

The logo features the word "AILERON" in a white, sans-serif font. A green swoosh, resembling an upward-pointing arrow, curves behind the letters from the bottom left to the top right.

AILERON

# Transforming the Experience of Chemotherapy for Cancer Patients

C O R P O R A T E   P R E S E N T A T I O N

O C T O B E R   2 0 2 1



## 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 anticipated; whether the Company will obtain sufficient cash resources to conduct its planned clinical trials; whether results obtained in clinical trials will be indicative of results obtained in future clinical trials; whether third-party data would be indicative of the data that would be obtained in a randomized clinical 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 be accepted by and 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; 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 quarterly report on Form 10-Q for the period ended June 30, 2021, filed on August 11, 2021, and risks described in other filings that Aileron may make with the Securities and Exchange Commission. Any forward-looking statements contained in this presentation 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.

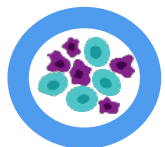
# Our Opportunity To Protect Against Chemotherapy-Induced Side Effects With ALRN-6924



## **Regulatory and commercial pathway established for ‘chemoprotection’**

FDA recently approved trilaciclib (COSELA™) by GTHX in Feb. 2021

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## **ALRN-6924: best-in-class potential among chemoprotective agents (“Triple Play Efficacy”)**

Clinical proof of concept demonstrated; protection against neutropenia, thrombocytopenia and anemia

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## **Core differentiator: p53 biomarker-enabled selective chemoprotection**

Nearly 1 million patients in the U.S. are diagnosed annually with p53-mutated cancer

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## **Expected milestones for new randomized placebo-controlled Phase 1b in frontline NSCLC**

Initiated: 2Q21 / Interim safety data: 4Q21 / Topline full results: mid-2022

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## **Activities ongoing to accelerate entry into late-stage development in NSCLC**

Strategic investments in CMC, companion diagnostic development and team scale-up

Clinical development strategy: ultimately pursue tumor-agnostic indication based on p53 mutation



The background image is a green-tinted photograph of a modern laboratory or clinical setting. It features various pieces of medical equipment, including monitors, carts, and large overhead devices. Several people in white lab coats are visible, working at different stations. The ceiling has exposed structural elements and large pendant lights. The overall atmosphere is professional and high-tech.

# Chemoprotection May Transform Chemotherapy Like Anesthesia Transformed Surgery

# Chemotherapy Remains The Essential Backbone Of The Majority Of Medical Cancer Treatment, But Its Side Effects Severely Limit Its Benefits To Patients

## MILLIONS OF PATIENTS

Benefit from chemotherapy, because it prolongs life and even cures some cancers

## CHEMOTHERAPEUTIC SIDE EFFECTS

Suffered by millions of cancer patients

## CHEMOTHERAPY UNSELECTIVE

Chemotherapy cannot distinguish between cancer cells and healthy cells, causing side effects

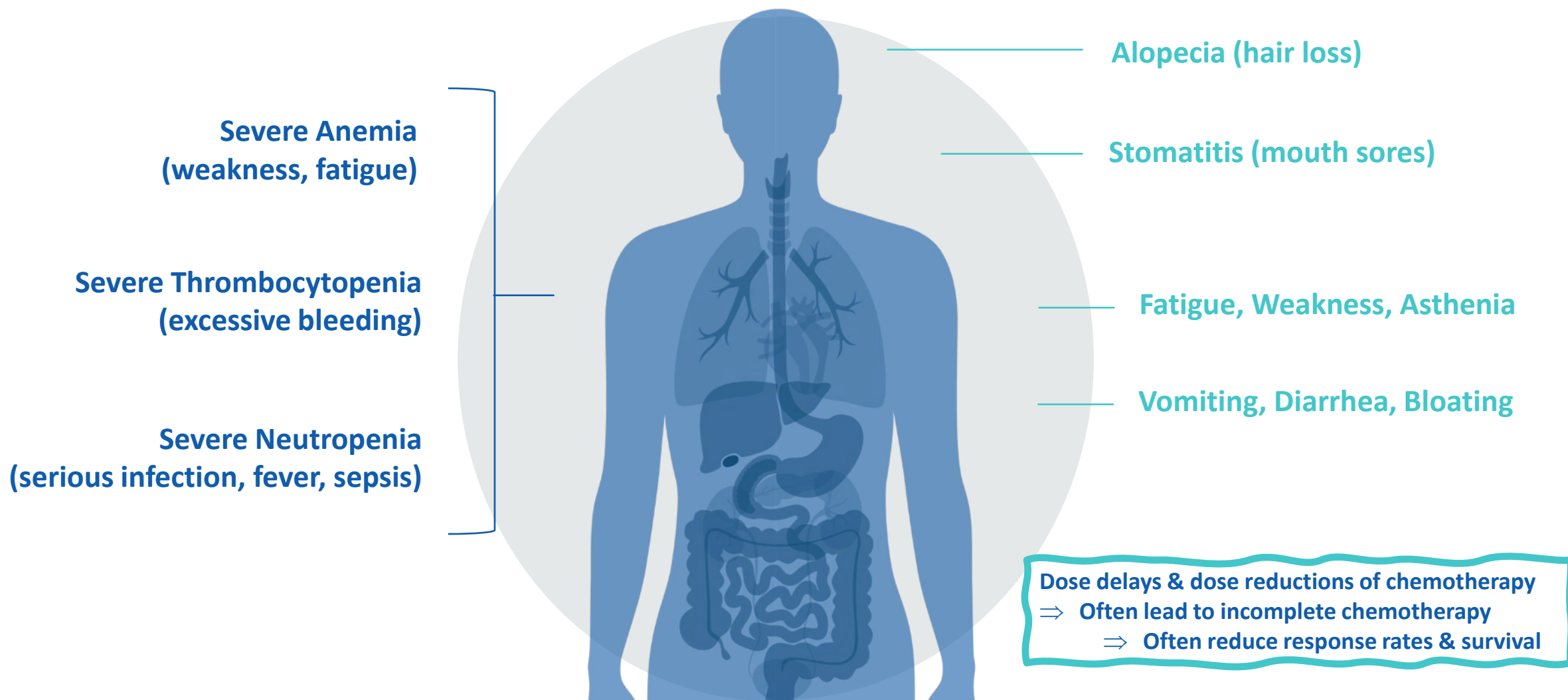
### TODAY'S APPROACH:

#### Resignation / Side Effects Accepted

- Multiple drugs; typically address only one toxicity
- Often ineffective; associated with harmful toxicities
- No options for some side effects (like hair loss)

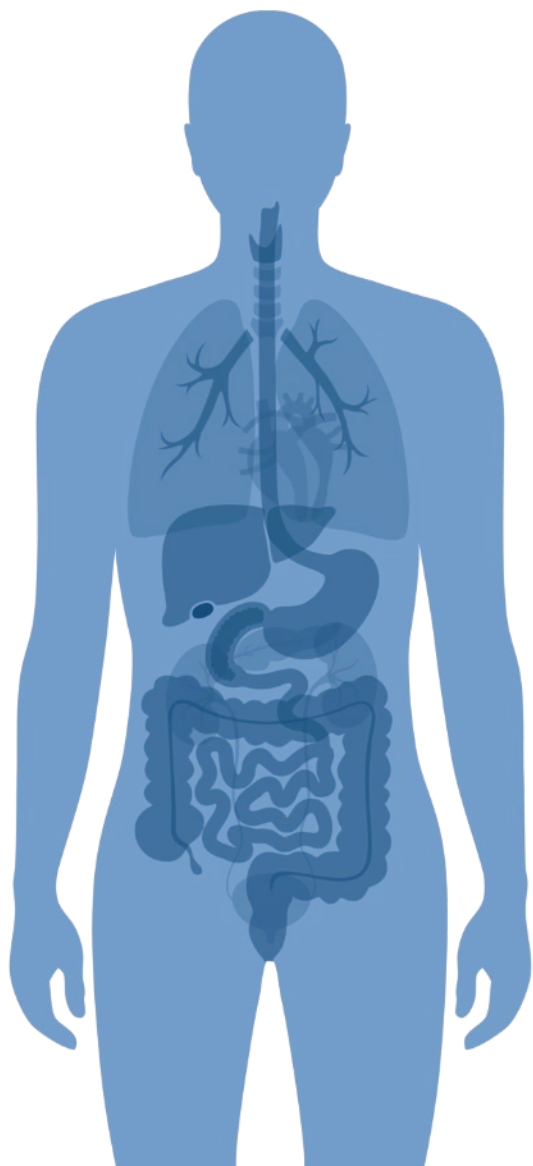
# Chemotherapy's Lack Of Selectivity Causes Side Effects – From Unpleasant To Life-Threatening

ALRN-6924 harnesses a universal mechanism common to normal cells to protect them against chemotherapy side effects



# Poor Standard Of Care For Management Of Bone Marrow Toxicities

Opportunity for ALRN-6924 to be Best-in-Class Medicine to Protect Against Chemotherapy Side Effects



## SEVERE ANEMIA

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

**Clinical Issues:**

- EPOs: promote tumor growth and thrombo-embolic events (black box warning ⚠)
- Limited efficacy
- Indicated only for hemoglobin < 10g/dL
- Transfusions: risk of infection; limited supply

## SEVERE NEUTROPENIA

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

**Clinical Issues:**

- Can promote tumor growth, can cause spleen rupture and bone pain
- Limited efficacy

## SEVERE THROMBOCYTOPENIA

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

**Clinical Issues:**

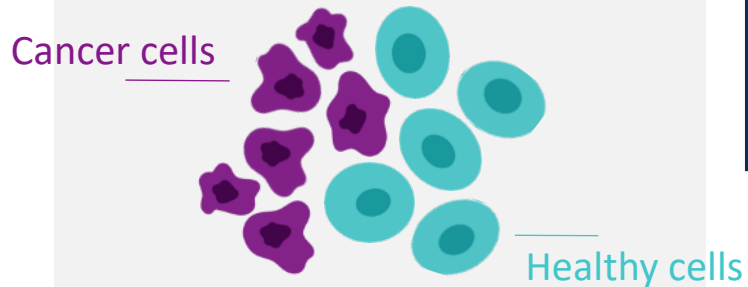
- Effects limited to 2-5 days maximum
- Patients can become transfusion-refractory
- Transfusion-related risk of infection; limited supply



# Basic Principles To Successfully Protect Against Chemotherapy-Induced Side Effects

## CURRENT PARADIGM:

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



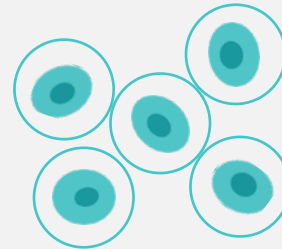
Normally, both healthy cells and cancer cells are destroyed by chemotherapy

PARADIGM SHIFT

## AILERON PARADIGM:

Temporarily pause cycling in healthy cells, shielding them from chemotherapy

No interruption of cycling in p53-mutant cancer cells, thus not protecting cancer cells from chemotherapy



