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# Corporate Presentation

March 2019

# Legal Matters

Any statements in this presentation about future expectations, plans and prospects for Aileron Therapeutics, Inc and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors, including: uncertainties inherent in the initiation of future clinical studies and in the availability and timing of data from ongoing clinical studies; whether results from preclinical studies or earlier clinical studies will be predictive of the results of ongoing and future studies; whether interim data from clinical studies such as the data reported in this presentation will be indicative of the final results of the study; whether results from clinical studies will warrant meetings with regulatory authorities or submissions for regulatory approval; whether submissions for regulatory approval will be made when anticipated or at all; whether the Company will receive will receive regulatory approvals to market products; whether the company can raise cash resources when needed on attractive terms or at all; whether the Company's cash resources will be sufficient to fund the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements; other matters that could affect the availability or commercial potential of the Company's therapeutic candidates; and other factors discussed in the "Risk Factors" section of the Company's most recent annual report on Form 10-K filed with the SEC on March 29, 2019, and in the Company's other filings that it may make from time to time with the SEC. In addition, the forward-looking statements included in this presentation represent the Company's views as of the date of this presentation and should not be relied upon as representing the Company's views as of any date subsequent to the date hereof. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so.

This presentation also contains market data and other statistical information that are based on independent industry publications, reports by market research firms or published independent sources. Some market data and statistical information are also based on the Company's good faith estimates, which are derived from management's knowledge of its industry and such independent sources referred to above. While the Company is not aware of any misstatements regarding the market and industry data presented herein, such data involve risks and uncertainties and are subject to change based on various factors, including those discussed under the headings “Forward-Looking Statements” and “Risk Factors” in the Company’s report on Form 10-K.

# Key Value Creation Opportunities

## ALRN-6924 + palbociclib combination in MDM2-amplified cancers

- Phase II combination trial ongoing in biomarker-defined cancer patients
- Preliminary data 4Q-2019
- CDK4/6 inhibitors (including palbociclib) currently a ≈ $5B/yr WW franchise
- Expansion opportunity in MDM2-amplified cancers: additional ≈ $2B/yr WW

## ALRN-6924 myelopreservation program

- Phase 1b/2 trial starting 3Q-2019; proof-of-concept data 1Q-2020
- Market opportunity in p53-mutant cancer chemotherapy: ≈ $2B/yr WW

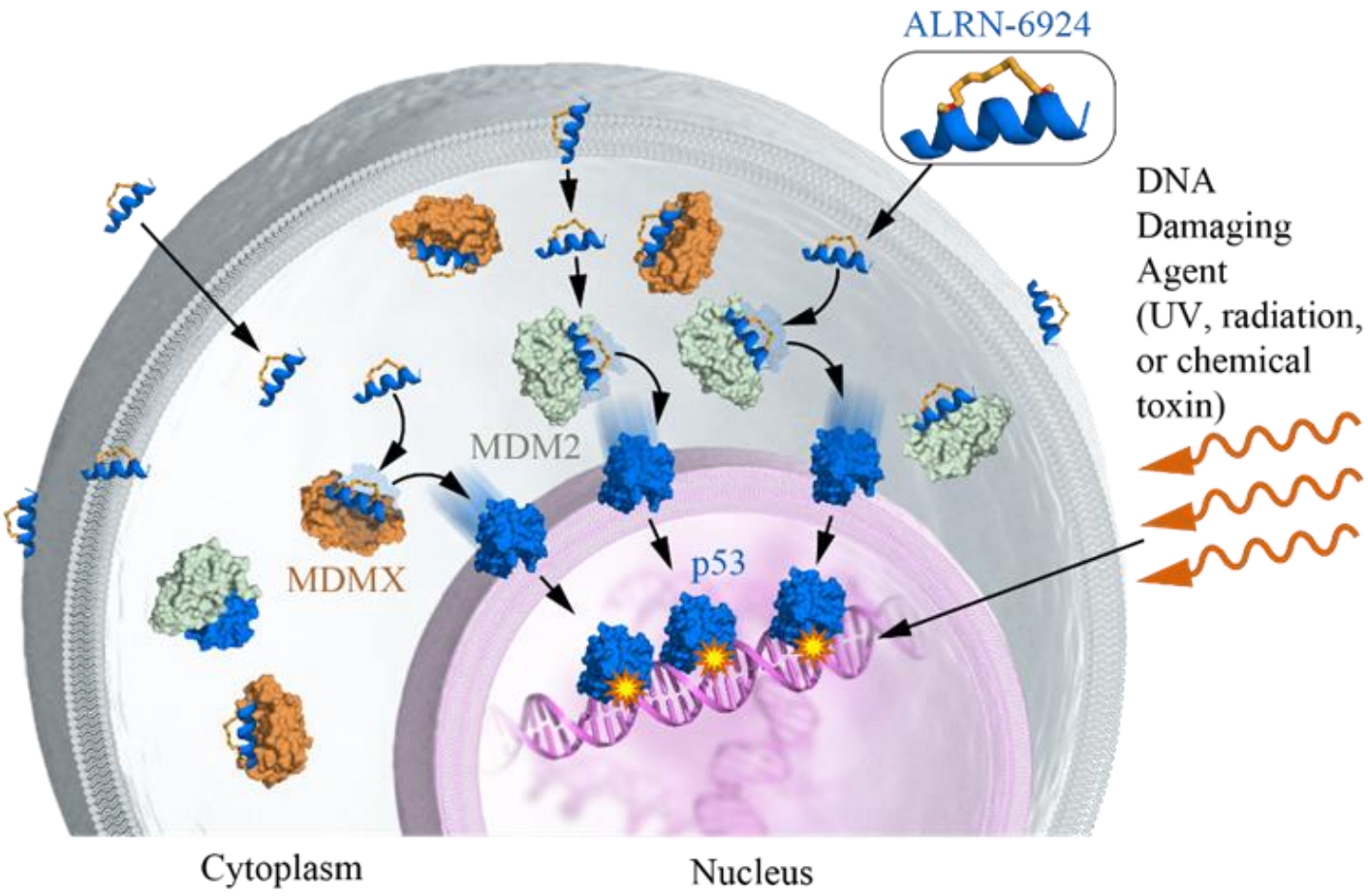
## Partnerships and out-licensing opportunities

