AILERON

Transforming the Experience of Chemotherapy for Cancer Patients

CORPORATE PRESENTATION

MAY 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 Aileron'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 or with respect to the matters 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 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 that could transform current standards of care for neutropenia, anemia and thrombocytopenia, as well as other 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

Three projected catalysts in 2022

2Q22 (June): Interim results from ongoing NSCLC clinical trial

4Q22: Topline results from ongoing NSCLC clinical trial

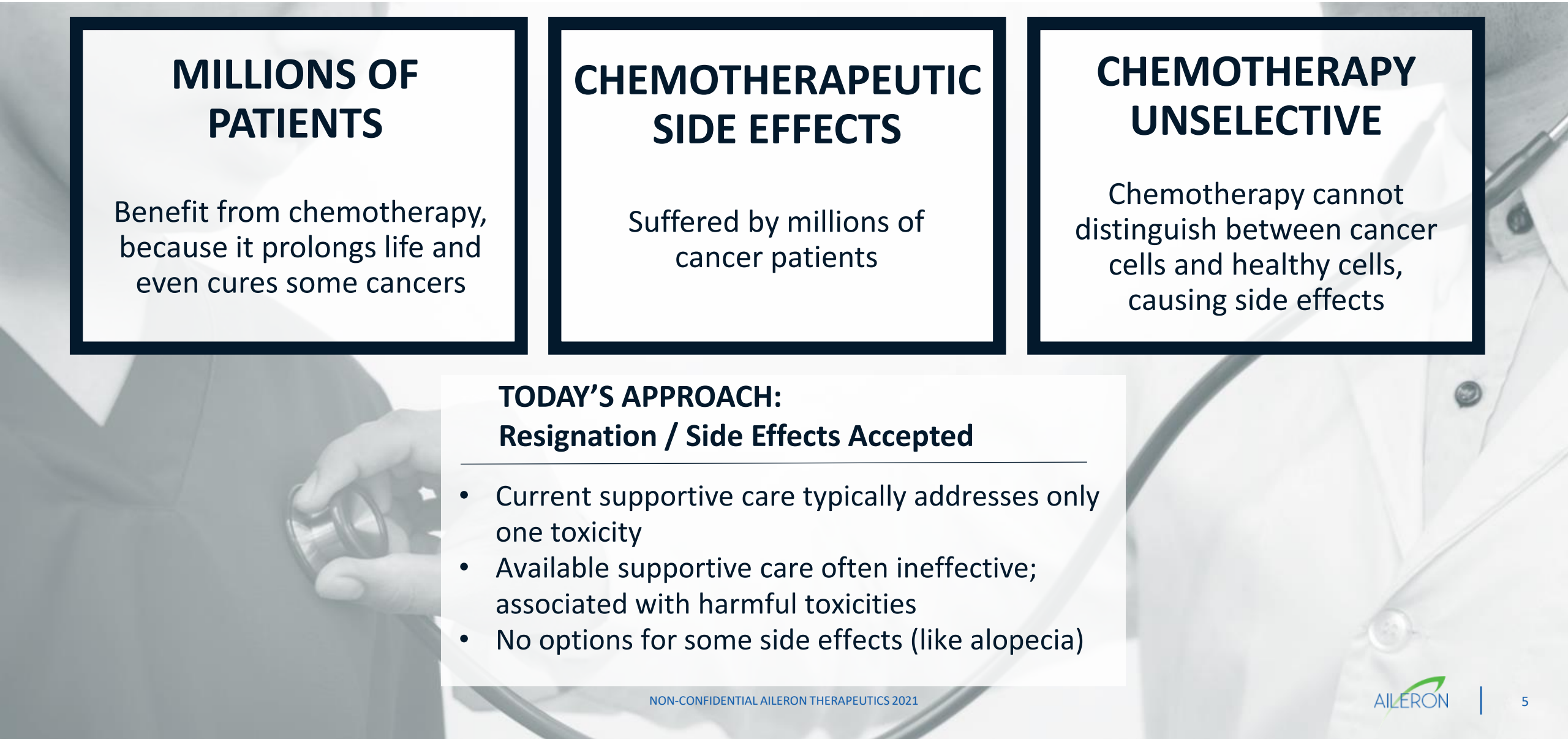
4Q22: Initial interim results from ongoing neoadjuvant breast cancer trial

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

NSCLC = non-small cell lung cancer

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, causing side effects

TODAY'S APPROACH:
Resignation / Side Effects Accepted

- Current supportive care typically addresses only one toxicity
- Available supportive care often ineffective; associated with harmful toxicities
- No options for some side effects (like alopecia)

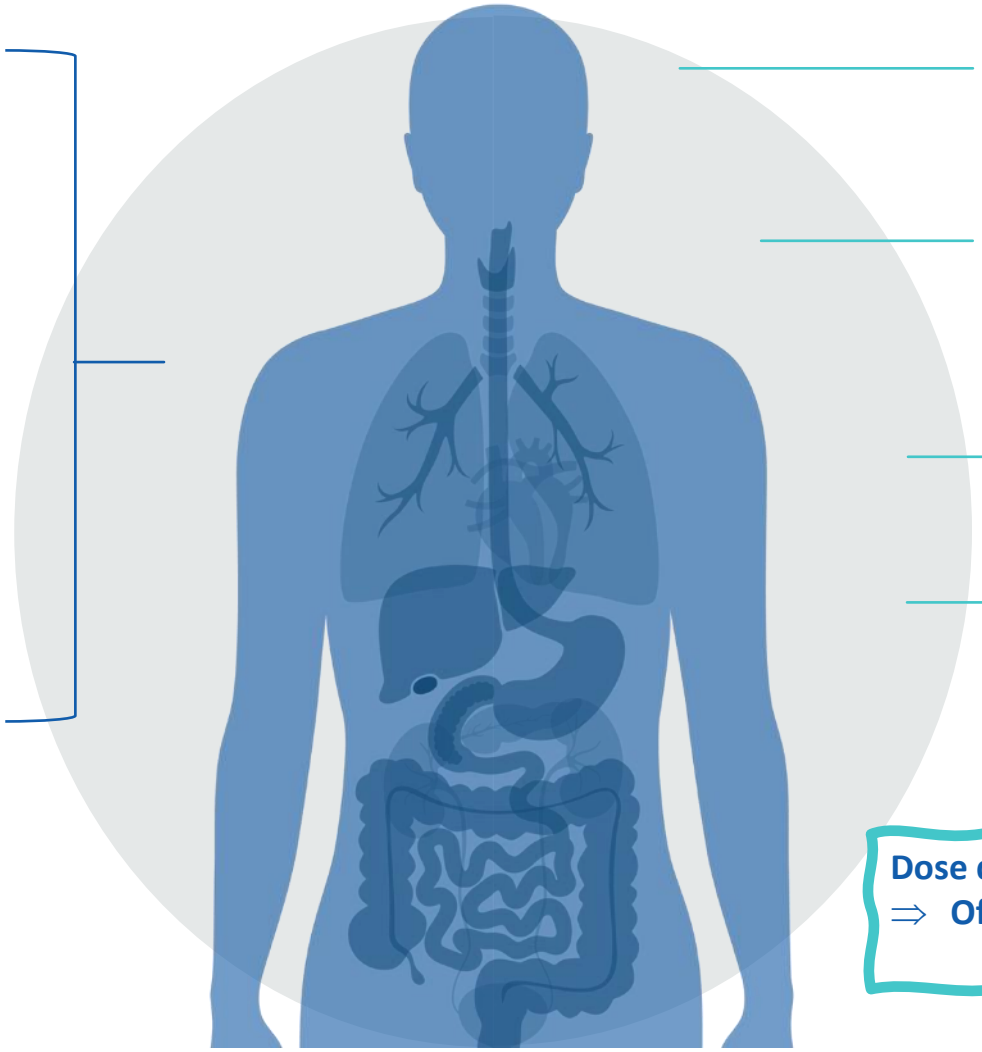
Broad Range of Chemotherapy-Induced Toxicities; Different Chemotherapies Have Different Toxicity Profiles

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; Different Chemotherapies Have Different Toxicity Profiles

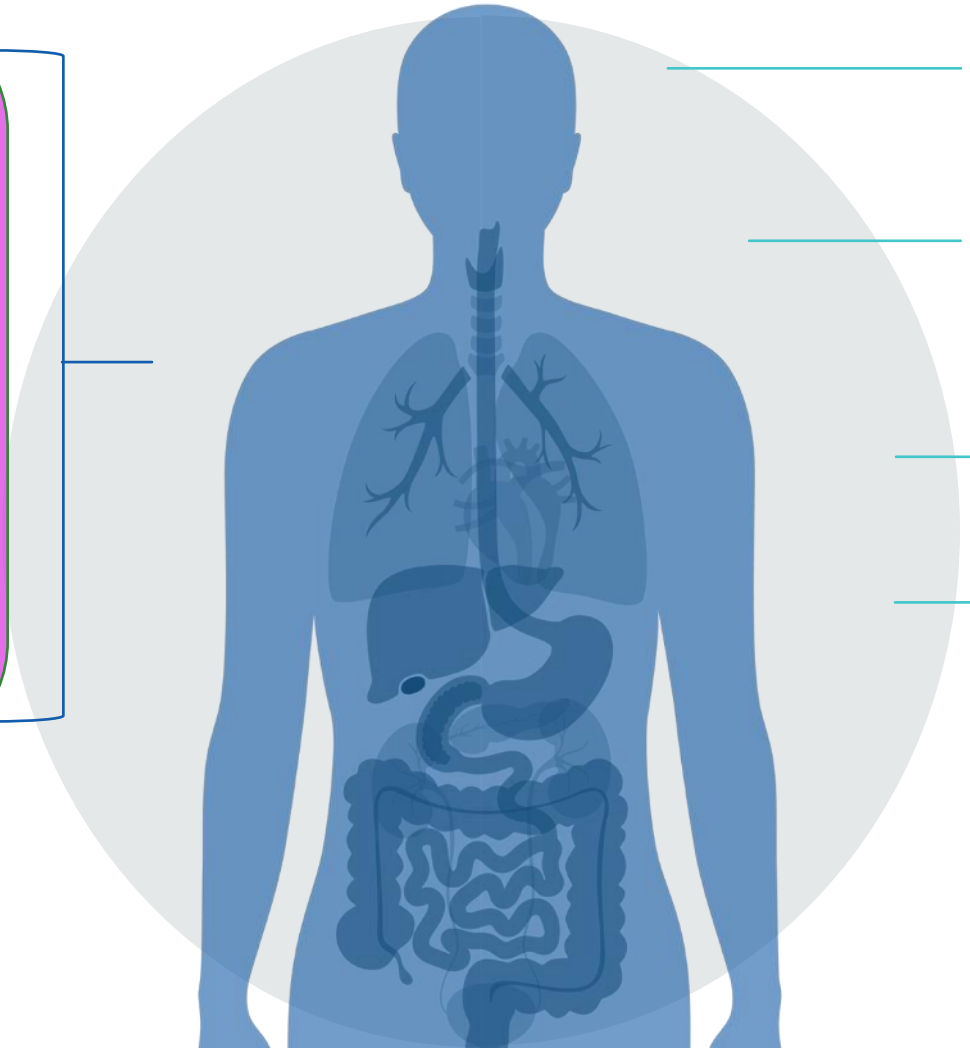
ALRN-6924 harnesses a universal mechanism common to normal cells to protect them against chemotherapy-induced side effects

Severe Neutropenia
(serious infection, fever, sepsis)

Severe Anemia
(weakness, fatigue)

Severe Thrombocytopenia
(excessive bleeding)

Focus of Trial with ALRN-6924 + topotecan in SCLC



Alopecia (hair loss)

Mucositis (mouth sores)

Fatigue, Weakness, Asthenia

Vomiting, Diarrhea, Bloating

Dark purple = occurs frequently
Light purple = occurs occasionally

Broad Range of Chemotherapy-Induced Toxicities; Different Chemotherapies Have Different Toxicity Profiles

