AILERON

Transforming the Experience of Chemotherapy for Cancer Patients

CORPORATE PRESENTATION

AUGUST 2022

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 potential of ALRN-6924 as a chemoprotective agent and the Company's 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 or with respect to the matters anticipated; whether the modifications to the Phase 1b breast cancer trial referred to in this presentation will have the effects anticipated, whether initial results of clinical trials will be indicative of final results of those trials; whether preclinical or clinical results will be indicative of results obtained in future clinical trials, including trials in different indications or with different chemotherapies; whether ALRN-6924 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 ALRN-6924 will receive approval from regulatory agencies on a timely basis or at all; whether, if product candidates obtain approval, it 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 annual report on Form 10-K for the year ended December 31, 2021, filed on March 28, 2022, and Form 10-Q for the quarter ended June 30, 2022, filed on August 15, 2022, 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.

We Aspire to Make Chemotherapy Safer and Thereby More Effective to Save More Lives

ALRN-6924: protecting against multiple chemotherapy-induced toxicities

- A single supportive care drug with the potential to prevent neutropenia, anemia and thrombocytopenia, as well as non-hematologic toxicities, including alopecia

Potentially the first precision medicine-based supportive care drug

- Targeting p53-mutant cancers = large market opportunity
- Nearly 1 million patients in the U.S. are diagnosed annually with p53-mutated cancer

Ongoing Phase 1b open-label trial in breast cancer patients

- Planned readouts include data from initial patients in 4Q 2022; interim analysis (n=12) in 2Q 2023; topline results (n=20) in 3Q 2023

Cash runway expected to fund operations through end of 1Q 2024

- Extended runway to fund topline results from breast cancer trial and pivotal trial preparations*

Our Vision: To deliver selective chemoprotection to all patients with p53-mutated cancer regardless of type of cancer or chemotherapy

* Pending breast cancer trial data

Strong Scientific Evidence Has Reliably and Reproducibly Demonstrated ALRN-6924's Chemoprotective Potential

Nonclinical Proof ALRN-6924 Works:

In vitro (mouse & human)

… in bone marrow stem cells

Carvajal et al., EORTC 2019

In vivo (mouse)

… in epithelial gut mucosa cells

Annis et al., ASH 2021

Ex vivo (human)

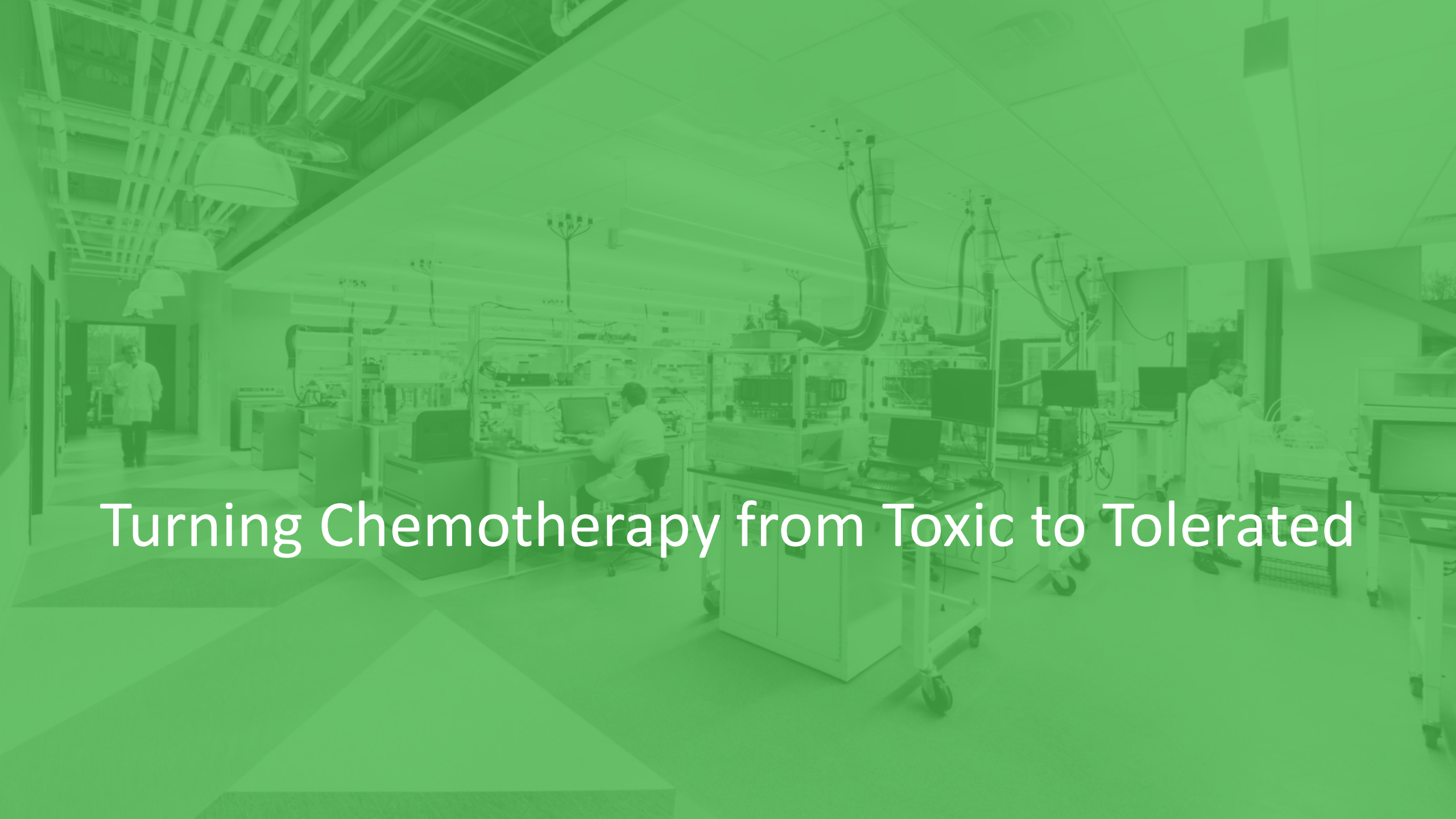
… in hair follicles and their stem cells

Gherardini et al., SID 2022

Clinical Development of ALRN-6924

Proof of Mechanism in Healthy Volunteers	*Supportive Clinical Trial Data*	*Current Focus and Anticipated Path to Pivotal Trial*	*Ultimate Goal*
Cell cycle arrest in bone marrow stem cells Voors-Pette et al., ESMO 2021	Reduced multilineage bone marrow toxicity in topotecan-treated, p53-mutated SCLC Andric et al., ESMO 2021	Evaluating severe neutropenia and other toxicities in TAC-treated, p53-mutated breast cancer → Phase 3 trial(s)	**Chemoprotection for all patients with p53-mutated cancer**
Cell cycle arrest in hair follicle cells Submitted for presentation in 2H 2022	More chemo cycles completed in carboplatin/ pemetrexed-treated, p53-mutated NSCLC Presented by Aileron in June 2022		

NSCLC=non-small cell lung cancer; SCLC=small cell lung cancer; TAC=taxane (docetaxel), adriamycin, cyclophosphamide



Turning Chemotherapy from Toxic to Tolerated

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, thus causing side effects

Today's supportive care options:

- Typically address only one toxicity
- Often have limited efficacy
- Associated with harmful side effects
- No pharmacological treatment options for multiple toxicities (e.g. alopecia)

Today's approach often leads to:

- Dose reductions and delays of chemotherapy
- Patients needing/seeking multiple supportive care drugs and treatments
- Poor quality of life for patients
- Resignation to the harm caused by chemo

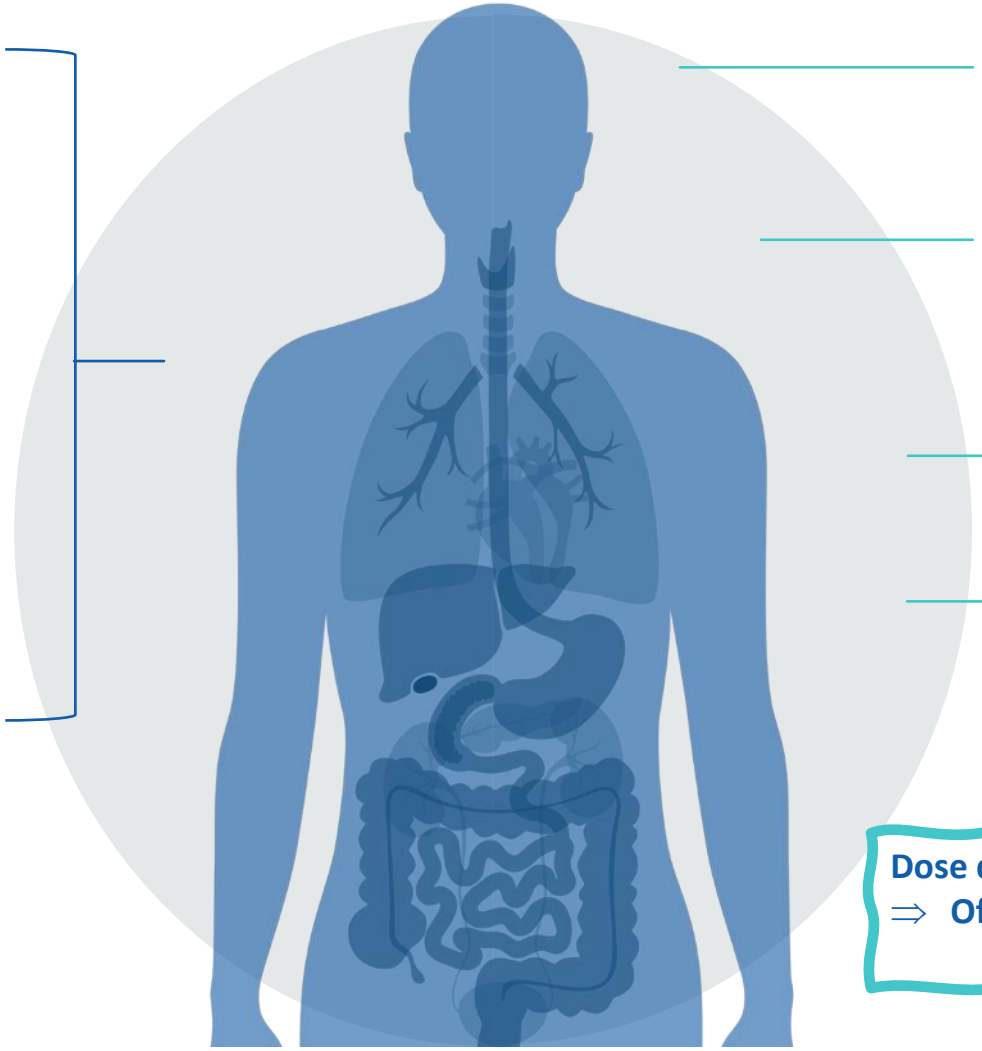
Broad Range of Chemotherapy-Induced Toxicities = Broad Potential for ALRN-6924

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

Severe Neutropenia
(serious infection, fever, sepsis)

Severe Anemia
(weakness, fatigue)

Severe Thrombocytopenia
(excessive bleeding)



Alopecia (hair loss)

Mucositis (mouth sores)

Fatigue, Weakness, Asthenia

Vomiting, Diarrhea, Bloating

Dose delays & dose reductions of chemotherapy
⇒ **Often lead to incomplete chemotherapy**
⇒ **Often reduce response rates & survival**

Broad Range of Chemotherapy-Induced Toxicities = Broad Potential for ALRN-6924

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

Severe Neutropenia
(serious infection, fever, sepsis)

Alopecia (hair loss)

Focus of Trial with ALRN-6924 + TAC Chemotherapy in Breast Cancer

Mucositis (mouth sores)

Severe Anemia
(weakness, fatigue)