- ALRN-6924 (regional or global rights)
- Platform expansion programs: PROTACs, Senolytics
- Discovery programs: HIF-1α, dual Bcl-2/Mcl-1-inhibitor
- >200 patents, worldwide exclusive rights to ALRN-6924 and platform

# Ongoing and Planned Trials

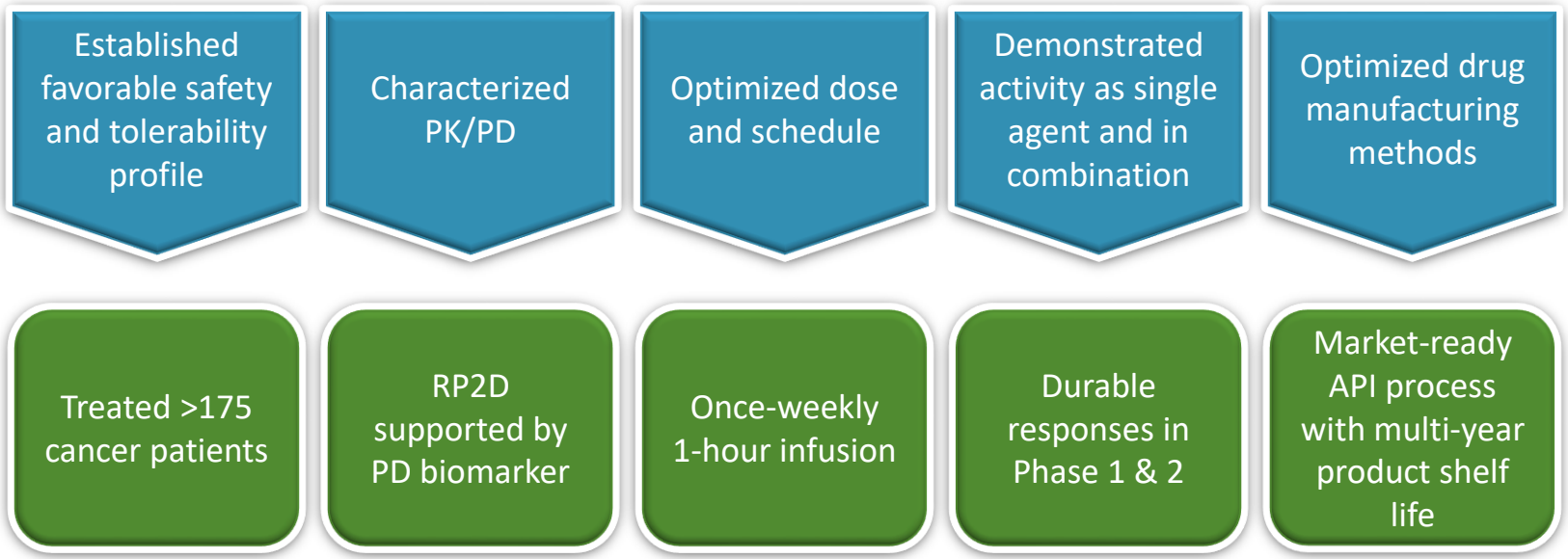
| Program | Indication | Preclinical | Phase 1 | Phase 2 | Milestone |
|---|---|---|---|---|---|
| **ALRN-6924**<br><br>**Dual MDMX- and MDM2 Inhibitor** | + Palbociclib in MDM2↑ tumors | | | | **Interim Data 4Q-2019** |
| | Myelopreservation for topotecan-induced chemotoxicity in 2L SCLC | Planned start Sept 2019 | | | **Proof of Concept 1Q-2020** |
| | + Paclitaxel in Breast cancer | | | | |
| | + Ara-C in Pediatric Leukemias | | | | |
| | Pediatric solid tumors | | | | |

