Transforming the Experience of Chemotherapy for Cancer Patients

CORPORATE PRESENTATION

January 2021

Forward Looking Statements

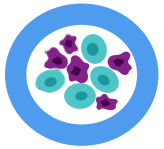
Statements in this presentation about Aileron's future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. These statements 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 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 September 30, 2020, filed on November 12, 2020, 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

Feb. 15, 2021: PDUFA date for first-generation chemoprotection drug (by G1-Therapeutics)
Establishes regulatory and commercial pathway for chemoprotection

ALRN-6924: Best-in-class potential among chemoprotective agents ("Triple Play Efficacy")
Clinical proof of concept demonstrated

Core differentiation
ALRN-6924 = Chemoprotection without protecting cancer cells by using p53 as biomarker



Large commercial opportunity
50% of all cancer patients have p53-mutated cancer / Millions worldwide

Read-outs from randomized placebo-controlled Ph1b in frontline NSCLC
Expected: Start Q2 2021 / **Initial data** Q4 2021 / **Final results** mid 2022

NSCLC = non-small cell lung cancer

Chemoprotection with ALRN-6924

Executive Summary

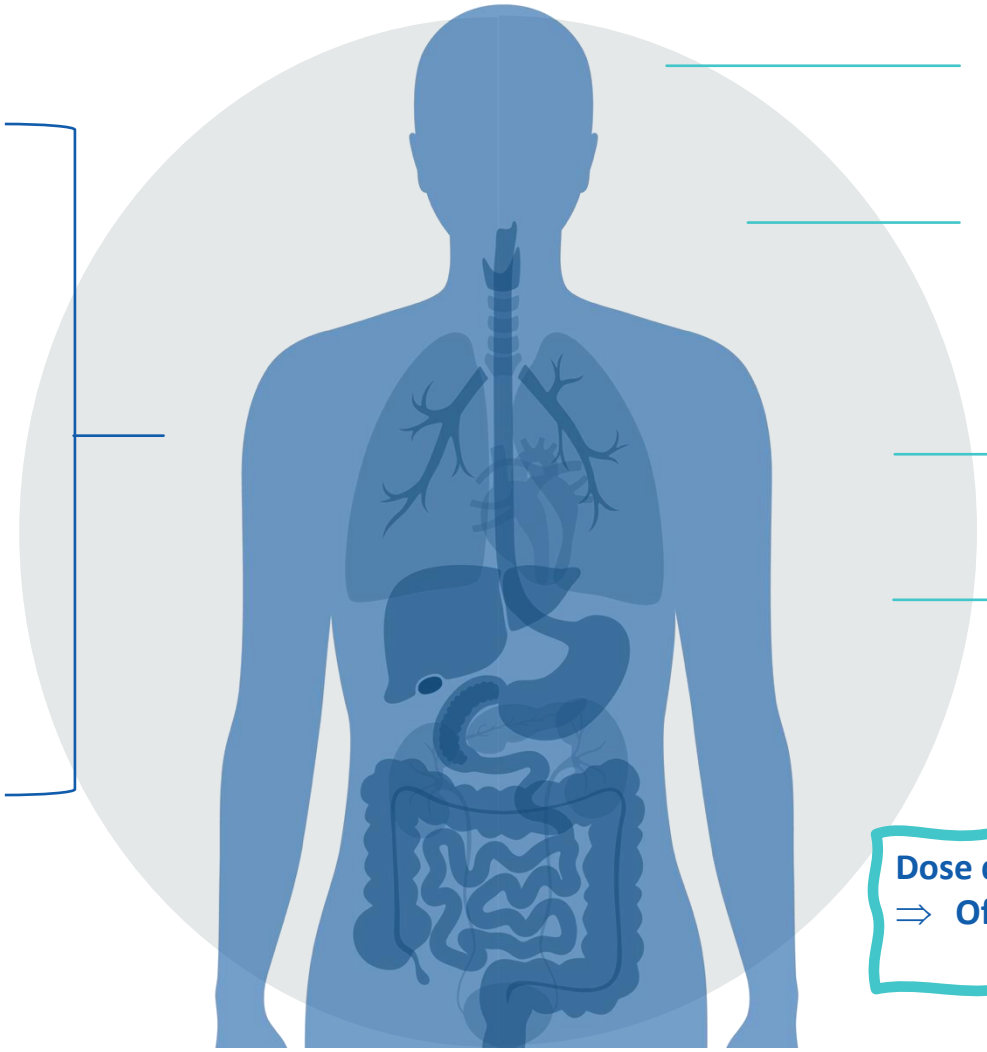
Chemotherapy's Lack Of Selectivity Causes Side Effects – From Unpleasant To Life-Threatening

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

Severe Anemia (weakness, fatigue)

Severe Thrombocytopenia (excessive bleeding)

Severe Neutropenia (serious infection, fever, sepsis)



Alopecia (hair loss)

Stomatitis (mouth sores)

Fatigue, Weakness, Asthenia

Vomiting, Diarrhea, Bloating

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

"Myelopreservation" = chemoprotection focused on limiting chemotherapy-induced bone marrow toxicities

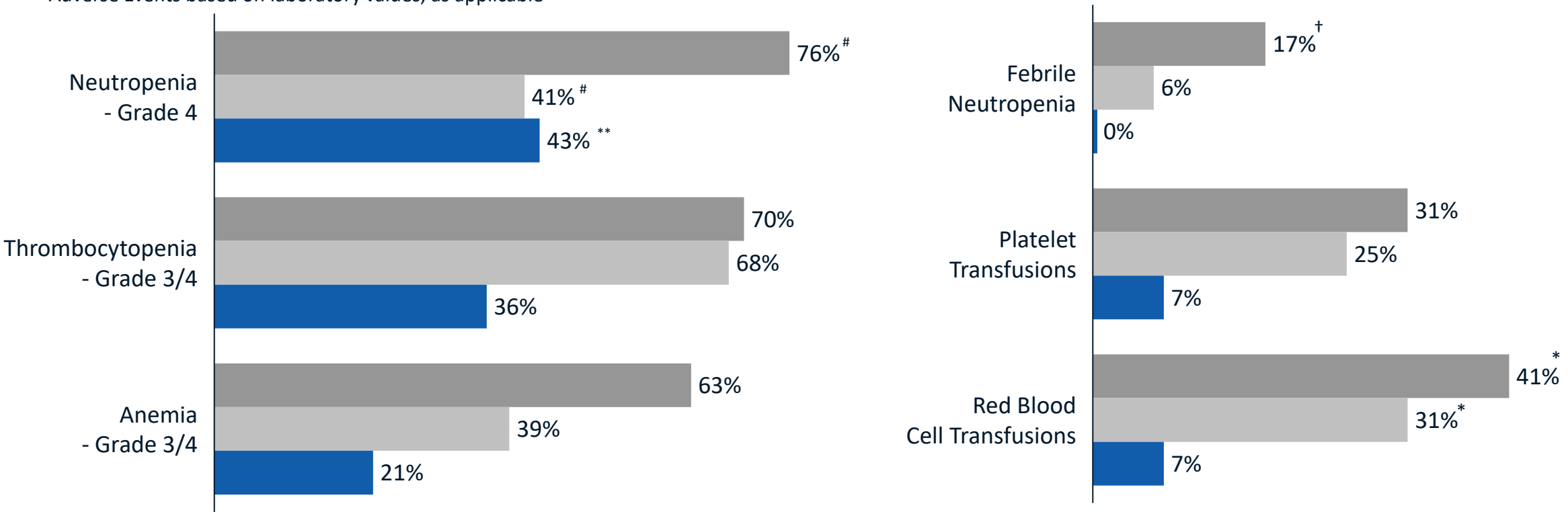
“Triple-play Efficacy” For Neutropenia, Thrombocytopenia, And Anemia, As Well As Fewer Transfusions With ALRN-6924 Than In Hart Et Al. (ASCO 2019) Trial

-24 Hour Cohort of Phase 1b Clinical Trial of ALRN-6924 as a Chemoprotection Agent in SCLC Patients Receiving Topotecan^

ALRN-6924 0.3mg/kg§ + Topotecan^, N=14

Hart et al. (ASCO 2019): Placebo + Topotecan‡, N=28 Trilaciclib + Topotecan‡, N=32

Adverse Events based on laboratory values, as applicable



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** For cycle 1 and for all treatment cycles

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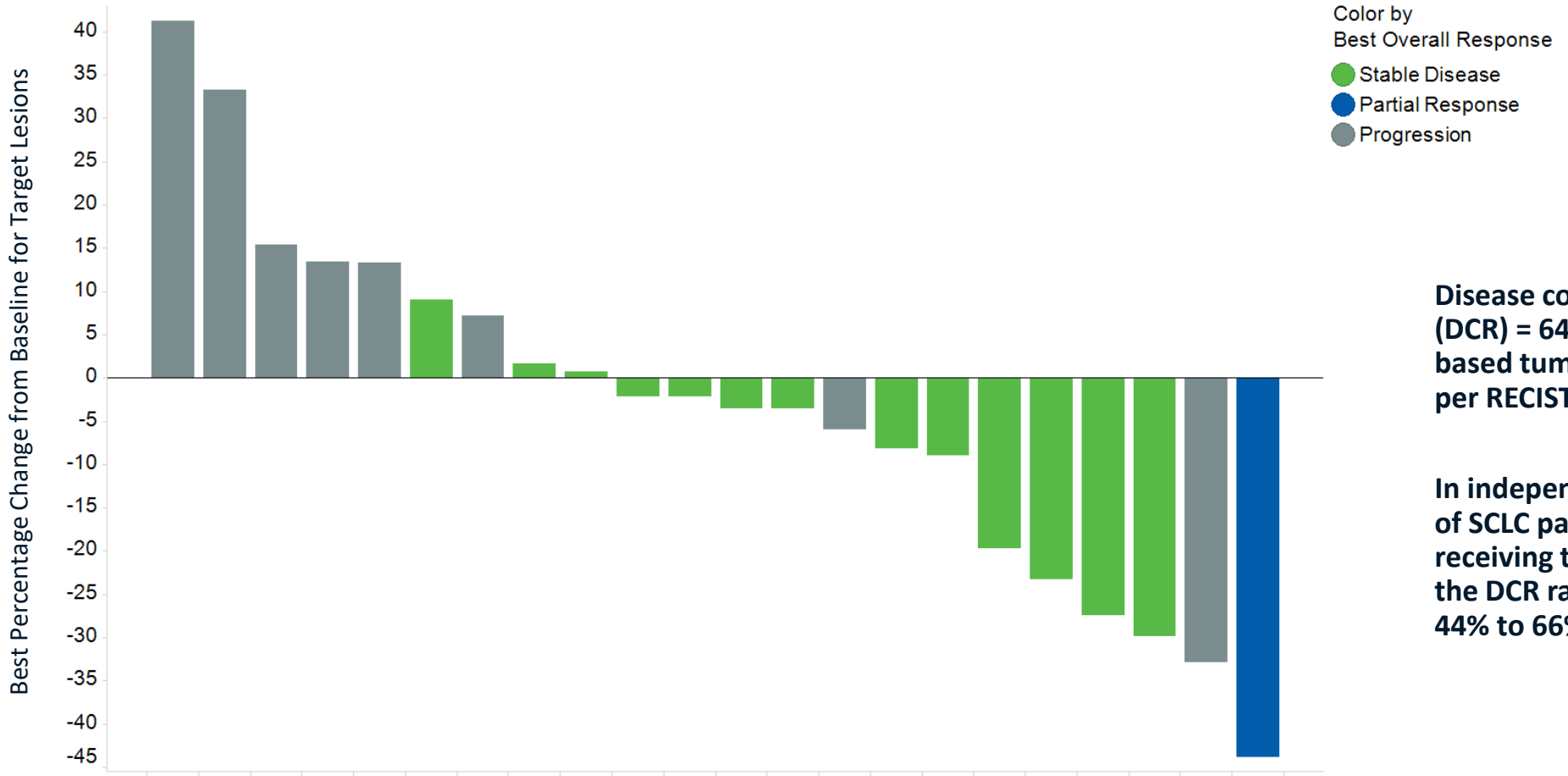