Fatigue, Weakness, Asthenia

Vomiting, Diarrhea, Bloating

Severe Thrombocytopenia
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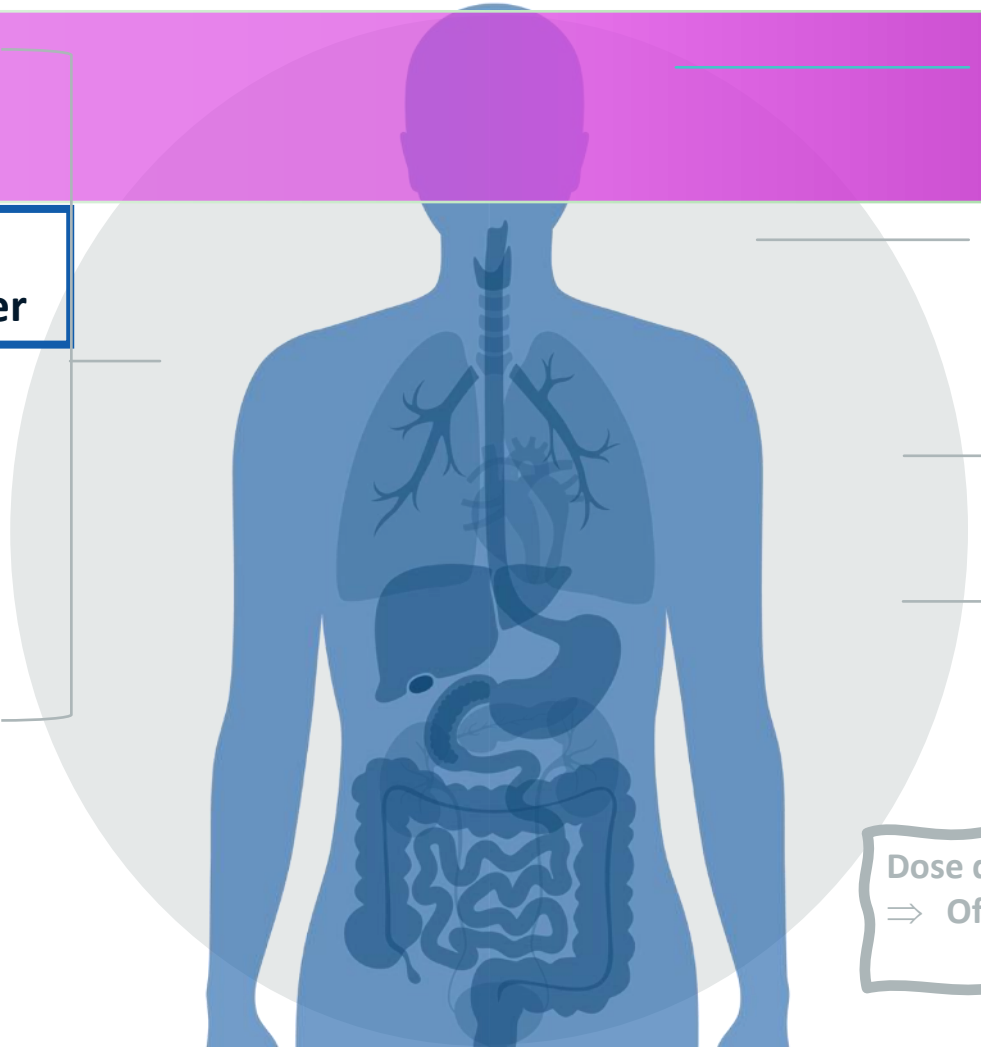


Dose delays & dose reductions of chemotherapy
⇒ Often lead to incomplete chemotherapy
⇒ Often reduce response rates & survival

TAC = docetaxel + doxorubicin + cyclophosphamide

Poor Standard of Care for Management of Bone Marrow Toxicities

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

SEVERE NEUTROPENIA

Standard of Care: G-CSF (e.g. Neulasta® [pegfilgrastim] /Neupogen® [filgrastim])

Clinical Issues:

- Can promote tumor growth, can cause spleen rupture and bone pain
- Limited efficacy (*Example: previous data has shown that up to 75% of breast cancer patients receiving prophylactic G-CSF still experience severe neutropenia in cycle 1.)**

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 THROMBOCYTOPENIA

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

Clinical Issues:

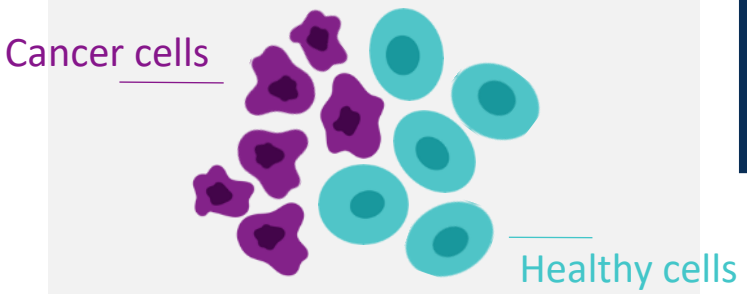
- Effects limited to 2-5 days maximum
- Patients can become transfusion-refractory
- Transfusion-related risk of infection; limited supply

* U.S. Food & Drug Administration Statistical Review of FULPHILA®

Basic Principles to Selectively Protect Against Chemotherapy-Induced Side Effects

CURRENT PARADIGM:

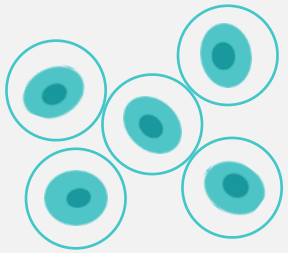
Chemotherapy destroys cells (healthy and cancer) that are cycling (= undergoing cell division process)



PARADIGM SHIFT

AILERON PARADIGM:

Temporarily pause cycling in healthy cells, shielding them from chemotherapy



Healthy cells always have normal p53 thus can be protected

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

Cancer cells with mutant p53 are not protected

A COUNTERINTUITIVE APPROACH:
Treat healthy cells, not cancer cells

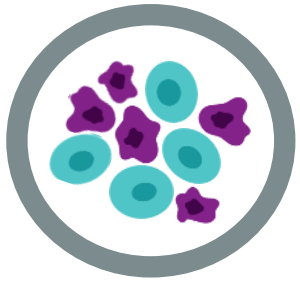
Healthy Cells Have Normal p53. ALRN-6924 Activates Normal p53, Pausing Cell Cycle in Normal Cells, but not in Cancer Cells with Mutant p53

Key Takeaway: We treat healthy cells using a precision medicine-based approach (p53 biomarker).

Patient with p53-mutant cancer receives ALRN-6924

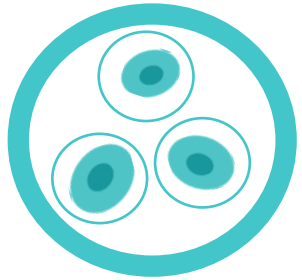
IV administration
1-hour infusion

→



ALRN-6924 activates normal p53 in healthy cells

→

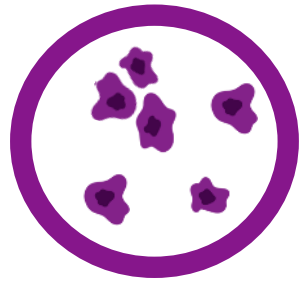


Activated normal p53 upregulates p21, which pauses cell cycling in healthy cells

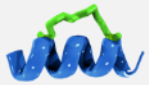
→

Patient with p53-mutant cancer receives chemotherapy

→



Chemotherapy's attack on cancer cells with mutant p53 is uninterrupted



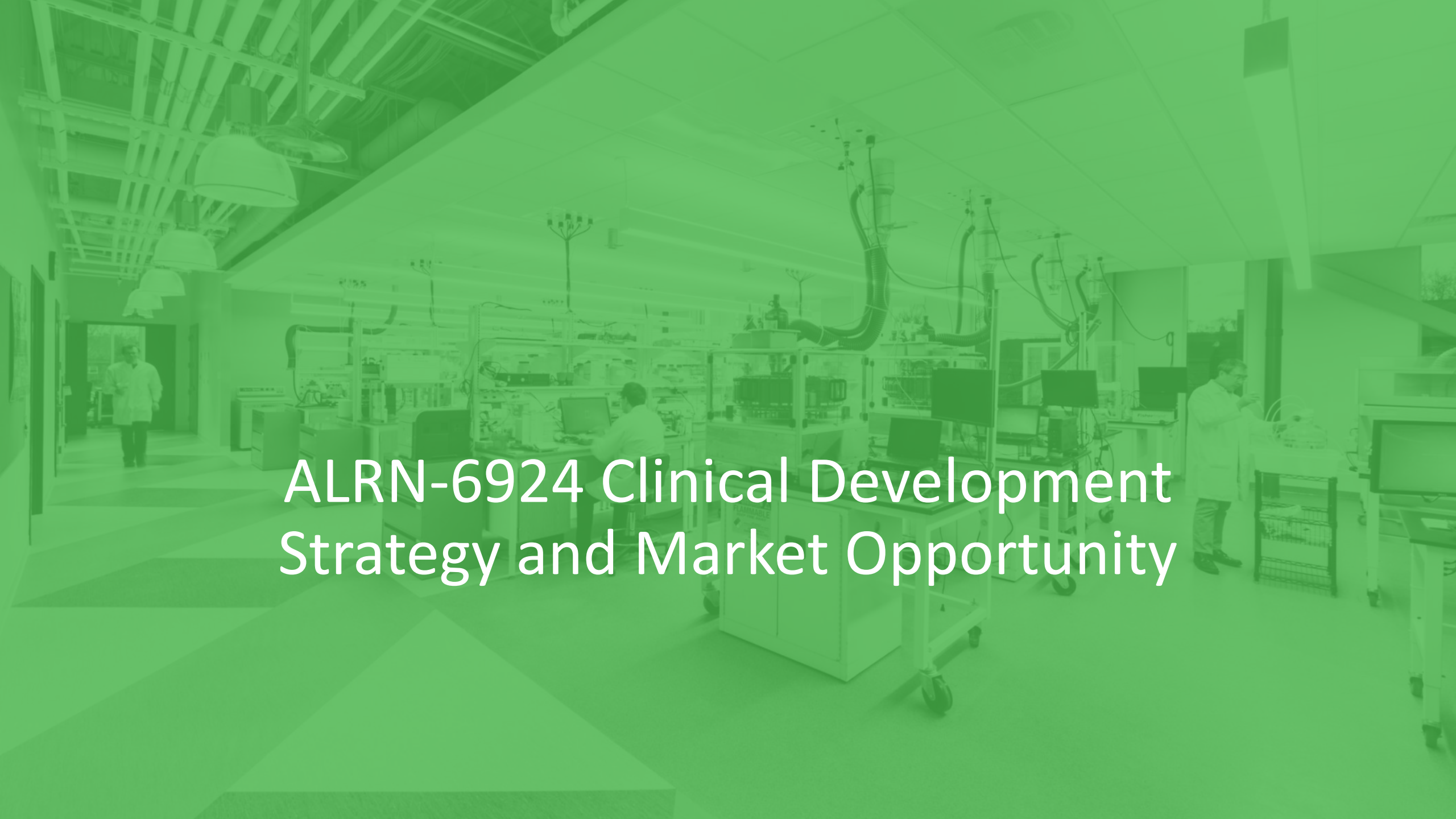
ALRN-6924

Selective chemoprotection of healthy cells

No protection of p53-mutant cancer cells

- > 50% of all cancer patients have p53 mutation†

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



ALRN-6924 Clinical Development Strategy and Market Opportunity

Strong Scientific Evidence Has Defined Path Toward Pivotal Trial Readiness

Nonclinical Proof ALRN-6924 Works:

In vitro (mouse & human)

… in bone marrow stem cells

Carvajal et al., EORTC 2019

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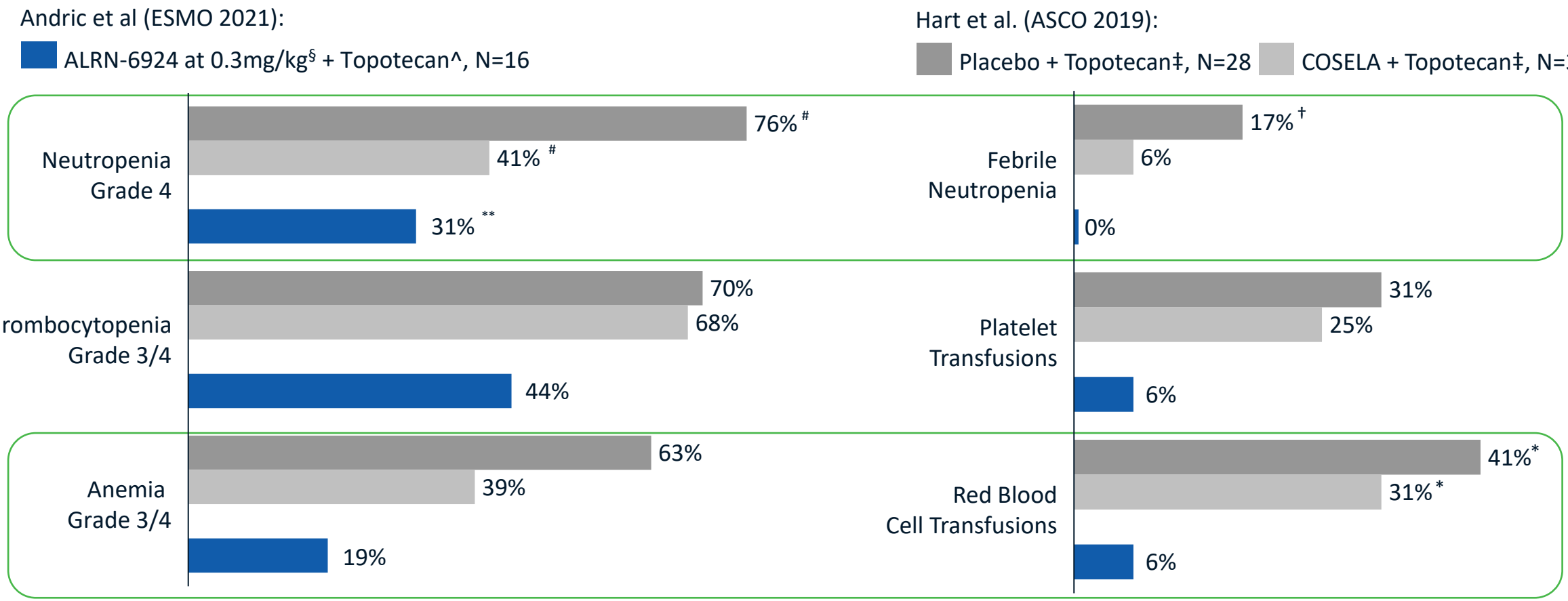
Proof-of-Concept in SCLC Patients Receiving Topotecan^