# ALRN-6924 is a First-in-Class p53 Activator

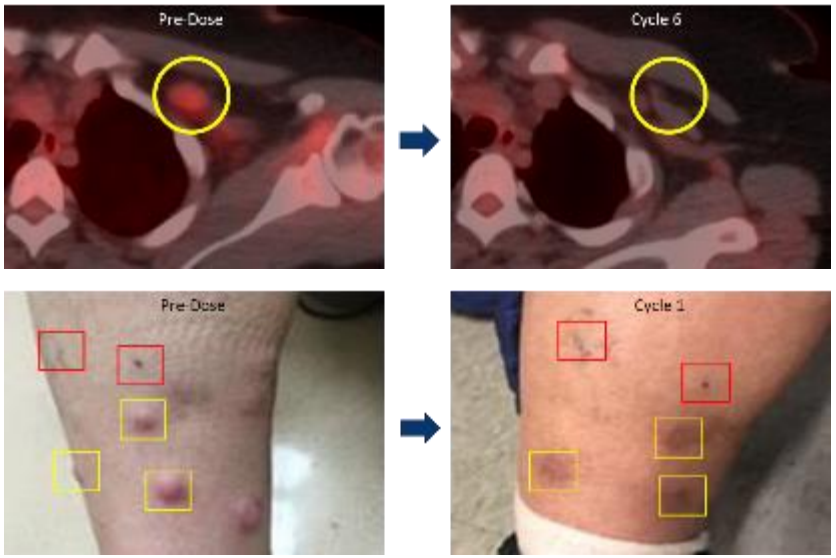


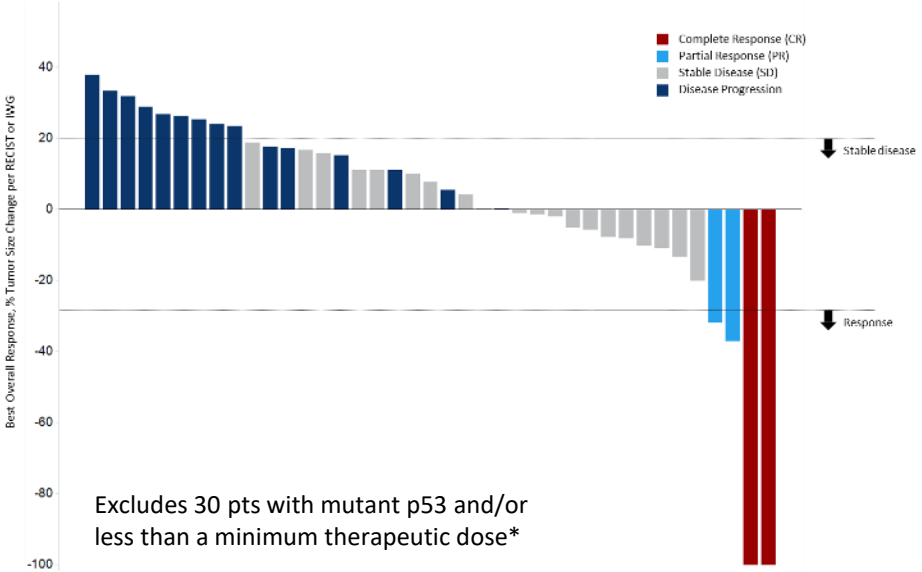

ALRN-6924 is a decoy that mimics p53 and selectively binds to MDMX + MDM2, releasing and reactivating p53 to induce cell cycle arrest and apoptosis