Healthy cells always have normal p53 thus can be protected



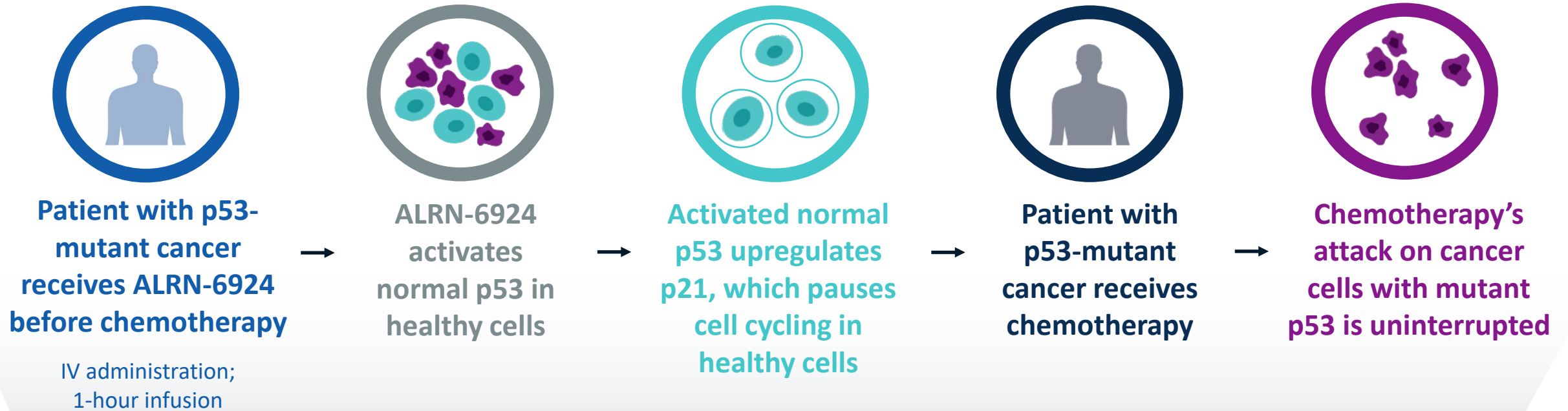
Cancer cells with mutant p53 are not protected

## A COUNTERINTUITIVE APPROACH:

Treat healthy cells, not cancer cells



# Healthy Cells Have Normal p53. ALRN-6924 Activates Normal p53, Thereby Upregulating p21, Which Pauses Cell Cycle In Normal Cells, But Not In Cancer Cells With Mutant p53



Selective chemoprotection of healthy cells (always normal p53)

No protection of p53-mutant cancer cells

- p53 = most common cancer mutation<sup>†</sup>
- > 50% of all cancer patients have p53 mutation<sup>†</sup>

# Potential Path To Tumor-Agnostic Indication For ALRN-6924

## Small Cell Lung Cancer (SCLC) (Topotecan)

### Phase 1b in SCLC (Completed)

- Achieved proof of concept

### Healthy Volunteer Study

- **Part 1** (optimal dose) and **Part 2** (time to onset, duration and magnitude of PD effects) **completed**
- **MOA confirmed**
- **Study ongoing**

## Non-Small Cell Lung Cancer (NSCLC) (1<sup>st</sup> line carboplatin + pemetrexed +/- immune checkpoint inhibitor)

### Registration Program

- **Randomized, Placebo-Controlled Phase 1b** (N=60 patients)
- **Initiated in 2Q21**
- **2<sup>nd</sup> randomized trial: start planned 2022<sup>†</sup>**

## Gastrointestinal (GI) and Other Cancers (Chemotherapies TBD)

### Registration Program<sup>†</sup>

- Start of trials planned for 2022



<sup>†</sup> Future trials are subject to clinical, regulatory, financial and other considerations

\*PD=pharmacodynamics; MOA=mechanism of action; Tx = Treatment

# **ALRN-6924 Phase 1b Trial in SCLC**

## Design & Final Results

European Society of Medical Oncology (ESMO) Virtual Congress  
September 2021



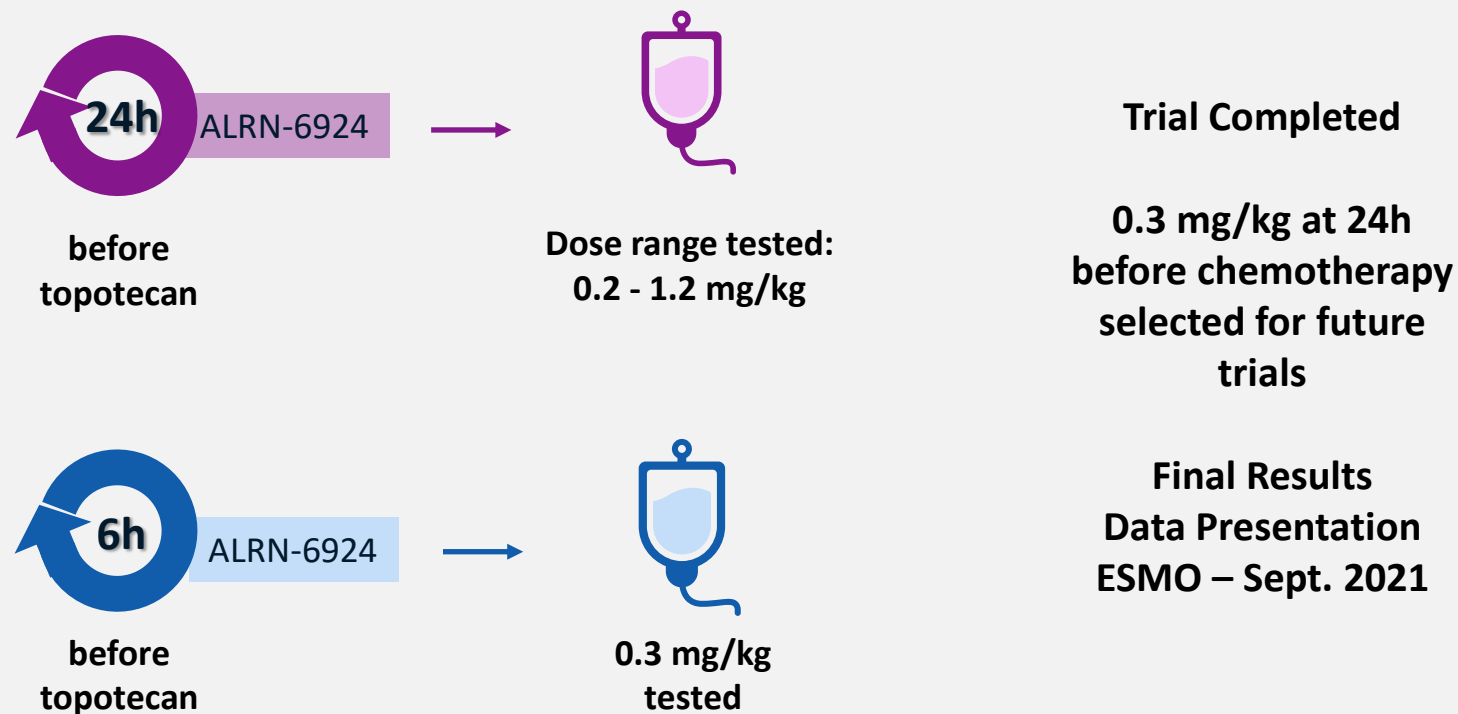
## ALRN-6924 Clinical Results: Key Takeaways

Meaningful reductions of multiple chemotherapy-induced hematologic toxicities as well as fewer RBC transfusions and platelet transfusions

Selective chemoprotection for normal cells without protecting cancer cells

Fewer dose reductions of chemotherapy  
=> potential for improved efficacy

# ALRN-6924 Proof-Of-Concept Phase 1b SCLC Trial Schema



Protocol highlights: Topotecan ( $1.5 \text{ mg/m}^2$ ) administered on days 1 through 5 of every 21-day treatment cycle. Prophylactic G-CSF treatment not permitted in cycle 1; Hb  $>9 \text{ g/dL}$ , ANC  $>1500/\mu\text{L}$ , Platelets  $>100\text{k}/\mu\text{L}$  at baseline

# ALRN-6924: “Triple-Play Efficacy” For Reduction Of Neutropenia, Thrombocytopenia, And Anemia, As Well As Fewer Transfusions In SCLC Patients Receiving Topotecan<sup>^</sup>

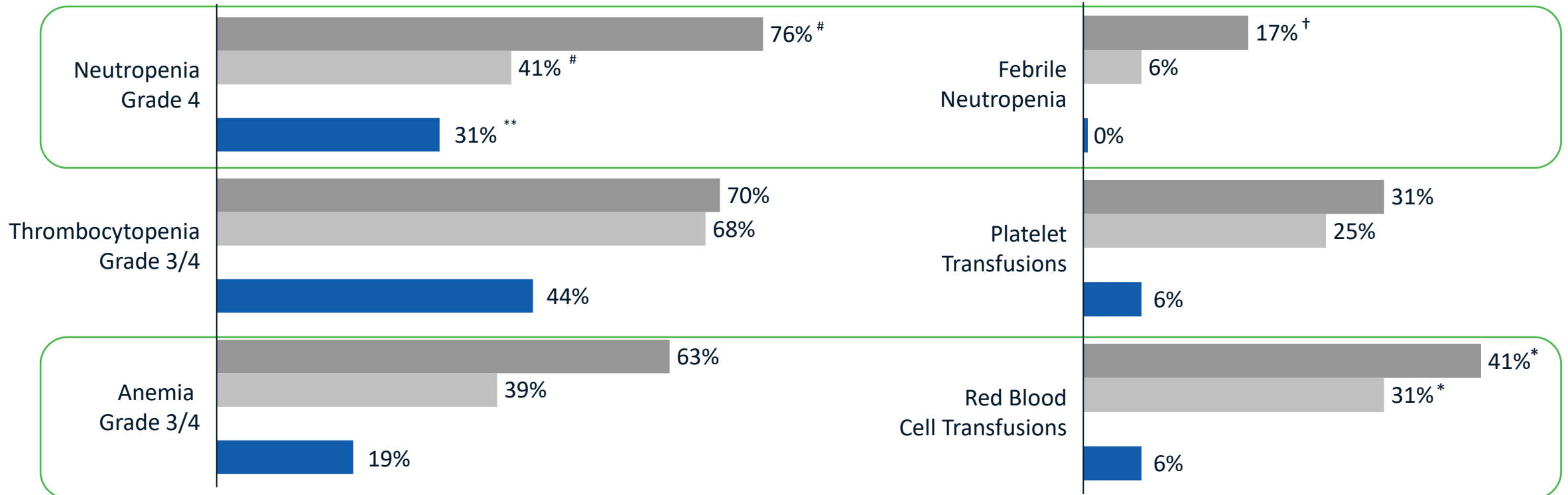
Results of ALRN-6924 Phase 1b Trial and Results of COSELA Trial – Both in SCLC Patients Receiving Topotecan

Andric et al (ESMO 2021):

■ ALRN-6924 0.3mg/kg<sup>§</sup> + Topotecan<sup>^</sup>, N=16

Hart et al. (ASCO 2019):

■ Placebo + Topotecan<sup>‡</sup>, N=28 ■ COSELA + Topotecan<sup>‡</sup>, N=32



AEs based on laboratory values, as applicable

<sup>^</sup> ALRN-6924 data cut July 29, 2021 (-24h cohort)

