)	Eribulin (3rd line)
Median PFS	4.6 months	4.2 months	2.9 months
ORR	14%	10%	1%

All FDA approvals of drugs for treatment of LPS were based on PFS

*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

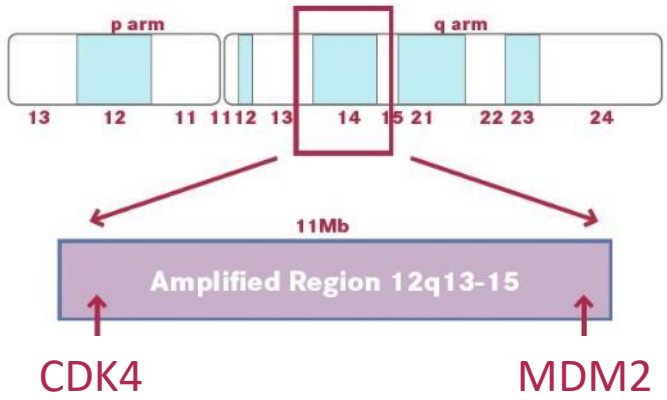
ALRN-6924 + Palbociclib Trial in Collaboration with Pfizer: Biomarker-driven, Tumor-agnostic Patient Selection



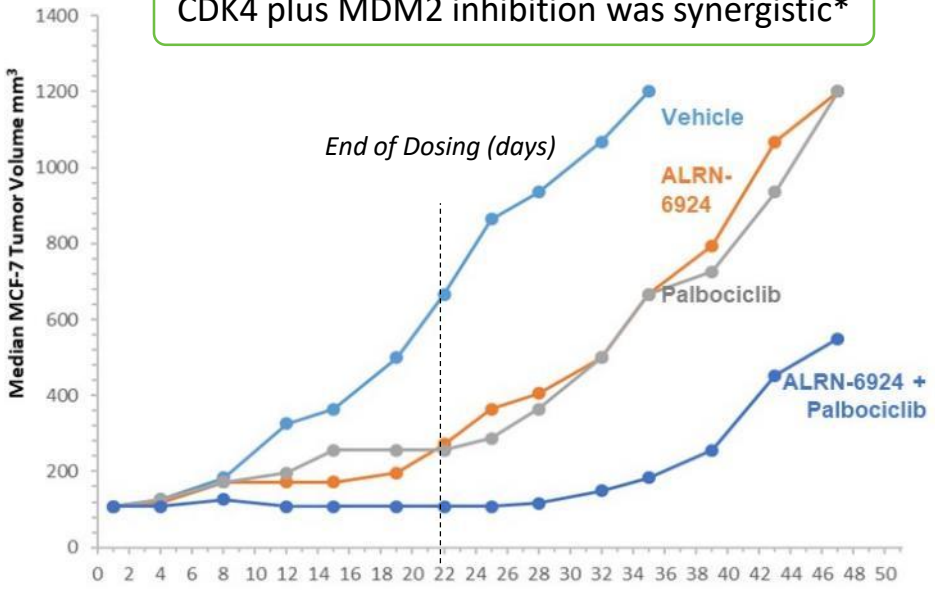
MDM2 amplification is found in up to **4% of all cancers.‡**

Most frequently found in liposarcomas, 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 + 10 additional pts to include a broader set of cancer types Objectives: Safety and Signal of activity 1st indication: Data-driven decision to be made based on signal from phase 2a
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 Liposarcoma (LPS) pts will be presented as a poster at ESMO on Sep 28, 2019. Expect to present results on all pts 2Q 2020.

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Myelopreservation

for Chemotherapy-induced Toxicity

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‡

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Chemotherapies Cause Significant Toxicities

Cancer patients suffer severe toxicities caused by unintended effects of chemotherapy on normal cells:

- The incidence of severe neutropenia in lung, breast and colorectal cancer patients treated with chemotherapy is 40-70%[1-3]
- Up to 3% of all cancer patients require transfusions of platelets and up to 14% transfusions of red blood cells[4]
- Other frequent debilitating side effects of chemotherapy include mucositis, neurotoxicity, diarrhea, hair loss, nausea and vomiting

In addition to patient suffering, chemotherapy toxicities also cause:

- Significant cost to health care systems
- Dose delays and dose reductions of chemotherapy, which can reduce its efficacy