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



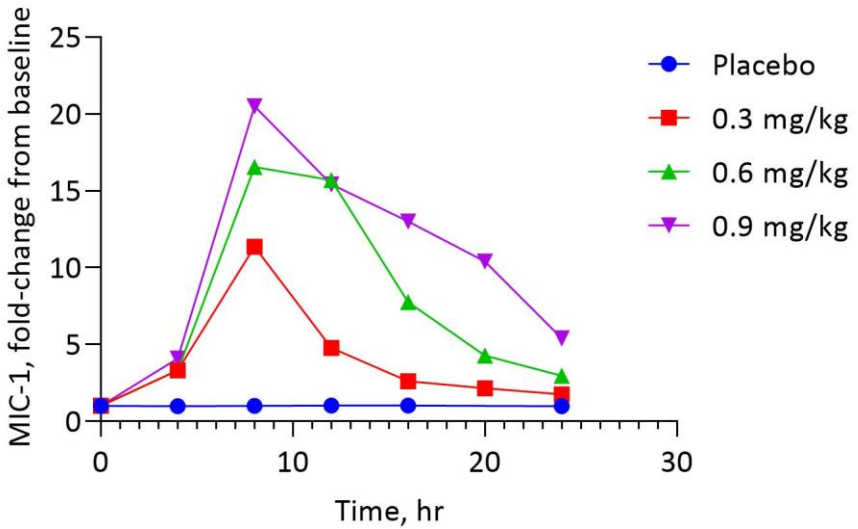
AEs based on laboratory values, as applicable

^ ALRN-6924 data cut July 29, 2021 (-24h cohort)
§ Identified as optimal dose
** In first treatment cycle
# Cycle not characterized

‡ Hart et al. ASCO 2019 (Slide 9) – G1 Therapeutics; clinical trial in SCLC patients receiving topotecan
* Excludes any RBC transfusions administered in the first 5 weeks
† Febrile neutropenia assessed for 29 patients

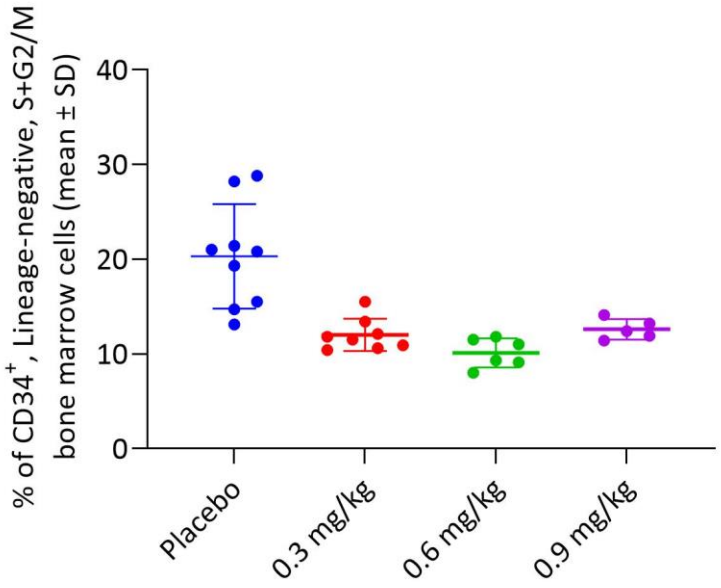
ALRN-6924 Activity in Serum, Bone Marrow, and Hair Follicles: Evidence from Phase 1 Healthy Volunteer Study

Serum MIC-1 levels increased after ALRN-6924 dosing, showing dose-dependent degree and duration of response†



† Macrophage Inhibitory Cytokine-1 (MIC-1, also known as Growth Differentiation Factor-15, or GDF-15) is a p53-dependent serum cytokine

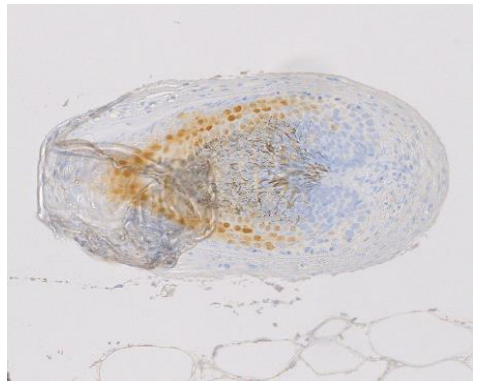
After a single dose, ALRN-6924 reduced the proportion of cycling bone marrow stem cells‡



‡ CD34+, lineage-negative cells measured by flow cytometry from bone marrow biopsies sampled 12 hrs post-dose

Immunohistochemistry in hair follicles 12 hrs after a single ALRN-6924 dose suggests ALRN-6924-dependent p21 induction§

p21 staining (brown) in placebo-treated subject



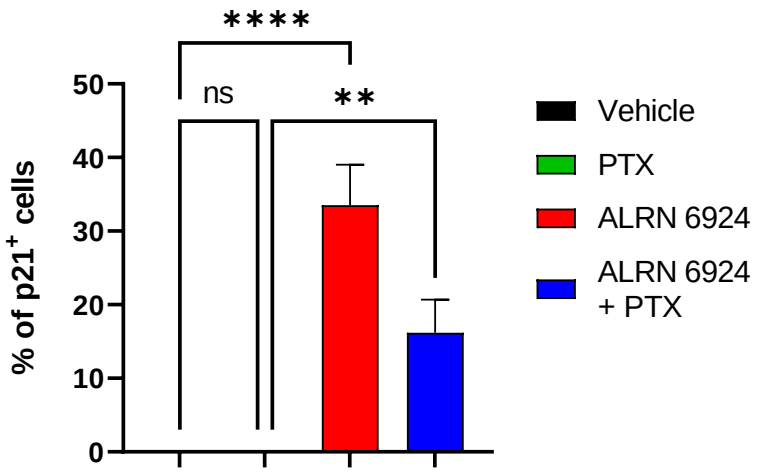
p21 staining (brown) in 0.6 mg/kg treated subject

§ For measurable anagen-phase hair follicles in 2 mm scalp skin punch biopsies sampled 12 hrs post-dose

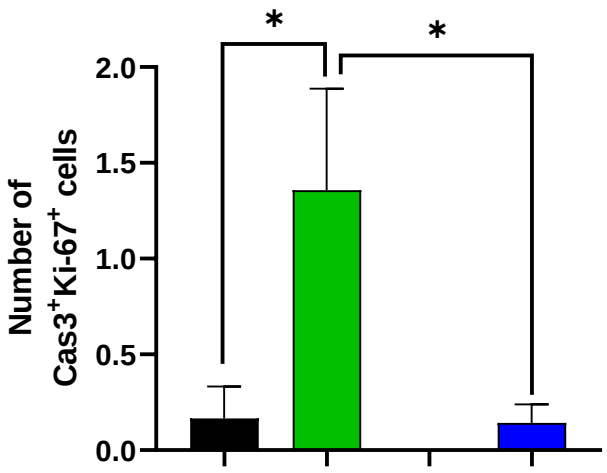
ALRN-6924 Protected Human Hair Follicles (HF) From Taxane-induced Toxicity *Ex Vivo*†

Research collaboration with chemo-induced alopecia expert Prof. Ralf Paus, U Miami, presented at Society for Investigative Dermatology Annual Meeting as late-breaking oral abstract

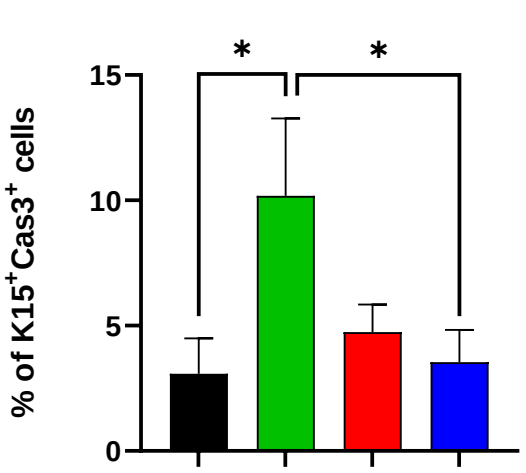
Significantly enhanced p21 in anagen hair matrix of human scalp HF *ex vivo*



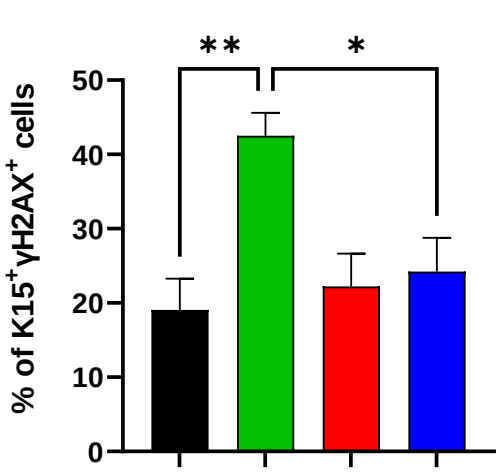
Significantly prevented paclitaxel (PTX)-induced mitotic catastrophe



Significantly protected HF stem cells from apoptosis



Significantly protected HF stem cells from DNA damage

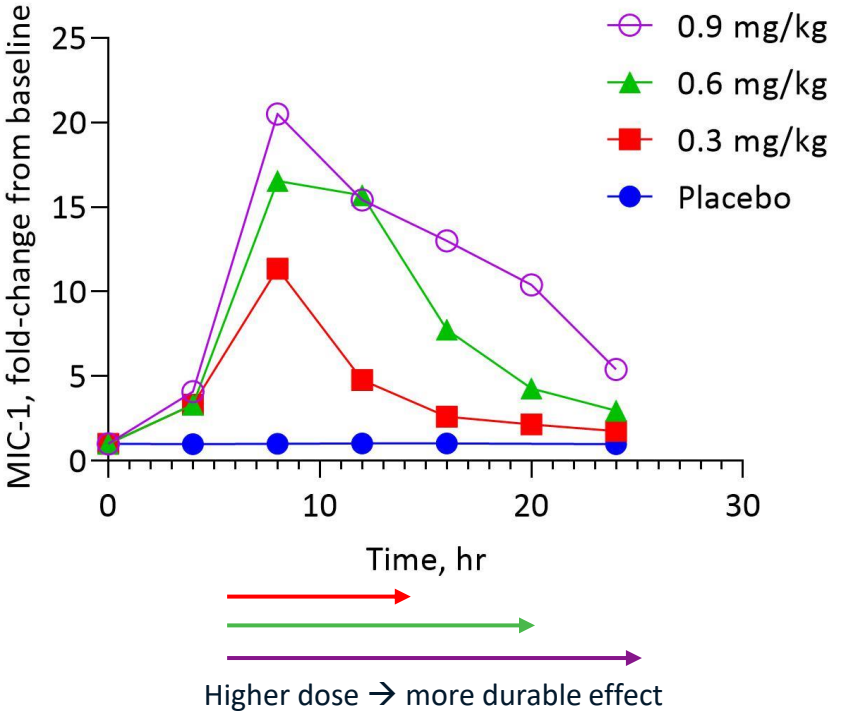


† Hair follicles were microdissected from human occipital scalp tissue from three healthy human donors. Cultured hair follicles were treated with vehicle or 1 µM ALRN-6924 18 hrs then vehicle or 100 nM paclitaxel (PTX) an additional 24 hrs prior to washout and analysis on Day 3.
*p<0.05, **p<0.01; ***p<0.001; ****p<0.0001 by Mann–Whitney test (p21) or Student's t test

Results from 3 Different Trials (Healthy Volunteers, NSCLC, and SCLC) Inform Ongoing Breast Cancer Trial

Key Healthy Volunteer Study Learning

Higher ALRN-6924 doses yielded more durable effects†

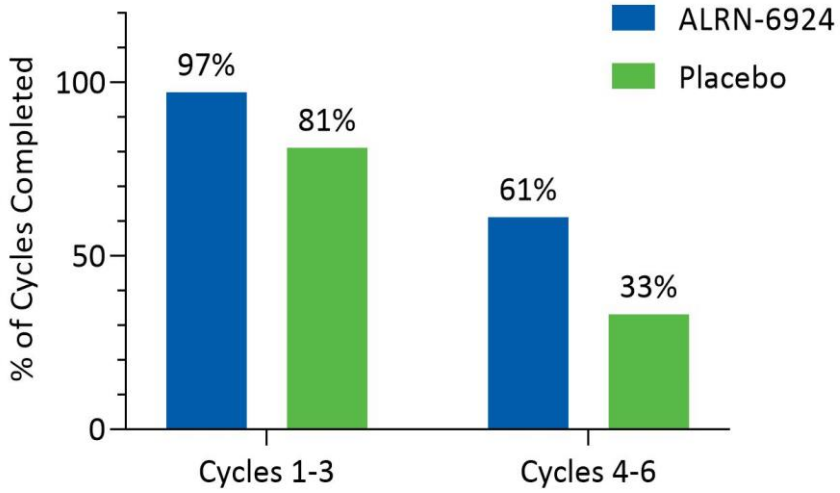


Applied Key Learnings to Breast Cancer Trial

- Increased ALRN-6924 dose: from 0.3 and 0.6 to 1.2 mg/kg
- New 1º endpoint: severe neutropenia in Cycle 1