<sup>§</sup> Identified as optimal dose

\*\* In first treatment cycle

# Cycle not characterized

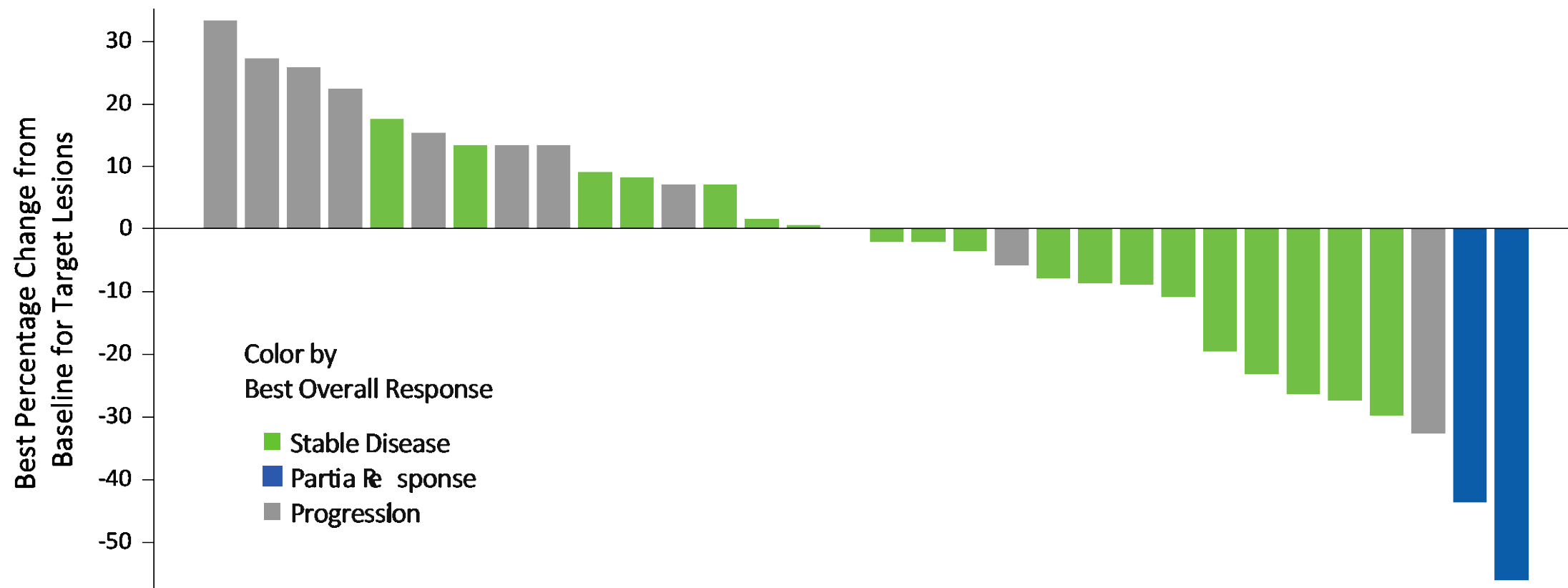
<sup>‡</sup> Hart et al. ASCO 2019 (Slide 9) – G1 Therapeutics; pivotal clinical trial in SCLC patients receiving topotecan

\* Excludes any RBC transfusions administered in the first 5 weeks

† Febrile neutropenia assessed for 29 patients



# Preservation Of Chemotherapy's Anti-Cancer Effects During Treatment With ALRN-6924



- The disease control rate (DCR) was 65.6% for 32 patients with radiological evaluation\*
- In historical trials of SCLC patients receiving topotecan, the DCR was between 47% and 61.5%‡

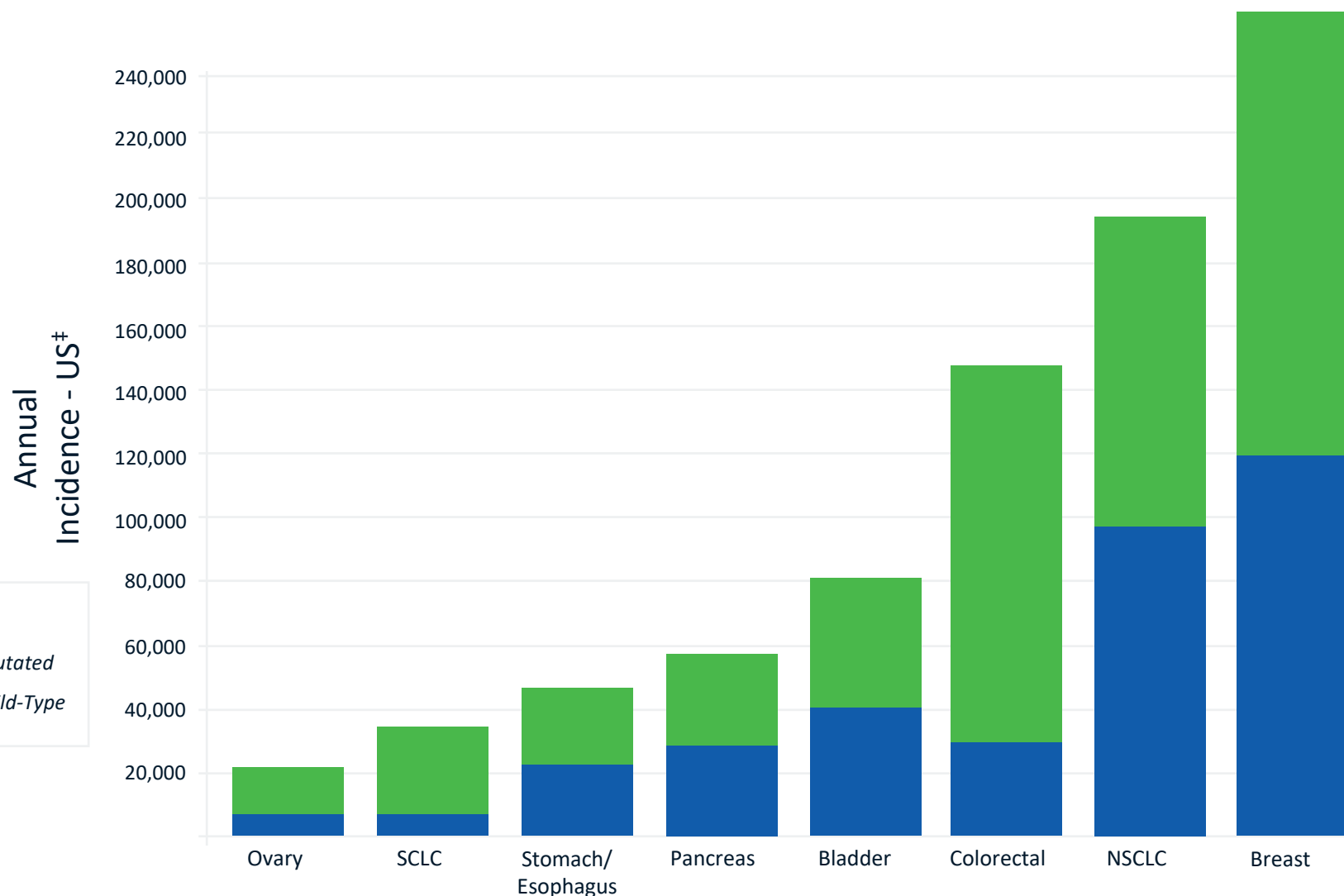
‡ O'Brien M., et al. J. Clinical Oncol. 24(34): 5441-5447, 2006.  
Eckhardt J.R., et al. J. Clin. Oncol. 25(15): 2086-2092, 2007.  
Inoue A., et al. J. Clin. Oncol. 26(33): 5401-5406, 2008  
Jotte R., et al. J. Clin. Oncol. 29(3): 287-293, 2011.  
Pawel J., et al. J. Clinical Oncol. 32(35): 4012-4019, 2014.

• As measured by CT-based tumor imaging per RECIST 1.1;  
7 patients did not have a post-baseline evaluation

The background image is a green-tinted photograph of a laboratory or clinical setting. It shows various pieces of medical equipment, including what appears to be a ventilator or respiratory system with large tubes. There are people in white lab coats working in the background. The floor has a geometric pattern. The overall scene is brightly lit with overhead lights.

# ALRN-6924 Opportunity and Clinical Development Strategy

# Large Market Opportunities In p53-Mutated Cancers Across Most Cancer Types



Newly diagnosed cancer patients per year:

- 18 M Worldwide
- 1.8 M in the US
  - ~50%, i.e. nearly 1M diagnosed annually with p53-mutant cancer in the US

† Siegel et al, "Cancer statistics, 2020" American Cancer Society journal CA: A Cancer Journal for Clinicians. Genetic alterations from Foundation "Insights" Database 18-May-2020 (297,209 sample set).

\* Hoe, K., et al. Nat. Rev. Drug Discov.; 13: 217-236, 2014.