Current Therapies for Chemotherapy-related Toxicities Are Inadequate

- Inefficient because they treat rather than prevent toxicities
- Incomplete because they only treat one problem at a time
  - E.g. G-CSF improves neutrophil counts, but has no effects on other bone marrow toxicities
- Risky due to their intrinsic side effects:
  - Erythropoietin increases risk of thromboembolic events
  - G-CSF and erythropoietin can promote cancer growth
- Do not address many of the side effects caused by chemotherapy:
  - mucositis, neurotoxicity, diarrhea, hair loss, thrombocytopenia

Cell Cycle Arrest is a Proven Approach to Achieve Myelopreservation

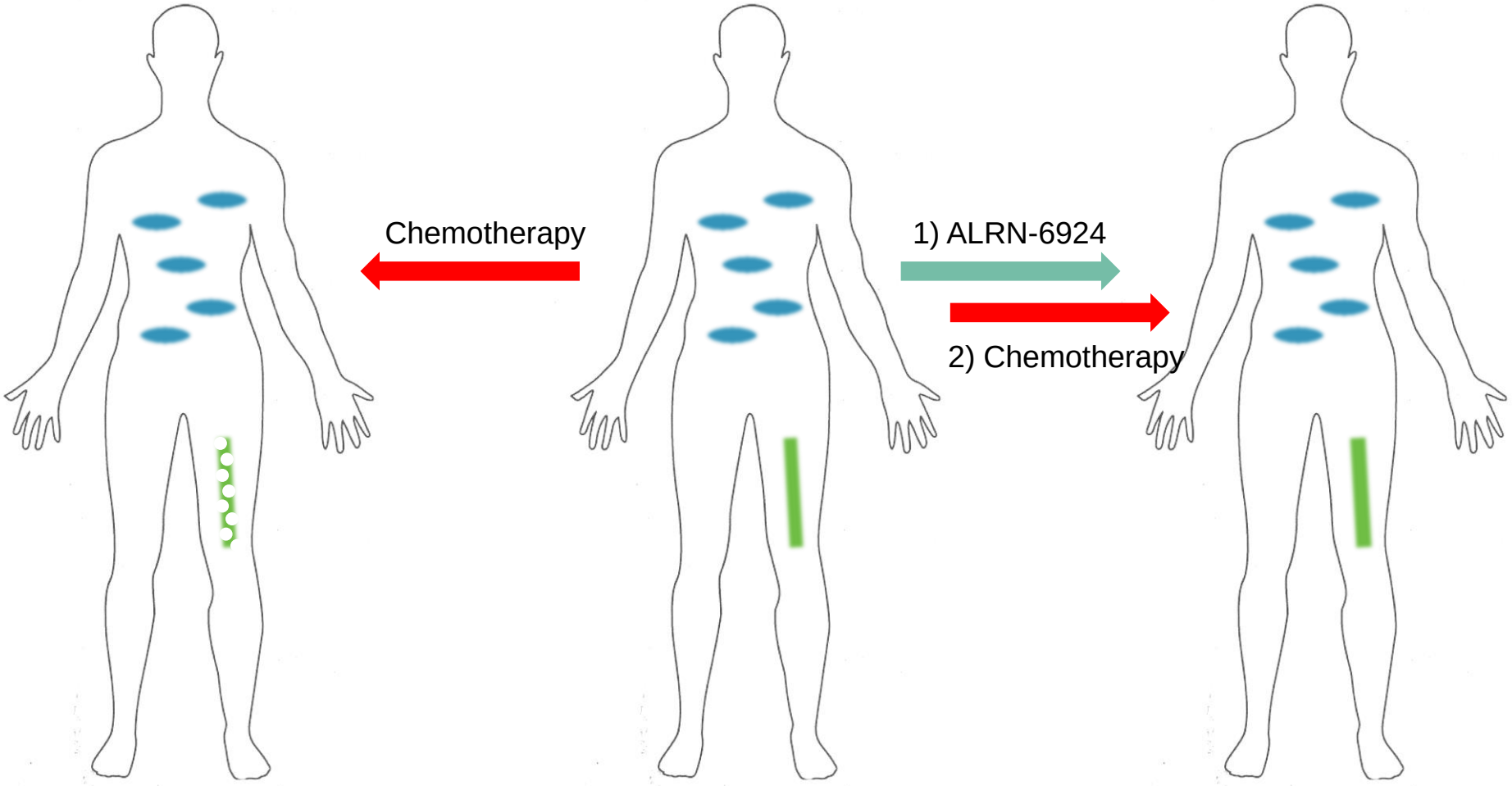
- Chemotherapy commonly damages proliferating cells
- A drug inducing cell cycle arrest in normal bone marrow cells will protect normal bone marrow cells from chemotherapeutic toxicity ("Myelopreservation")
- G1-Therapeutics (NASDAQ: GTHX) has proven that pharmacologically induced cell cycle arrest reduces chemotherapeutic toxicity in Rb1-deficient cancers
  - 4/4 positive randomized placebo-controlled clinical trials
  - FDA-agreement on regulatory path to NDA for myelopreservation with existing data