Key NSCLC Trial Learning

ALRN-6924-treated pts received more chemo than placebo, thus at greater risk to experience toxicities



Median PFS: ALRN-6924 = 4.6 months
Placebo = 3.2 months

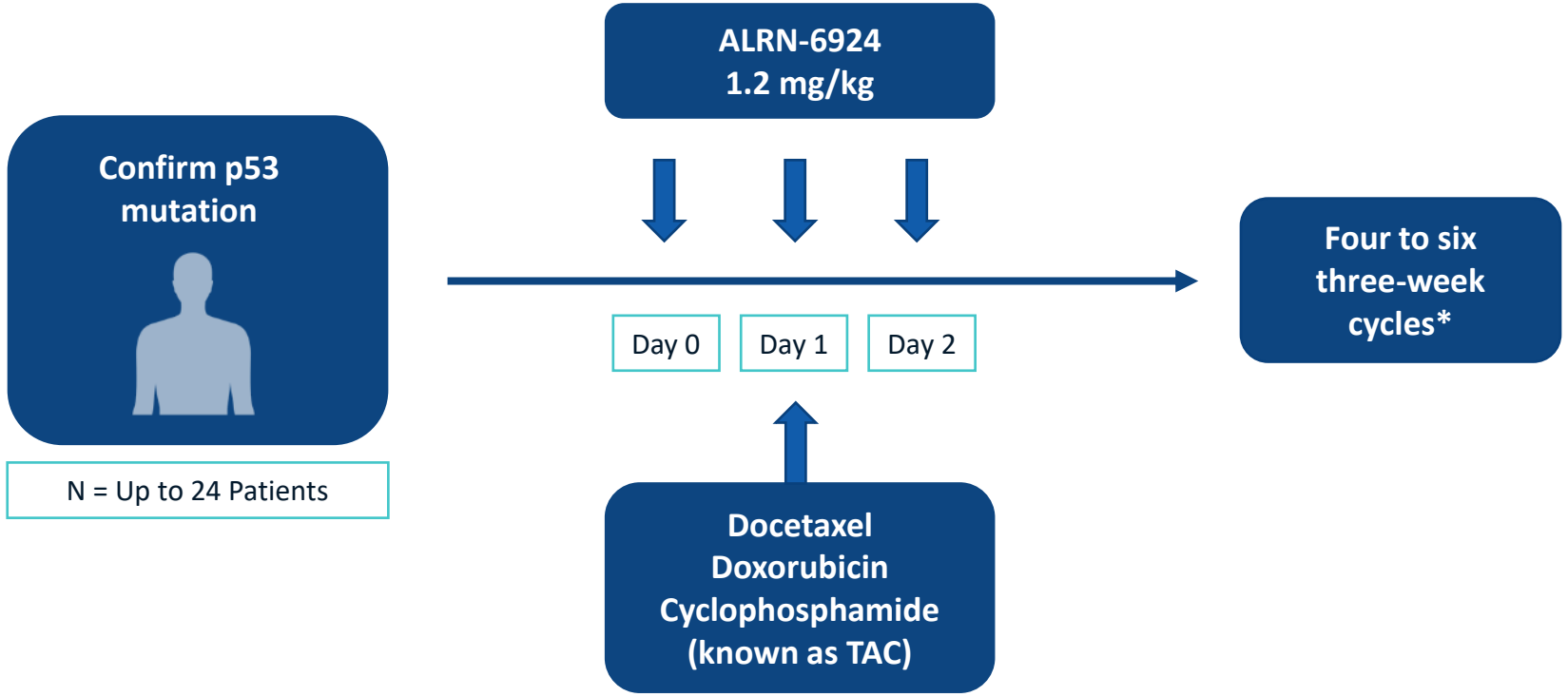
Key SCLC Trial Learning

1.2 mg/kg was well-tolerated and demonstrated robust chemoprotective effect when co-administered w/ topotecan daily for 5 consecutive days‡

†topotecan clearance < 12 hrs vs. longer clearance time (12 to 48+ hrs) for carboplatin, pemetrexed, docetaxel, doxorubicin, cyclophosphamide; ‡ Andric et al., ESMO 2021

Phase 1b Trial in p53-Mutated Breast Cancer Patients Receiving TAC Chemotherapy

Primary endpoint: duration and incidence of severe neutropenia in cycle 1
Key secondary endpoints: chemoprotective effect of ALRN-6924 on alopecia, as well as other toxicities



Protocol Highlights:

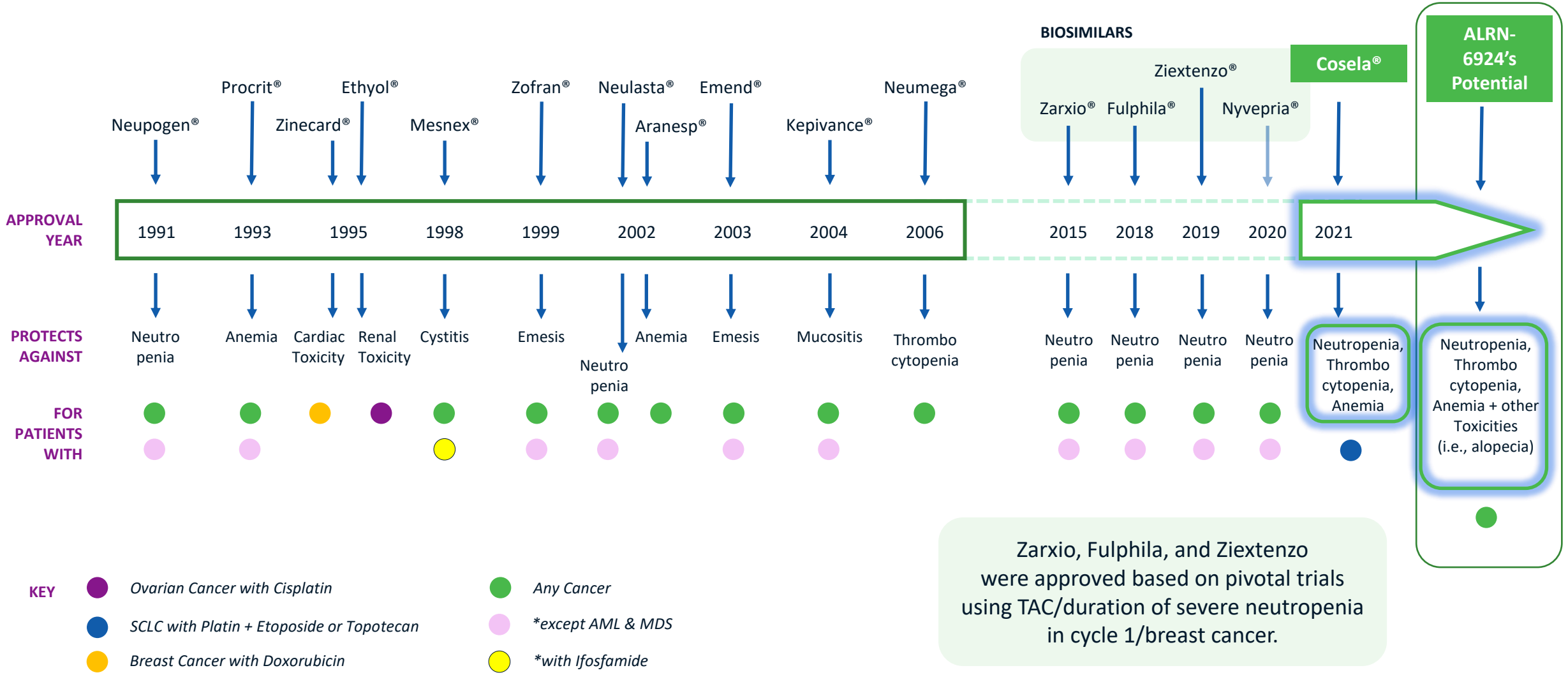
Prophylactic G-CSF not allowed in Cycle 1 (Rescue mandated at 1st occurrence of severe neutropenia)

Patients: non-metastatic, HER2-negative receiving (neo-)adjuvant TAC chemotherapy

* Based on investigators' discretion

Historical Landscape: Single Toxicity Drugs with Primarily Broad Labels (i.e., Indicated to Treat Most Cancers); Innovation Gap from 2006 - 2021

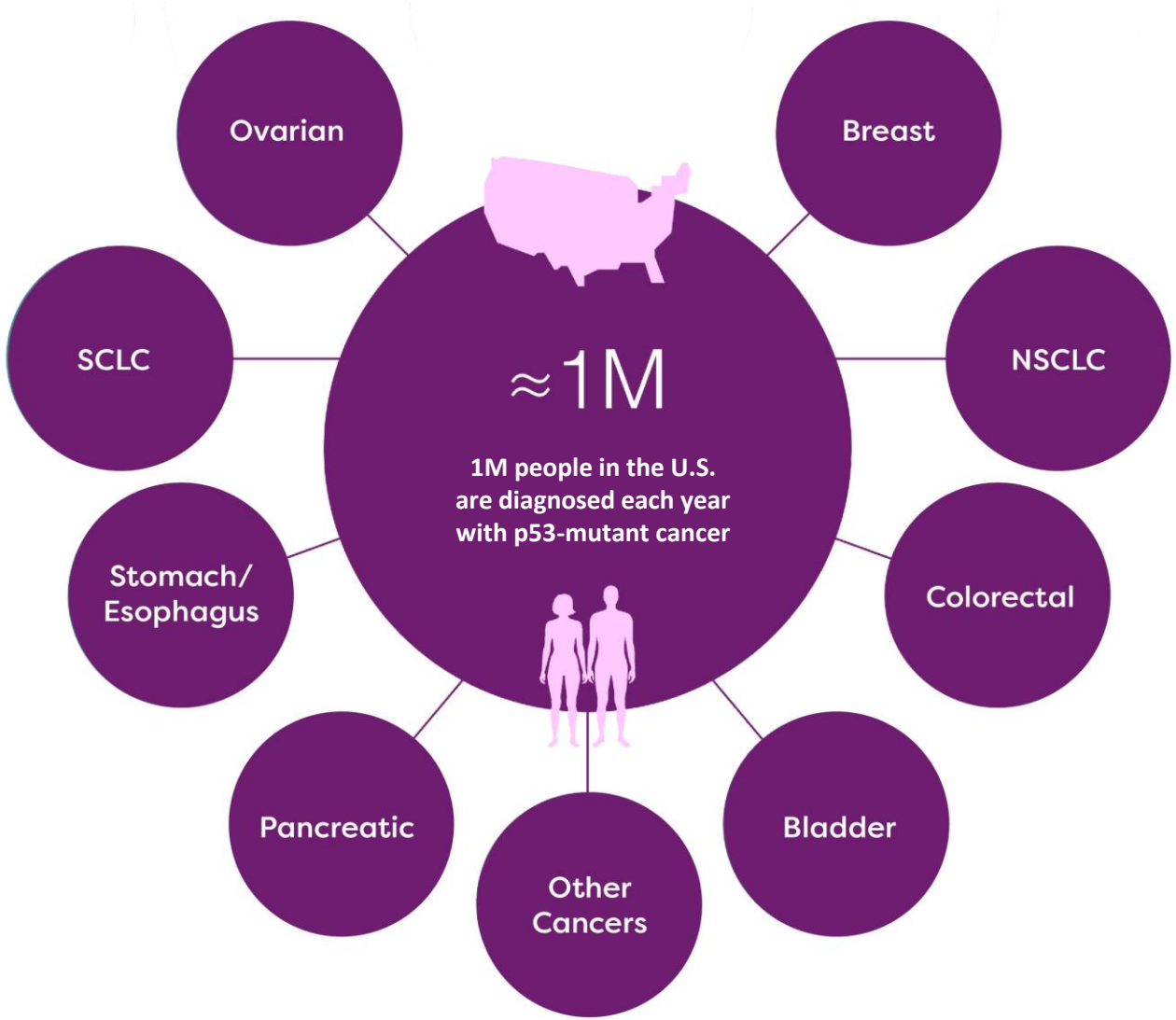
Cell Cycle Arresting Agents Are Poised to Bring New Era of Innovation to Supportive Care



Zarxio, Fulphila, and Ziextenzo were approved based on pivotal trials using TAC/duration of severe neutropenia in cycle 1/breast cancer.

Chemoprotection for p53-Mutated Cancers Is a Large Market Opportunity

p53 mutation is prevalent across most major cancers. We have the potential to bring selective chemoprotection to millions of patients.