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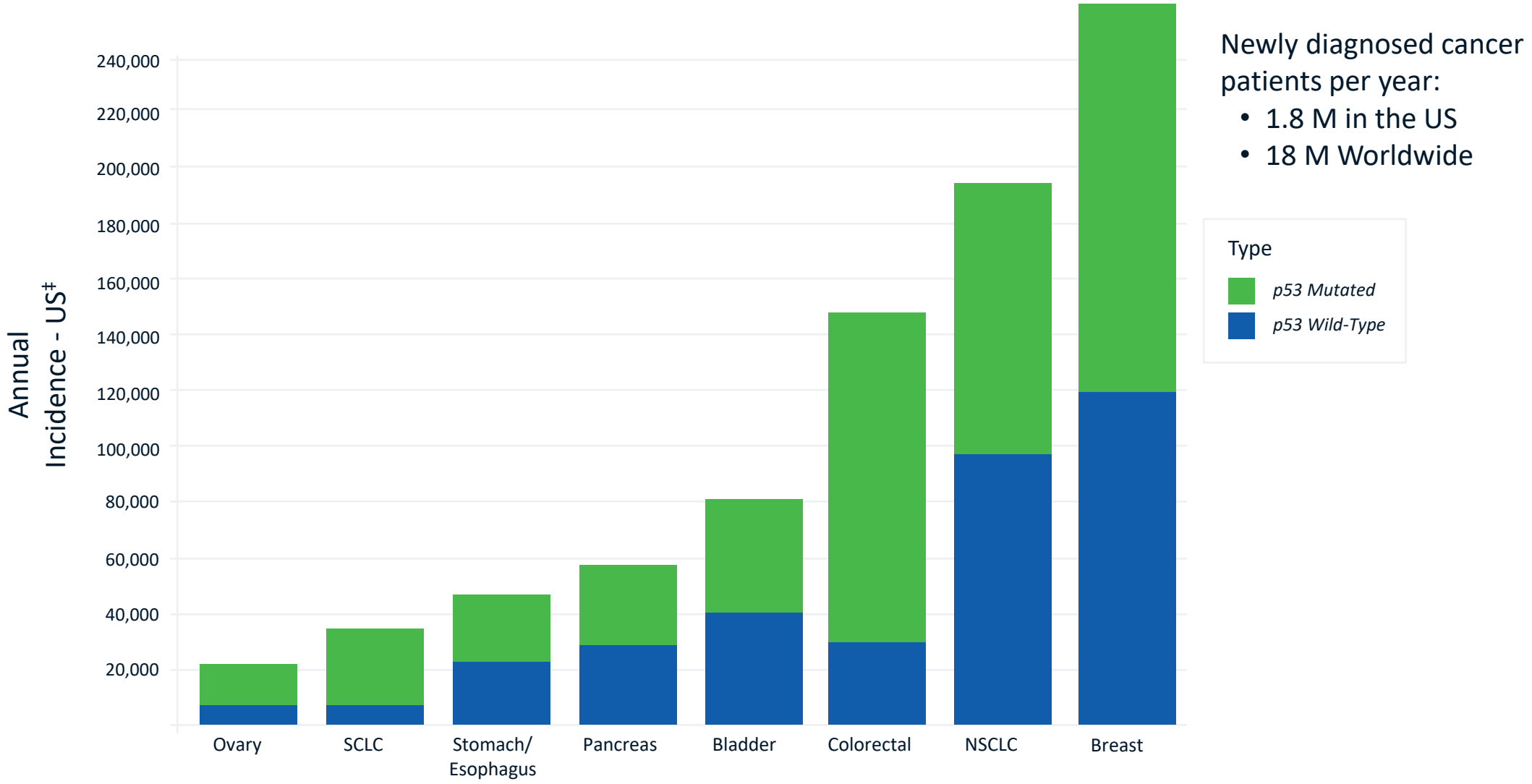
-24h cohort, data cut August 31, 2020

Large Market Opportunities In p53-mutated Cancers Across Most Cancer Types



Newly diagnosed cancer patients per year:

- 1.8 M in the US
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Chemoprotection May Transform Chemotherapy Like Anesthesia Transformed Surgery

Potential Path To Approval For ALRN-6924 In Multiple p53-Mutant Cancers & Chemotherapies

Small Cell Lung Cancer (Topotecan)

Ongoing Phase 1b Trial

- 24h-schedule Proof-of-Concept results: Oct. 2020
- 6h-schedule results and add'l 24h-schedule results (including exploratory 0.2 mg/kg cohort): expected Q1 2021

Healthy Volunteer Study

- Results expected mid-2021

Non-Small Cell Lung Cancer (1st Line Platinum Doublet +/- immune checkpoint inhibitor)

Registration Program†

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  - *** Start Q2 2021**
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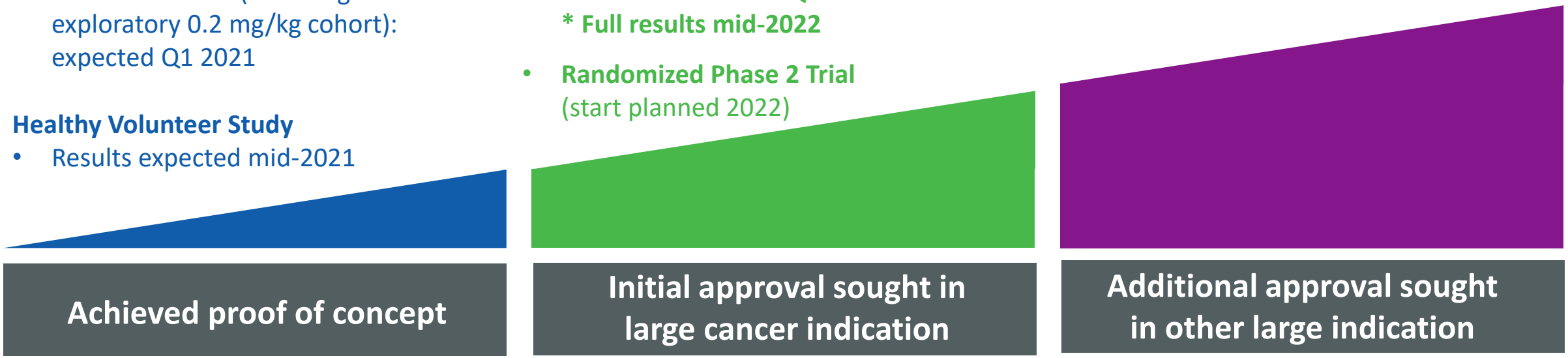
Gastrointestinal and Other Cancers (Chemotherapies TBD)

Registration Program†

- Start of trials planned for 2022



Achieved proof of concept

Initial approval sought in large cancer indication

Additional approval sought in other large indication

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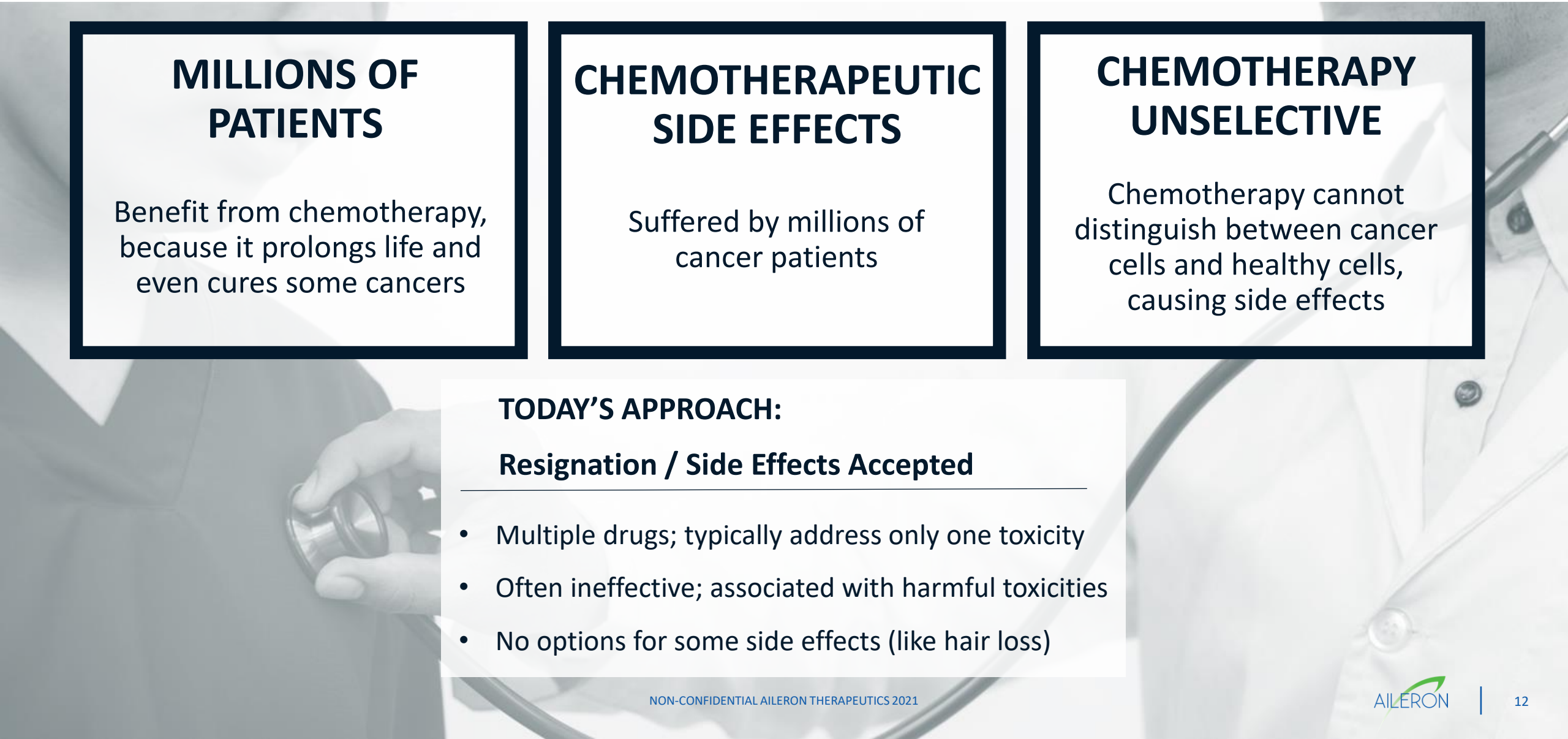
Chemoprotection with ALRN-6924
Background