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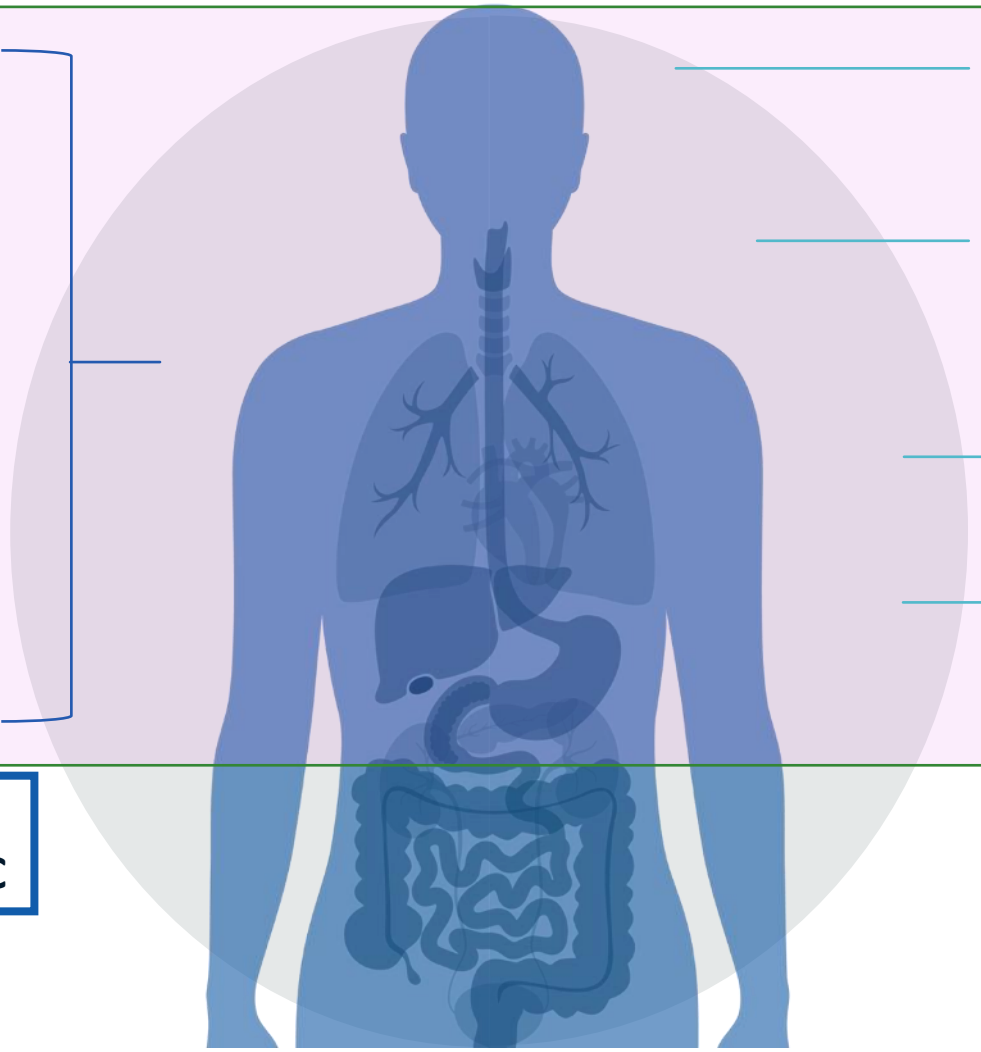


Alopecia (hair loss)

Mucositis (mouth sores)

Fatigue, Weakness, Asthenia

Vomiting, Diarrhea, Bloating

Focus of Trial with ALRN-6924 + carboplatin/pemetrexed in NSCLC

Dark purple = occurs frequently
Light purple = occurs occasionally

Broad Range of Chemotherapy-Induced Toxicities; Different Chemotherapies Have Different Toxicity Profiles

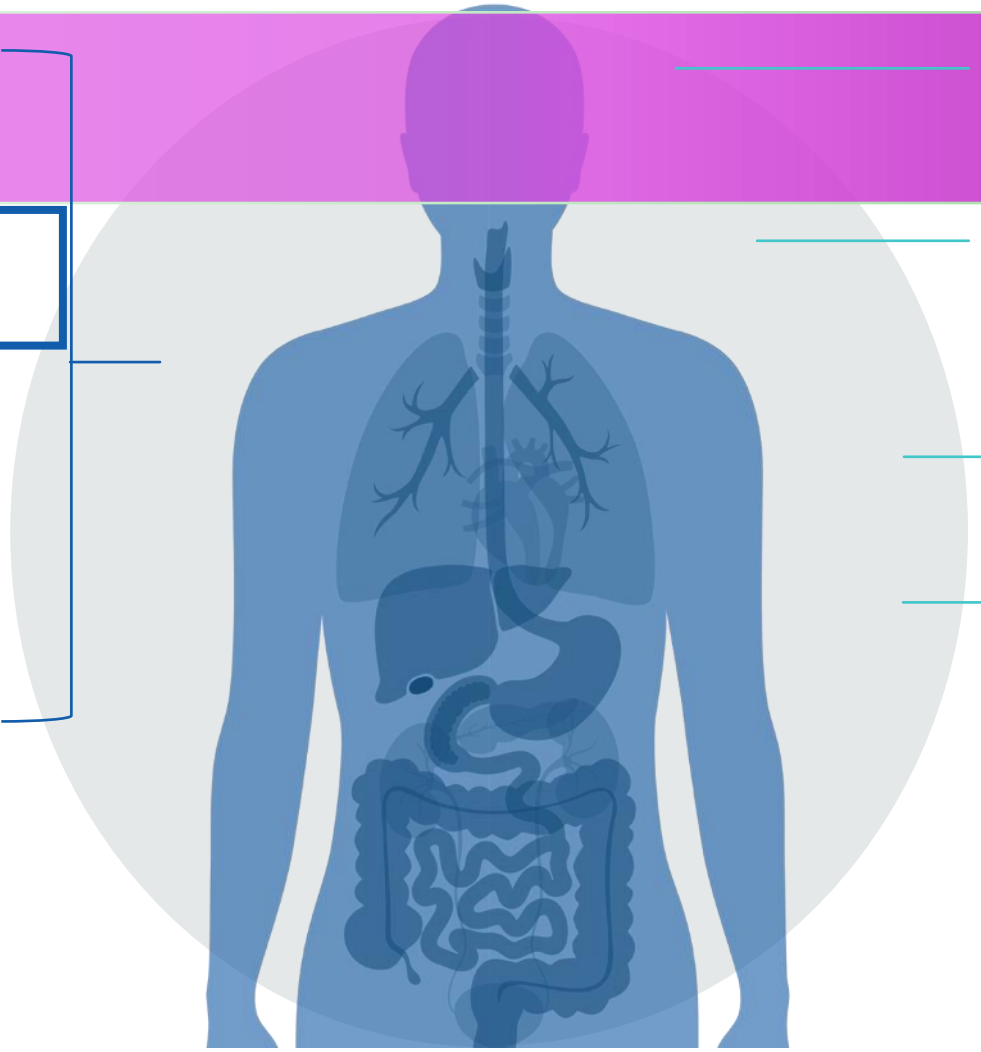
ALRN-6924 harnesses a universal mechanism common to normal cells to protect them against chemotherapy-induced side effects

Severe Neutropenia
(serious infection, fever, sepsis)

Focus of Trial with ALRN-6924 + AC and D in Breast Cancer

Severe Anemia
(weakness, fatigue)

Severe Thrombocytopenia
(excessive bleeding)



Alopecia (hair loss)

Mucositis (mouth sores)

Fatigue, Weakness, Asthenia

Vomiting, Diarrhea, Bloating

Dark purple = occurs frequently
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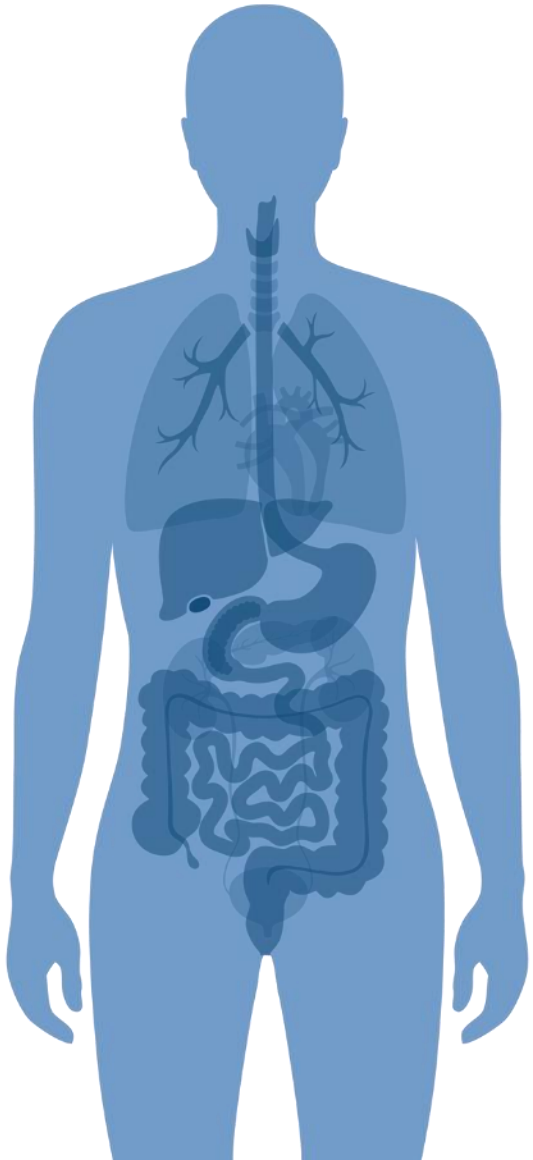
Poor Standard of Care for Management of Bone Marrow Toxicities

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



SEVERE 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

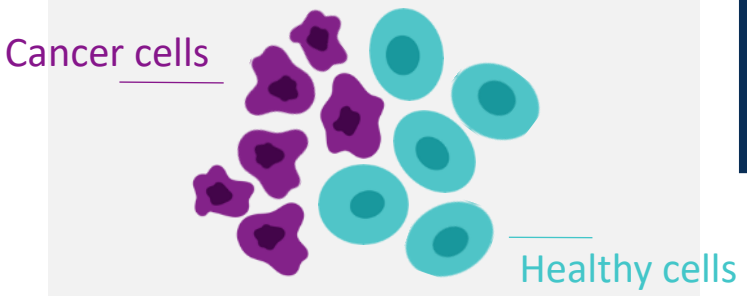
Standard of Care: No drugs used as standard of care – platelet transfusions instead
Clinical Issues:

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

Basic Principles to Selectively Protect Against Chemotherapy-Induced Side Effects

CURRENT PARADIGM:

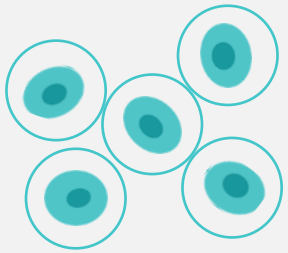
Chemotherapy destroys healthy cells and cancer cells that are cycling (= undergoing cell division process)



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

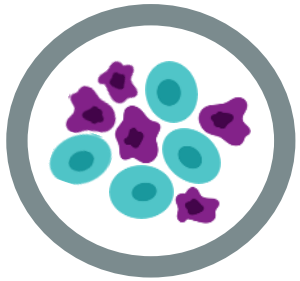
Healthy Cells Have Normal p53. ALRN-6924 Activates Normal p53, Pausing Cell Cycle in Normal Cells, but not in Cancer Cells with Mutant p53