50%

Of all cancer patients
have p53-mutated cancer

p53

Most common
cancer mutation

Strong Intellectual Property (IP) Portfolio, Exclusive Worldwide Rights

- Aileron's robust IP portfolio comprises over 160 U.S. and foreign patents, including an additional composition of matter patent for ALRN-6924 in China secured in 2Q 2022.

- These patents and applications include ALRN-6924 methods of manufacture, methods of use, drug product formulations, and compositions of matter.

- Composition of matter patent in the US expires in 2033 with up to 5 additional years subject to patent term extensions.

Aileron maintains exclusive worldwide rights to its proprietary peptide drug technology and ALRN-6924.

Key Financial Highlights

Cash, Cash Equivalents and Investments (as of June 30, 2022)	$32.4M
Expected to Support Operations	Through End of 1Q 2024
Common Shares Outstanding (as of June 30, 2022)	90.8M
Analyst Coverage by H.C. Wainwright, Jones Trading, Ladenburg Thalmann, William Blair	

We Aspire to Make Chemotherapy Safer and Thereby More Effective to Save More Lives

ALRN-6924: Selective chemo-protection without protecting cancer cells

Demonstrated protection against multiple heme toxicities & blood transfusions

Potential to protect multiple tissue types against chemotherapeutic toxicities

Planned breast cancer trial readouts:
Initial data – 4Q 2022
Interim data – 2Q 2023
Topline readout – 3Q 2023

OUR VISION

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

~1 million

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

*HVS=Healthy Volunteer Study

AILERON

Chemoprotection May Transform Chemotherapy Like Anesthesia Transformed Surgery

NASDAQ: ALRN

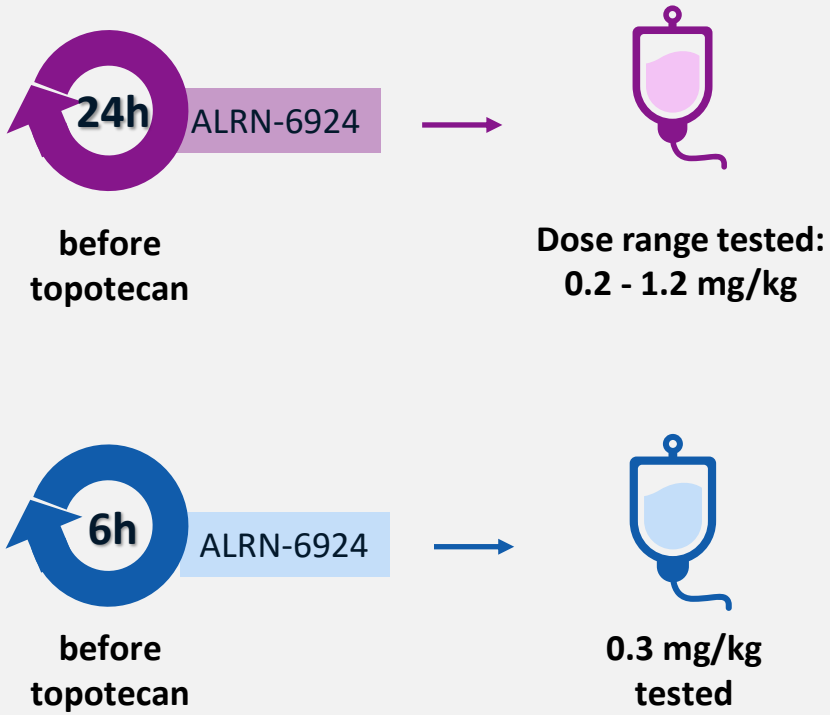
WWW.AILERONRX.COM

Supplementary Information

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

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

ALRN-6924 Proof-of-Concept Phase 1b SCLC Trial Schema



Trial Completed

0.3 mg/kg at 24h before chemotherapy selected for future trials

Final Results Data Presentation ESMO – Sept. 2021

Protocol highlights: Topotecan (1.5 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 g/dL, ANC >1500/µL, Platelets >100k/µL at baseline

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

SCLC Phase 1b: Status and Results

Safety/Tolerability	0.2 mg/kg 24h (N=4)	0.3 mg/kg 24h (N=16)	0.3 mg/kg 6h (N=7)	0.6 mg/kg 24h (N=5)	1.2 mg/kg 24h (N=6)	Total (N=38)
Topotecan cycles (months, median)	5	4	3	1	2.5	3
Topotecan dose reductions (%)	0	19	14	0	17	13
G-CSF use (%)	75	63	71	60	67	66
EPO use (%)	0	0	0	0	0	0
Plt transfusion (%)	0	6	14	40	17†	13
RBC transfusion (%)	0	6	14	60	50‡	21
Neutropenia Grade 4 all cycles (%)	25	44	57	40	17	40
Neutropenia Grade 4 1st cycle (%)	25	**31**	43	40	**17**	37
Febrile neutropenia (%)	0	0	14	0	0	3
Neutropenia Grade 3/4 (%)	75	81	100	100	100	90
Thrombocytopenia Grade 3/4 (%)	50	44	71	40	33	47
Anemia Grade 3/4 (%)	0	19	14	20	17	16

† in one patient in Cycle 8

‡ of the 3 pts in 1.2-cohort, one required multiple RBC Tx from C1D12, and one pt received RBC Tx on C1D17, which would be excluded in a standard RBC Tx analysis (e.g. COSELA, Procrit or Lenalidomide, i.e., excluding initial weeks - 5 weeks in most cases)

Chemoprotection Led to Fewer Dose Reductions of Chemotherapy

Topotecan dose reductions in SCLC patients:

- Without Chemoprotection: 29%[^] to 32%[*] of patients
- With Chemoprotection:
  - with COSELA[#]: 19% of patients
  - with ALRN-6924[§]: 19% of patients

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

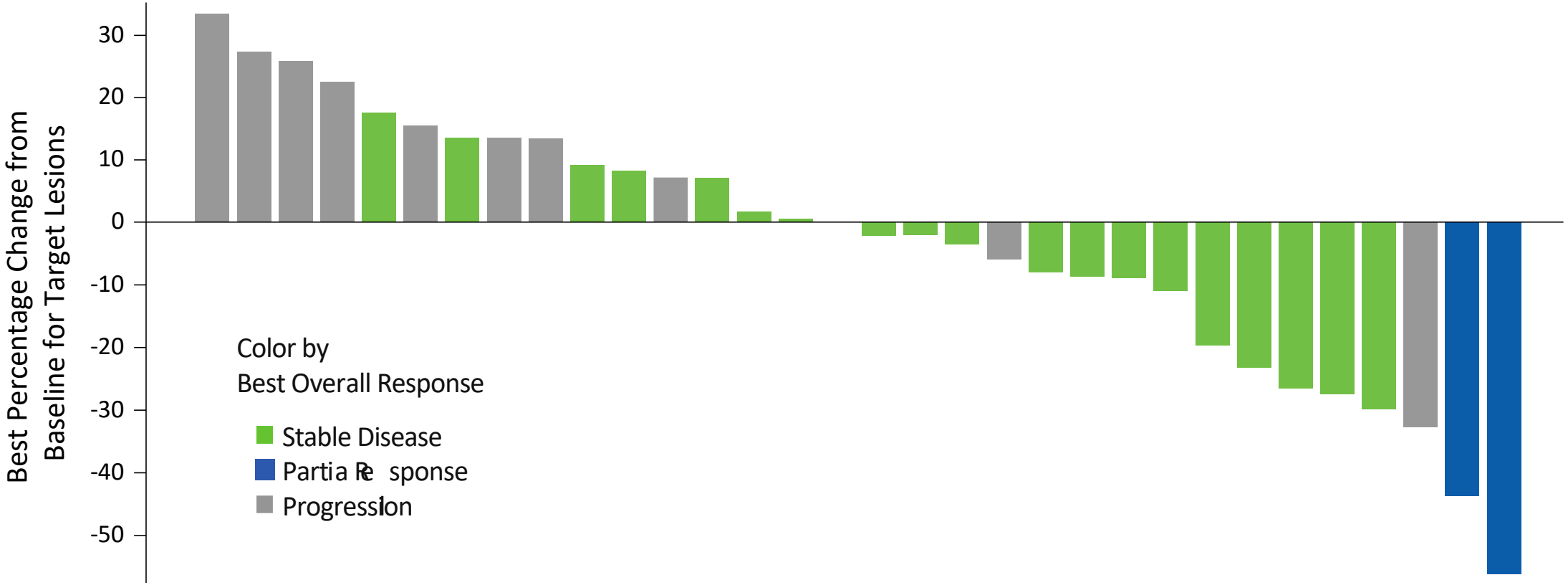
* Hart et al., Adv Ther 2020; topotecan + *placebo*-treated patients (G1-Therapeutics' clinical trial in SCLC patients receiving topotecan)

^ U.S. Prescribing Information for topotecan (2019)

§ 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

Preservation of Chemotherapy's Anti-Cancer Effects During Treatment with ALRN-6924



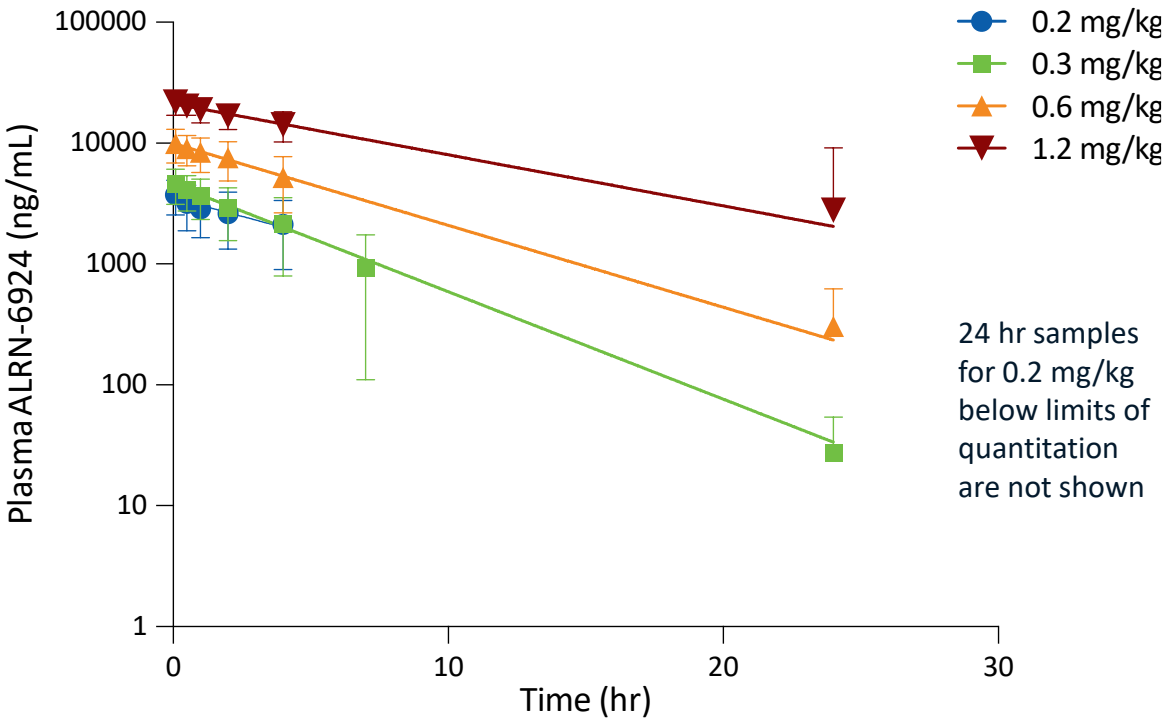
- **The disease control rate (DCR) was 65.6% for 32 patients with radiological evaluation***
- **In historical trials of SCLC patients receiving topotecan, the DCR was between 47% and 61.5%‡**

‡ 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

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



24 hr samples for 0.2 mg/kg below limits of quantitation are not shown

- Mean ± 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†	6	6
$AUC_{0\text{-}24\ hr}$ µg·hr/mL (% CV)	31.8 (53.6)	34.4 (57.0)	83.0 (45.4)	211.9 (26.3)
C_{max} µg/mL (% CV)	3.8 (32.2)	4.9 (31.3)	10.0 (30.9)	22.0 (21.6)
$t_{½}$, 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 $t_{½}$) 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_{max}, slightly greater than dose-proportional AUC