NON-CONFIDENTIAL AILERON THERAPEUTICS 2021

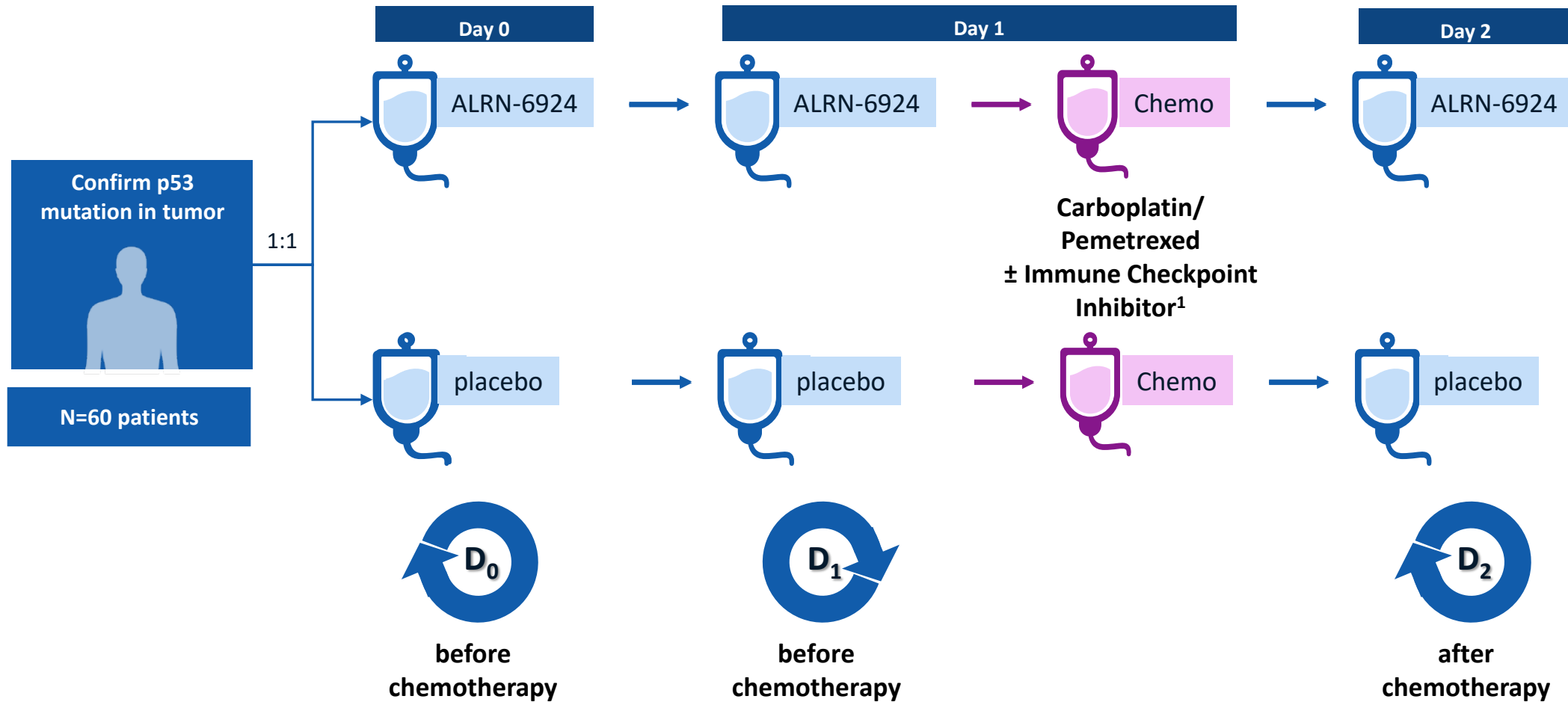


# Advanced p53-Mutated NSCLC Patients Treated In First Line With Carboplatin/Pemetrexed ± Immune Checkpoint Inhibitor<sup>1</sup> And ALRN-6924 Or Placebo

Randomized, double-blind, placebo-controlled Phase 1b clinical trial initiated in 2Q21; topline full results mid-2022

Composite 1° Endpoint: proportion of treatment cycles free of severe heme toxicities, dose reductions, transfusions and use of growth factors

Other Endpoints: proportion of patients with NCI CTCAE Grade 3/4 TEAEs, quality of life, overall response rate and progression-free survival



<sup>1</sup> Combination of ALRN-6924 with immune checkpoint inhibitors evaluated in Zhou X. et al, Cancer Discovery, July 6, 2021; DOI: 10.1158/2159-8290.CD-20-1741

## Strong Intellectual Property Portfolio

- Aileron owns or has exclusive license to over 200 U.S. and foreign patents, with another 100+ applications in prosecution.
- These patents and applications include ALRN-6924 methods of manufacture, methods of use, drug product formulations, and compositions of matter.
- Composition of matter patent expiration in 2033 (+ up to 5 additional years subject to patent term extensions).
- Of note, Aileron maintains global exclusive rights to its proprietary peptide drug technology and ALRN-6924 worldwide.

## Key Financial Highlights

**Cash, Cash Equivalents and Investments (as of June 30, 2021 )**

**\$59.5M**

**Expected to Support Operations Into**

**2<sup>nd</sup> Half 2023**

**Common Shares Outstanding (June 30, 2021)**

**90.5M**

**Analyst Coverage by William Blair, H.C. Wainwright and Jones Trading**



# Our Belief: Chemoprotection Will Transform Chemotherapy Like Anesthesia Transformed Surgery

## Validated Core Differentiator

Selective chemoprotection without protecting cancer cells

## Achieved Proof-of-Concept

Reduction of multiple hematological toxicities and blood transfusions

## Stepwise Clinical Development Strategy

Phase 1b Trial in NSCLC: planned start in Q2 2021

Seek NSCLC indication 1st, then seek other large cancer indications

Ultimately pursue tumor-agnostic indication

## OUR VISION

Chemoprotection for patients with p53-mutated cancers across  
all cancer types and chemotherapies

**~1 million**

patients diagnosed  
annually in U.S. with  
p53-mutated cancer



AILERON

# Chemoprotection May Transform Chemotherapy Like Anesthesia Transformed Surgery

NASDAQ: ALRN

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# **Supplementary Information**

## **ALRN-6924 Phase 1b Trial in SCLC Design & Final Results**

European Society of Medical Oncology (ESMO) Virtual Congress  
September 2021

# Phase 1b SCLC Study: Demographics And Key Baseline Disease Characteristics

		24H SCHEDULE				6H SCHEDULE	TOTAL
		0.2 N=4	0.3 N=16	0.6 N=6	1.2 N=6	0.3 N=7	N=39
AGE, MEDIAN		65	68.5	66.5	58	69	67
GENDER N (%)	MALE	2 (50)	16 (100)	3 (50)	4 (67)	4 (57)	29 (74)
	FEMALE	2 (50)	0	3 (50)	2 (33)	3 (43)	10 (26)
BASELINE LDH N (%)	<ULN	1 (25)	9 (56)	2 (33)	4 (67)	1 (14)	17 (44)
	≥ULN	3 (75)	7 (44)	4 (67)	2 (33)	6 (86)	22 (56)
TIME SINCE COMPLETION OF PREVIOUS THERAPY N (%)	<60 DAYS	1 (25)	8 (50)	1 (17)	5 (83)	3 (43)	18 (46)
	≥60 DAYS	3 (75)	7 (44)	5 (83)	1 (17)	4 (57)	20 (51)
	MISSING	0	1 (6)	0	0	0	1 (3)
BASELINE ECOG STATUS N (%)	0	3 (75)	12 (75)	3 (50)	3 (50)	2 (29)	23 (59)
	1	1 (25)	4 (25)	3 (50)	3 (50)	4 (57)	15 (39)
	2	0	0	0	0	1 (14)	1 (2)
	≥3	0	0	0	0	0	0
STAGE AT SCLC DIAGNOSIS N (%)	LIMITED	0	0	0	0	0	0
	EXTENSIVE	4 (100)	16 (100)	6 (100)	6 (100)	7 (100)	39 (100)
p53 MUTATION STATUS N (%)	MUTATED	4 (100)	16 (100)	6 (100)	6 (100)	7 (100)	39 (100)
	WILD TYPE	0	0	0	0	0	0



# Chemoprotection Led To Fewer Dose Reductions Of Chemotherapy

Topotecan dose reductions in SCLC patients:

- Without Chemoprotection: 29%<sup>^</sup> to 32%<sup>\*</sup> of patients
- With Chemoprotection:
  - with COSELA<sup>#</sup>: 19% of patients
  - with ALRN-6924<sup>§</sup>: 19% of patients

<sup>#</sup> Hart et al., Adv Ther 2020; topotecan + *COSELA*-treated patients (G1-Therapeutics' pivotal clinical trial in SCLC patients receiving topotecan)

<sup>\*</sup> Hart et al., Adv Ther 2020; topotecan + *placebo*-treated patients (G1-Therapeutics' pivotal clinical trial in SCLC patients receiving topotecan)

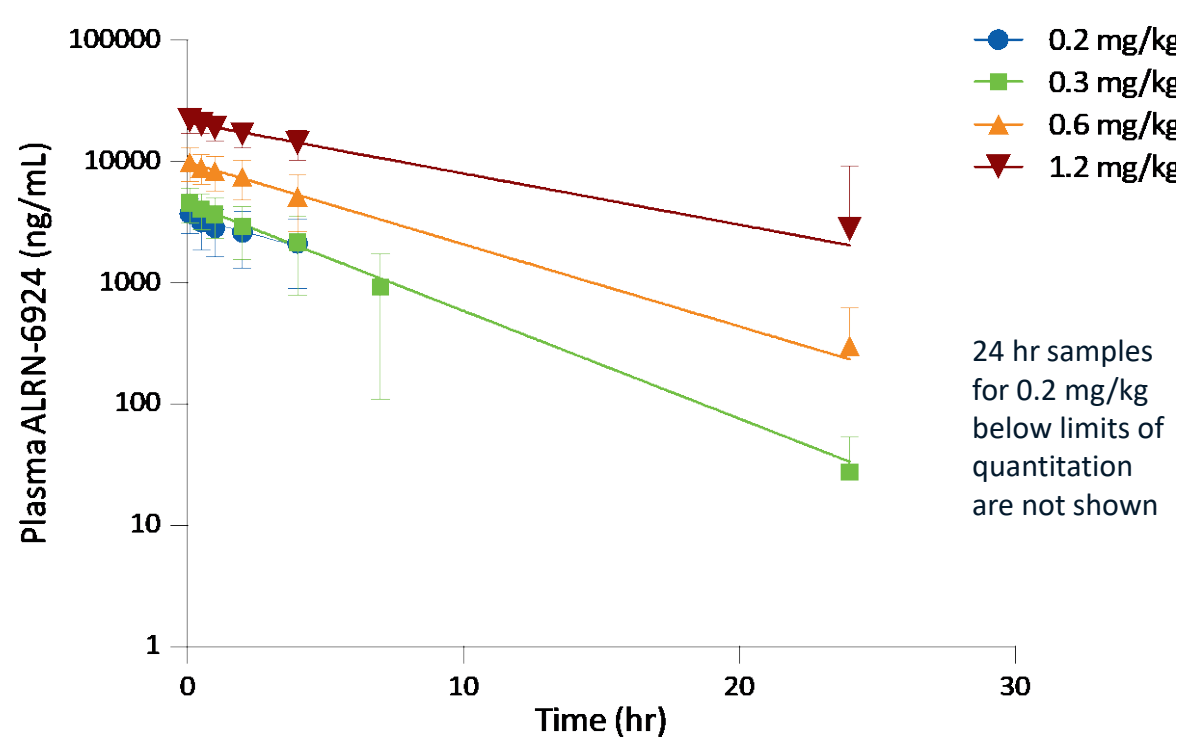
<sup>^</sup> U.S. Prescribing Information for topotecan (2019)

<sup>§</sup> Andric et al, ESMO 2021; patients receiving topotecan + ALRN-6924 (0.3 mg/kg -24 h cohort, N=16)

Vision: Chemoprotection → fewer dose reductions → better outcomes

# ALRN-6924 Shows Dose-Dependent PK Profile In SCLC Patients

ALRN-6924 Plasma PK For Patients Dosed 0.2, 0.3, 0.6, and 1.2 mg/kg



- Mean  $\pm$  st. dev. following first dose of ALRN-6924

	0.2 mg/kg	0.3 mg/kg	0.6 mg/kg	1.2 mg/kg
n of patients	4	22 <sup>†</sup>	6	6
AUC <sub>0-24 hr</sub> $\mu\text{g}\cdot\text{hr}/\text{mL}$ (% CV)	31.8 (53.6)	34.4 (57.0)	83.0 (45.4)	211.9 (26.3)
C <sub>max</sub> $\mu\text{g}/\text{mL}$ (% CV)	3.8 (32.2)	4.9 (31.3)	10.0 (30.9)	22.0 (21.6)
t <sub>1/2</sub> , hr (95% C.I.)	4.9 (2.0 - n.c.)	3.4 (2.5 - 4.7)	4.4 (2.6 - 9.2)	7.1 (3.9 - 12.4)

- Slower clearance (longer t<sub>1/2</sub>) at higher ALRN-6924 doses. 3.4 to 7.1 hr half-life yields no accumulation on repeated dosing
- Plasma exposure after a single ALRN-6924 dose: Dose-proportional C<sub>max</sub>, slightly greater than dose-proportional AUC