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

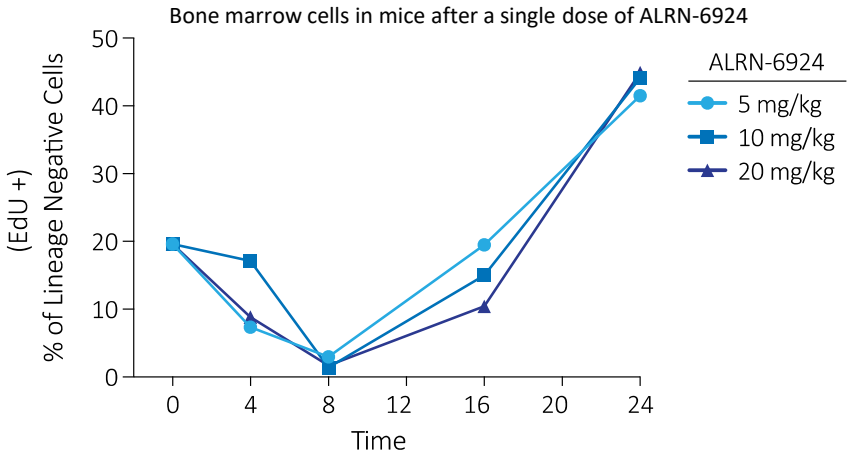
Patient with p53-mutant tumors, p53-wild-type bone marrow

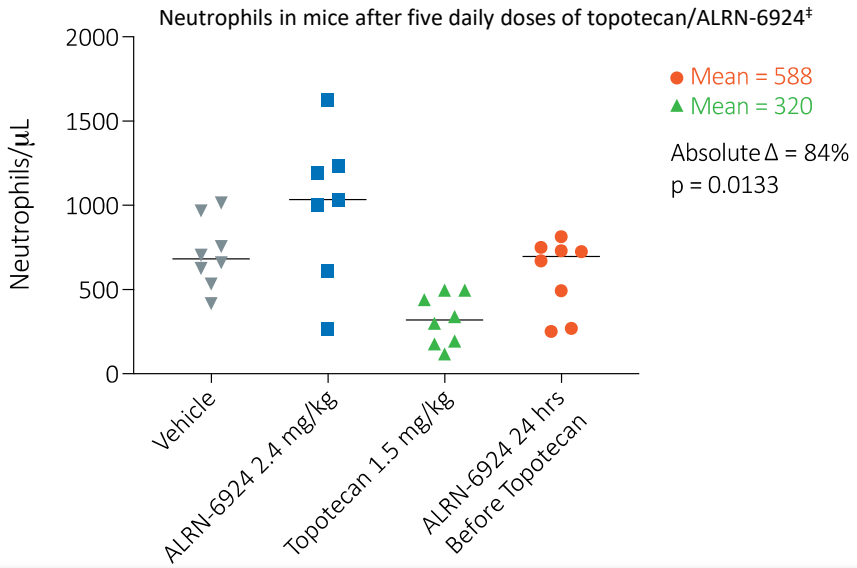
Pre-treatment with ALRN-6924 preserves p53-wild-type bone marrow to prevent toxicity



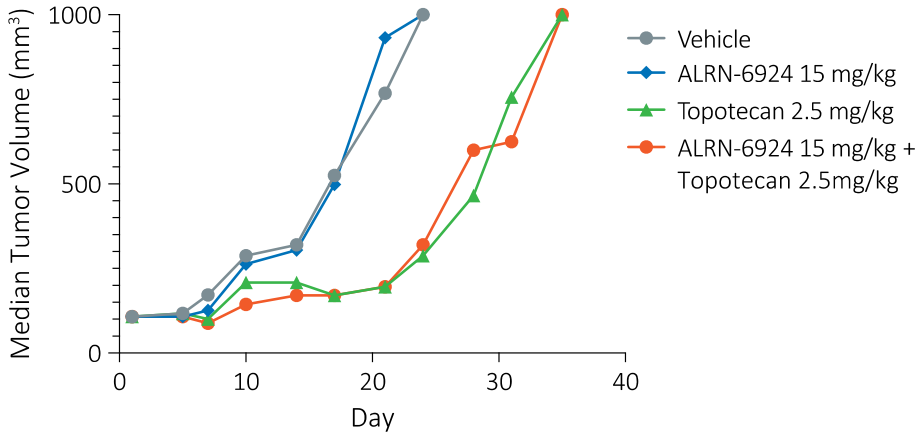
ALRN-6924 Is an Effective Myelopreservation Agent in Preclinical Studies