Chemotherapy Remains Essential Backbone Of 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:

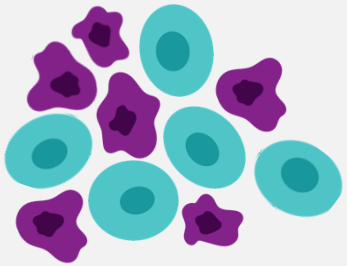
Resignation / Side Effects Accepted

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

Basic Principles To Successfully Protect Against Chemotherapy-induced Side Effects

CURRENT PARADIGM:

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



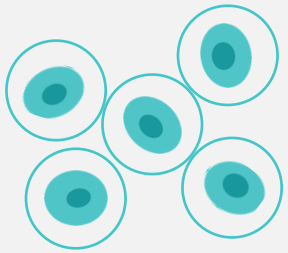
Normally, both healthy cells and cancer cells are destroyed by chemotherapy

PARADIGM SHIFT

AILERON PARADIGM:

Temporarily pause cycling in healthy cells, shielding them

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:

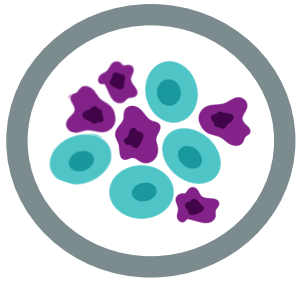
Treat healthy cells, not cancer cells

Healthy Normal Cells Have Normal p53. Normal p53 Is Activated By ALRN-6924, Which Pauses Cell Cycle In Normal Cells, But Not In Cancer Cells With Mutant p53

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

IV administration;
1-hour infusion

→



ALRN-6924 activates normal p53 in healthy cells

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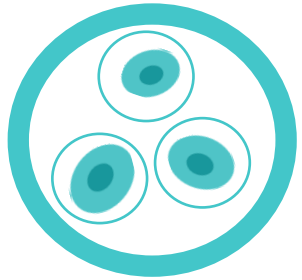
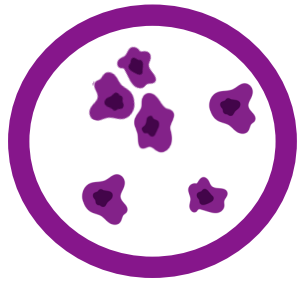


Activated normal p53 pauses cell cycling in healthy cells

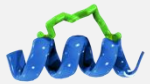
→

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 (always normal p53)

No protection of cancer cells with p53-mutation

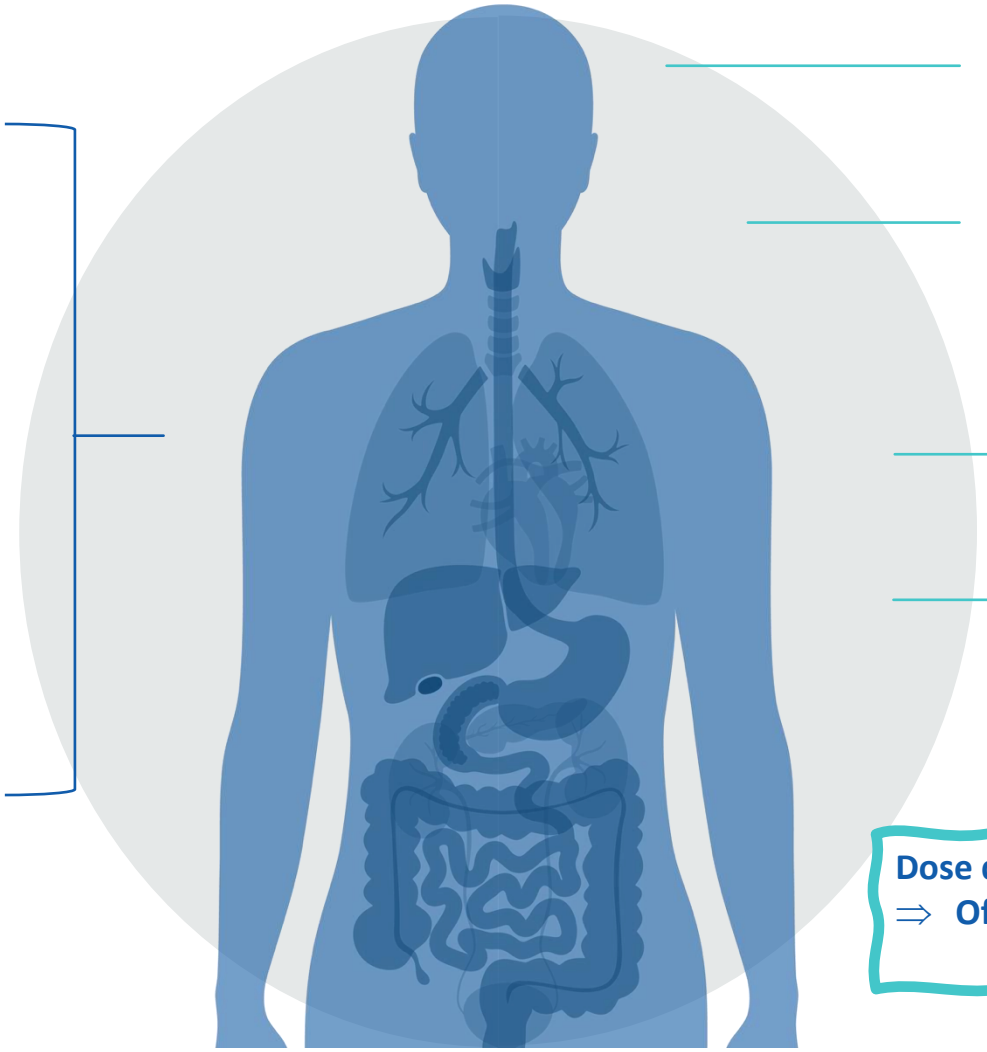
Chemotherapy's Lack Of Selectivity Causes Side Effects – From Unpleasant To Life-Threatening

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

Severe Anemia (weakness, fatigue)

Severe Thrombocytopenia (excessive bleeding)

Severe Neutropenia (serious infection, fever, sepsis)



Alopecia (hair loss)

Stomatitis (mouth sores)

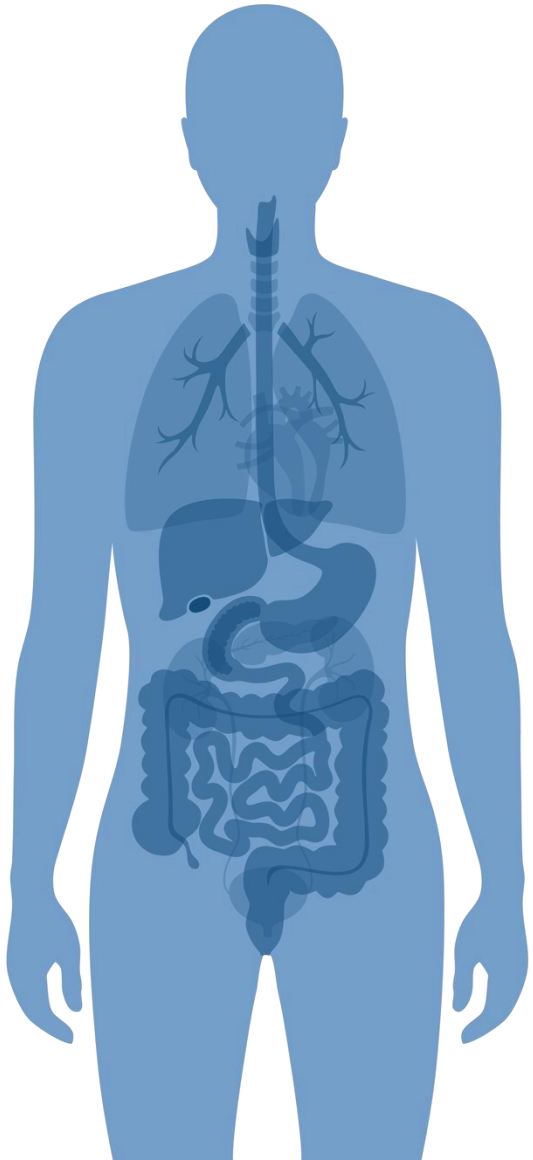
Fatigue, Weakness, Asthenia

Vomiting, Diarrhea, Bloating

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

"Myelopreservation" = chemoprotection focused on limiting chemotherapy-induced bone marrow toxicities

Poor Standard Of Care For Management Of Bone Marrow Toxicities



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
- 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