# ALRN-6924 Clinical Development Accomplishments



# ALRN-6924 Phase 1: Compelling Single-agent Activity, Oral ASCO Presentation, Selected for "Best of ASCO"



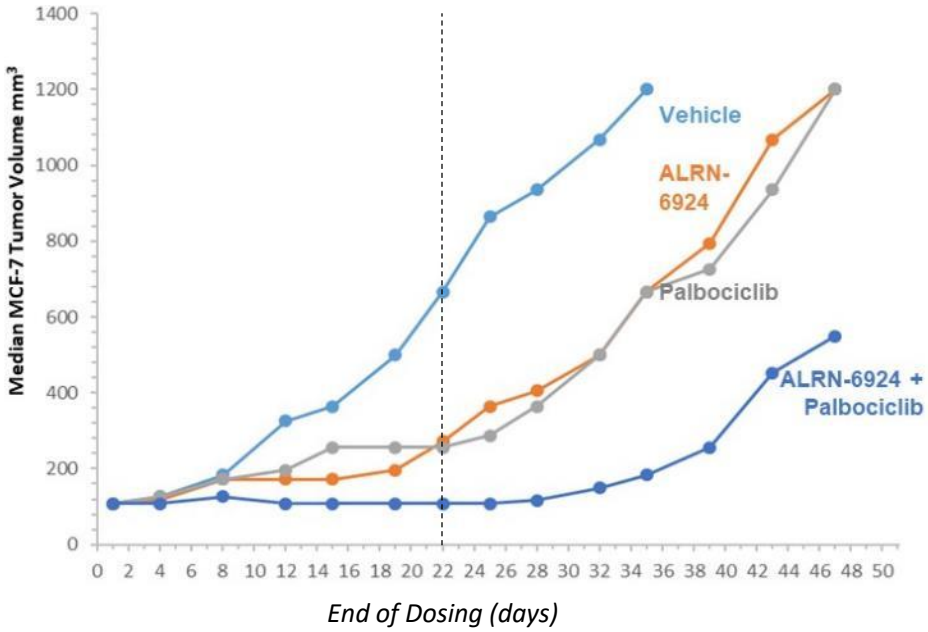

- 71 pts monotherapy dose-escalation
- 2 CRs (Merkel and PTCL), 2 PRs (liposarcoma and CRC), 11/20 SDs w/ shrinkage
- Durable responses: 4 pts >2 yrs. (70-100+ doses of ALRN-6924)
- Activity in MDM2↑ liposarcoma pt and T-cell-related malignancies

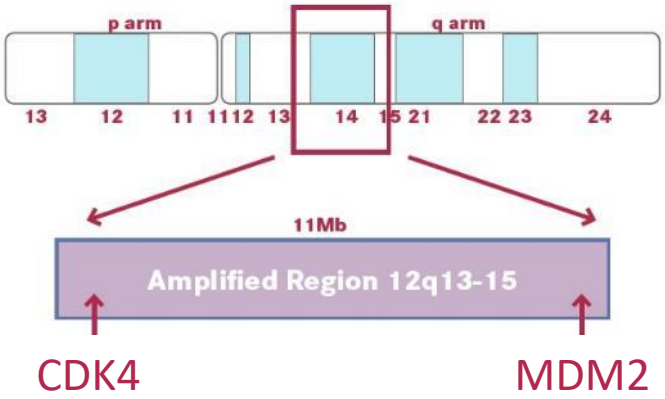
** <0.8 mg/kg per dose (Recommended Phase 2 Dose = 3.1 mg/kg per dose)*

# ALRN-6924 Shows a Differentiated Safety Profile vs. MDM2-only Inhibitors

| First-in-Human Phase 1 Trial | # pts | Dose range | Thrombo-cytopenia Grade ≥ 3 | Neutropenia Grade ≥ 3 |
|---|---|---|---|---|
| **ALRN-6924** | **71** | **28x** | **0%** | **3%** |
| AMG 232 | 39 | 32x | 33% | 21% |
| DS-3032b | 103 | 22x | 19% | 12% |
| HDM201 | 107 | 28x | 24% | 23% |
| RO6839921 | 41 | 8x | 15% | 20% |
| RG7388 | 95 | 16x | 33% | 21% |
| MK-8242 | 47 | 8x | 15% | 19% |