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

Patient with p53-mutant cancer receives ALRN-6924 before chemotherapy

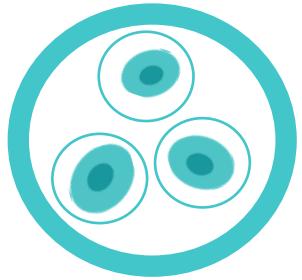
IV administration
1-hour infusion

→



ALRN-6924 activates normal p53 in healthy cells

→

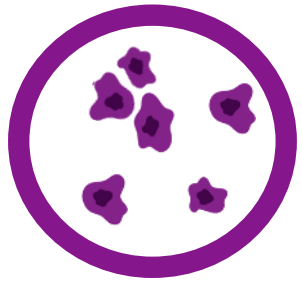


Activated normal p53 upregulates p21, which pauses cell cycling in healthy cells

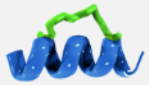
→

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

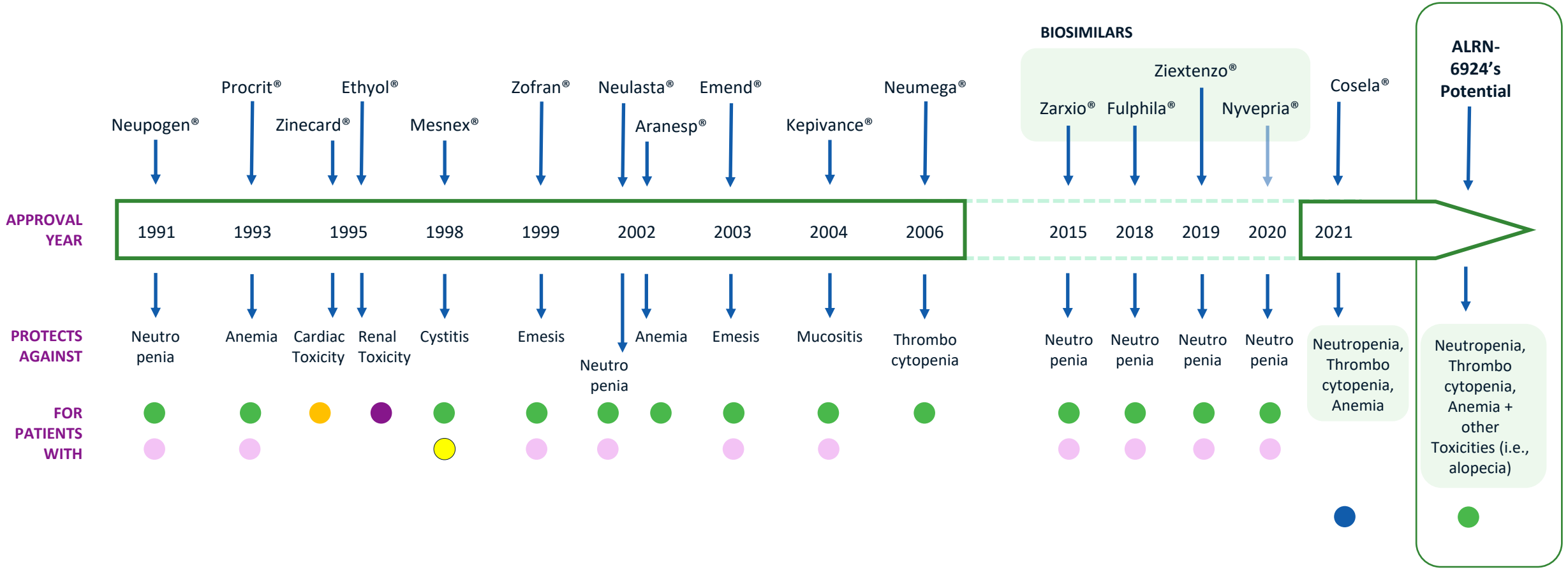
No protection of p53-mutant cancer cells

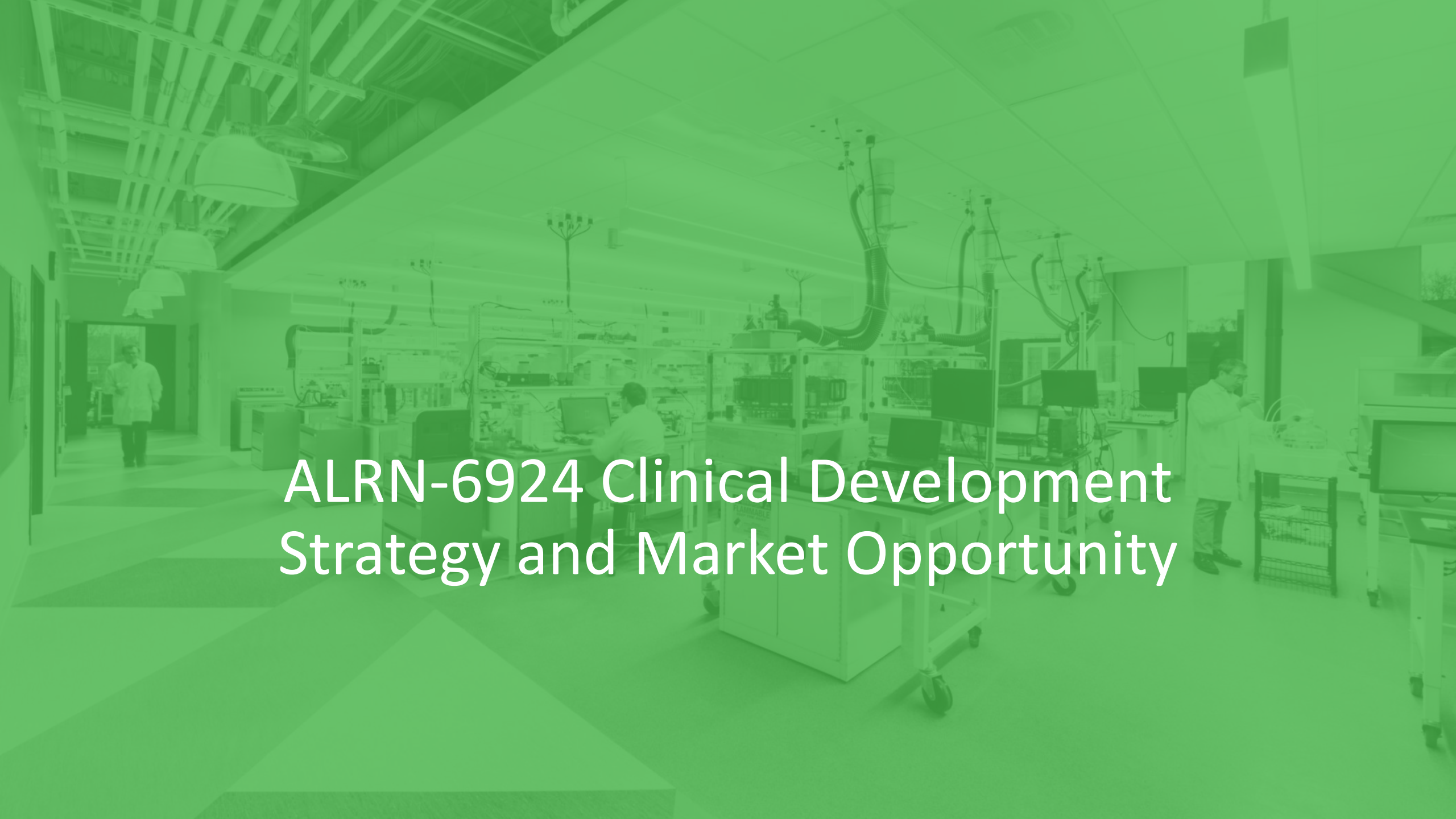
- > 50% of all cancer patients have p53 mutation†
- p53 = most common cancer mutation†

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

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

Historical landscape: primarily broad labels (i.e., indicated to treat all/most cancers); single toxicity drugs; innovation gap from 2006 - 2021





ALRN-6924 Clinical Development Strategy and Market Opportunity

Developing ALRN-6924 as a Selective CCA Agent to Protect Patients with p53-Mutant Cancers from Multiple Chemotherapy-Induced Side Effects

Nonclinical Proof of Mechanism

In vitro (mouse & human)

Bone marrow stem cells

Carvajal et al., EORTC 2019

In vivo (mouse)

Epithelial gut mucosa cells

Annis et al., ASH 2021

Ex vivo (human)

Hair follicles and their stem cells

Gherardini et al., SID 2022

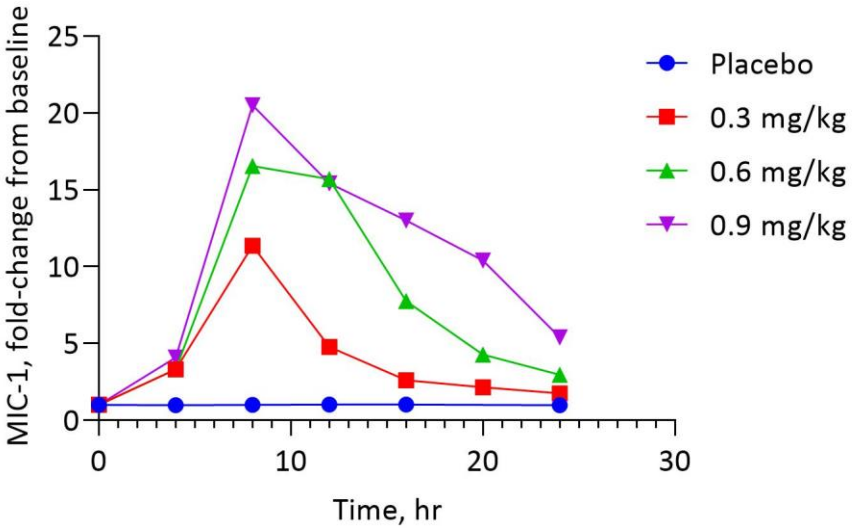
Clinical Development

Proof of Mechanism in Healthy Volunteers	*Proof of Concept in Phase 1*	*Path to Approval: Randomized Clinical Trials*	*Ultimate Goal*
CCA in BM stem cells after single and repeated doses of ALRN-6924 Voors-Pette et al., ESMO 2021	Reduced multilineage BM toxicity in topotecan-treated, p53-mutant SCLC Andric et al., ESMO 2021	Ongoing clinical trial in carboplatin/ pemetrexed-treated, p53-mutant NSCLC • Planned interim (n=20 pts): 2Q22 • Planned topline (n=60 pts): 4Q22	**Chemoprotection for all patients with p53-mutated cancer**
CCA in hair follicle cells after single dose of ALRN-6924 To be presented 2H 2022		Ongoing clinical trial in doxorubicin/ cyclophosphamide + docetaxel-treated, p53-mutant BC • Planned interim: 4Q22 • Up to 30 pts	

Phase 3 trial(s)

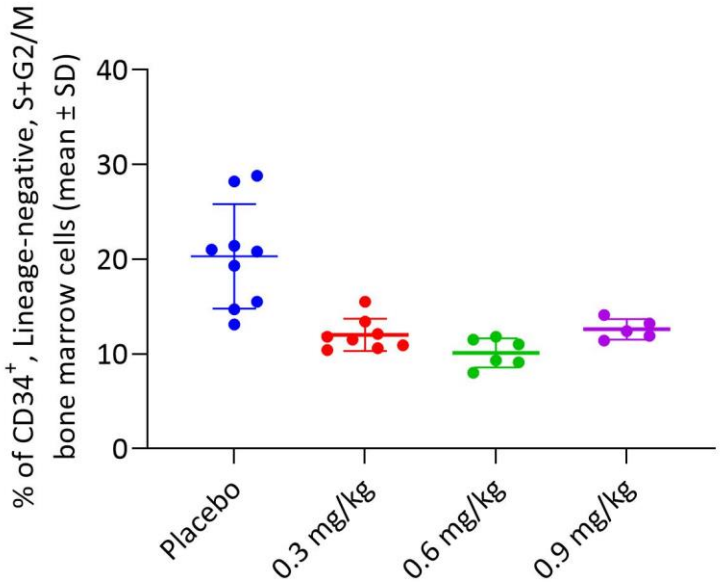
Phase 1 Healthy Volunteer Study: Pharmacodynamic Effects in Serum, Bone Marrow, and Hair Follicles Show ALRN-6924 Activated p53 to Induce p21 and CCA

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

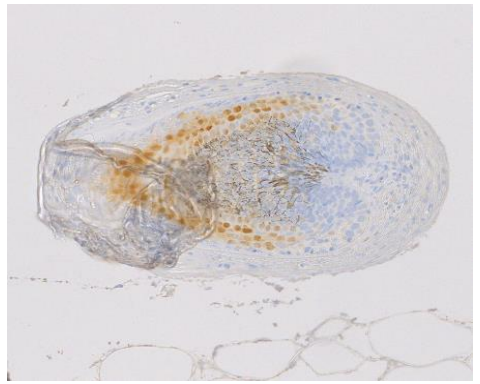
After a single dose, ALRN-6924 reduced the proportion of cycling bone marrow stem cells‡