<sup>†</sup> PK samples unavailable for one 0.3 mg/kg patient

## **Supplementary Information**

# **Phase 1 Pharmacology Study of ALRN-6924 in Healthy Volunteers (Ongoing) Design & Initial Results**

European Society of Medical Oncology (ESMO) Virtual Congress  
September 2021

# Phase 1 Study Of ALRN-6924 In Healthy Human Volunteers: Study Schema

## PART 1



### Determination of Optimal Dose (Completed)

**3** groups of subjects were treated with a single dose of placebo (n=6), ALRN-6924 0.3 mg/kg (n=4), or ALRN-6924 0.6 mg/kg (n=4)

## PART 2



### Kinetics of Pharmacodynamic Effects in the Bone Marrow (Completed)

**23** subjects were treated with a single dose of 0.3 mg/kg ALRN-6924, with bone marrow sampled from **3** subjects at each successive time points 4-48 hrs post-infusion

## Ongoing



### Confirmation of a Universal Treatment Schedule for ALRN-6924; Testing Effects of ALRN-6924 on Epithelial Cells

## ALRN-6924 Phase 1 Healthy Volunteer Study: Key Takeaways

Study findings (Parts 1 and 2 completed to date) consistent with prior PK-PD non-clinical results

Optimal dose (0.3 mg/kg) and MOA (p53-activated p21 upregulation, p21-mediated cell cycle arrest) confirmed

Time to onset, duration and magnitude of PD effects to inform dosing schedules for future clinical trials of ALRN-6924



# Adverse Events: All Events Were Grade 1 Only; No SAEs Or AEs Led To Discontinuation Of Study Participation

Parameter	Part 1			Part 2	
	Placebo (N=6)	ALRN-6924 0.3 mg/kg (N=4)	ALRN-6924 0.6 mg/kg (N=4)	ALRN-6924 0.3 mg/kg (N=23)	Total ALRN-6924 0.3 mg/kg (N=27)
<b>TEAEs Occurring in &gt;10% of Subjects</b>					
ANY TEAE	3 (50)	2 (50)	4 (100)	21 (91)	23 (85)
NAUSEA	0	1 (25)	3 (75)	5 (22)	6 (22)
VOMITING	0	1 (25)	1 (25)	2 (9)	3 (11)
BIOPSY SITE PAIN	3 (50)	0	0	11 (48)	11 (41)
FATIGUE	0	0	1 (25)	1 (4)	1 (4)
HEADACHE	0	0	2 (50)	9 (39)	9 (33)
DIZZINESS	0	1 (25)	1 (25)	3 (13)	4 (15)
<b>SAEs Occurring in &gt;10% of Subjects</b>					
ANY SAE	0	0	0	0	0

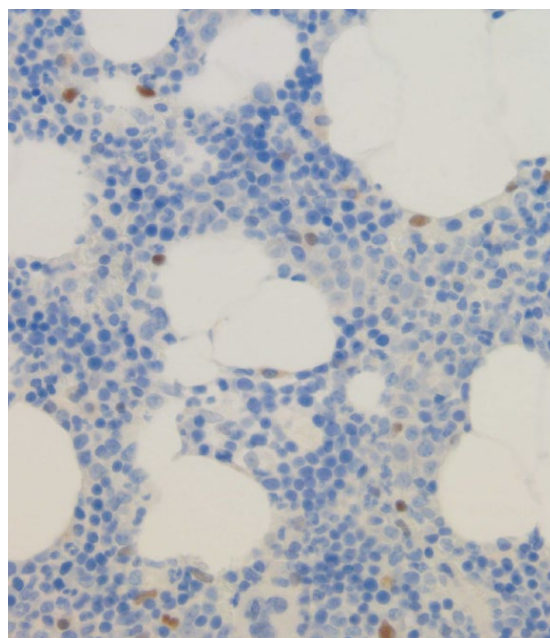
\*Following submission of poster to ESMO Virtual Congress 2021, a “totals” column mistakenly combining placebo- and ALRN-6924-treated subjects was removed from this table.

## Both 0.3 And 0.6 mg/kg ALRN-6924 Doses Induced p21 In 3-7% Of Bone Marrow Cells<sup>†</sup>

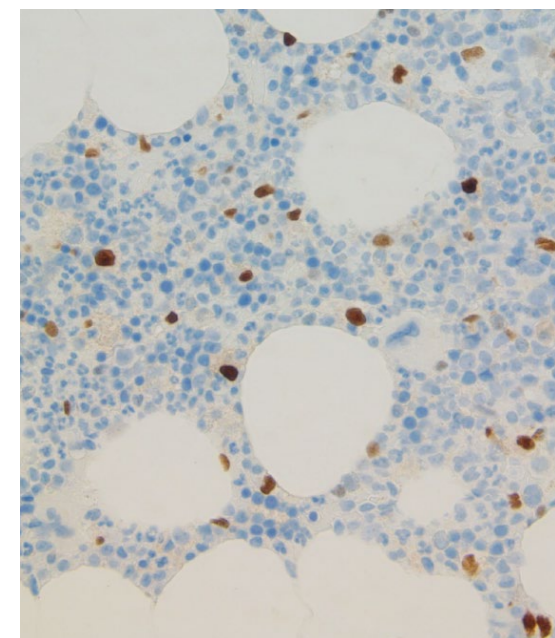
Subject	Group	p21, % at Differential Intensities <sup>†</sup>				cPARP <sup>‡</sup> # cells per HPF
		0	1+	2+	3+	
1	Plac.	100	0	0	0	2
2	"	100	0	0	0	1
3	"	100	0	0	0	19
4	"	100	0	0	0	12
5	"	100	0	0	0	19
6	"	100	0	0	0	21
<hr/>						
7	0.3 mg/kg	94	0	2	4	19
8	"	96	0	2	2	21
9	"	96	0	1	3	7
10	"	95	0	1	4	85
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11	0.6 mg/kg	94	0	1	5	17
12	"	93	0	2	5	61
13	"	97	0	3	0	70
14	"	95	3	2	0	96

### Representative p21 Staining

Placebo-treated Subject



ALRN-6924-treated Subject



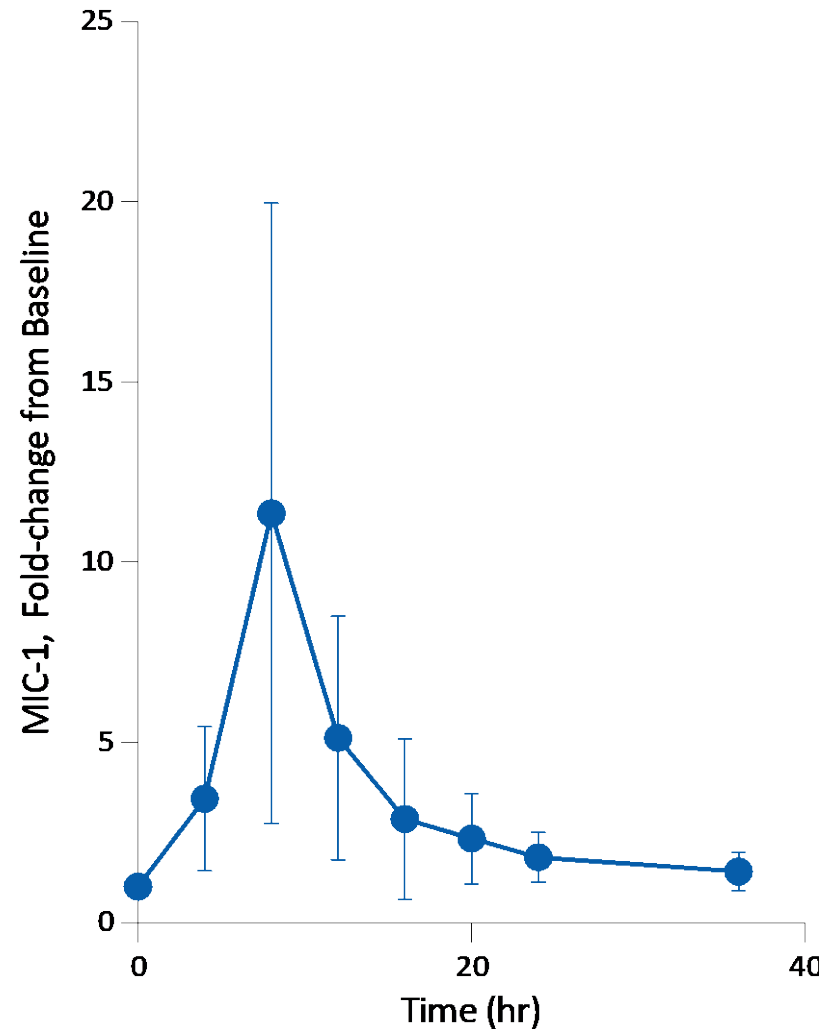
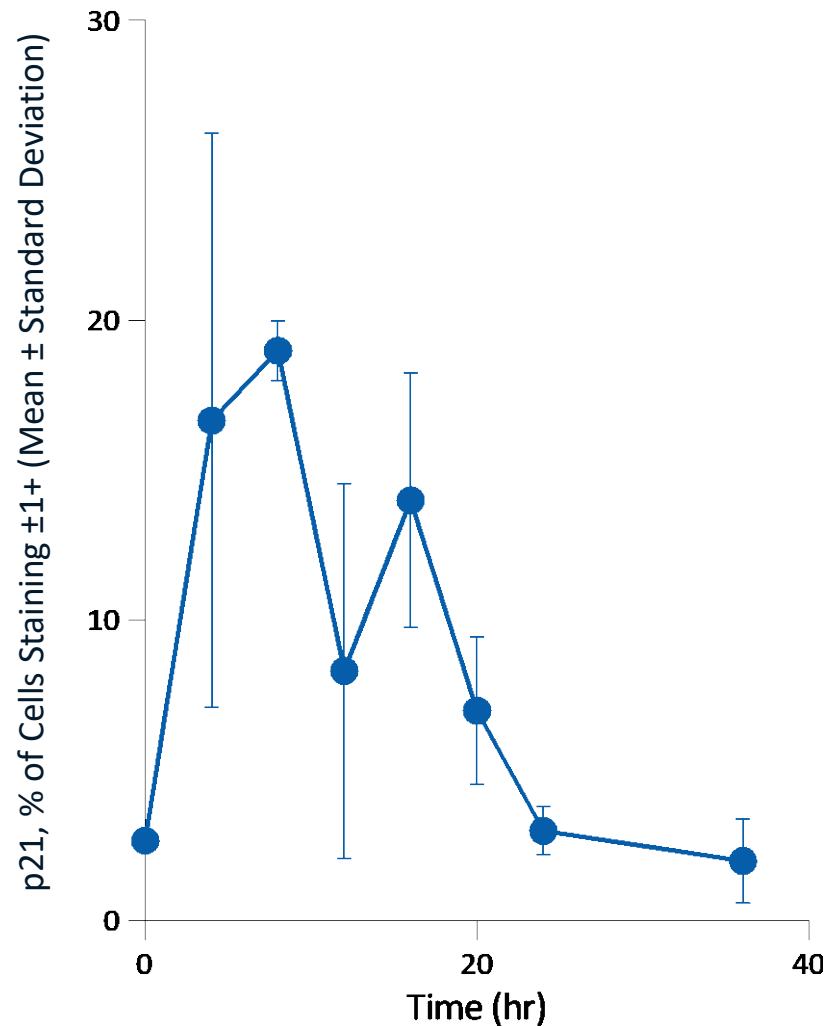
<sup>†</sup>Note: bone marrow is largely composed of quiescent stem cells or nonproliferating immature, differentiating cells; only 5% to 20% of cells are actively cycling<sup>1,2</sup>

<sup>‡</sup>Due to low % of cells with positive staining, results are shown as actual number of cells per high-power field (HPF). Scoring in bone marrow core biopsies sampled 8 hrs post-dose was conducted by a pathologist blinded to experimental conditions.