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



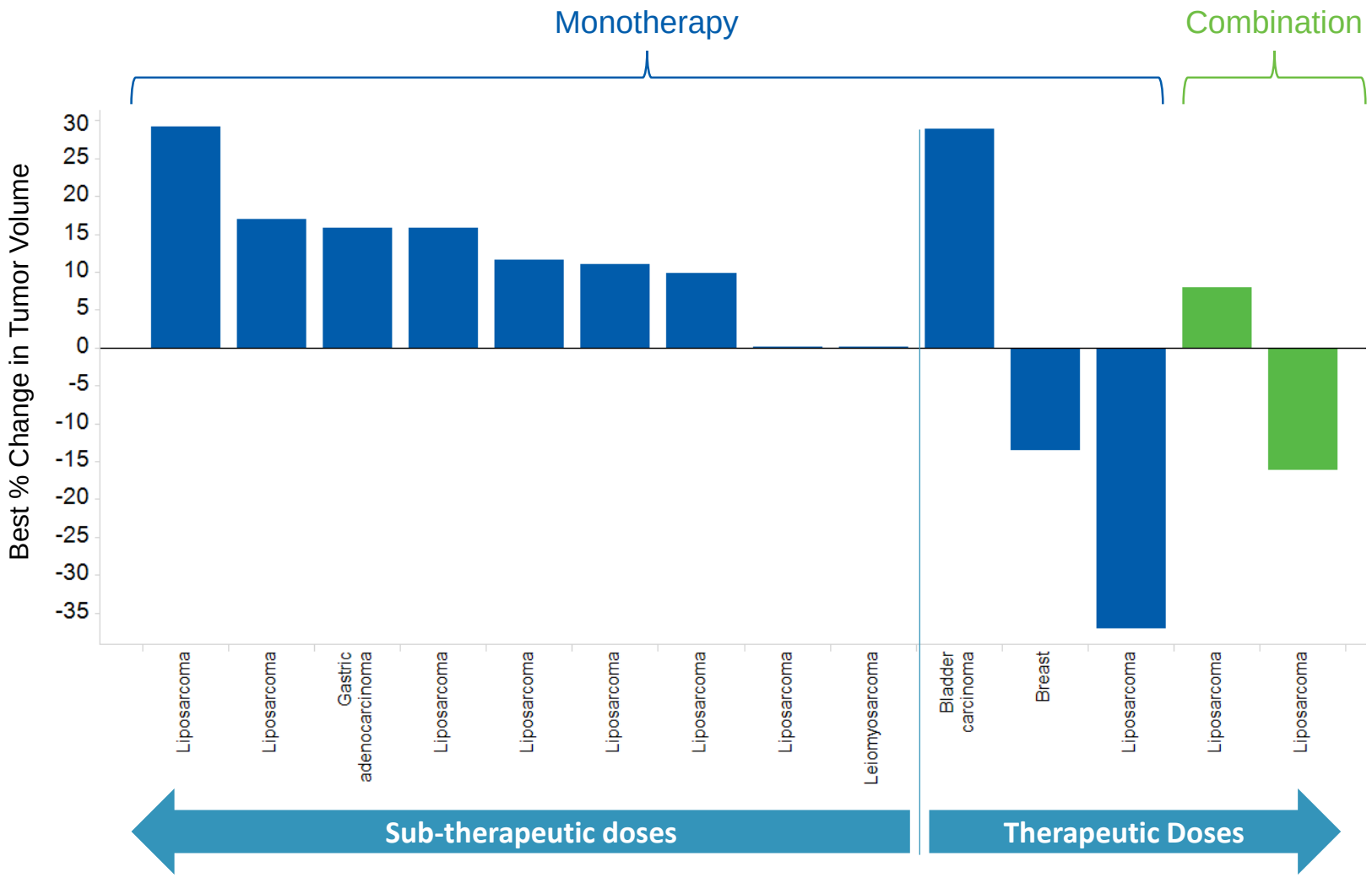




**Palbociclib Phase 2 combination trial ongoing: interim data (n =15) in 4Q-2019**

- Precision medicine approach: patient selection based on genetic biomarker (MDM2 amplification or MDM2/CDK4 co-amplification) detected by routine genetic testing
- Tumor-agnostic: MDM2 amplification found in up to **4% of all cancers.**‡ Most frequent tumor types include sarcomas, breast and lung cancer, glioblastoma, etc.
- Palbociclib provided by Pfizer, supported by Joint Development Committee