‡ 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

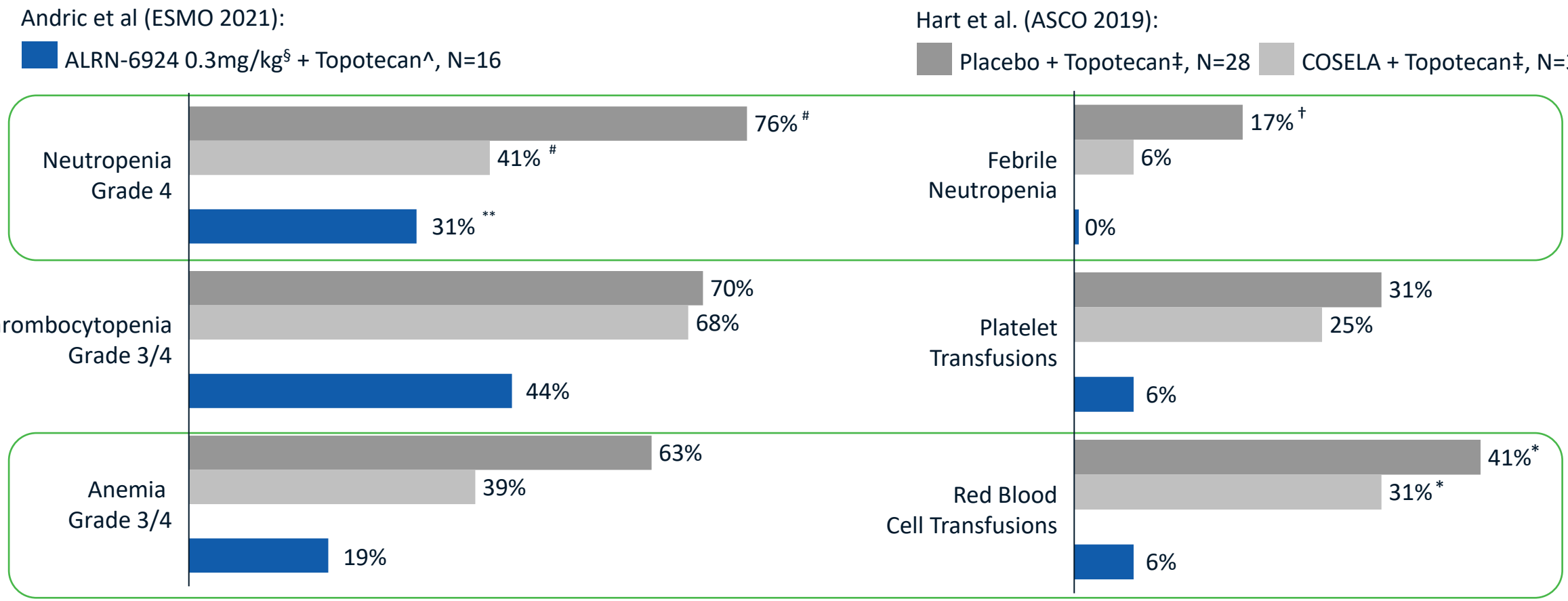


p21 staining (brown) in 0.6 mg/kg treated subject

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

ALRN-6924 Proof-of-Concept Chemoprotection Data in SCLC Patients Receiving Topotecan^

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



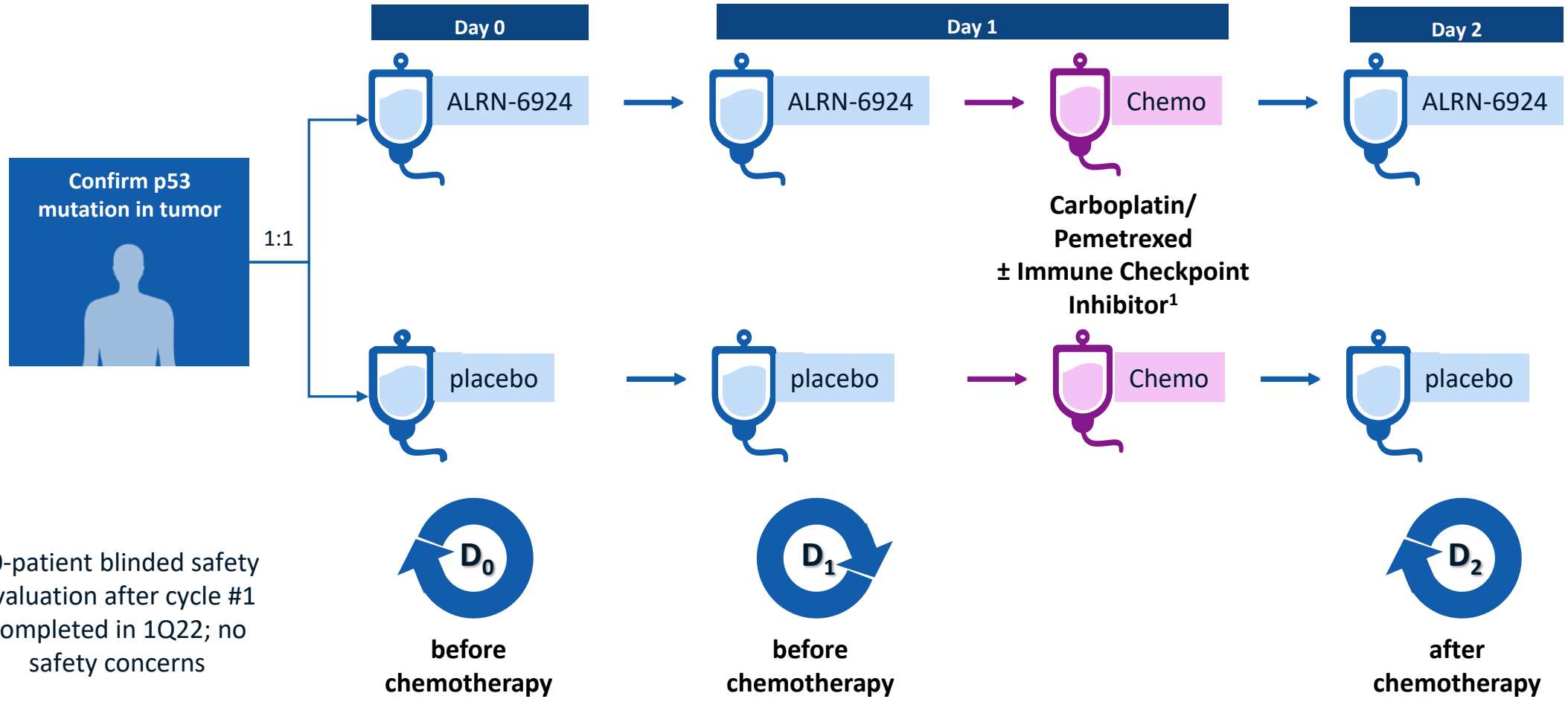
AEs based on laboratory values, as applicable

^ 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

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

Planned interim data from 20 patients in 2Q22; planned topline results from 60 patients in 4Q22

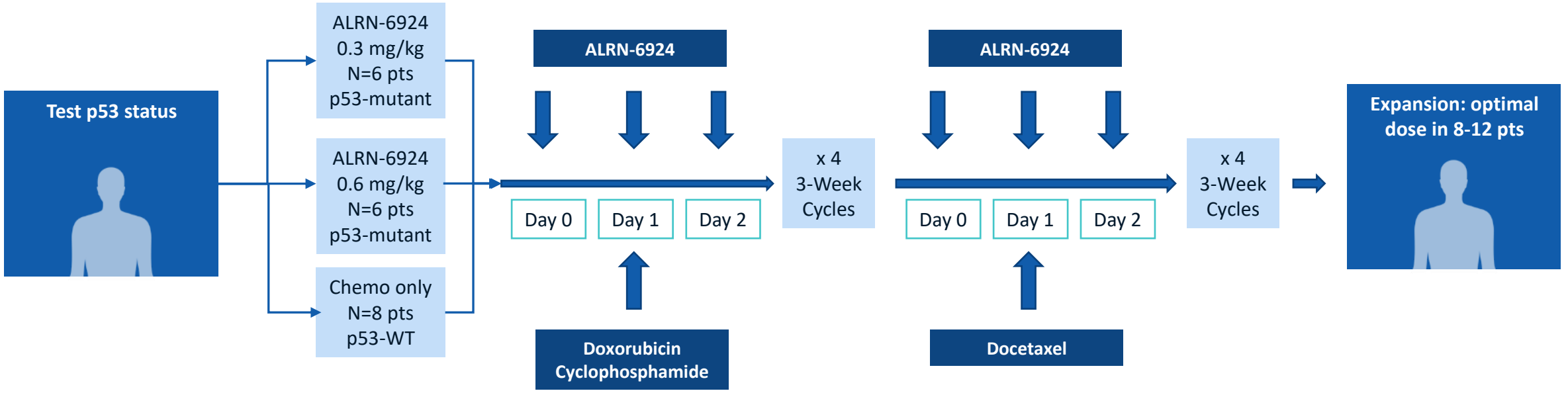


10-patient blinded safety evaluation after cycle #1 completed in 1Q22; no safety concerns

[1] 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

p53-Mutated Breast Cancer Patients Receiving Neoadjuvant Chemotherapy[1]

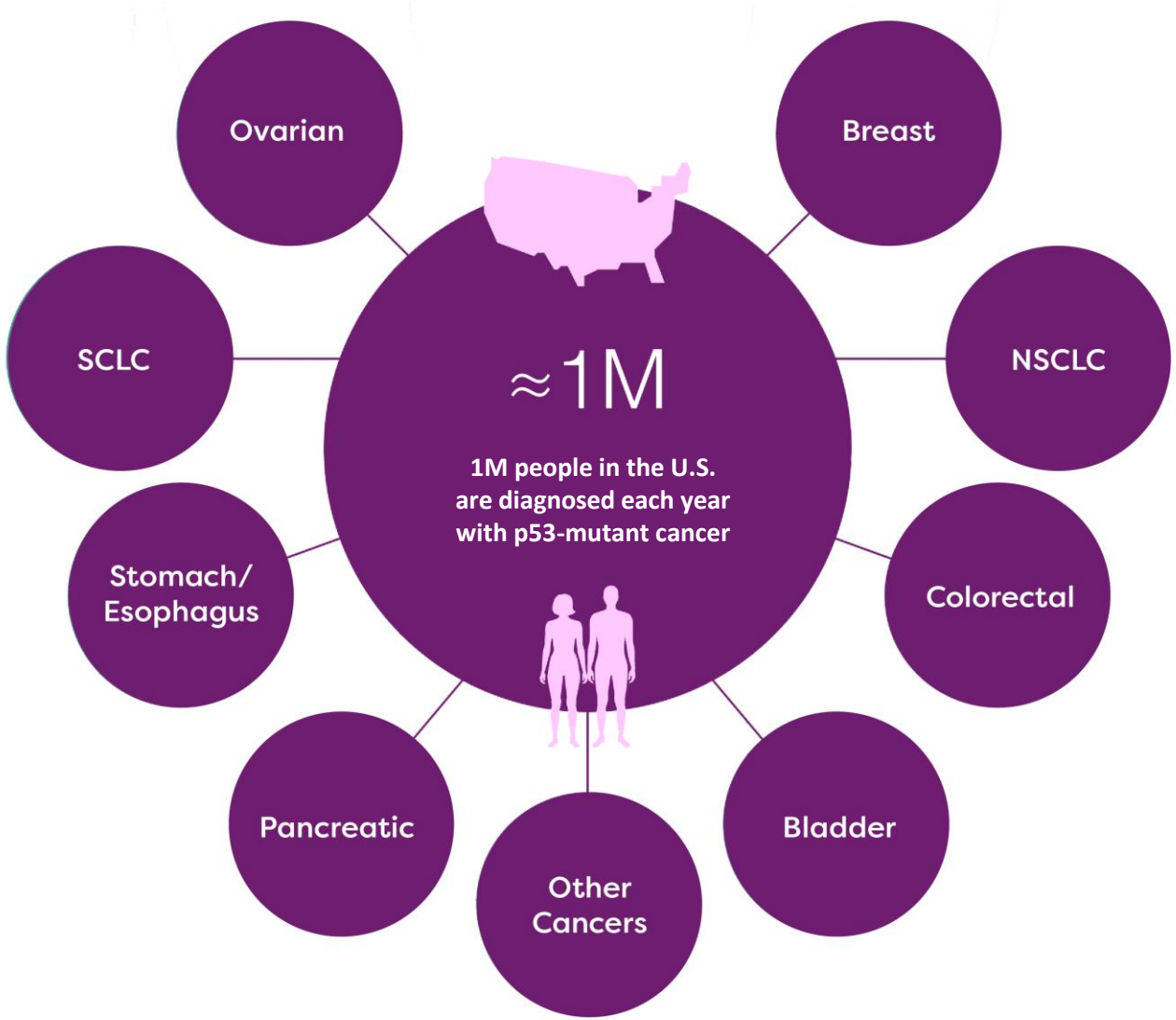
Ongoing Phase 1b randomized, controlled clinical trial; planned initial interim data 4Q22
***Note:* AC+D chemotherapy causes severe neutropenia in ≥75% of patients and alopecia in ≥90% of patients[2]**



[1] AC+D: Adriamycin (doxorubicin) + Cyclophosphamide, followed by Docetaxel
[2] Doxorubicin Prescribing Information; Docetaxel Prescribing Information (https://www.accessdata.fda.gov/)

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 Portfolio

- In 2021, Aileron was issued 7 new international patents, including new patent protection for ALRN-6924 in China, and 4 U.S. patents, adding to its strong intellectual property portfolio comprising over 160 U.S. and foreign patents.