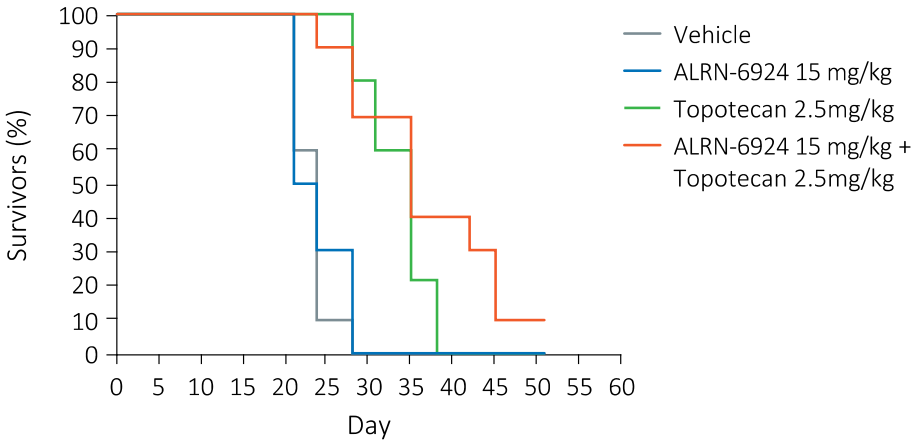
ALRN-6924 induces cell cycle arrest in bone marrow to protect against topotecan-induced DNA damage





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





C57BL/6 mice bearing syngeneic MC38 colon cancer tumors after five daily doses of topotecan/ALRN-6924‡

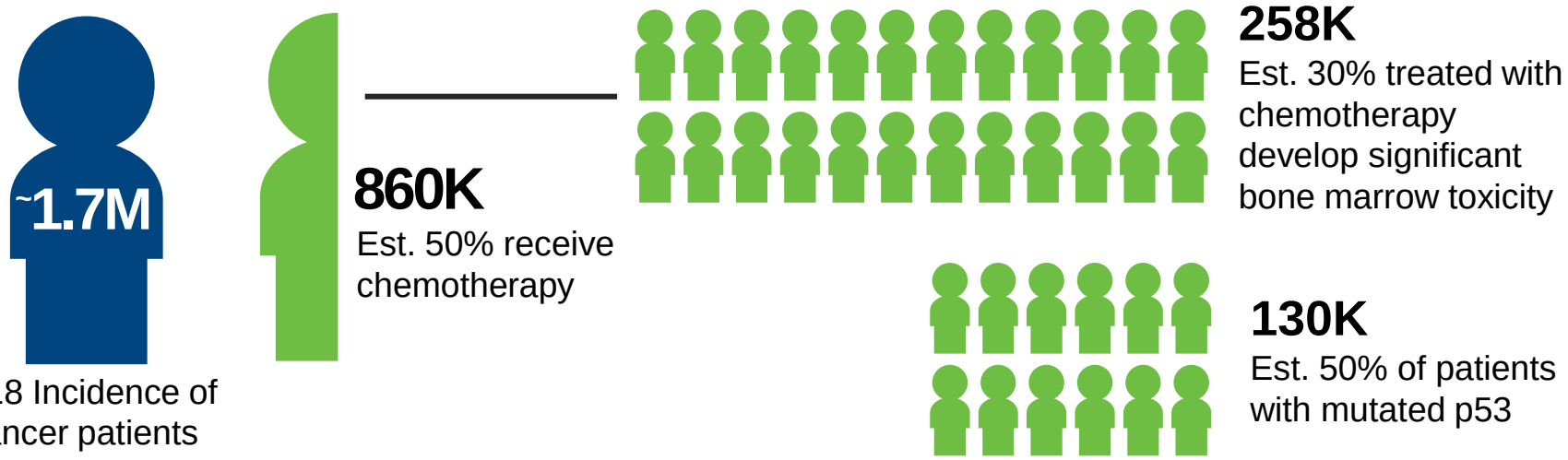
‡ Mice dosed with topotecan on days 1-5 preceded by ALRN-6924 by 24 hrs