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

# ALRN-6924 Alone and in Combination with Palbociclib Shows Activity in MDM2-amplified Solid Tumor Patients



# Market Opportunity for MDM2-amplified Tumors

| Patients | Factor |
|---|---|
| 1,735,350 | 2018 Incidence of cancer patients in USA* |
| 69,000 | 4% of cancers have amplified MDM2‡ |
| 52,000 | Est. 75% identified with routine genetic testing |
| 39,000 | 75% of patients with wildtype TP53‡ |

Market opportunity for combo: US ≈ $1.2B/yr; worldwide ≈ $2B/yr
Assumptions include: tumor agnostic label, treatment duration 6 months, market penetration 60%

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

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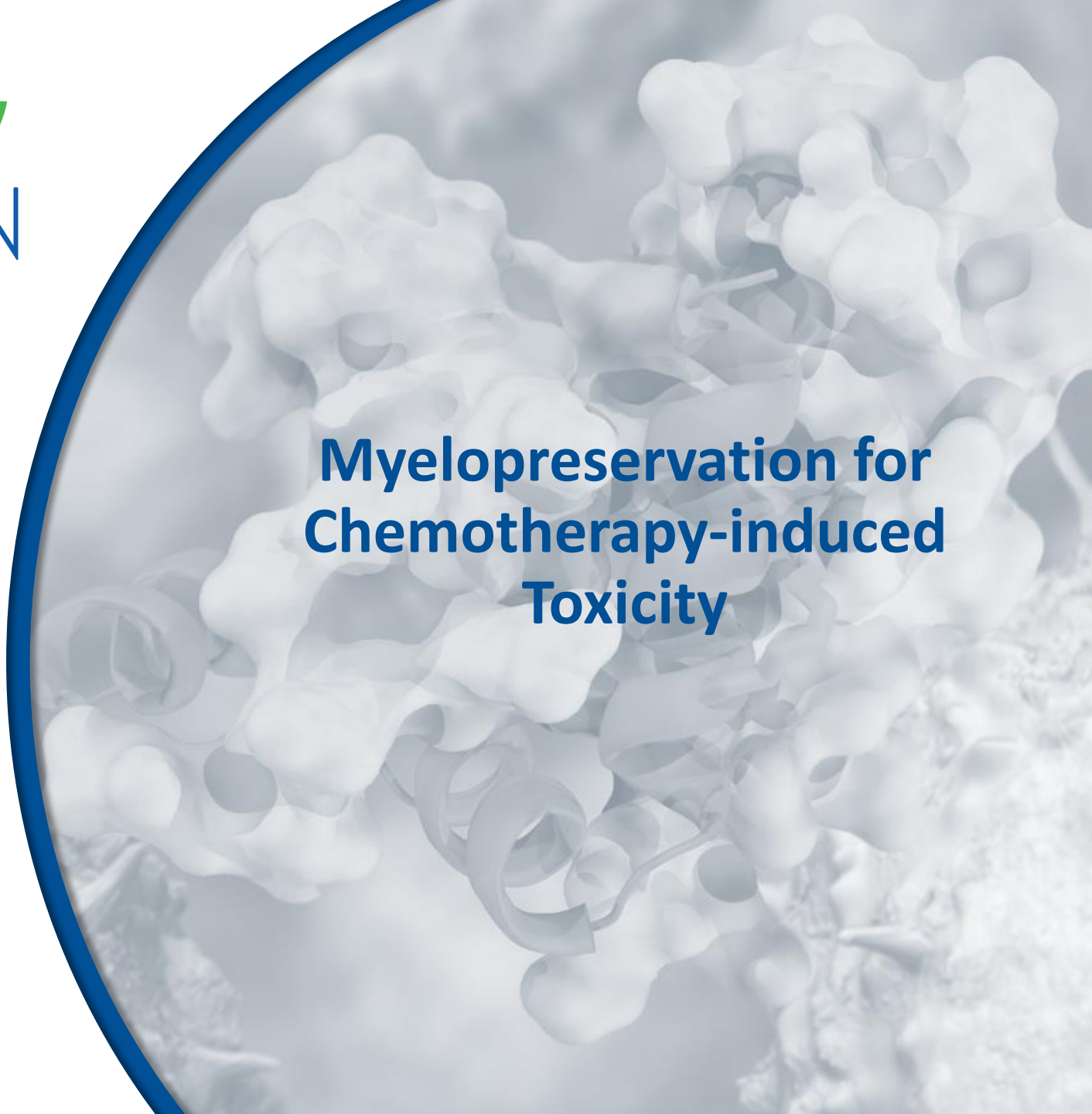
# Myelopreservation for Chemotherapy-induced Toxicity