1. Zhang S., et al. Study of different phases in growth cycle of human bone marrow cells and their growth speed, using rat-human cell hybridization, premature chromosome condensation, and sister chromatid differentiation techniques. *Exp Hematol.* 16(3):221-5, 1988.

2. Hayman et al. Distribution Of Proliferating Bone Marrow in Adult Cancer Patients Determined Using FLT-PET Imaging. *Int. J. Radiation Oncology Biol. Phys.* 79(3):847-852, 2011.

## p21 Protein In Bone Marrow And Serum MIC-1, Both p53-Dependent, Were Transiently Elevated Up To 20 hrs Following A Single 0.3 mg/kg Dose of ALRN-6924

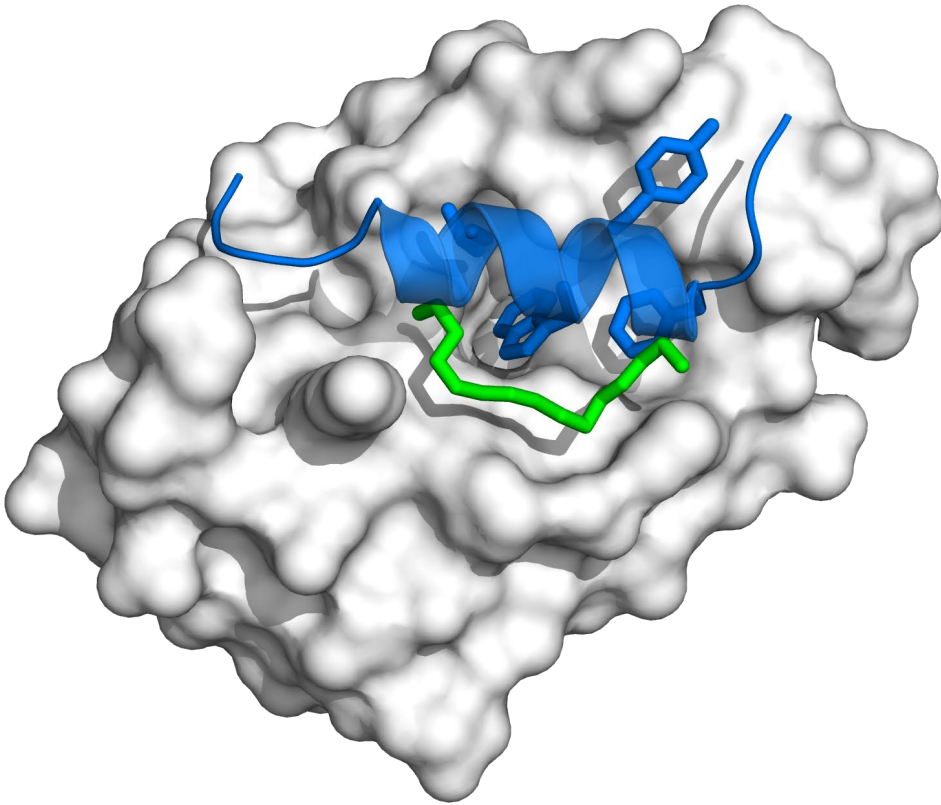


- p21 immunohistochemistry scoring was conducted by an independent pathologist blinded to experimental conditions
- Macrophage Inhibitory Cytokine-1 (MIC-1, also known as Growth Differentiation Factor-15, or GDF-15) was quantified by a qualified ELISA assay
- MIC-1 results are shown as mean change from baseline value prior to first ALRN-6924 dose

**Supplementary  
Non-Clinical Information About ALRN-6924**

# Structure And Key Design Properties Of ALRN-6924

Structure based on the  $\alpha$ -helical domain of p53, with chemical modifications



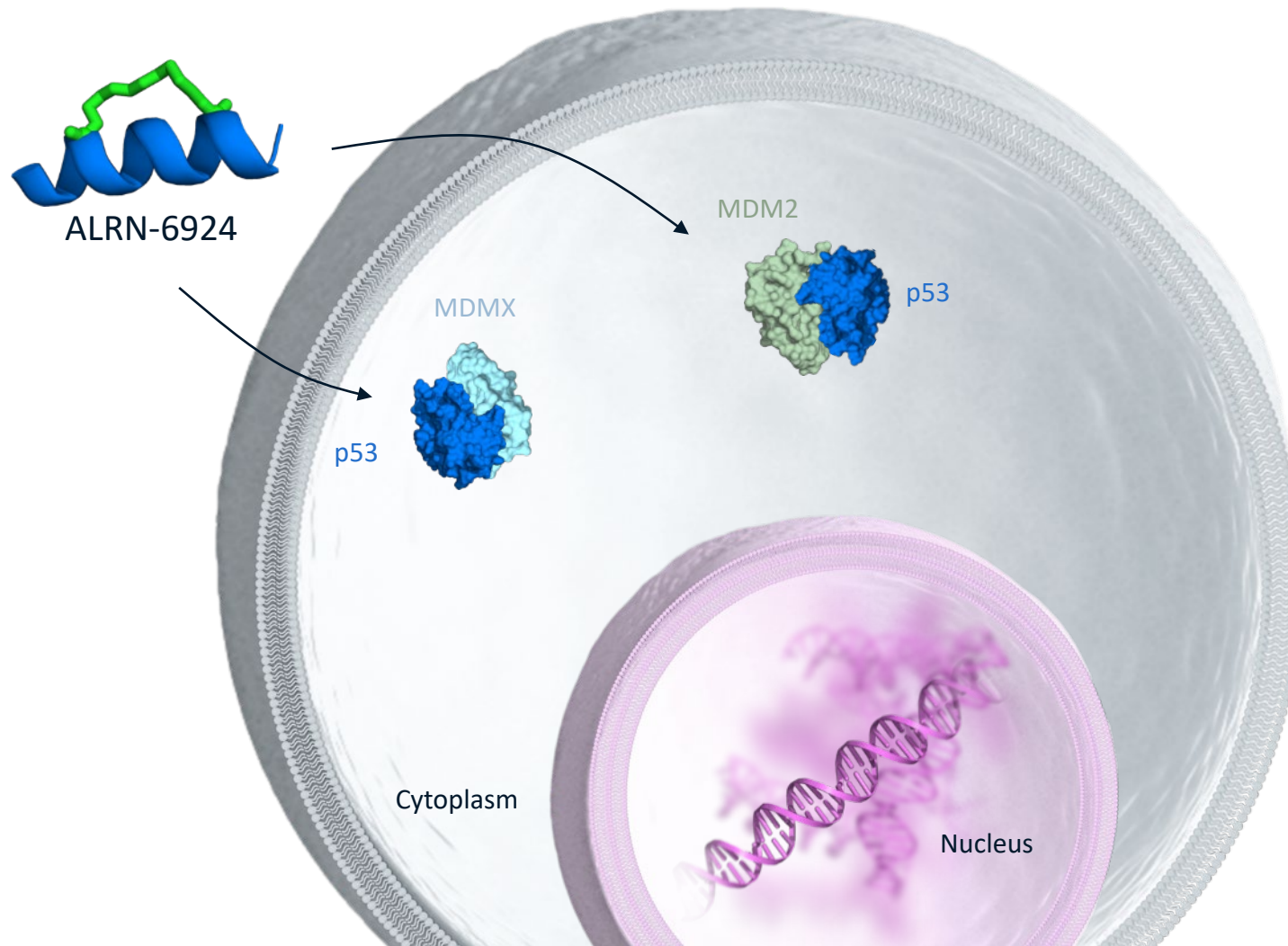
ALRN-6924-MDMX co-crystal structure

The hydrocarbon staple and other modifications ensure:

- I. Protection from proteolytic cleavage
- II. Permeation of cell membranes and cell entry
- III. High affinity binding to its targets
- IV. Preclinical and clinical on-target, on-mechanism effects