- 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 March 31, 2021)	$38.1M
Expected to Support Operations	Into 4Q 2023
Common Shares Outstanding (March 31, 2021)	90.7M
Analyst Coverage by William Blair, H.C. Wainwright and Jones Trading	

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

NSCLC trial ongoing, readouts 2Q22 and 4Q22; Breast cancer trial ongoing, first readout 4Q22

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

Chemoprotection May Transform Chemotherapy Like Anesthesia Transformed Surgery

NASDAQ: ALRN

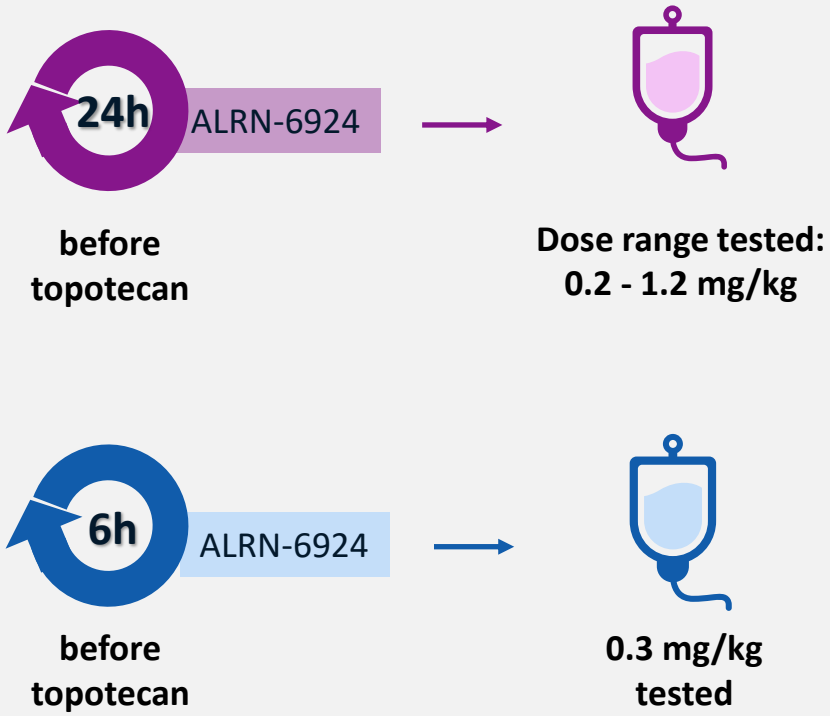
WWW.AILERONRX.COM

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

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)

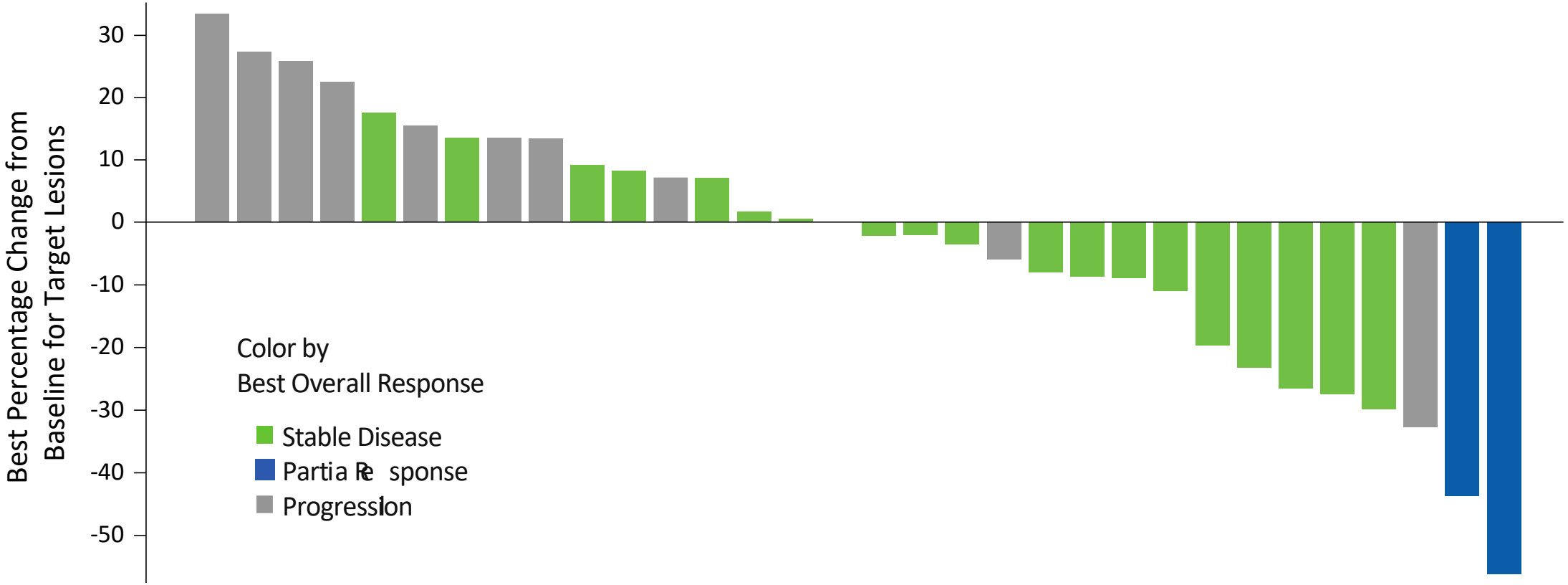
* Hart et al., Adv Ther 2020; topotecan + *placebo*-treated patients (G1-Therapeutics' clinical trial in SCLC patients receiving topotecan)

^ 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



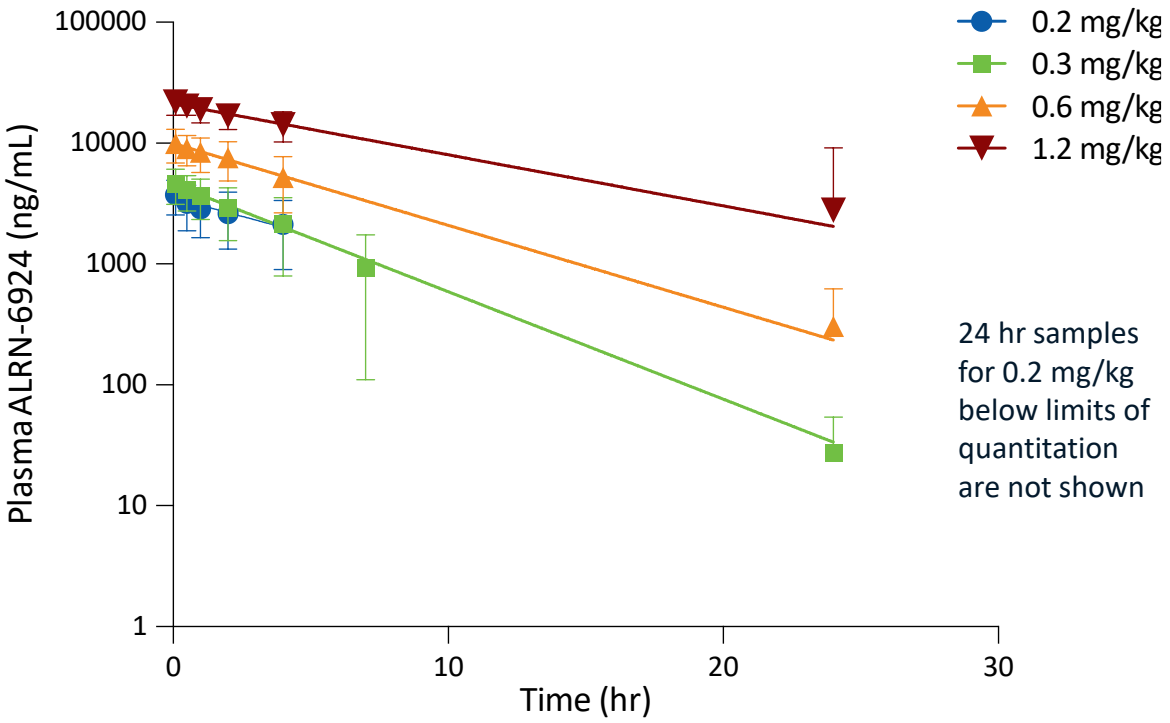
- **The disease control rate (DCR) was 65.6% for 32 patients with radiological evaluation***
- **In historical trials of SCLC patients receiving topotecan, the DCR was between 47% and 61.5%‡**

‡ 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 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

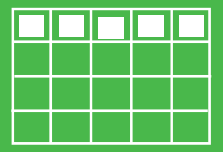
3 groups of subjects were treated with a single dose of placebo (n=6), ALRN-6924 0.3 mg/kg (n=4), or ALRN-6924 0.6 mg/kg (n=4)

PART 2

Kinetics of Pharmacodynamic Effects in the Bone Marrow

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

PART 3



Confirmation of a Universal Treatment Schedule for ALRN-6924; Testing Effects of ALRN-6924 on Epithelial Cells Additional data readout planned in 2H22

ALRN-6924 Phase 1 Healthy Volunteer Study: Key Takeaways

Study findings 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

	Part 1			Part 2	
Parameter	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)
TEAEs Occurring in >10% of Subjects					
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)
SAEs Occurring in >10% of Subjects					
ANY SAE	0	0	0	0	0

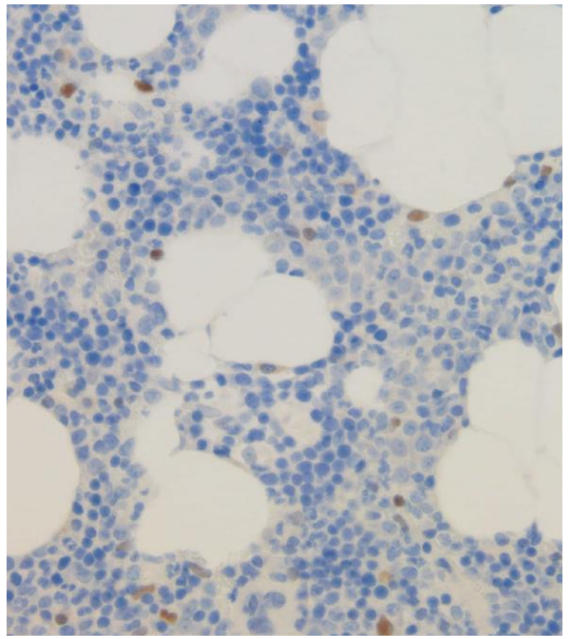
*Following submission of poster to ESMO Virtual Congress 2021, a “totals” column mistakenly combining placebo- and ALRN-6924-treated subjects was removed from this table.