† PK samples unavailable for one 0.3 mg/kg patient

Supplementary Information

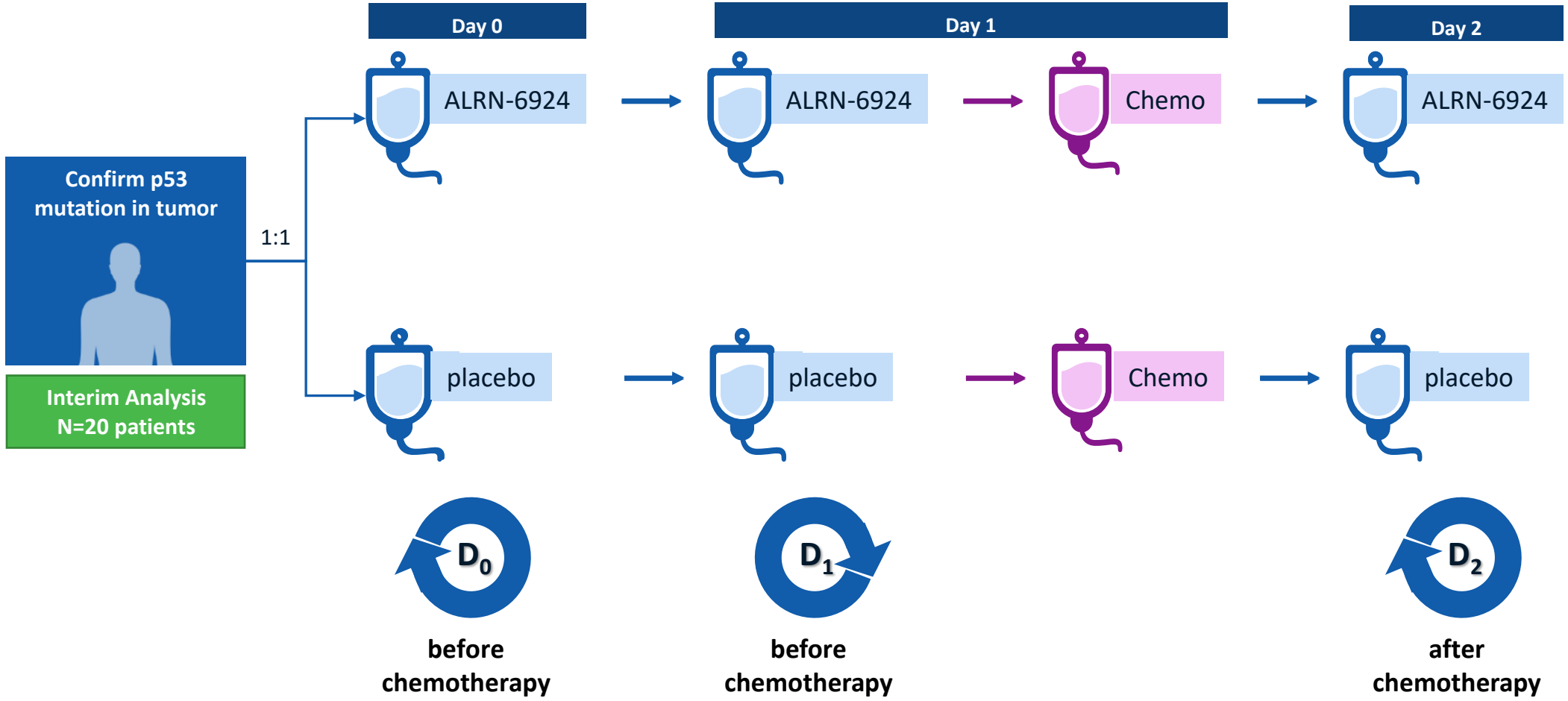
Phase 1b Trial of ALRN-6924 in Patients with Advanced p53-Mutated NSCLC Treated in First Line with Carboplatin/Pemetrexed ± Immune Checkpoint Inhibitor and ALRN-6924 or Placebo

Interim Results
June 2022

NSCLC Trial: Overview & Protocol Highlights

- **Carboplatin/Pemetrexed:** Historically not associated with high frequency of Grade 3/4 hematologic toxicities; no single standout hematologic toxicity
- **Exploratory composite primary endpoint:** Proportion of treatment cycles free of severe neutropenia, thrombocytopenia and anemia, blood transfusions, and the use of growth factors, as well as dose reductions or dose delays in the first 4 cycles
- **Measures to maximize detection of hematologic toxicities:** Hematologic AEs coded using lab values; frequent blood testing; carboplatin dose = AUC6
- **ALRN-6924 was dosed at 0.3 mg/kg:** Based on successful SCLC/topotecan chemoprotection trial (Andric, ESMO 2021)
- **None of the 20 patients in the interim analysis received checkpoint inhibitors (CPI):** Standard of care with CPI = 4 cycles; Standard of care without CPI = 6 cycles

Phase 1b Trial of ALRN-6924 in Advanced p53-Mutated NSCLC Patients Treated in First Line with Carboplatin/Pemetrexed ± Immune Checkpoint Inhibitor† and ALRN-6924 or Placebo



Demographics and Baseline Characteristics

	ALRN-6924 (n=11)†	Placebo (n=9)	Overall (n=20)
Age, mean (range)	66.3 (54, 74)	70.0 (62, 78)	68.0 (54, 78)
Gender (n, % male)	9 (88.1)	4 (44.4)	13 (65.0)
Race (%)			
Caucasian	11 (100)	9 (100)	20 (100)
Ethnicity (n, %)			
Hispanic or Latino	0	1 (11)	1 (5)
Not Hispanic or Latino	11 (100)	8 (89)	19 (95)
Baseline ECOG, n (%)			
0	8 (72.7)	7 (77.8)	15 (75.0)
1	3 (27.3)	2 (22.2)	5 (25.0)
2+	0	0	0

† One patient was randomized to the placebo arm, but treatment was initiated with ALRN-6924 due to a dispensing error, and the decision was made to maintain that patient on ALRN-6924.

Max Grade of Neutropenia, Thrombocytopenia, or Anemia per Patient per Cycle

		Neutropenia						Thrombocytopenia						Anemia					
Treatment	**Patient**	**1**	**2**	**3**	**4**	**5**	**6**	**1**	**2**	**3**	**4**	**5**	**6**	**1**	**2**	**3**	**4**	**5**	**6**
ALRN-6924 (n=11)	1	1	2	0	1	1	0	1	0	0	0	0	0	0	0	0	0	0	0
	2	1	1	0	0	0	1	1	3	1	1	1	3	0	1	1	1	1	2
	3	2	3	3	2			1	1	2	1			1	1	2	1		
	4*	3	4	3	3	4	3	0	3	3	4	4	4	1	2	3	3	3	3
	5	1	2					1	3					2	2				
	6	0	1	1	1	1	1	0	1	0	0	0	0	0	1	2	2	2	2
	7	0	1	1				0	1	0				1	1	2			
	8	1	2	3	3	3	2	1	2	2	2	1	1	1	1	1	1	1	1
	9	0	1	3	0	0		1	1	3	1	0		0	1	2	2	2	
	10	3	2	1	0			1	2	3	3			0	1	1	1		
	11	0	1	0	0			0	0	0	0			1	1	1	1		
Placebo (n=9)	12	0						0						1					
	13	1	1	2	2	1	1	2	1	2	3	2	3	1	1	1	2	1	2
	14	0	1	0	3			0	0	0	4			2	2	3	3		
	15	1	0					1	0					2	2				
	16	0	0	0	1			2	0	1	4			0	0	0	1		
	17	0						1						3					
	18	1	0	2	0	0		1	1	1	0	1		0	1	2	2	2	
	19	1	2	2	2			0	1	0	1			0	0	0	1		
	20	1	1	2	3			1	2	2	3			1	1	1	2		

* Despite 15 instances of Grade ≥3 heme toxicities, patient completed 6 cycles, achieved partial response, investigator reported patient "felt great"

Completed 6 cycles

- Of 83 cycles administered, Grade ≥3 toxicities were observed in 25 (30%). Only 3 were in Cycle 1 (12%)
- Grade 4 toxicities were infrequent, occurring in one pt on ALRN-6924 and two pts on placebo
- 5/11 (45%) on ALRN-6924 completed 6 cycles, vs. 1/9 (11%) on placebo
- 18 cycles showed 28 Grade ≥3 toxicities on ALRN-6924; 7 cycles with 10 instances on placebo
- One pt (#4) on ALRN-6924 accounted for 15 of 28 Grade ≥3 instances (53%)*

Results by Treatment Group

Average cycles of chemotherapy completed by patients: 4.7 on ALRN-6924, 3.4 on Placebo

	Treatment (n of pts)	Primary composite endpoint: Cycles without Grade ≥3 cytopenia or DD, DR, transfusion, growth factor	Pts with grade ≥3 neutropenia n (%)	Pts with grade ≥3 thrombo-cytopenia n (%)	Pts with grade ≥3 anemia n (%)	Total cycles completed†
Cycles 1-4	ALRN-6924 (n=11)	23 / 41 (56%)	5 (45%)	5 (45%)	1 (9%)	41 / 44 possible (93%)
	Placebo (n=9)	14 / 28 (50%)	2 (22%)	4 (44%)	2 (22%)	28 / 36 possible (78%)
Cycles 1-6	ALRN-6924 (n=11)	29 / 52 (56%)	5 (45%)	5 (45%)	1 (9%)	52 / 66 possible (79%)
	Placebo (n=9)	16 / 31 (52%)	2 (22%)	4 (44%)	2 (22%)	31 / 54 possible (57%)

DD Dose Delay, DR Dose reduction

† Completed cycles = received ≥1 dose of ALRN-6924 and chemotherapy.

Summary of Safety Findings

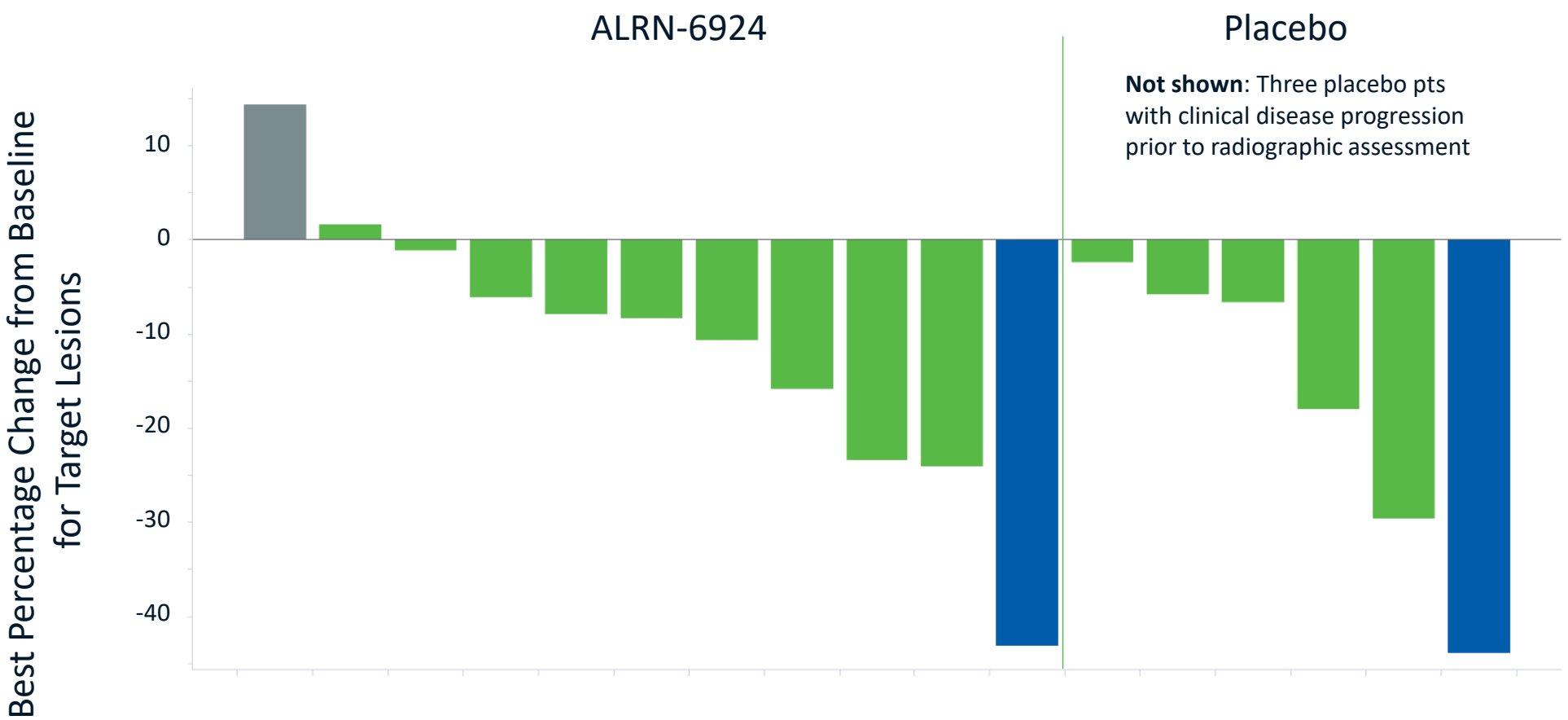
	ALRN-6924 (N=11) n (%)	Placebo (N=9) n (%)
Any TEAE	8 (72.7)	8 (88.9)
Serious TEAEs	2 (18.2)	2 (22.2)
Grade ≥3 Higher TEAEs	7 (63.6)	5 (55.6)
TEAEs Leading to Discontinuation of ALRN-6924/Placebo	0	1 (11.1)[&]
TEAEs Leading to Discontinuation of Pemetrexed	0	1 (11.1)
TEAEs Leading to Discontinuation of Carboplatin	0	1 (11.1)
TEAEs Leading to Death	1 (9.1)*	0
TEAEs Related to ALRN-6924/Placebo	0	1 (11.1)
TEAEs Related to pemetrexed	7 (63.6)	7 (77.8)
Serious TEA Related to pemetrexed	2 (18.2)	1 (11.1)
TEAEs Related to carboplatin	7 (63.6)	7 (77.8)
Serious TEA Related to carboplatin	2 (18.2)	1 (11.1)