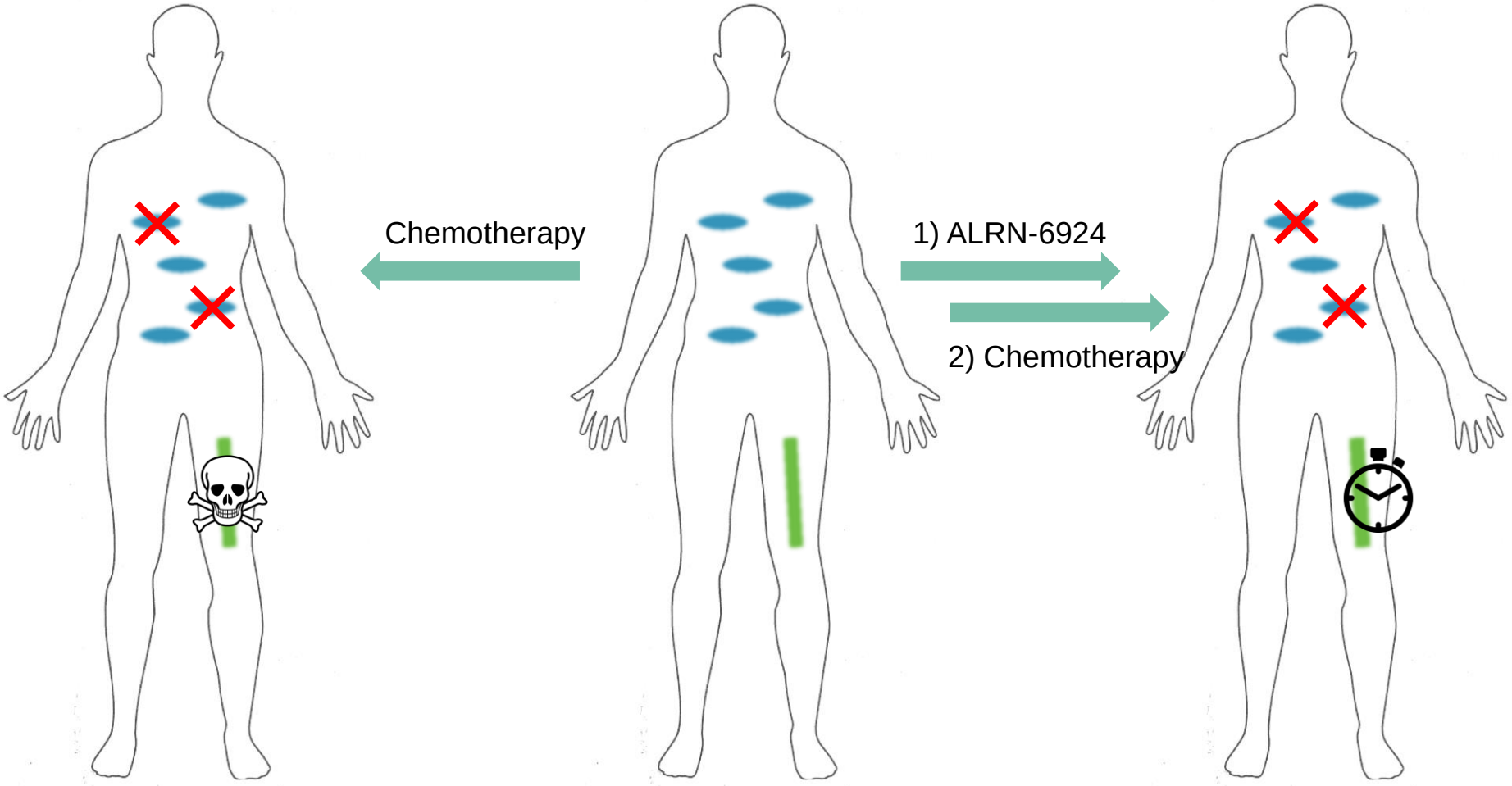


# ALRN-6924 can be a Myelopreservative Agent for Chemotherapy Treatment of p53-mutant Cancers

Chemotherapy can affect both p53-mutant tumors and p53-wild-type bone marrow

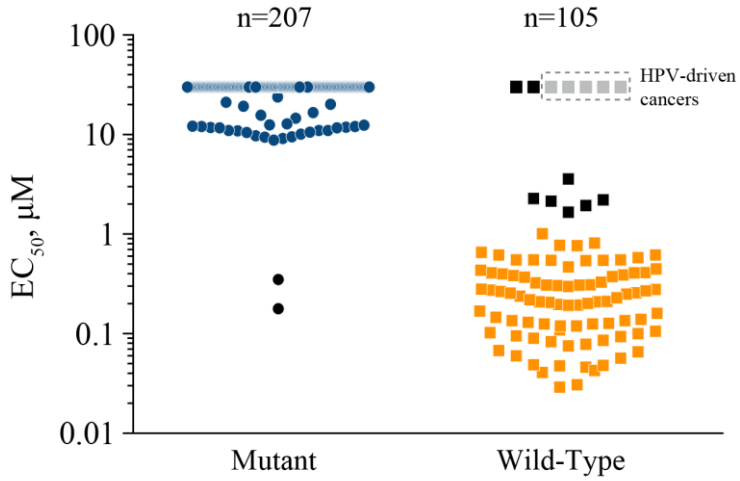
Patient with p53-mutant tumors, p53-wild-type bone marrow

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

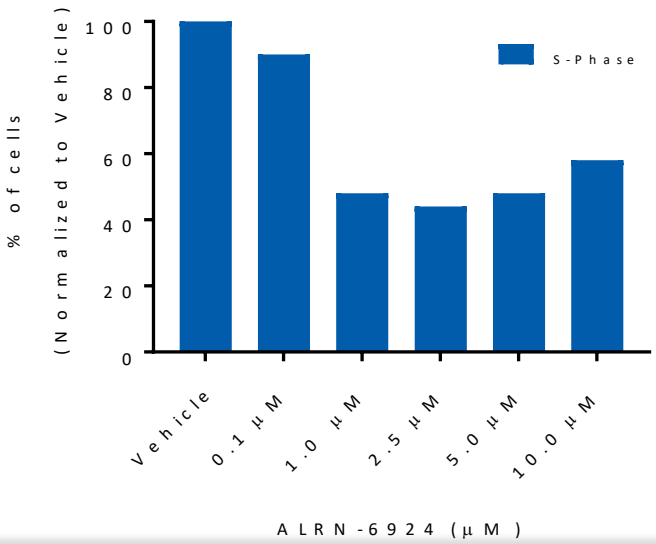


# ALRN-6924 is Active in p53-WT Cells Only and Causes Cell Cycle Arrest in Human Bone Marrow Cells

ALRN-6924 is active in wt p53 cells only




ALRN-6924 arrests human bone marrow cells



# Market Opportunity for Myelopreservation

Bone marrow toxicity is an area of unmet medical need, leading to severe complications, treatment delays and chemotherapy dose reductions

| Patients | Factor |
|---|---|
| 1,735,350 | 2018 Incidence of cancer patients in USA* |
| 860,000 | Est. 50% of cancer patients receive chemotherapy |
| 258,000 | Est. 30% of patients treated with chemotherapy develop significant bone marrow toxicity |
| 130,000 | 50% of patients with mutated TP53 |

Market opportunity: US ≈ $1.2B/yr; worldwide ≈ $2B/yr.
Assumptions include: chemotherapy agnostic label, average number of 4 treatment cycles, cost per cycle $4k (based on G-CSF pricing), market penetration 60%

*SEER database

# New Indications and Targets in Discovery Stage:
*Opportunities for Partnership*


Discovery programs: HIF-1α, dual Bcl-2/Mcl-1-inhibitor

Proteolysis targeting chimeras (PROTACs)

Bifunctional peptides that connect ubiquitin ligases to unwanted proteins resulting in degradation of the target protein

*In vitro* Proof-of-Mechanism: Stabilized peptide conjugates to degrade MDM2 and Myc

Therapeutics that eliminate senescent (aging) cells

First drug now in trials: Unity Bio's MDM2 inhibitor

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# Outlook

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# Financial Summary

## Financial Position

- $21M in cash and equivalents as of December 31, 2018
- $26M raised in a private placement, April 2, 2019 closing
- Current expected cash runway into December, 2020
- Future projected quarterly cash burn rate ≈ $6M

## Key Value Drivers

- Combination with palbociclib in MDM2↑ cancers
- Myelopreservation trial in small cell lung cancer

## Research & Opportunities for Partnering

- Selected novel applications for Aileron's peptide technology:
  - Targeted protein degradation (PROTACs)
  - Dual Bcl-2/Mcl-1, ß-Catenin, HIF-1α inhibitor
  - Senolytics

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# Thank You

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