Both 0.3 and 0.6 mg/kg ALRN-6924 Doses Induced p21 in Bone Marrow Cells†

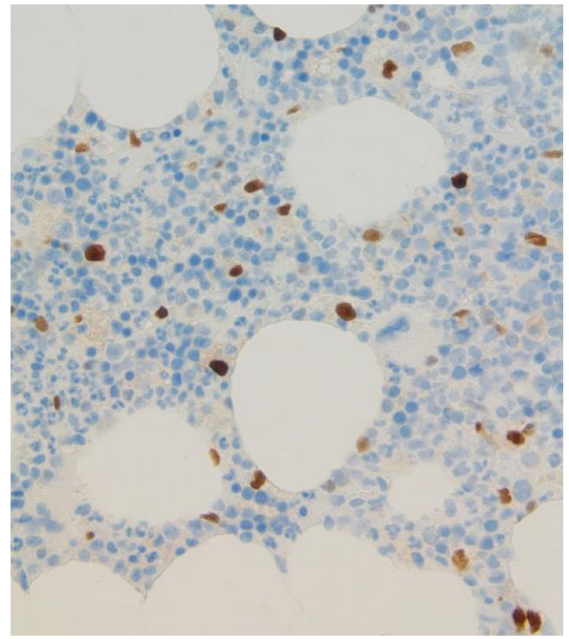
Subject	Group	p21, % at Differential Intensities† 0	1+	2+	3+	cPARP‡ # cells per HPF
1	Plac.	100	0	0	0	2
2	"	100	0	0	0	1
3	"	100	0	0	0	19
4	"	100	0	0	0	12
5	"	100	0	0	0	19
6	"	100	0	0	0	21
7	0.3 mg/kg	94	0	2	4	19
8	"	96	0	2	2	21
9	"	96	0	1	3	7
10	"	95	0	1	4	85
11	0.6 mg/kg	94	0	1	5	17
12	"	93	0	2	5	61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

Representative p21 Staining

Placebo-treated Subject



ALRN-6924-treated Subject



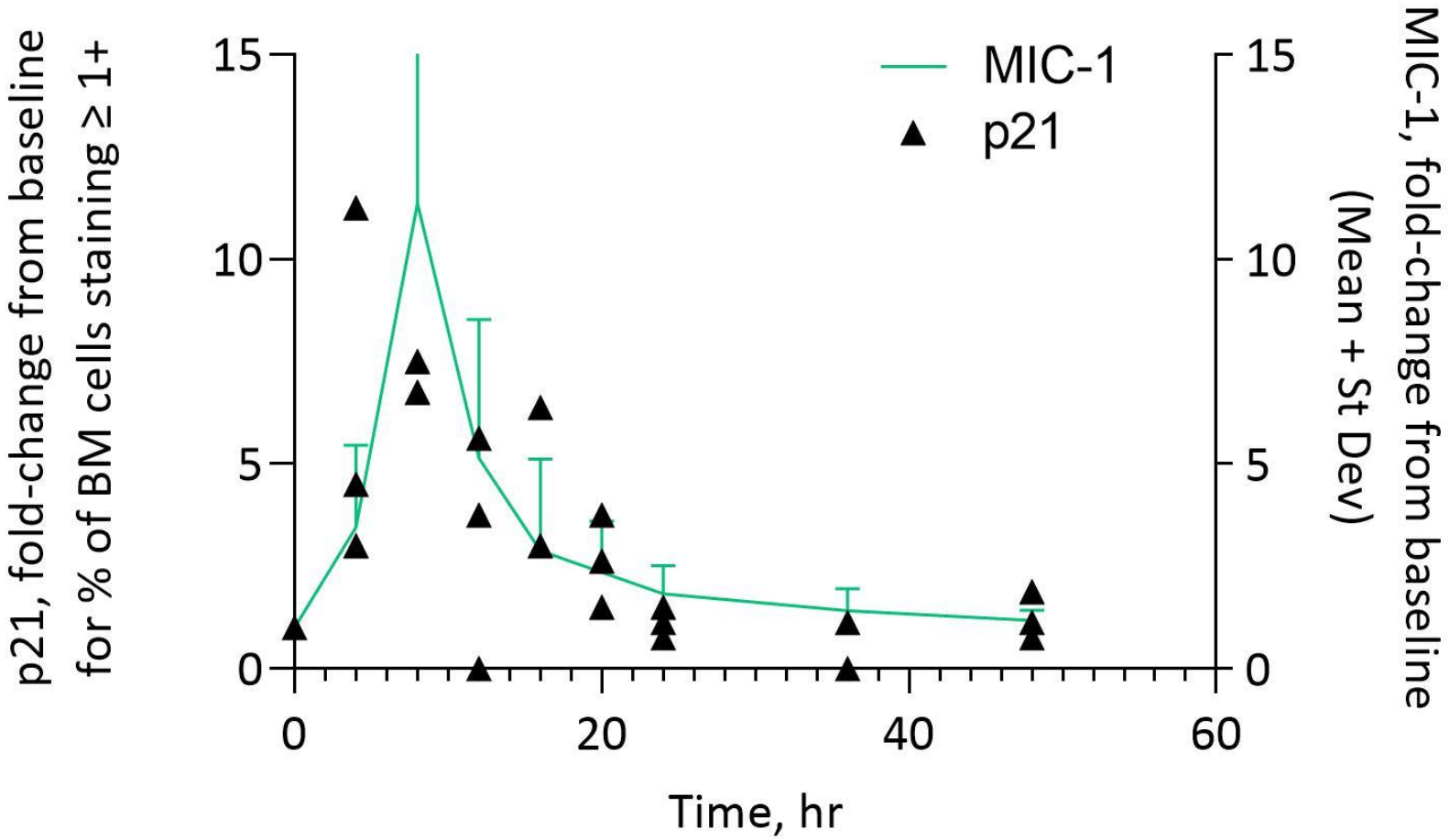
†Note: bone marrow is largely composed of quiescent stem cells or nonproliferating immature, differentiating cells; only 5% to 20% of cells are actively cycling[1,2]

‡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



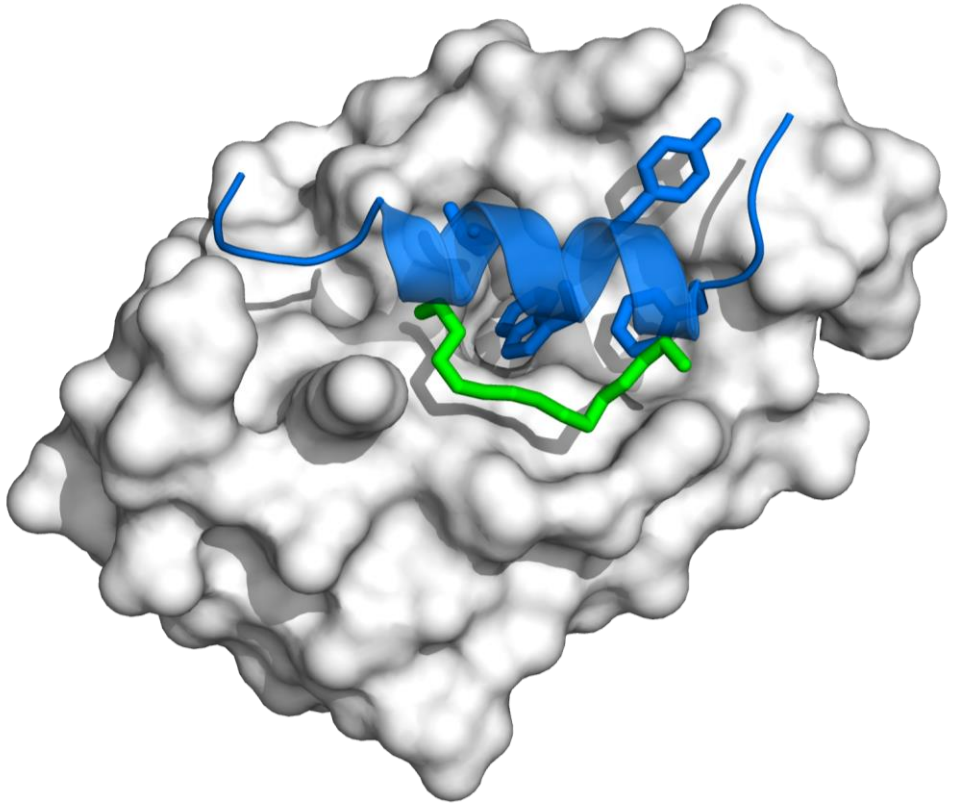
- p21 immunohistochemistry scoring was conducted by an independent pathologist blinded to experimental conditions
- Macrophage Inhibitory Cytokine-1 (MIC-1, also known as Growth Differentiation Factor-15, or GDF-15) was quantified by a qualified ELISA assay
- MIC-1 results are shown as mean change from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

MIC-1 = macrophage inhibitory cytokine-1

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:

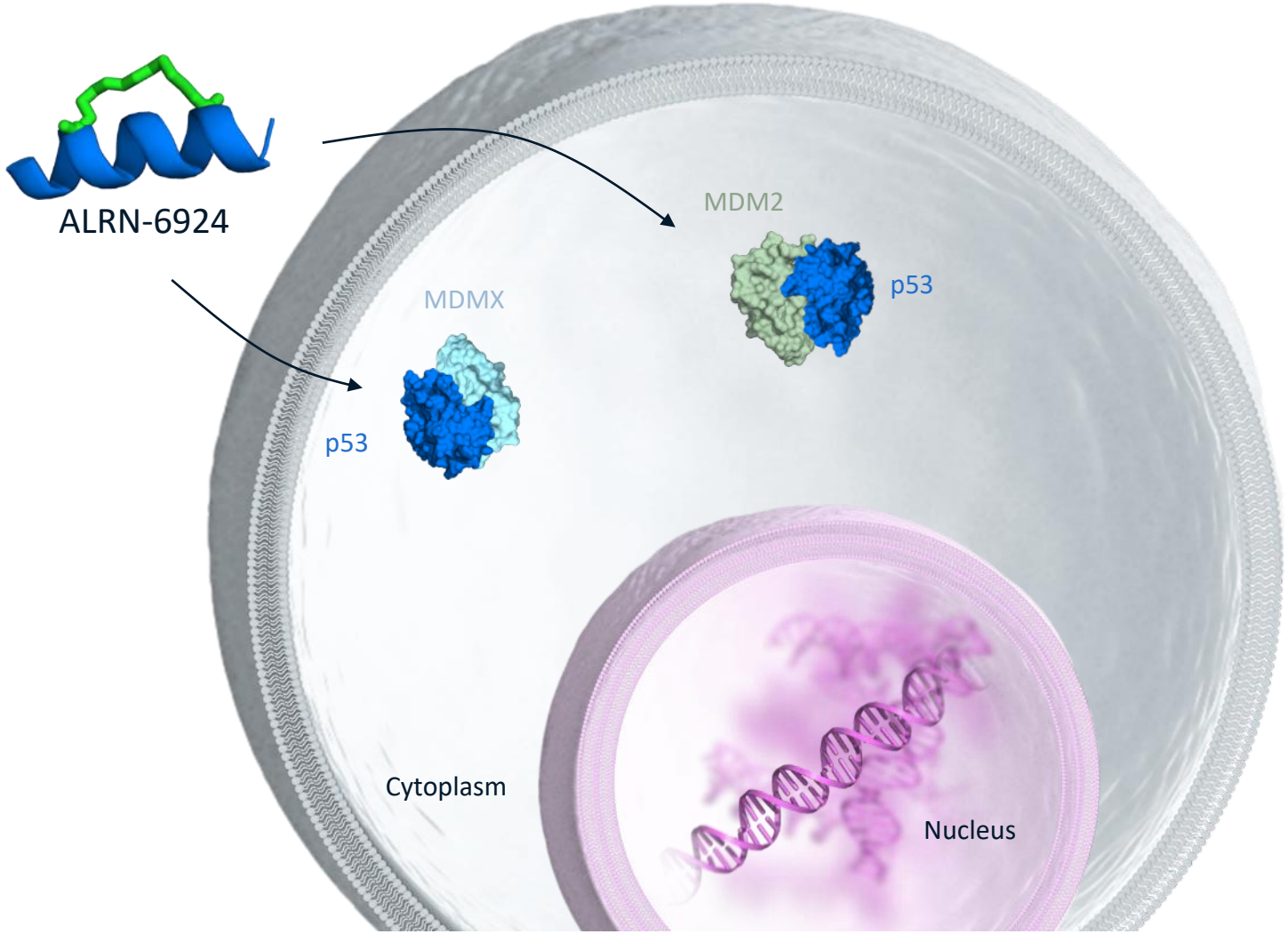
I. Protection from proteolytic cleavage

II. Permeation of cell membranes and cell entry

III. High affinity binding to its targets

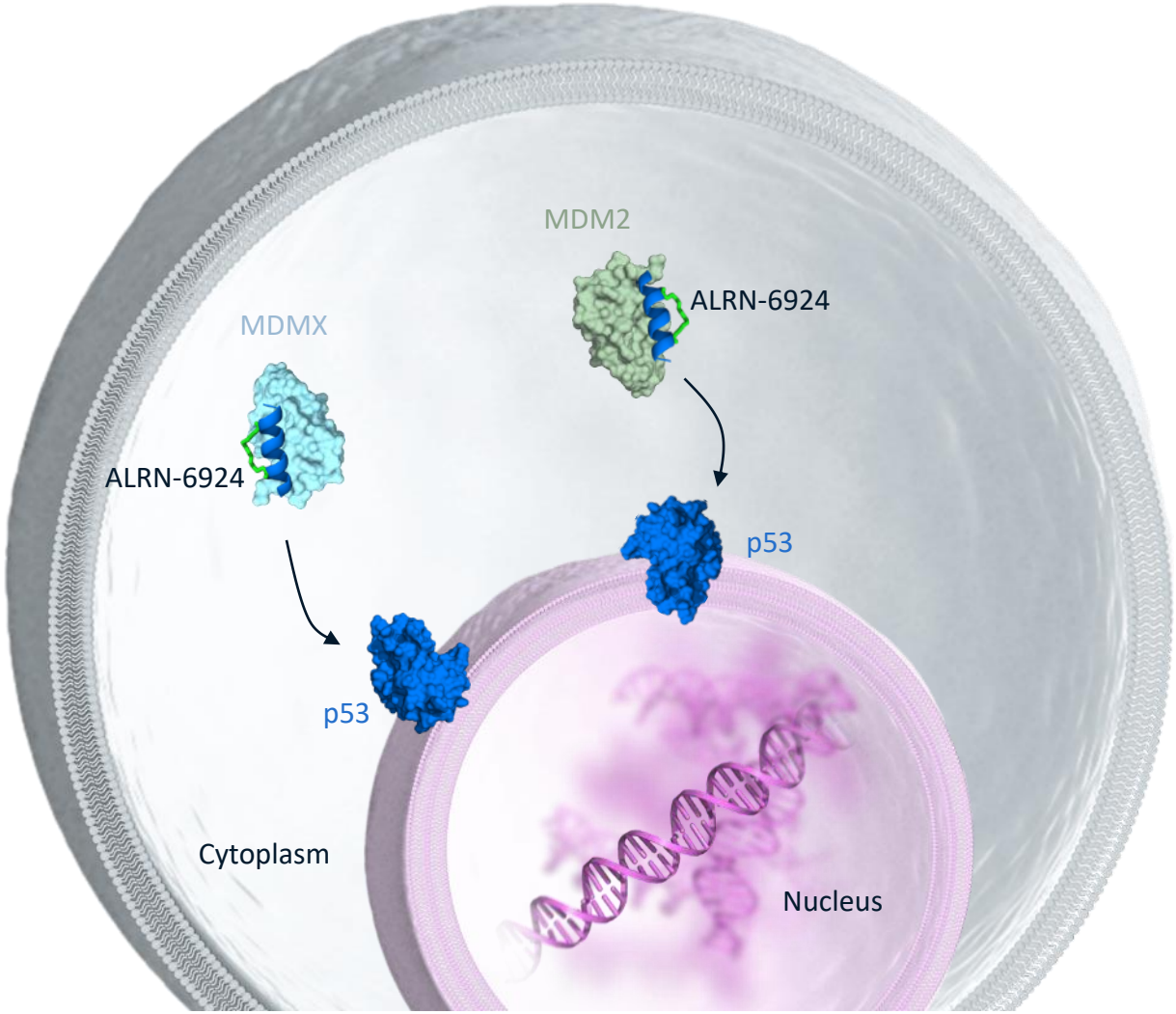
IV. Preclinical and clinical on-target, on-mechanism effects

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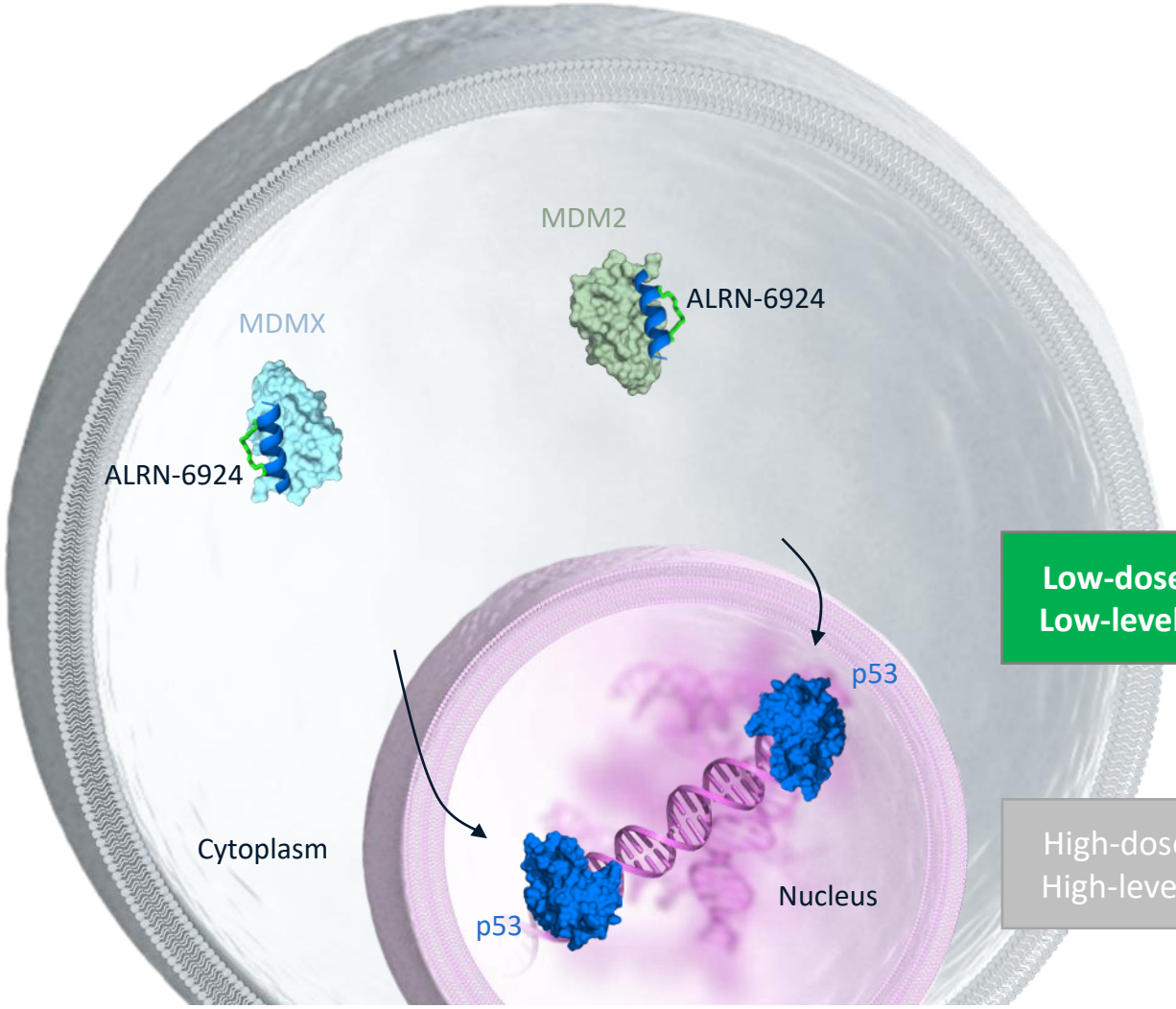
ALRN-6924 Mechanism of Action in Wild-Type p53 Cells



Low-dose ALRN-6924
Low-level p53 release

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

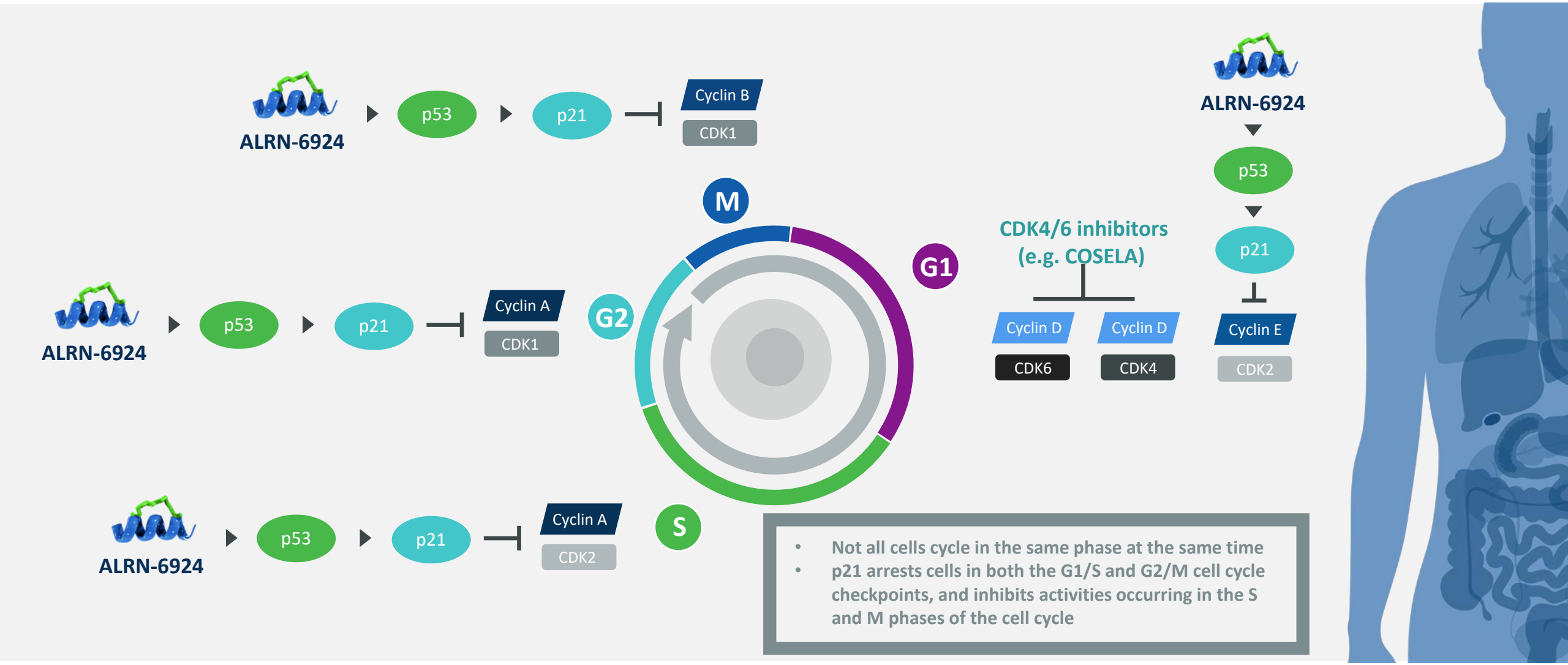
High-dose ALRN-6924
High-level p53 release