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

Potential Market Opportunity for Myelopreservation



*SEER database

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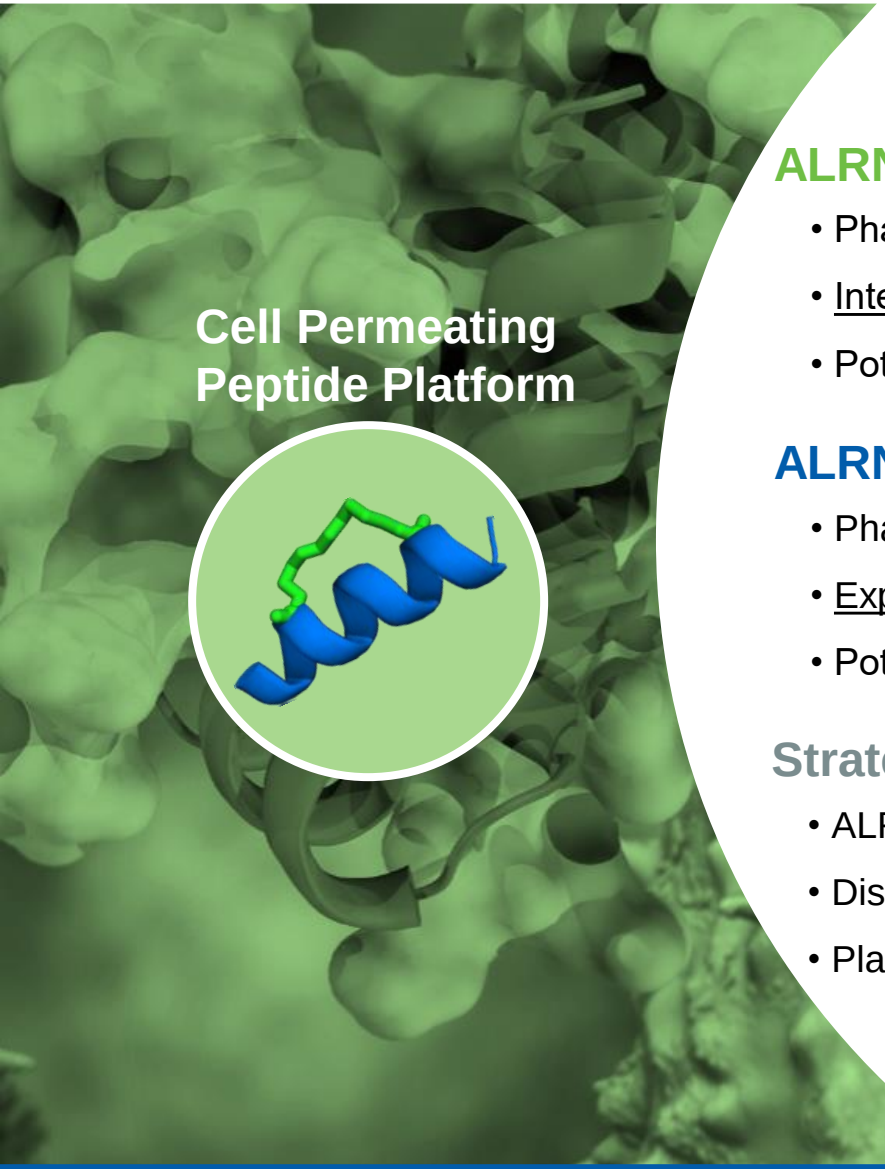
Corporate Development

Financial Summary

- As of June 30, 2019, $31.5M in cash and equivalents
- Current expected cash runway into the fourth quarter, 2020
- As of August 6, we have 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
- Potential medical need in ≈39,000 patients in US alone

ALRN-6924 for Myelopreservation

- Phase 1b/2 planned start September 2019
- Expected to present results on 30-40 pts from ph1b 2Q2020
- Potential medical need in ≈130,000 patients in US alone

Strategic alliances & out-licensing opportunities

- ALRN-6924 (regional or global rights)
- Discovery programs: HIF1/2-α inhibitor, dual Bcl-2/Mcl-1 inhibitor
- Platform expansion programs: PROTACs, Senolytics

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Thank You

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