SEVERE THROMBOCYTOPENIA

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

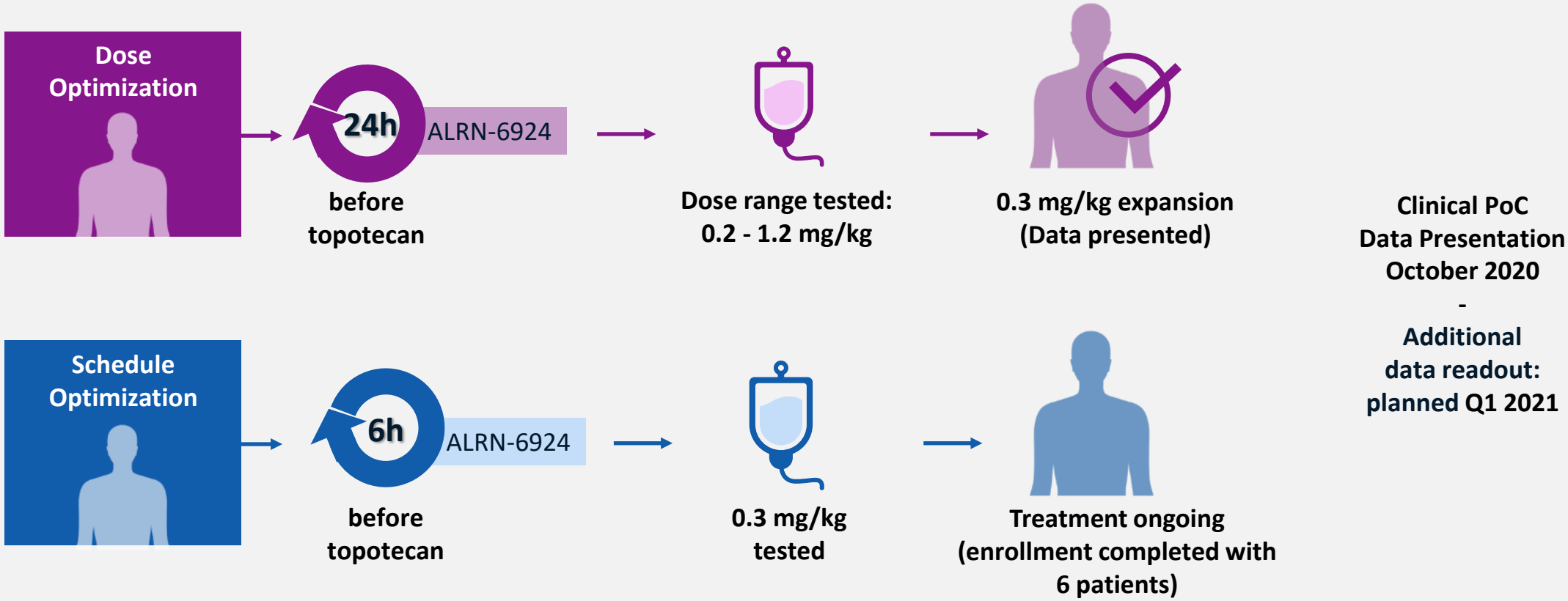
Clinical Issues:

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

ALRN-6924 Ongoing Phase 1b Trial
Design & Results

Data presented in late-breaking poster presentation at
EORTC-NCI-AACR conference (October 24, 2020)

ALRN-6924 Ongoing Proof-Of-Concept Phase 1b Study Schema



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

Representative Demographics And Key Baseline Characteristics

		0.3 mg/kg N (%) N=14	0.6 mg/kg N (%) N=5	1.2 mg/kg N (%) N=6	Total N (%) N=25
AGE	Median	68.5	67	58	67
GENDER	Male	14 (100)	2 (40)	4 (67)	20 (80)
ECOG PS	0	10 (71)	2 (40)	3 (50)	15 (60)
	1	4 (29)	3 (60)	3 (50)	10 (40)
BASELINE LDH	≥ULN	5 (36)	3 (60)	2 (33)	10 (40)
TIME SINCE PREVIOUS THERAPY	<60 days	7 (50)	1 (20)	5 (83)	13 (52)
STAGE AT INITIAL TUMOR DIAGNOSIS	Extensive Disease	6 (100)	5 (100)	6 (100)	25 (100)
P53 MUTATION STATUS	Mutated	13 (93)	5 (100)	6 (100)	24 (96)

-24h cohort, data cut August 31, 2020

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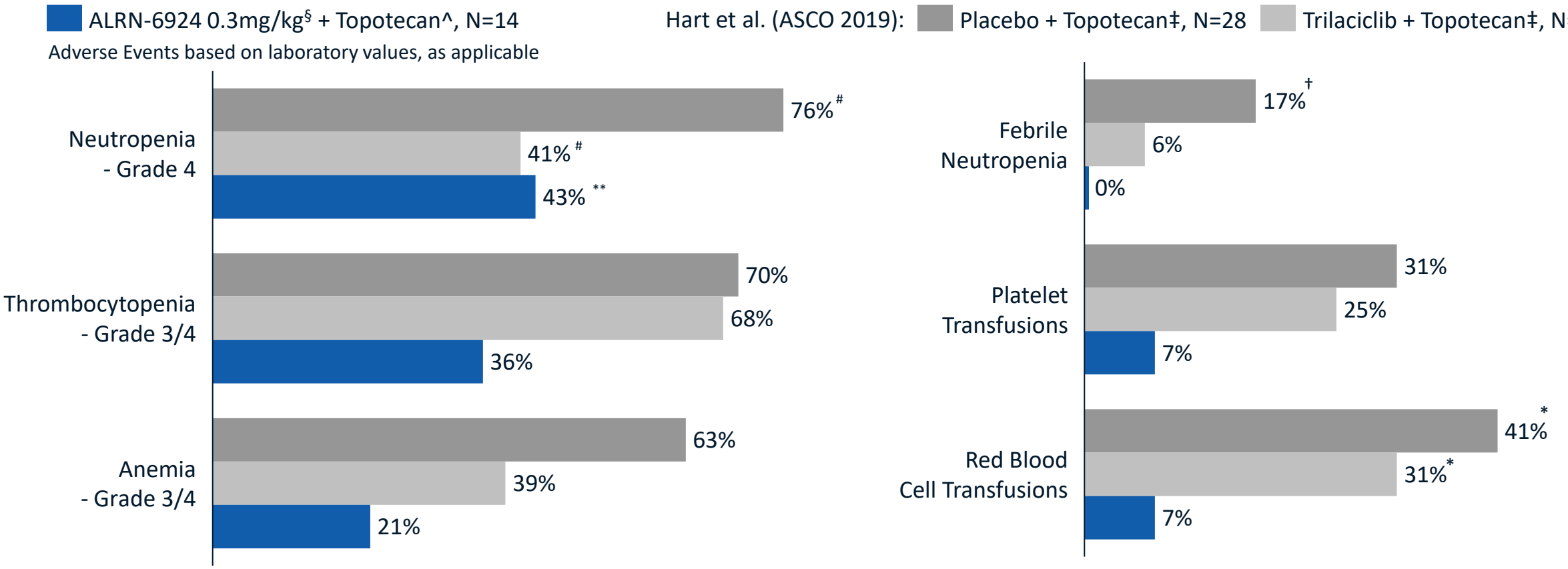

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* Excludes any RBC transfusions administered in the first 5 weeks
† Febrile neutropenia reported for 29 patients

Impact Of Chemoprotection On Other Side Effects, Dose Reductions Of Topotecan, And Other Metrics

- Topotecan-treated SCLC patients (%) experiencing Grade 3 or Grade 4 nausea or fatigue:
  - Without Chemoprotection: Nausea: 4%* to 8%^ , Fatigue: 6%^ to 7%*
  - With Chemoprotection:
    - with trilaciclib#: Nausea: 0%, Fatigue: 6%
    - with ALRN-6924§: Nausea: 0%, Fatigue: 0%

- Topotecan dose reductions in SCLC patients:
  - Without Chemoprotection: 29% ^ to 32%* of patients
  - With Chemoprotection:
    - with trilaciclib#: 19% of patients
    - with ALRN-6924§: 14% of patients

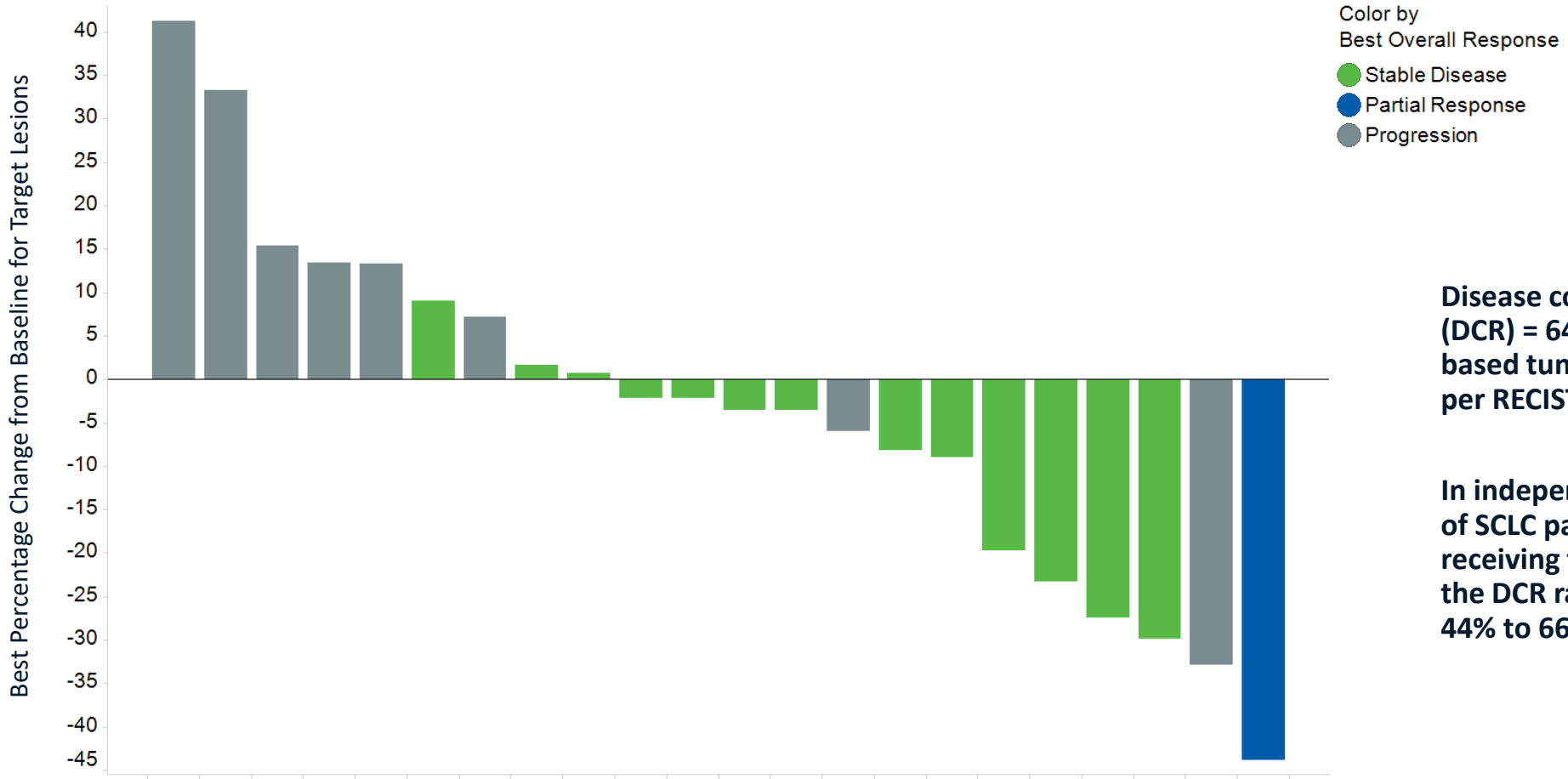
Hart et al., Adv Ther 2020; topotecan + trilaciclib-treated patients (G1-Therapeutics' Phase 2 Clinical Trial)