→ 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

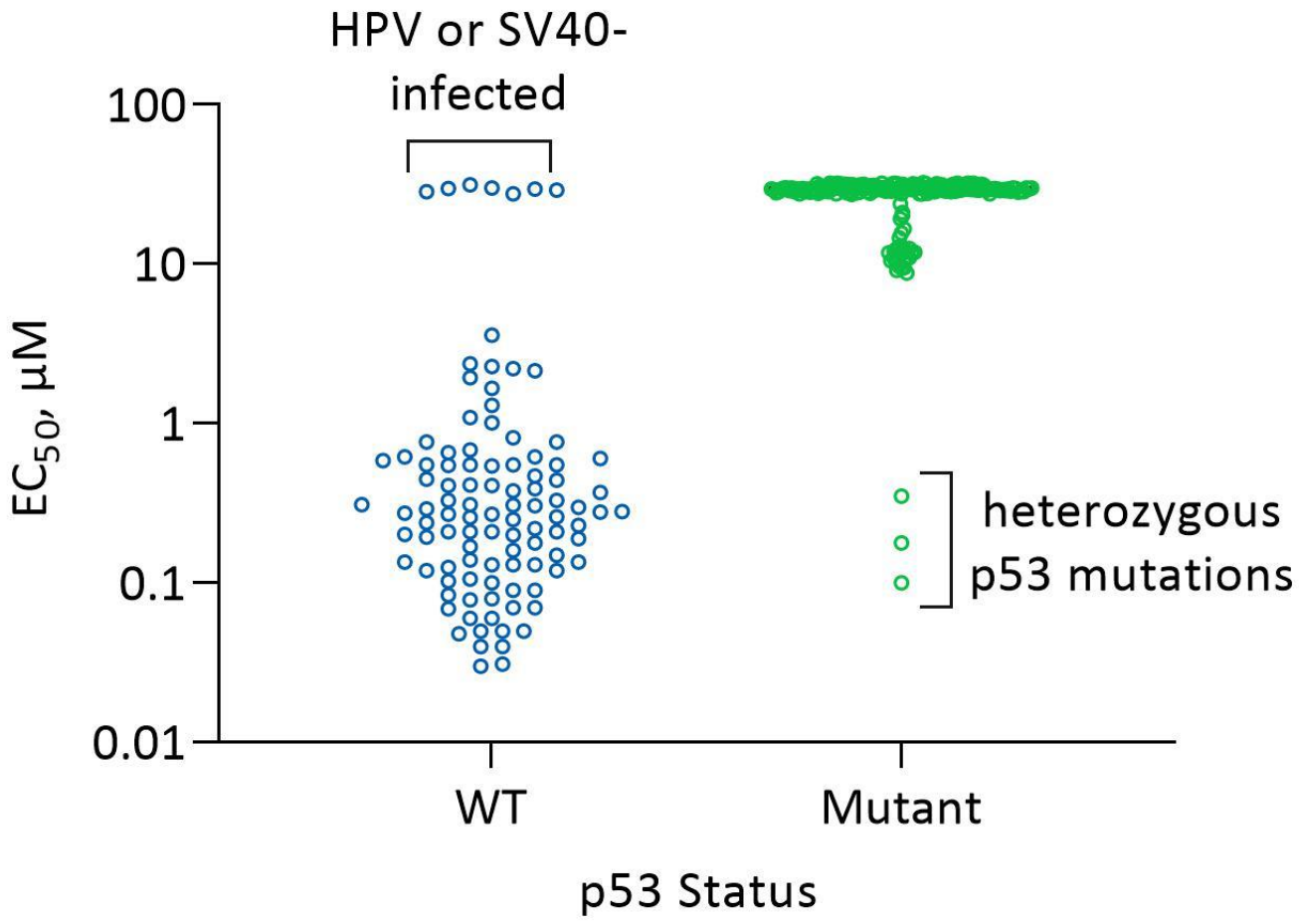
[1] Chen; Cold Spring Harb Perspect Med. 2016 Mar 1

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



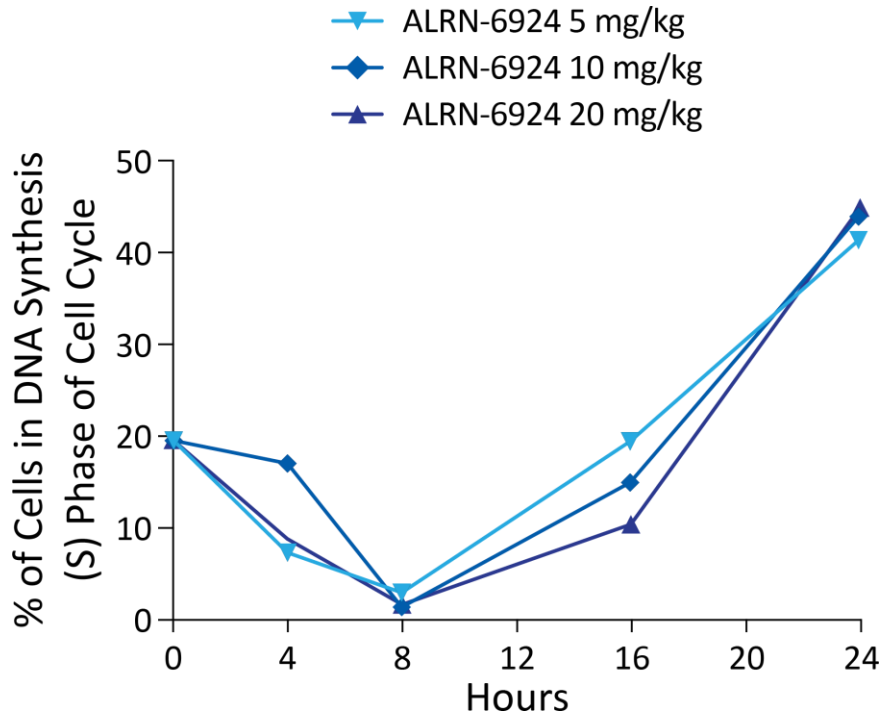
ALRN-6924 Potently Inhibits Proliferation in Wild-Type p53 Cells; Mutant Cells Are Insensitive

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



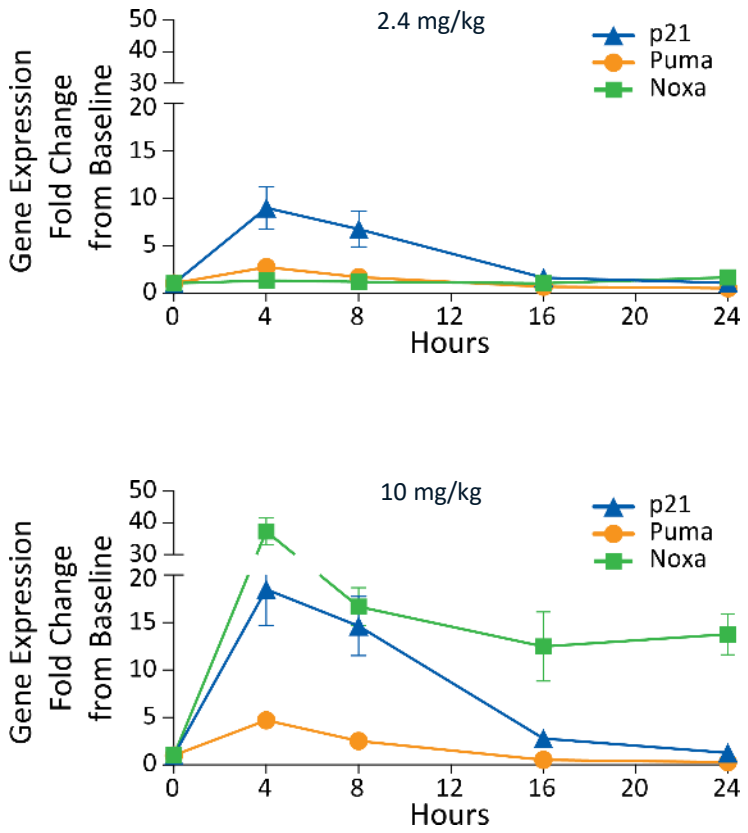
Pairawan et al, "First in class dual MDM2/MDMX inhibitor ALRN-6924 enhances antitumor efficacy of chemotherapy in TP53 wild-type hormone receptor-positive breast cancer models." Breast Cancer Research, 2021; 23: 29.

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

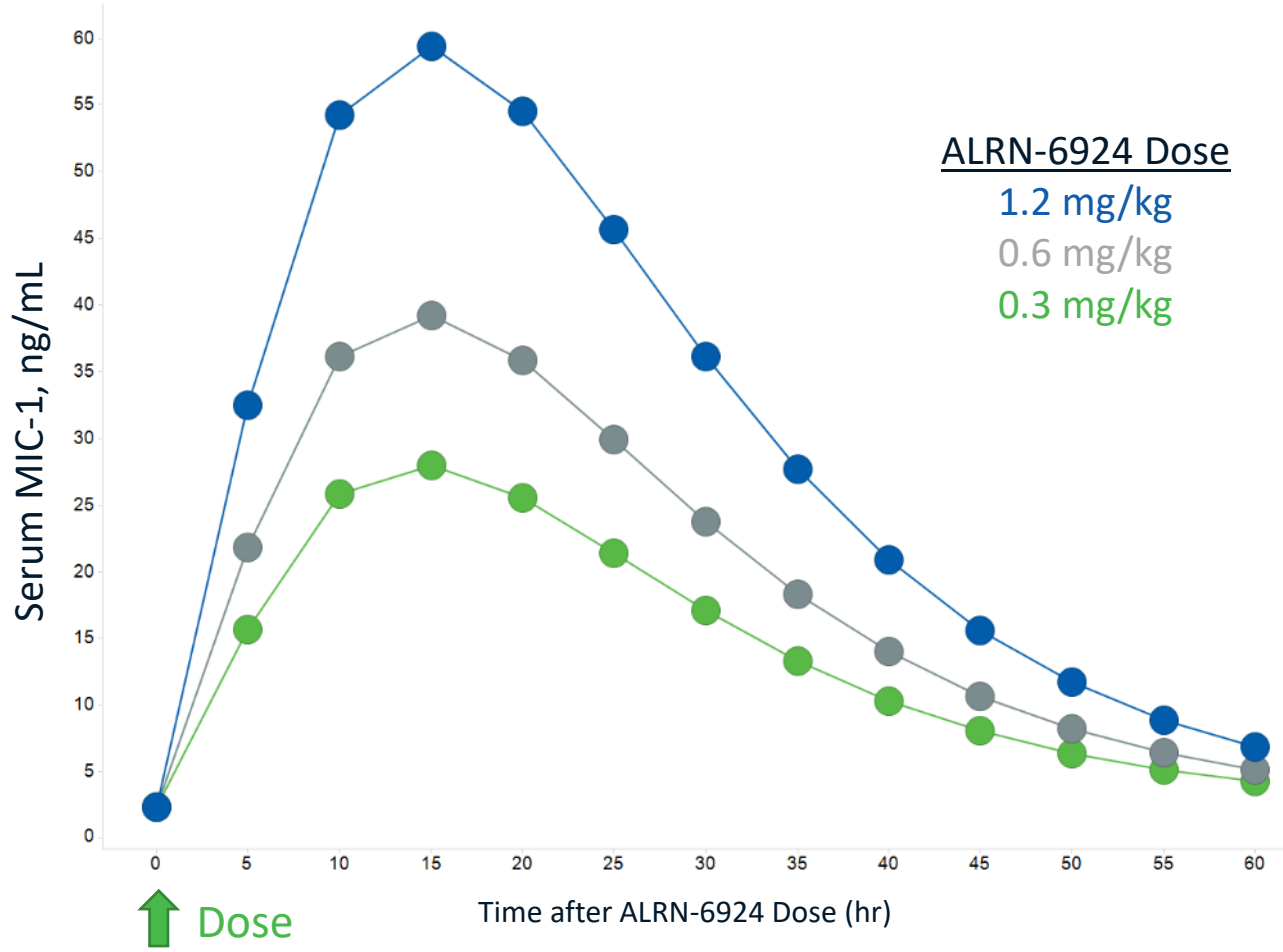


Biomarkers of CCA (p21) and Apoptosis (Puma, Noxa, And MIC-1)

Non-clinical studies†



MIC-1 levels in SCLC trial‡



† 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

‡ Data modelled from this trial and other ALRN-6924 clinical studies: Meric-BernstamF., 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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NASDAQ: ALRN

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