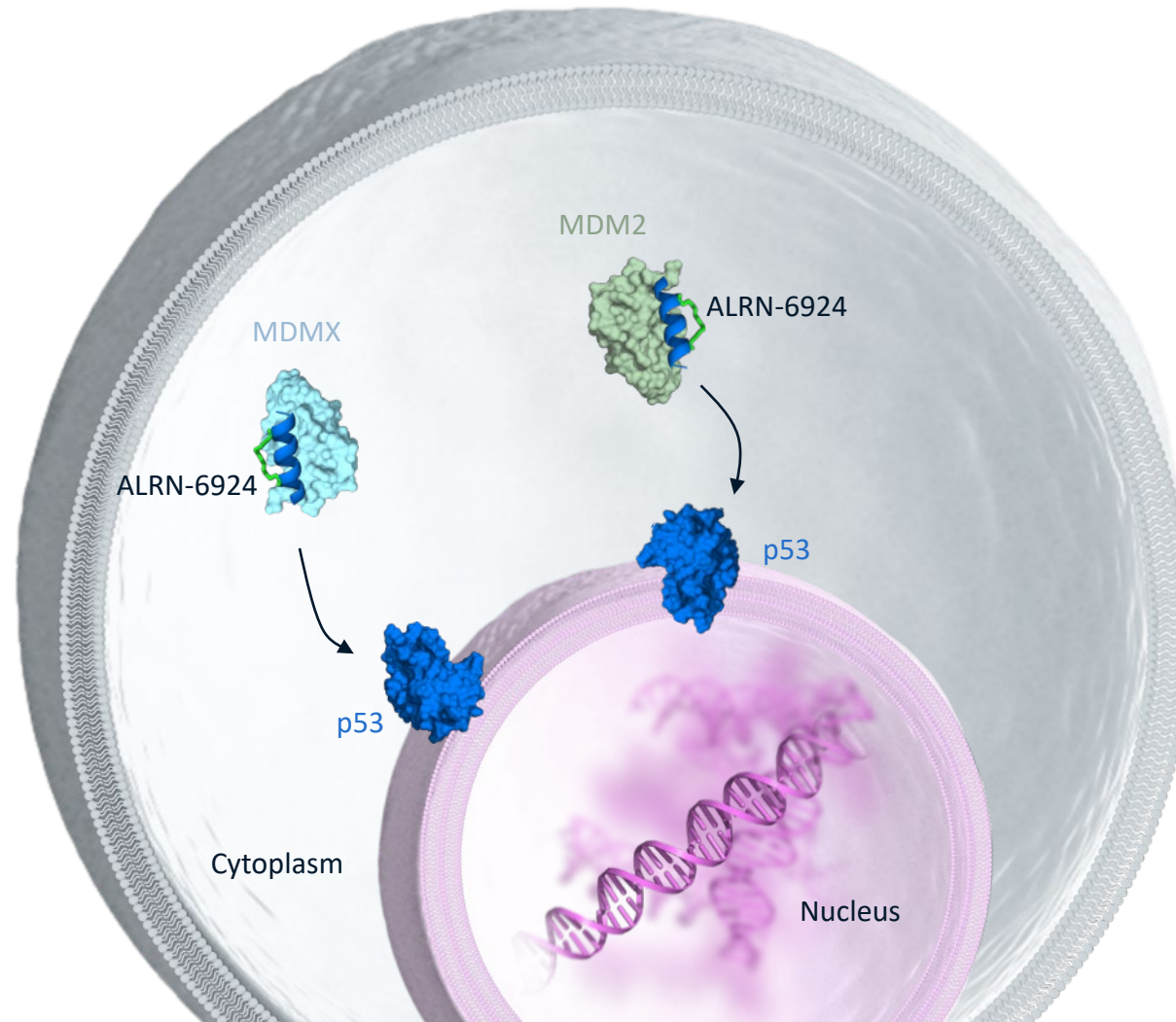


## ALRN-6924 Mechanism Of Action In Wild-Type p53 Cells



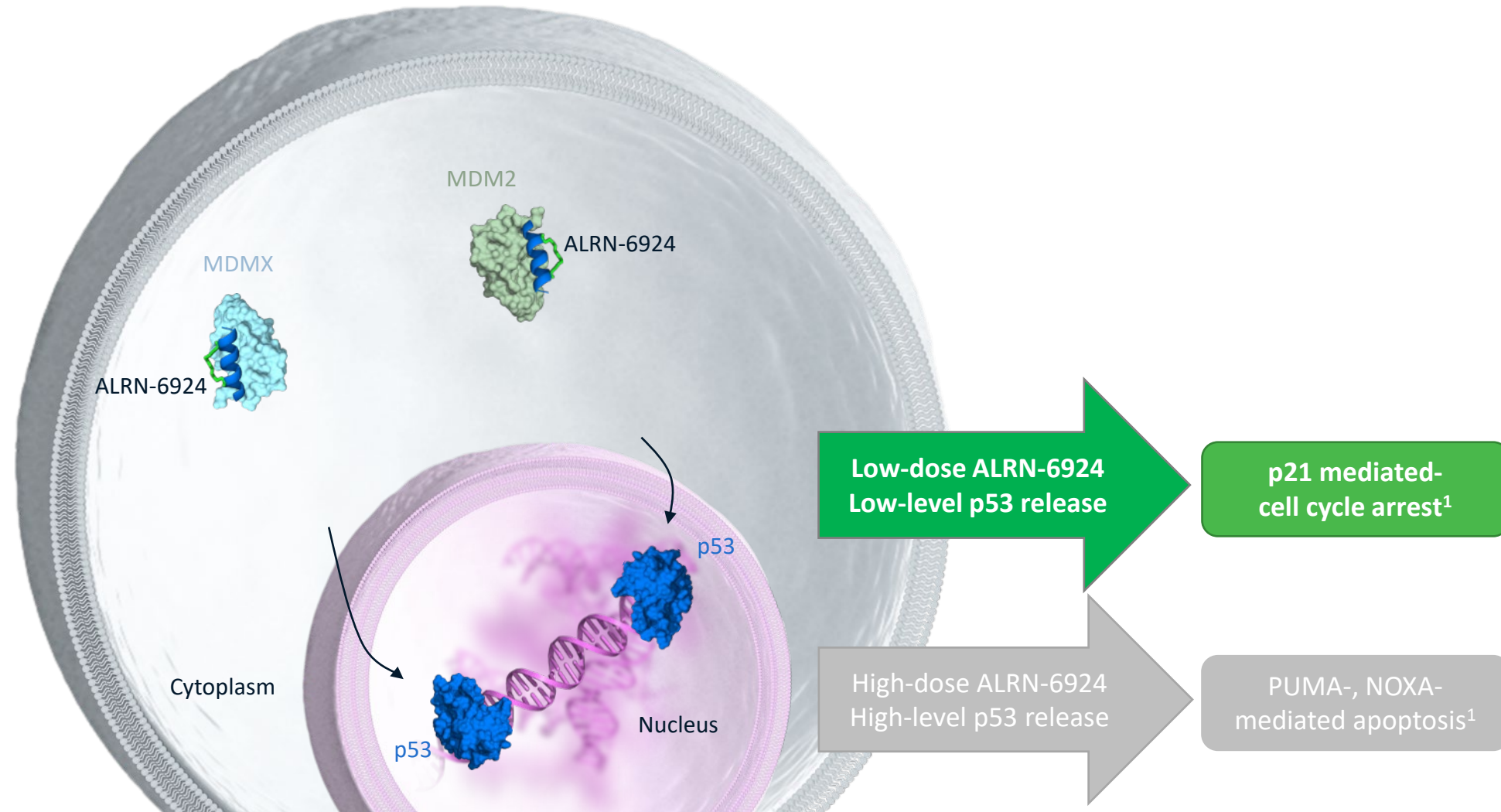
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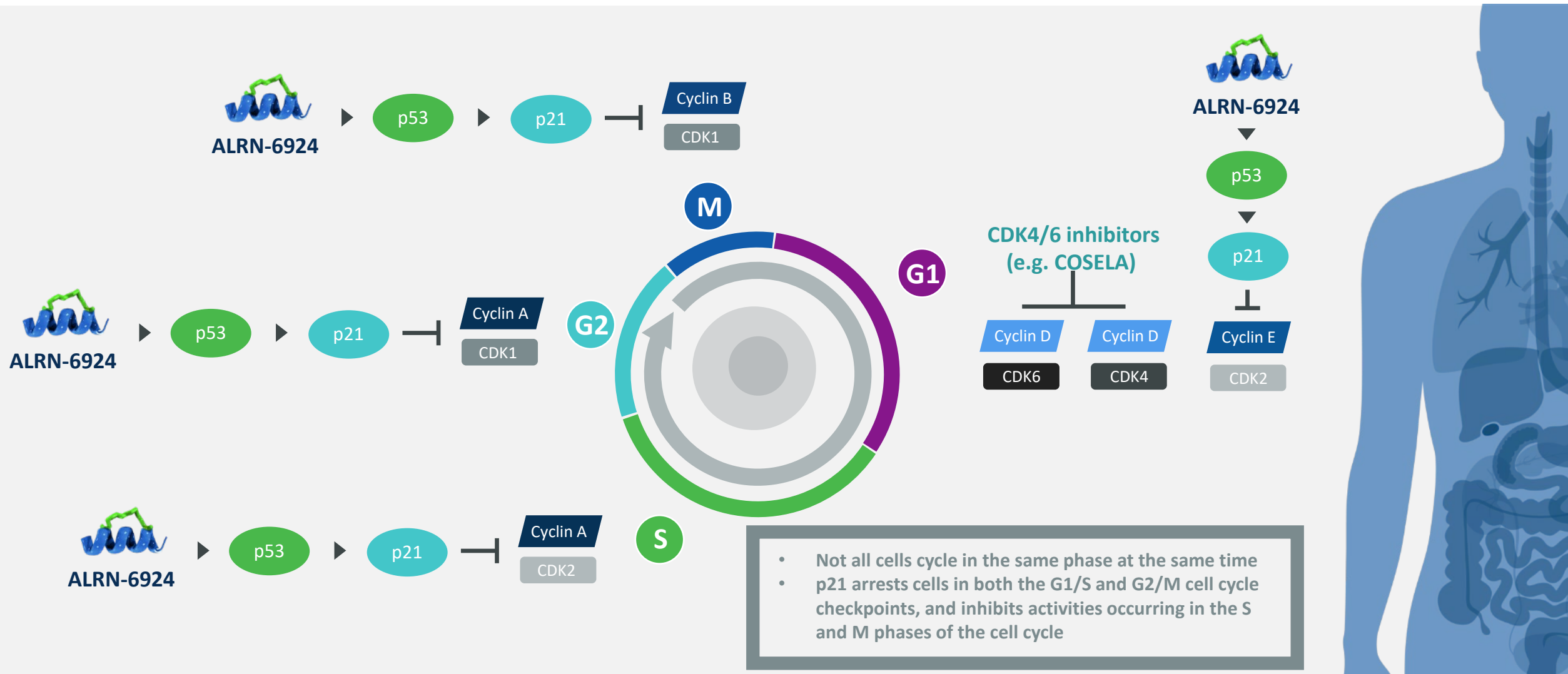
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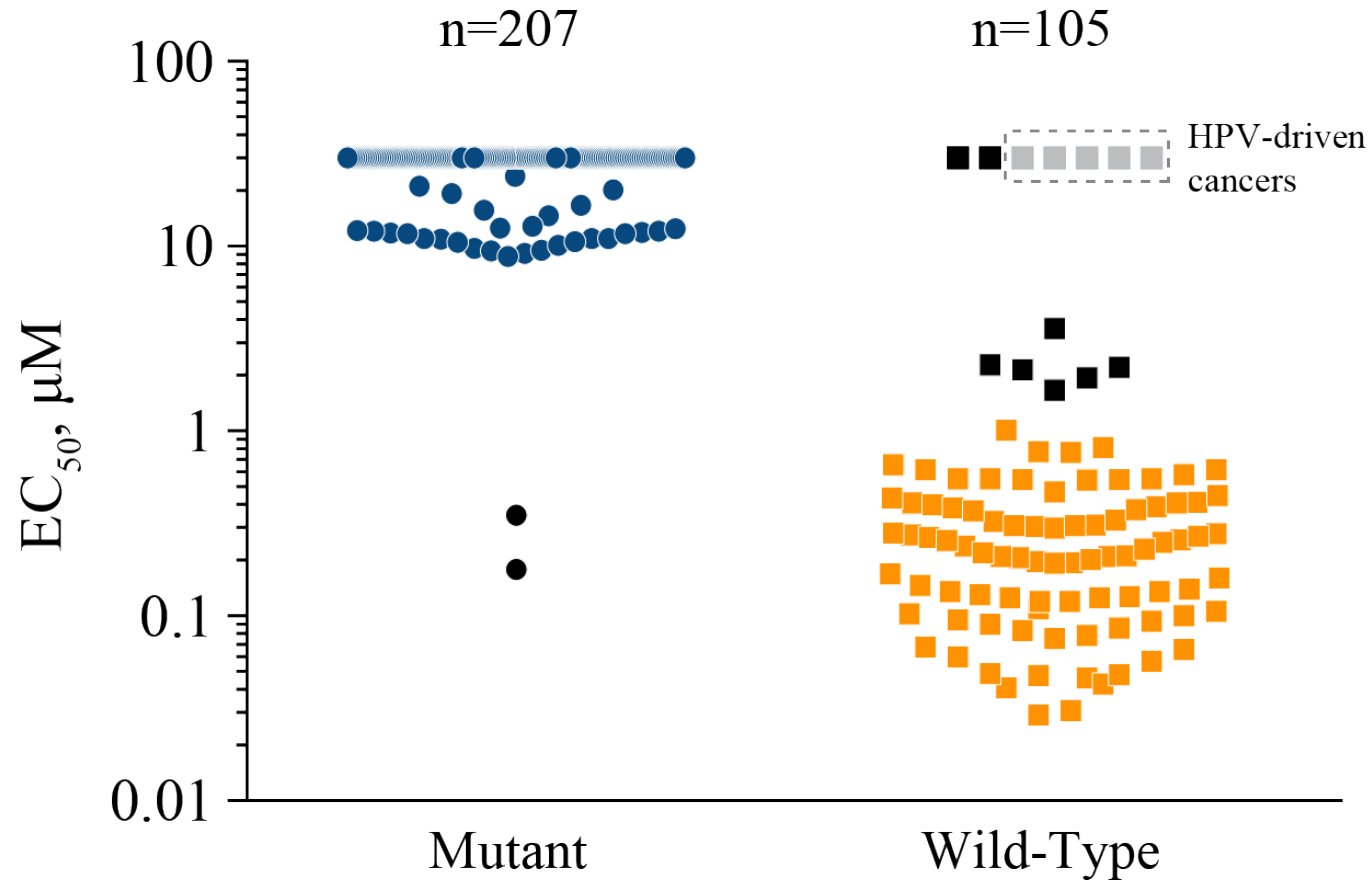
<sup>1</sup> Chen; Cold Spring Harb Perspect Med. 2016 Mar 1