* Hart et al., Adv Ther 2020; topotecan + placebo-treated patients (G1-Therapeutics' Phase 2 Clinical Trial)

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

§ Andric et al, ENA 2020; patients receiving topotecan + ALRN-6924 (0.3 mg/kg, N=14)

Preservation Of Chemotherapy's Anticancer Effects During Treatment With ALRN-6924 And Topotecan As Reflected By Disease Control Rate



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ALRN-6924 Clinical Results: Key Takeaways

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

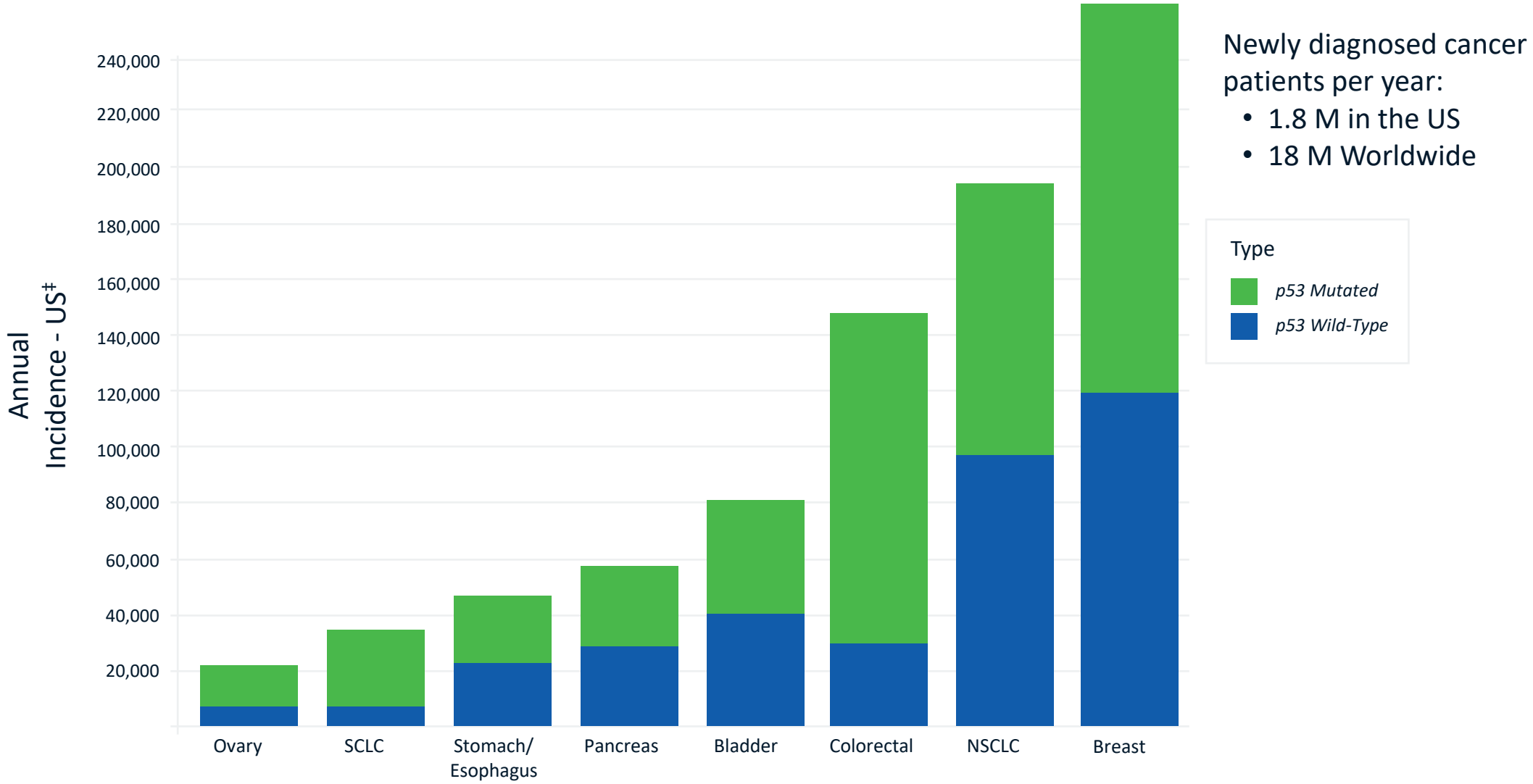
Chemoprotection for normal cells without protecting cancer cells

Fewer dose reductions of chemotherapy
=> potential for improved efficacy

0.3 mg/kg established as optimal dose for upcoming trial of ALRN-6924 in first-line chemotherapy in NSCLC

ALRN-6924 Opportunity and Clinical Development Strategy

Large Market Opportunity: High Rate Of p53 Mutation In Many Cancer Types



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Gastrointestinal and Other Cancers (Chemotherapies TBD)

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ALRN-6924: Next-Generation = Chemoprotection Without Protecting Cancer Cells

	1st Generation: Trilaciclib (GTHX) - PDUFA Feb. 2021	Next Generation: ALRN-6924
MoA to Induce Cell Cycle Arrest	CDK4/6 inhibitor that activates RB1	p53-agonist that activates p21
Genetic characteristic that avoids cell cycle arrest in cancer cells	RB1-Deficiency	p53-Mutation
Percentage of cancer patients:	10%	50%
Use of genetic characteristic as biomarker to select patients	NO	YES
Strategy to ensure chemoprotection without protecting cancer cells	NO	YES

Key Financial Highlights

January 2021	
Cash, Cash Equivalents and Investments	>$50M
Expected to support operations into	2nd Half 2023
Common Shares Outstanding	84M

Our Belief: Chemoprotection Will Transform Chemotherapy Like Anesthesia Transformed Surgery

Validated Core Differentiator	**Chemoprotection Without Protecting Cancer Cells**
Achieved Proof-of-Concept	**Reduction of multiple hematological toxicities and blood transfusions**
p53-Focused Clinical Development	**Trials in NSCLC: planned start in Q2 2021** **Trials in gastrointestinal and other cancers: planned start in 2022**

OUR VISION

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

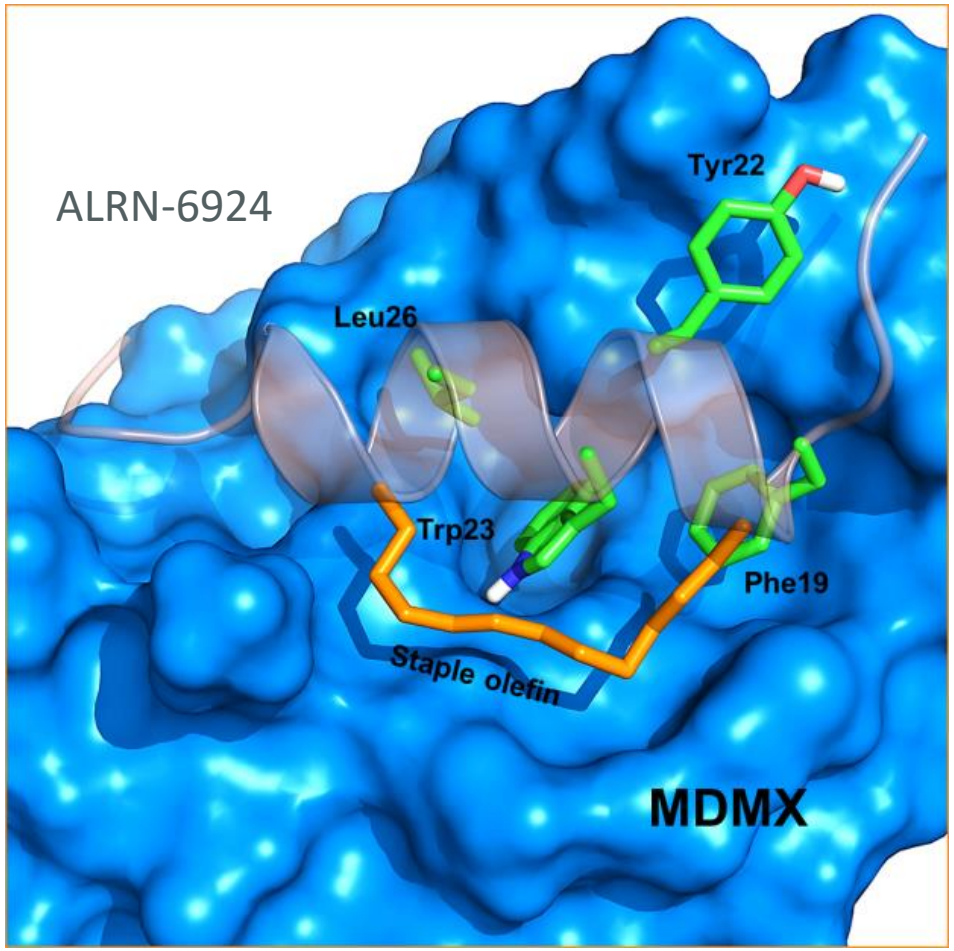
50%
of cancer patients have p53-mutated cancer

Supplementary Information I

ALRN-6924 - Mechanism of Action, Pharmacokinetics and Pharmacodynamics

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:

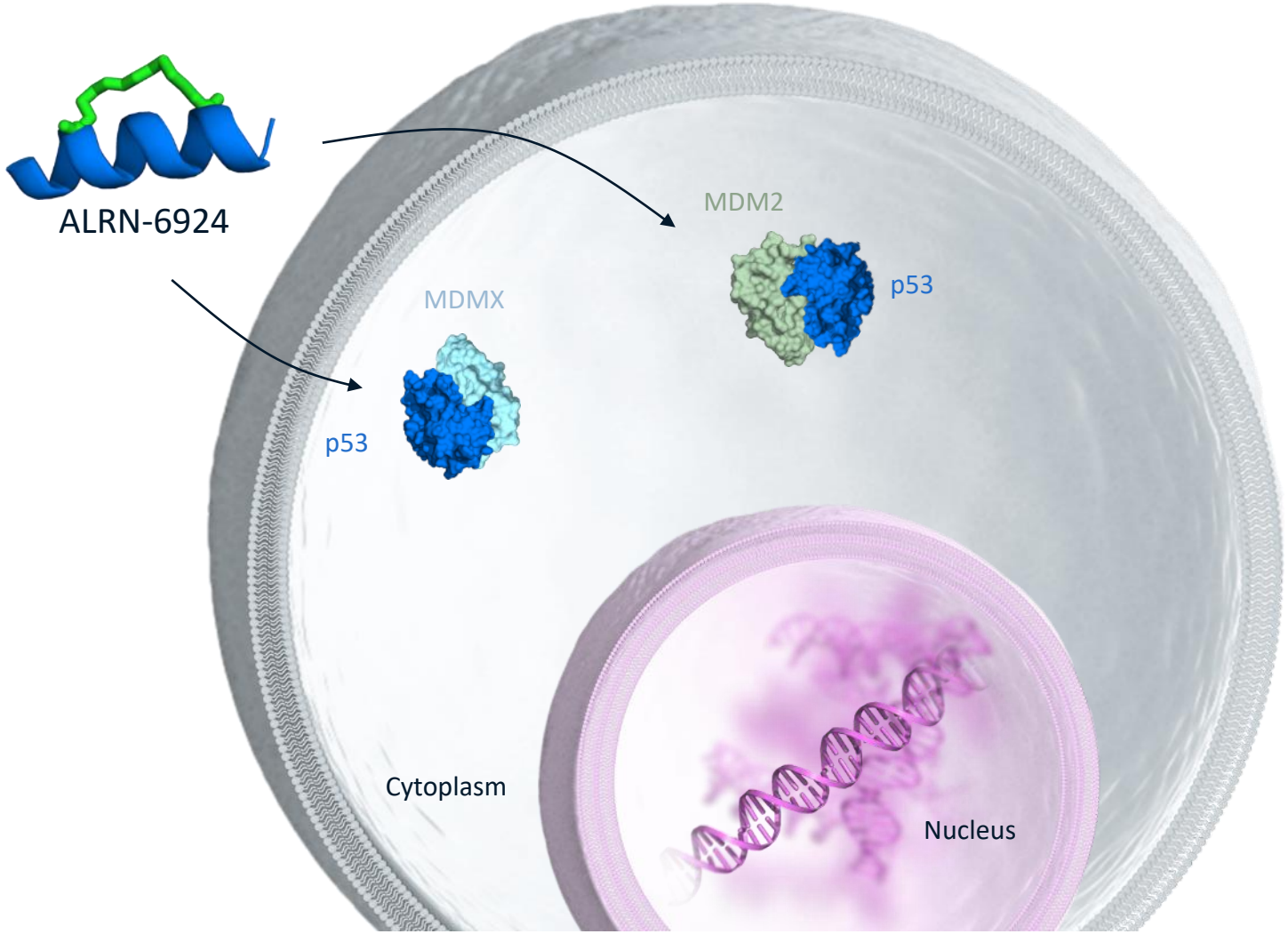
I. Protection from proteolytic cleavage

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 to induce cell cycle arrest

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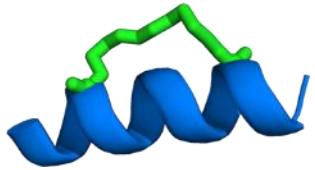
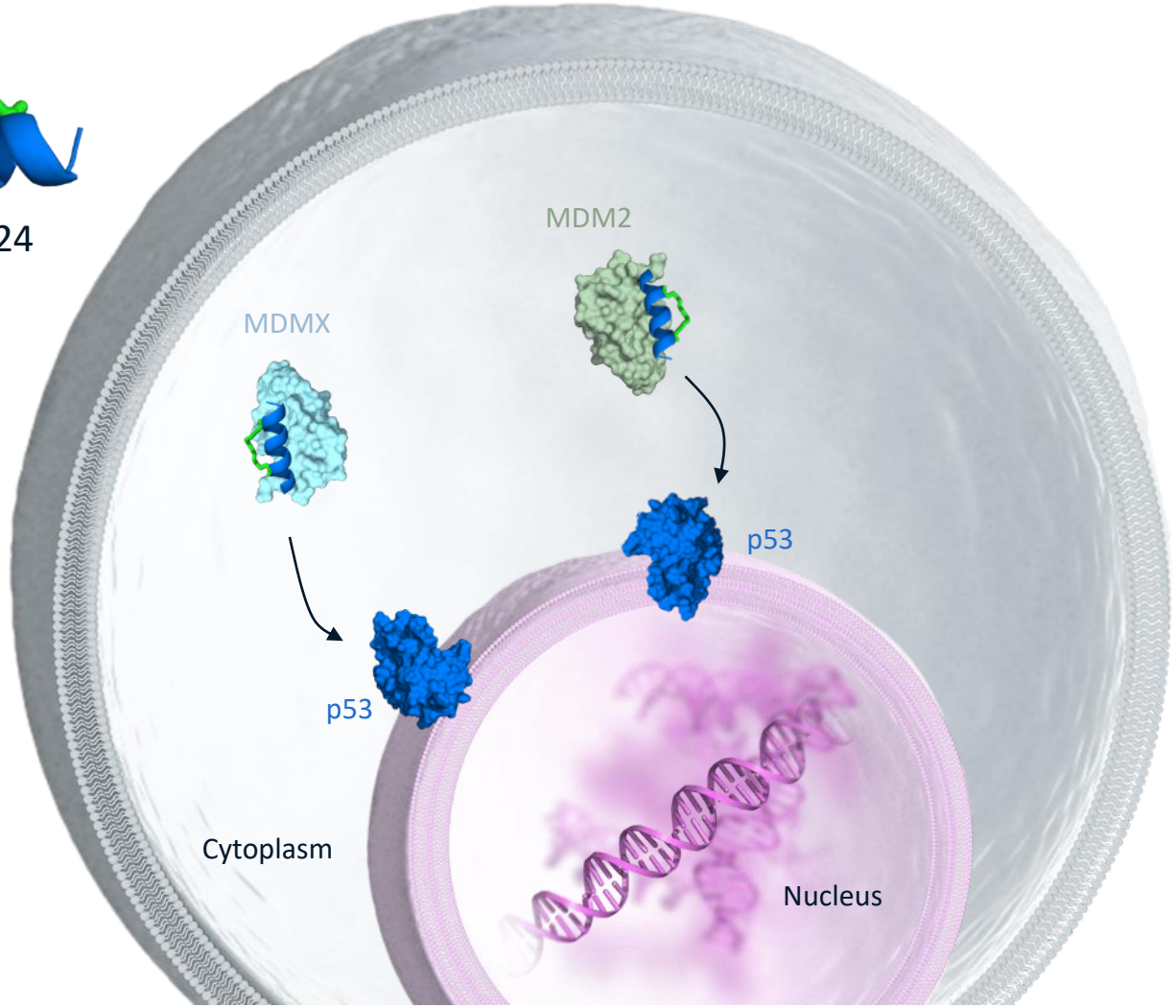


ALRN-6924



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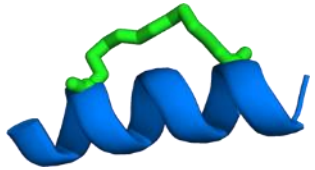
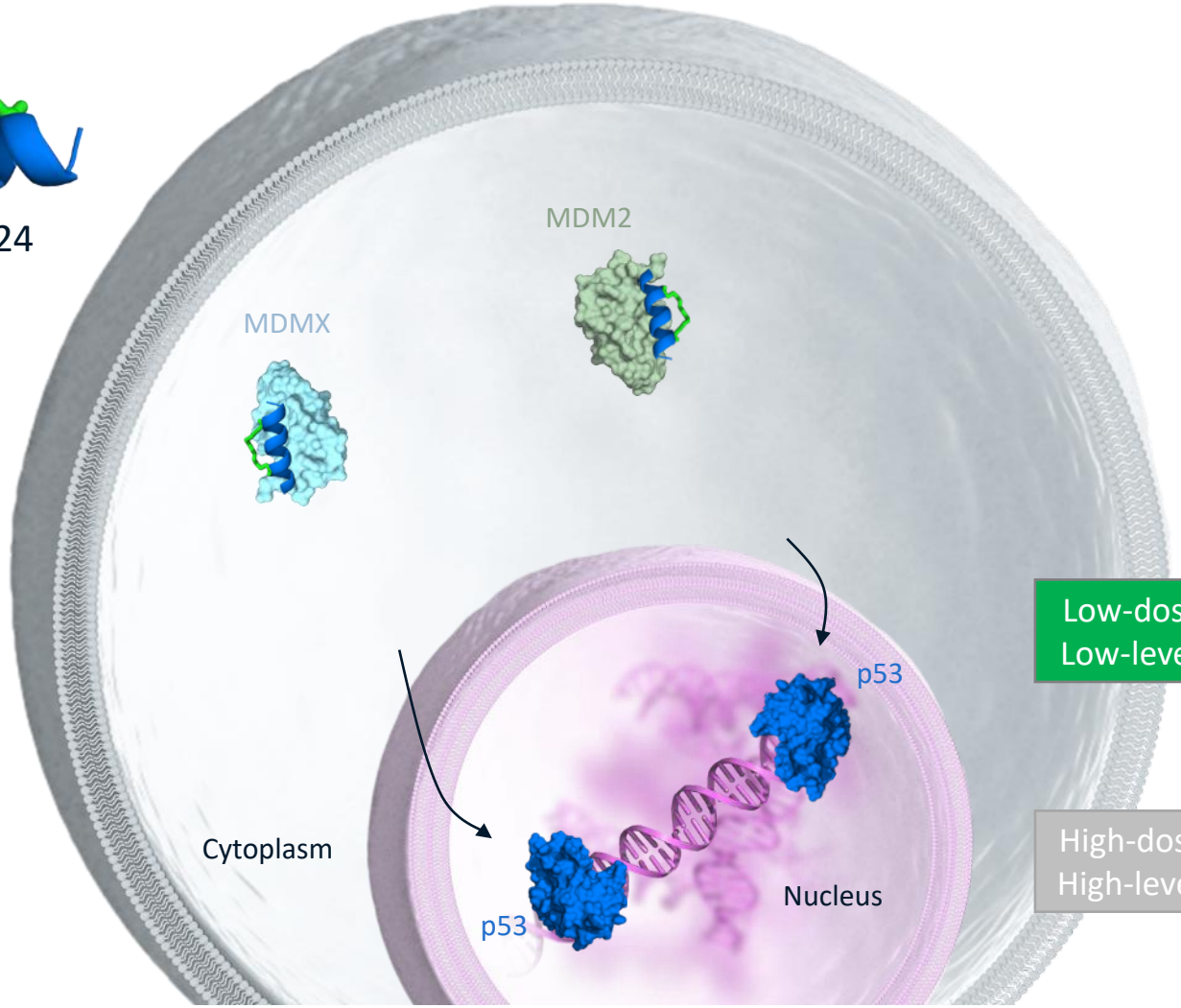


ALRN-6924



Low-dose ALRN-6924
Low-level p53 release

Cell cycle Arrest[1]