- **Anemia (any grade): 4/11 (36%) on ALRN-6924 vs. 6/9 (67%) on placebo**
- **Fatigue (any grade): 2/11 (18%) on ALRN-6924 vs. 5/9 (56%) on placebo**

TEAE Treatment-emergent Adverse Event
* Death due to disease progression after completing 2 cycles of chemotherapy
[&] TEAE deterioration of general health

No evidence that ALRN-6924 Protected p53-mutant Tumors

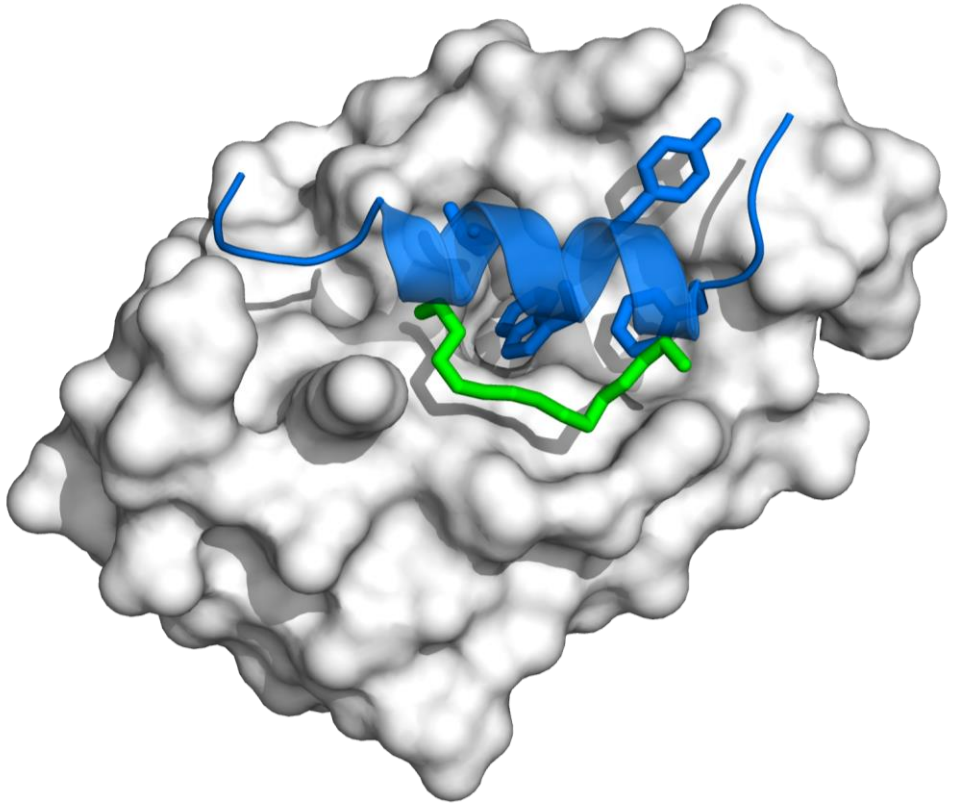
Median progression-free survival: 4.6 months ALRN-6924, 3.2 months placebo



Supplementary
Non-Clinical Information About ALRN-6924

Structure and Key Design Properties of ALRN-6924

Structure based on the α-helical domain of p53, with chemical modifications



ALRN-6924·MDMX co-crystal structure

The hydrocarbon staple and other modifications ensure:

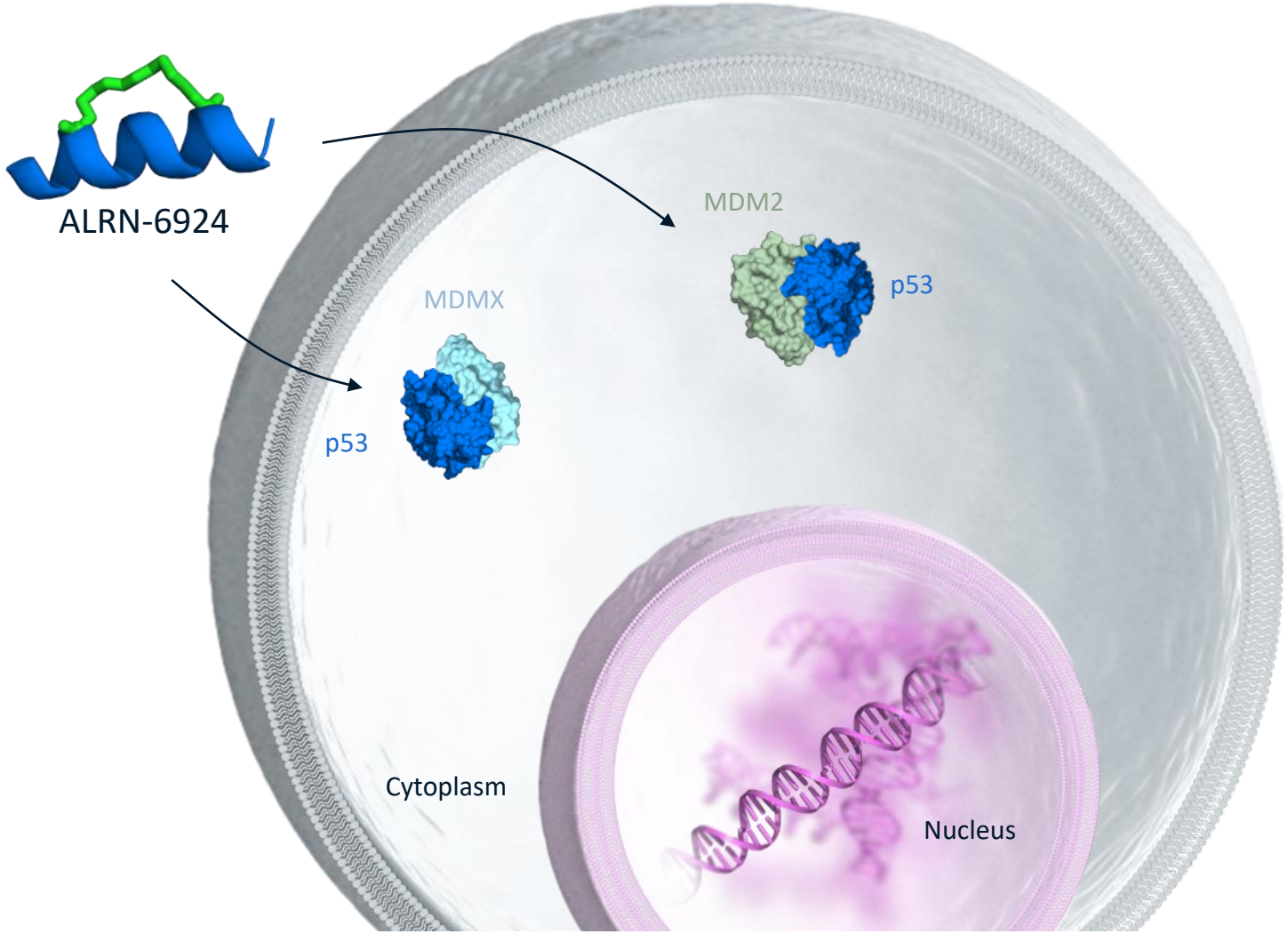
I. Protection from proteolytic cleavage

II. Permeation of cell membranes and cell entry

III. High affinity binding to its targets

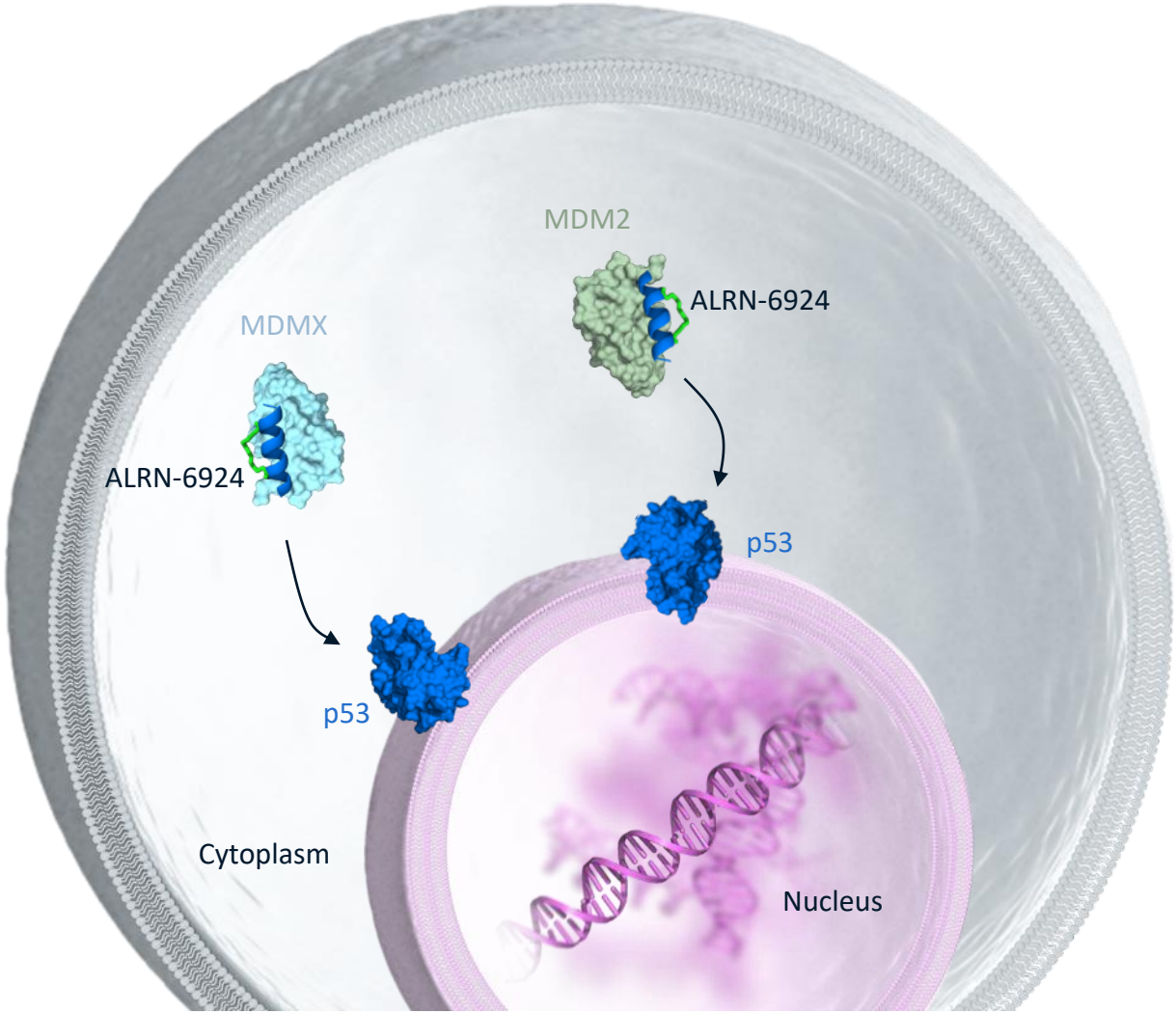
IV. Preclinical and clinical on-target, on-mechanism effects

ALRN-6924 Mechanism of Action in Wild-Type p53 Cells



ALRN-6924 is a decoy that mimics p53 and selectively binds to MDMX + MDM2, releasing p53 and, thereby, upregulating p21 to induce cell cycle arrest