# ALRN-6924 Best-In-class Potential In Chemoprotection: Effects On All Phases Of Cell Cycle



# ALRN-6924 Does Not Work In Cells With Mutant p53

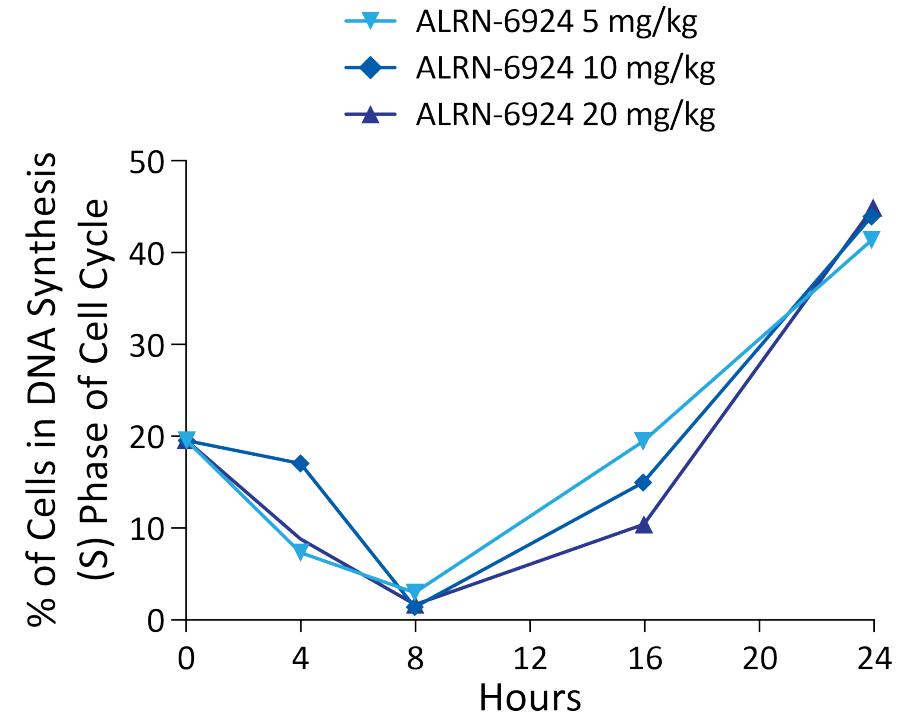
ALRN-6924 Studies in >300 Cell Lines Show Potent, On-mechanism Cellular Activity



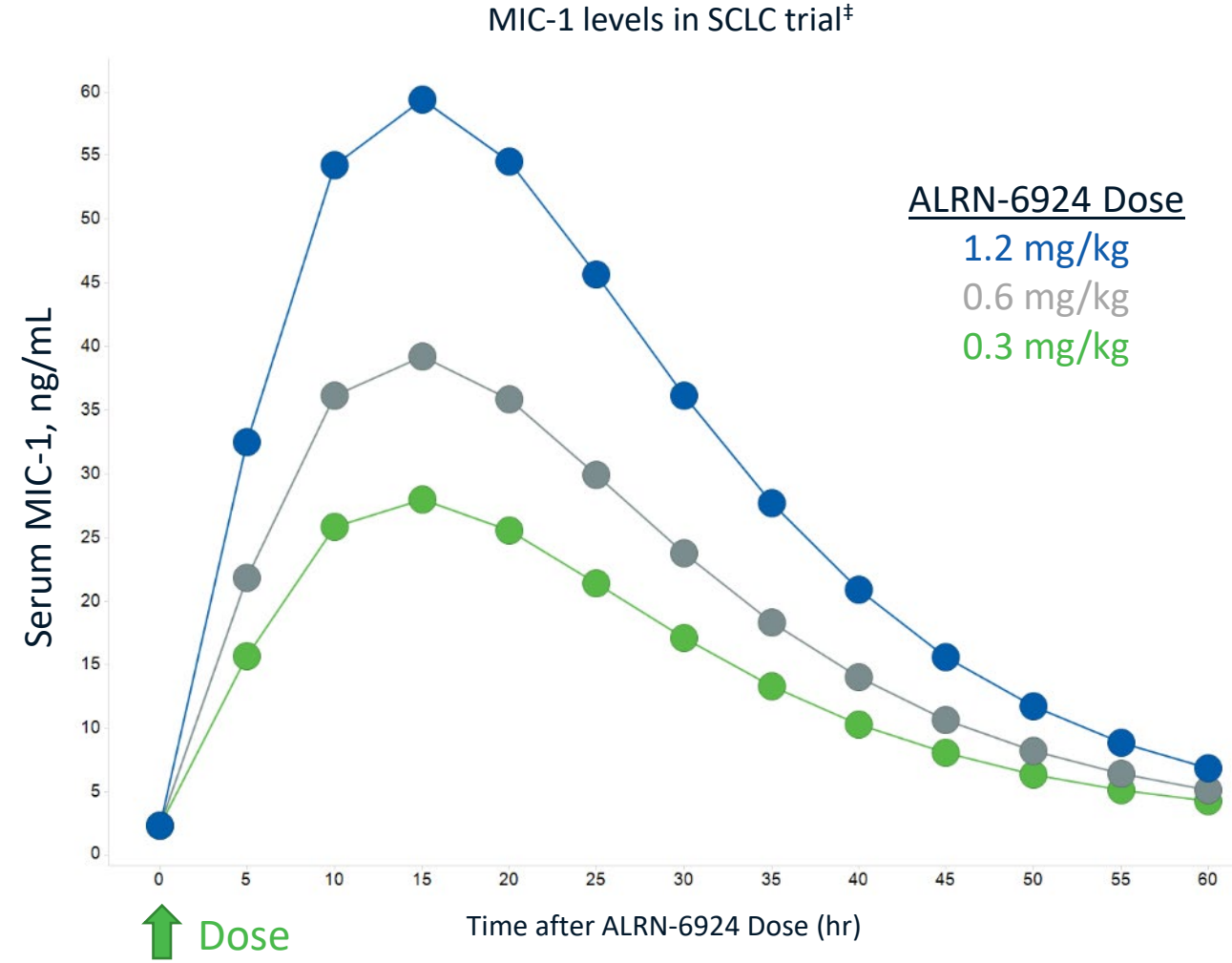
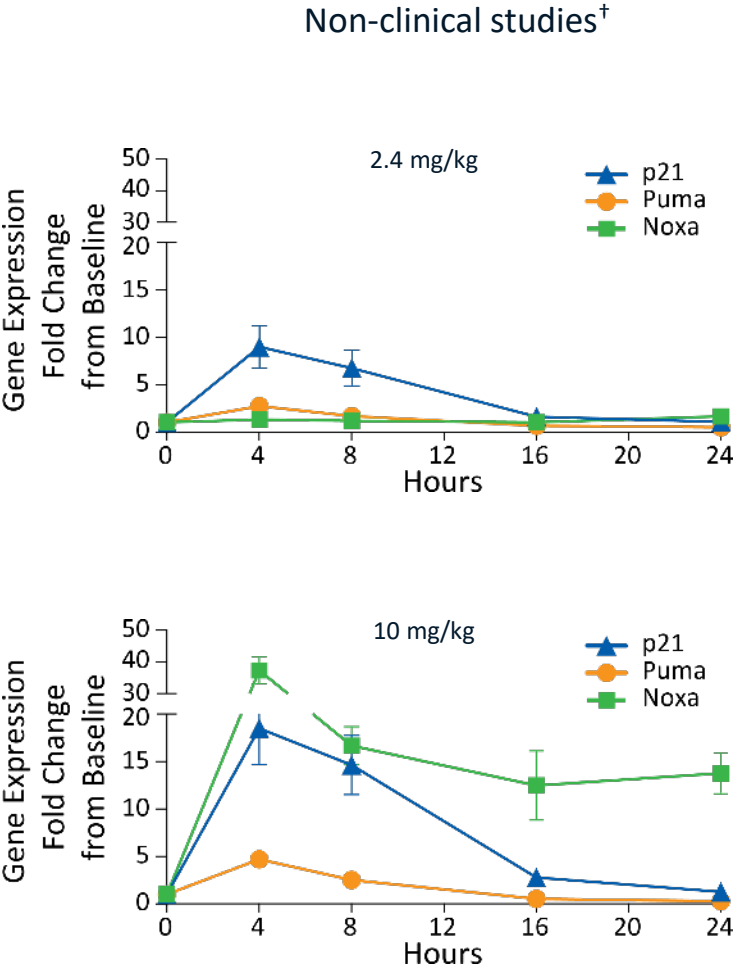
$EC_{50}$  = Drug conc. at which 50% of tumor cells are killed  
 $EC_{50}$  values  $\geq 30 \mu M$  are shown as 30  $\mu M$



# ALRN-6924 Induces Transient, Reversible Cell Cycle Arrest In Murine Hematopoietic Stem And Progenitor Cells (HSPCs) *in vivo*



# Biomarkers Of Cell Cycle Arrest (p21) And Apoptosis (Puma, Noxa, And MIC-1)



<sup>†</sup> Carvajal et al, "The Investigational Peptide Drug ALRN-6924, a Dual Inhibitor of MDMX and MDM2, is an Effective Myelopreservation Agent. AACR-NCI-EORTC Conference October 2019

<sup>‡</sup> Data modelled from this trial and other ALRN-6924 clinical studies: Meric-Bernstam F, et al Phase I trial of a novel stapled peptide ALRN-6924 disrupting MDMX and MDM2-mediated inhibition of WTP53 in patients with solid tumors and lymphomas. J. Clin. Oncol. 35(15): 2505, 2017.



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