High-dose ALRN-6924
High-level p53 release

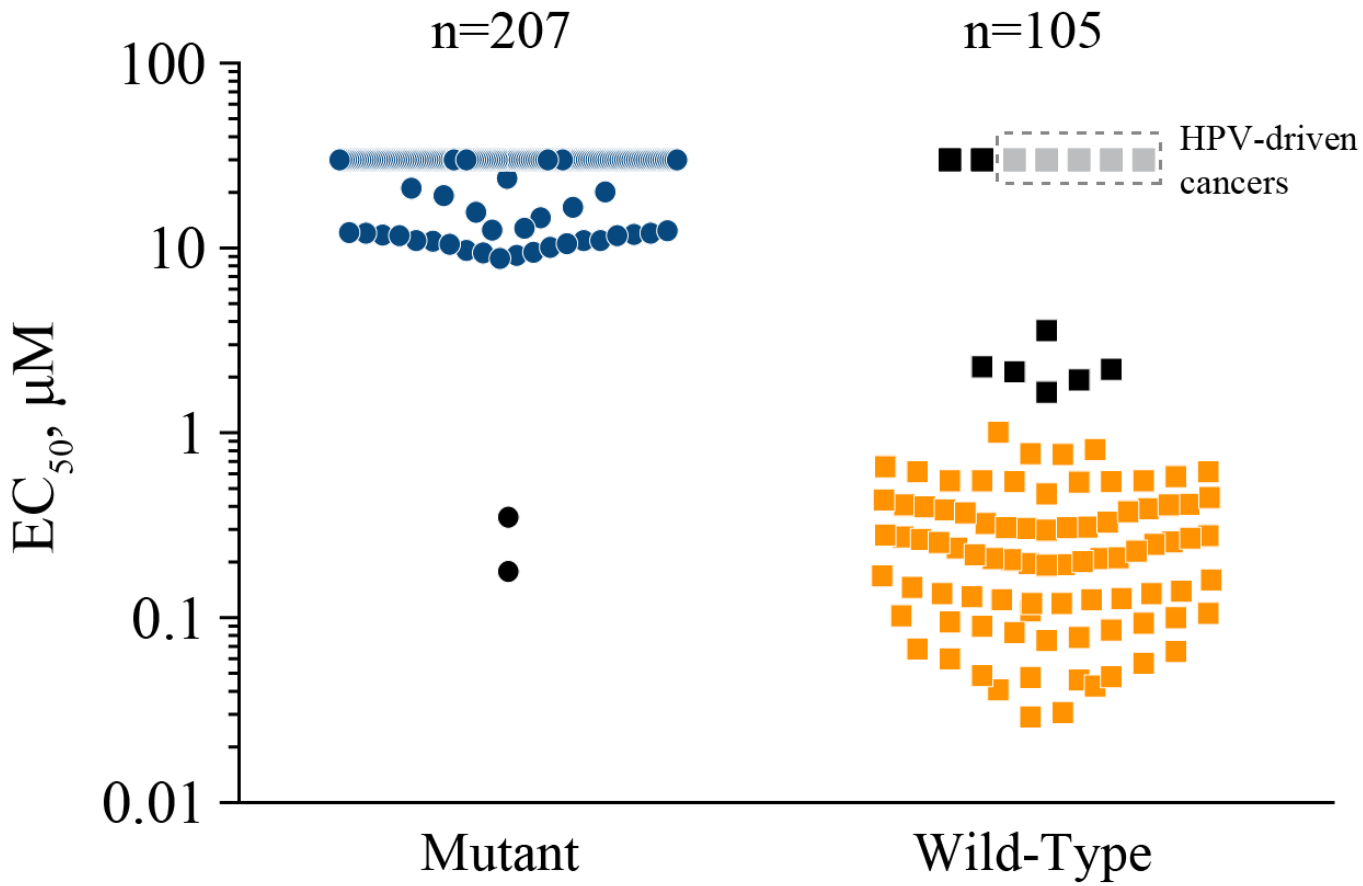
Apoptosis[1]

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

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

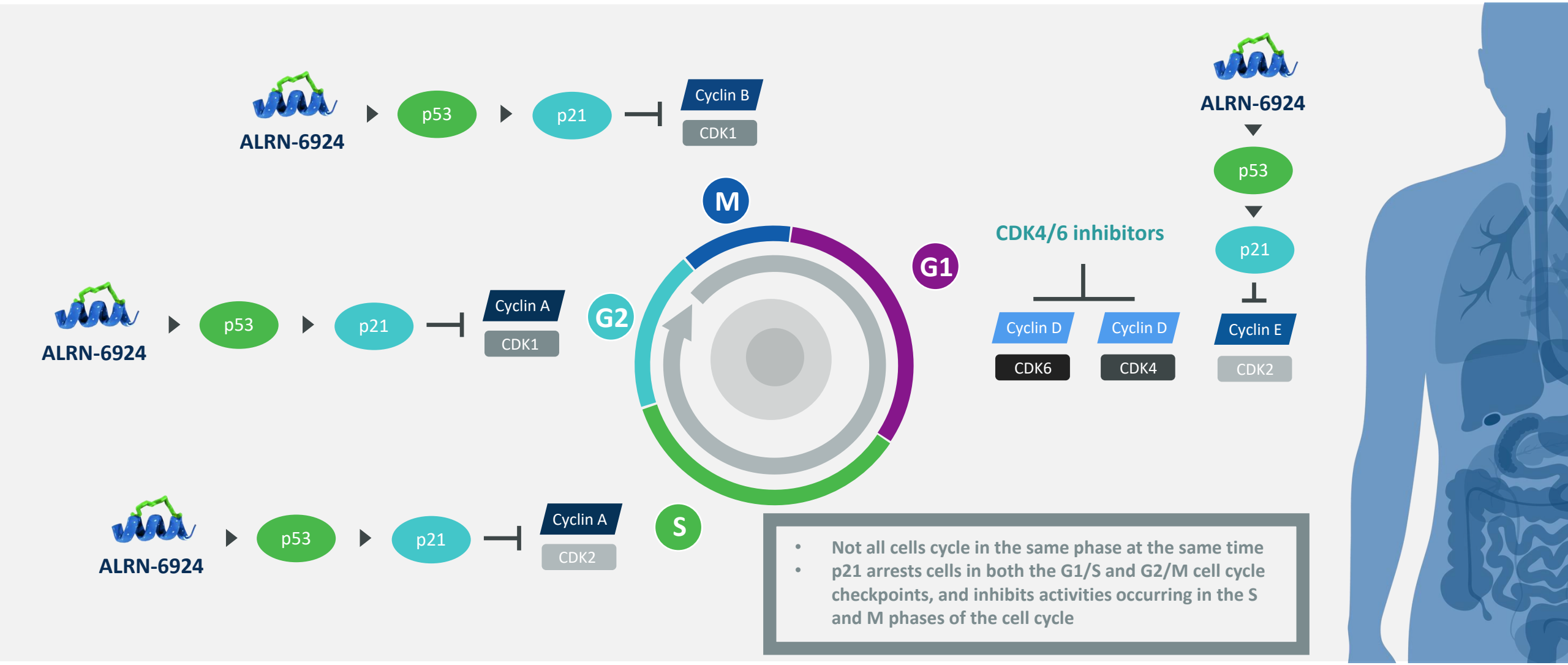
ALRN-6924 Does Not Work In Cells With Mutant p53

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



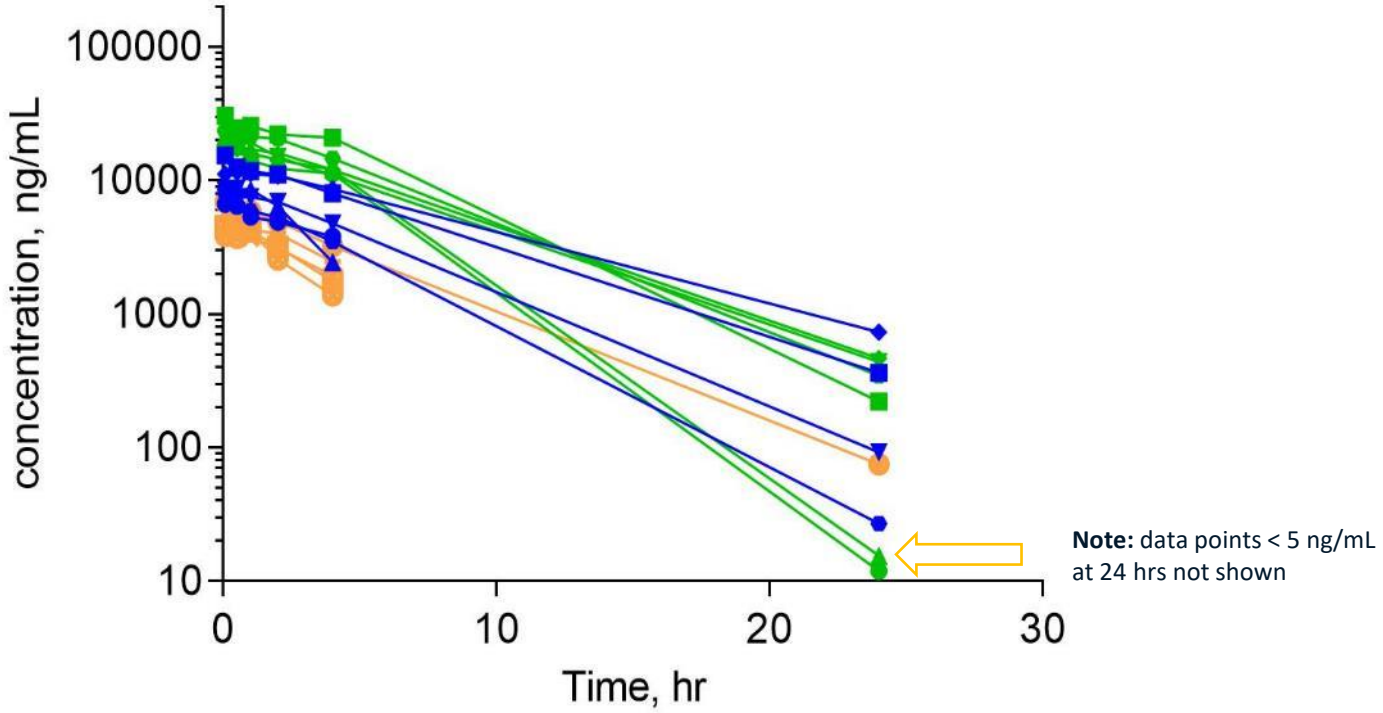
EC_{50} = Drug conc. at which 50% of tumor cells are killed
EC_{50} values ≥ 30 µM are shown as 30 µM