ALRN-6924 Mechanism of Action in Wild-Type p53 Cells



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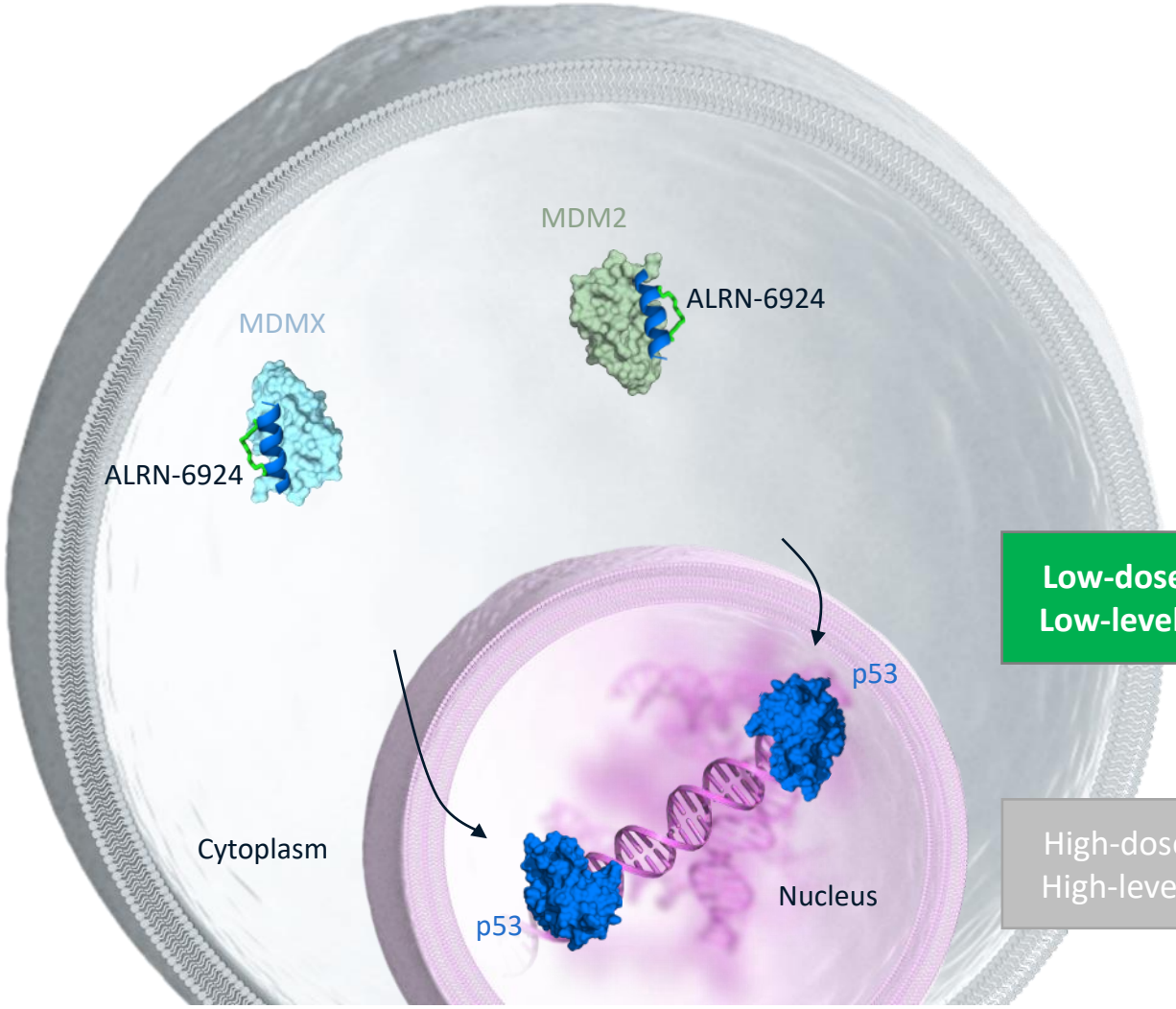
ALRN-6924 Mechanism of Action in Wild-Type p53 Cells



Low-dose ALRN-6924
Low-level p53 release

→ **p21 mediated-cell cycle arrest[1]**

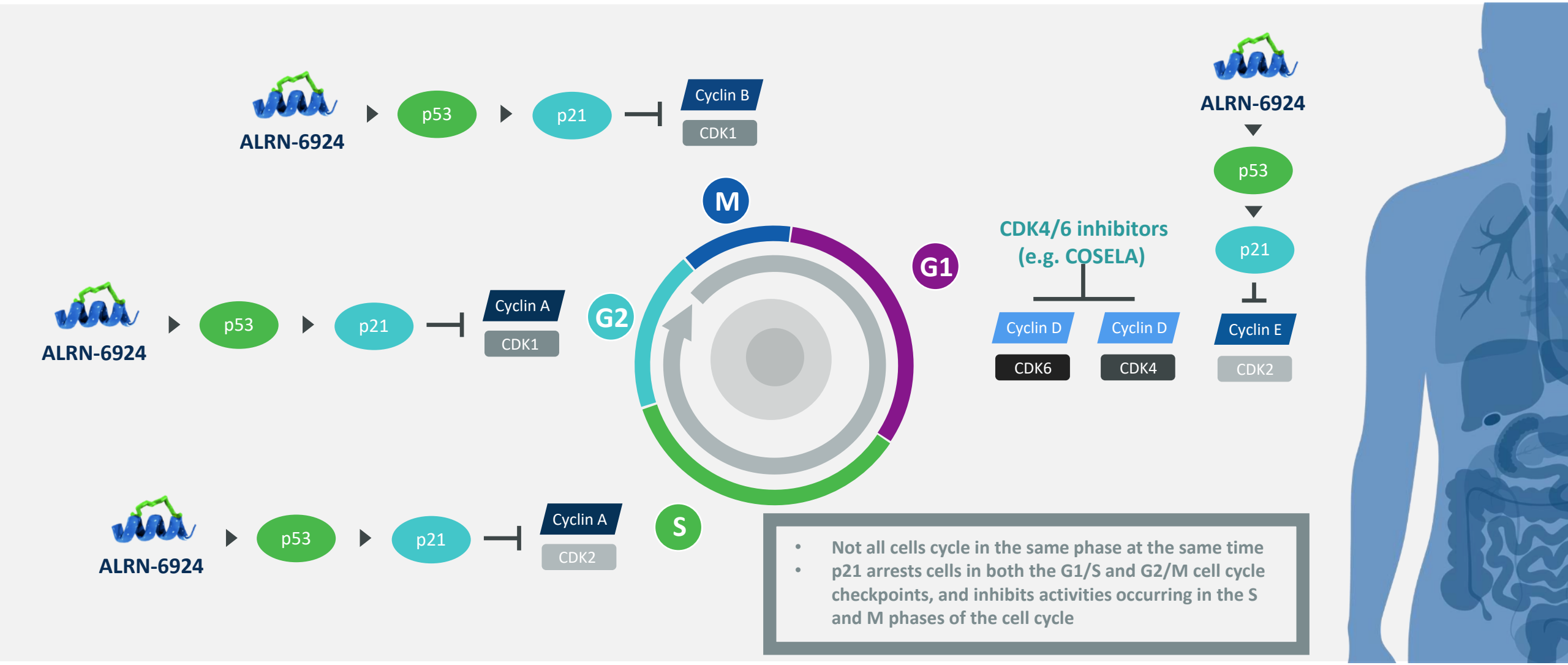
High-dose ALRN-6924
High-level p53 release

→ PUMA-, NOXA-mediated apoptosis[1]

ALRN-6924 is a decoy that mimics p53 and selectively binds to MDMX + MDM2, releasing p53 and, thereby, upregulating p21 to induce cell cycle arrest

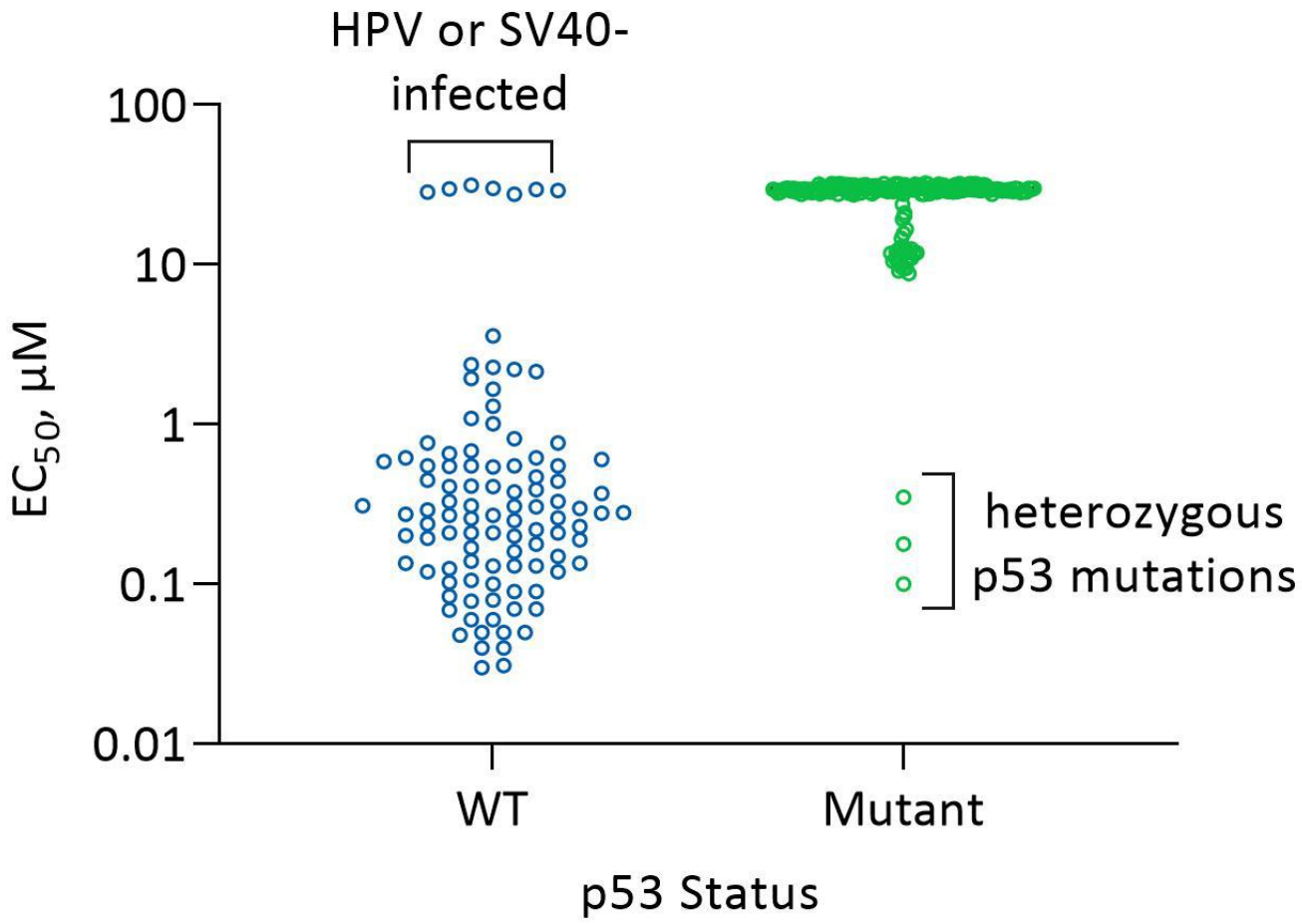
[1] Chen; Cold Spring Harb Perspect Med. 2016 Mar 1

ALRN-6924 Best-in-Class Potential in Chemoprotection: Effects on All Phases of Cell Cycle



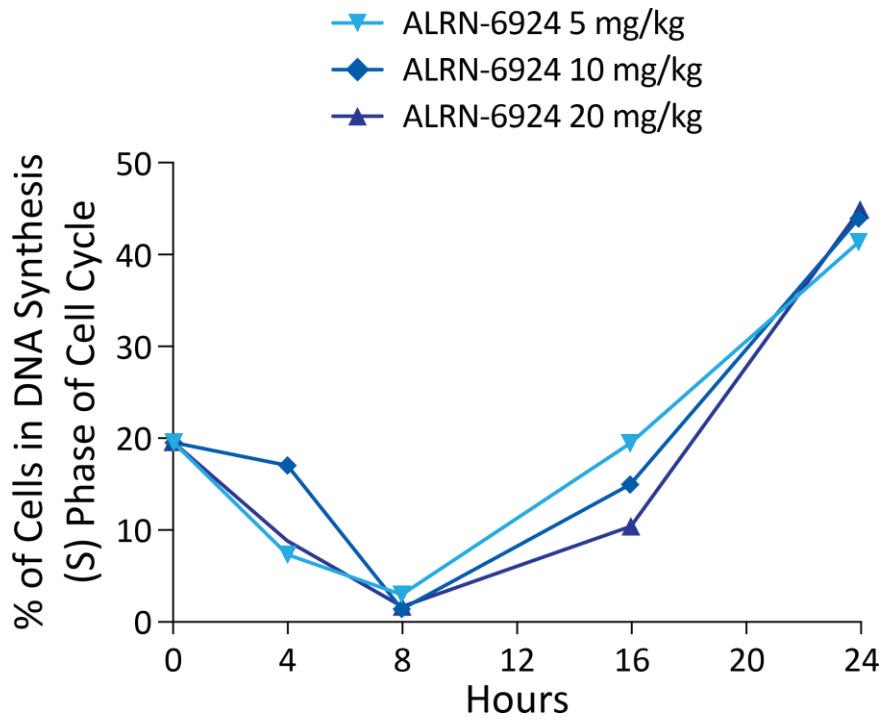
ALRN-6924 Potently Inhibited Proliferation in Wild-Type p53 Cells; Mutant Cells Are Insensitive

ALRN-6924 studies in 300 cell lines show potent, on-mechanism cellular activity



Pairawan et al, "First in class dual MDM2/MDMX inhibitor ALRN-6924 enhances antitumor efficacy of chemotherapy in TP53 wild-type hormone receptor-positive breast cancer models." Breast Cancer Research, 2021; 23: 29.

ALRN-6924 Induced Transient, Reversible CCA in Murine Hematopoietic Stem and Progenitor Cells (HSPCs) *in vivo*



AILERON

Chemoprotection May Transform Chemotherapy Like Anesthesia Transformed Surgery

NASDAQ: ALRN

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