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



ALRN-6924 Shows Dose-dependent PK Profile In SCLC Patients

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



Note: data points < 5 ng/mL at 24 hrs not shown

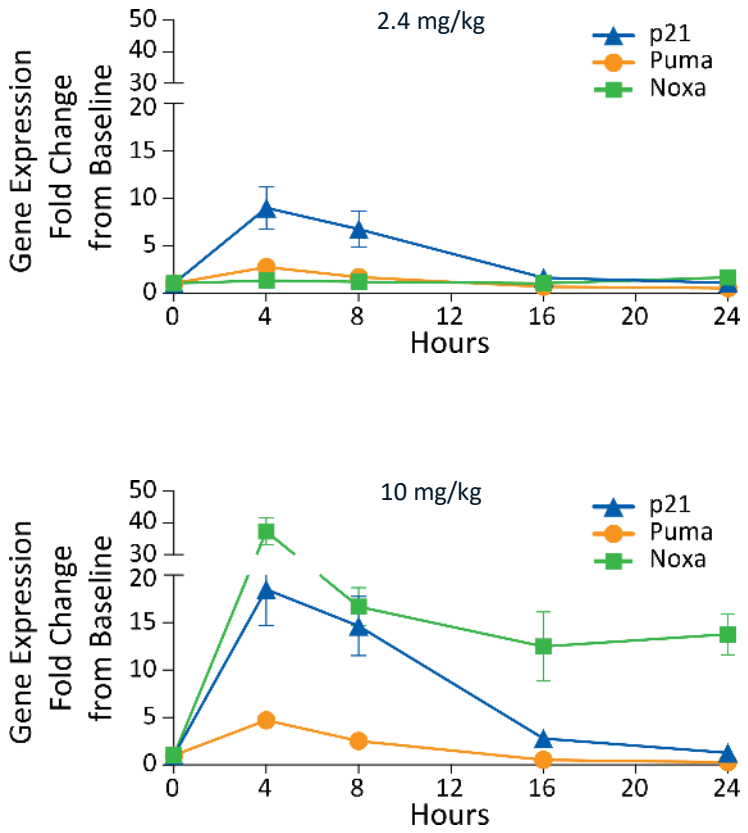
Parameter (average)	0.3 mg/kg	0.6 mg/kg	1.2 mg/kg
C_{max} µg/mL	5.0	9.9	21.9
$AUC_{0\text{-}24hr}$ ng·hr/mL	35,862	83,030	250,519
$t_{½}$ hr	3.4	4.5	7.1

- Monophasic clearance, low patient-to-patient variability
- Slightly less than dose-proportional exposure
- 3.4 to 7.1 hr half-life yields no accumulation on repeated dosing

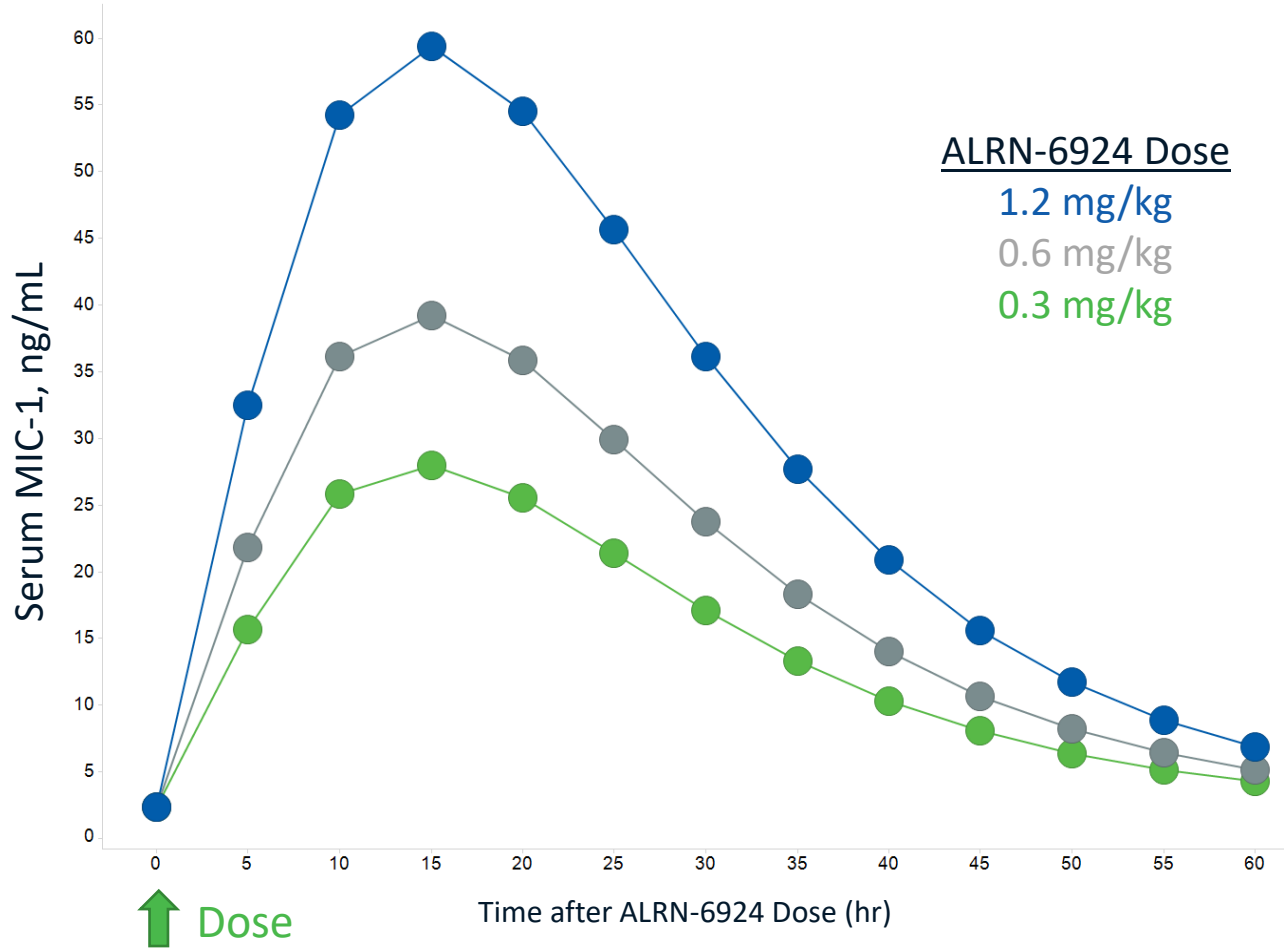
-24h cohort, data cut May 13, 2020

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

Non-clinical studies†



MIC-1 levels in ongoing SCLC trial‡

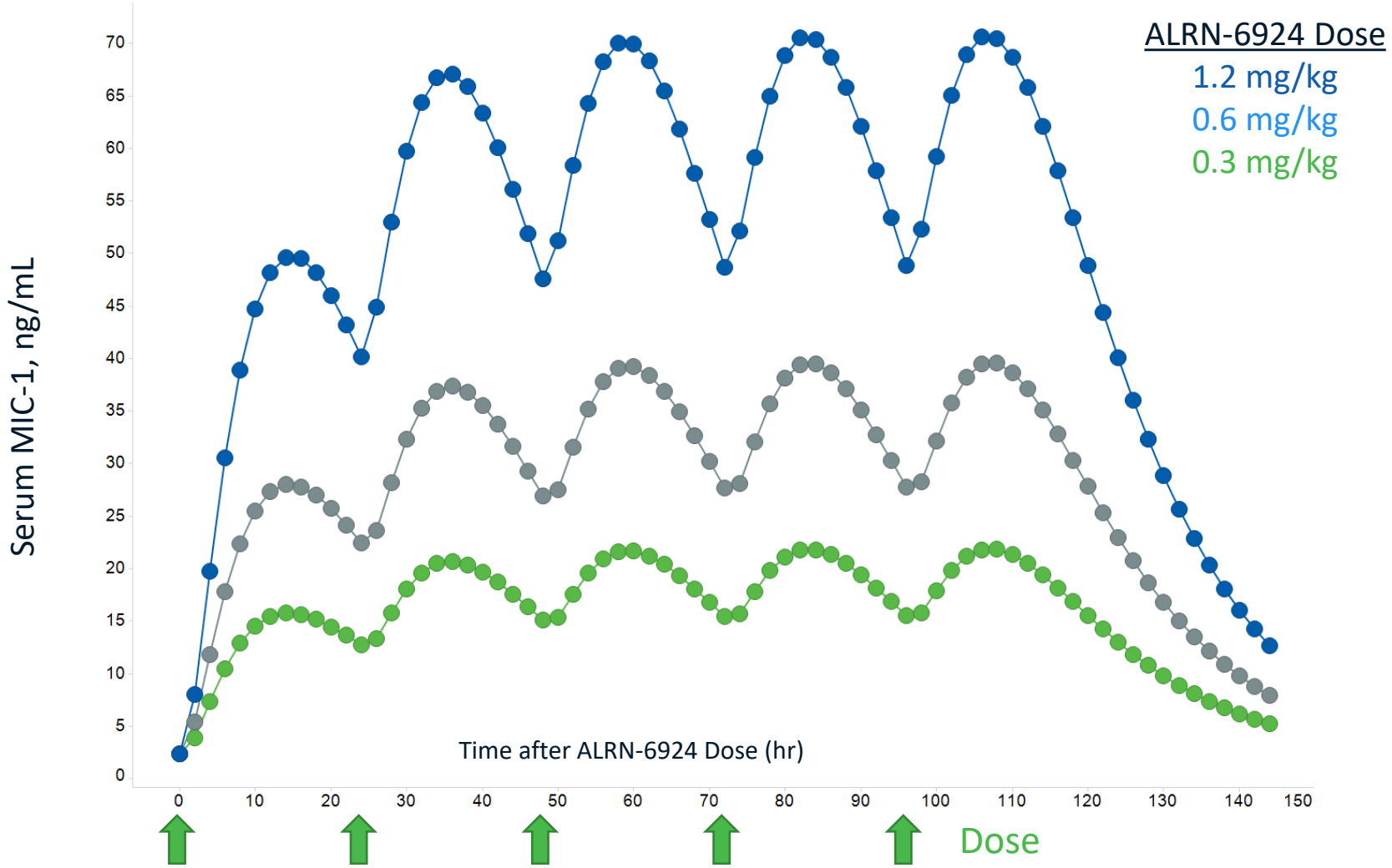


† Carvajal et al, "The Investigational Peptide Drug ALRN-6924, a Dual Inhibitor of MDMX and MDM2, is an Effective Myelopreservation Agent. AACR-NCI-EORTC Conference October 2019

‡ 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.

Repeat-dosing Of 6924 Leads To Sustained Activation Of P53 As Reflected By Sustained MIC-1 Levels

Data modelled from chemoprotection trial MIC-1 data plus earlier 71-patient first-in-human ALRN-6924 clinical trial results‡



‡ 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):2505-2505 (2017).

Chemoprotection May Transform Chemotherapy Like Anesthesia Transformed Surgery

NASDAQ: ALRN

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