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- Clinical-stage leader in stapled peptide therapeutics for cancer and other diseases
- Clinical proof-of-concept with multiple complete and partial remissions showing that stapled peptides successfully engage with intracellular targets
- Clinical compound ALRN-6924
  - has potential to be **best-in-class** p53-activating therapy, and
  - is the **first-in-class** dual MDMX/MDM2 inhibitor
- Clinical programs in PTCL, AML and MDS indications may allow fast-to-market development in areas of large unmet medical need
- Preclinical data and clinical safety profile support exploration of opportunities for combination therapies with immune checkpoint inhibitors, kinase inhibitors and chemotherapeutics
- Strong IP patent portfolio protecting ALRN-6924 and stapled peptide platform



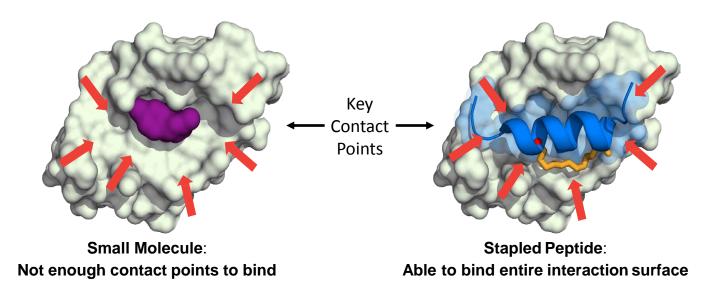
# Aileron Pipeline

Programs	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
	All-comers solid tumors & lymphomas				Enrollment completed 1Q2017; patients ongoing	
ALRN-6924 Reactivating p53	PTCL					
	AML & MDS (Monotherapy)					
	AML & MDS (Combo w/ Ara-C)					
	Combination therapies for solid tumors					
p53 Next generation	Solid & liquid tumors					
Pipeline	Undisclosed Targets					

PTCL: Peripheral T-cell Lymphoma; AML: Acute Myeloid Leukemia; MDS: Myelodysplastic Syndrome



# Stapled Peptide Technology Platform: Opens Opportunity to Address Unmet Needs

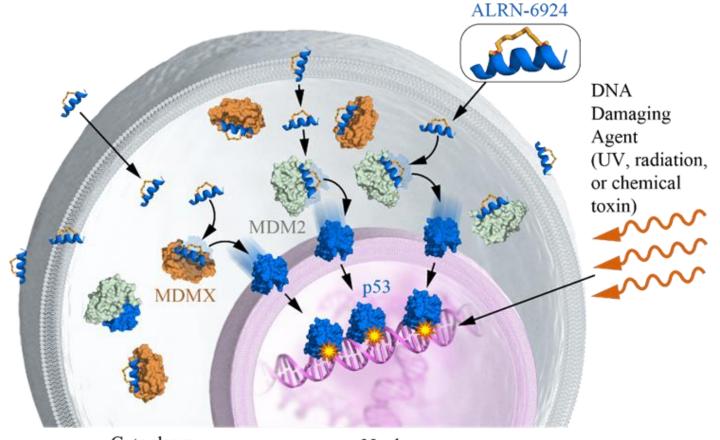


### Advantages of Stapled Peptides over Small Molecules:

- 1. Larger surface area
  - Provides superior binding properties reducing off-target effects
  - More resistant to mutation of targets
- 2. Technology enables single compound to engage with multiple targets, potentially increasing potency, e.g. MDMX + MDM2 or Bcl-2 + Mcl-1
- 3. Easier design: stapled peptides largely replicate natural peptide sequences



### ALRN-6924 Reactivates p53: First-in-Class Dual Inhibitor



Cytoplasm

Nucleus

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



### **Recent Recognitions by Scientific Community**:

- ASCO 2017 Oral presentation and selected for "Best of ASCO"
- **ISEH 2017** Oral presentation and gold medal investigator award
- **ASH 2017** Two oral presentations
- Inclusion in JCO's Clinical Cancer Advances 2018:
  - Heymach et al., JCO 2018 Apr 1;36(10):1040
- Collaborative Research Papers:
  - Carvajal et al., Science Translational Medicine 2018 Apr 11;10(436)
  - Koch et al., accepted for publication in **Nature Communications**



Targeted Cancers	WT P53 Frequency	Incidence (US)	ALRN-6924 Pre-Clinical Proof	ALRN-6924 Clinical Activity
Breast Cancer (ER+HER2+/ER+HER2-)	75/90%	252,710	$\checkmark$	✓
Colorectal Cancer	20%	135,430	$\checkmark$	PR
Melanoma/Merkel Cell	80%	87,110	$\checkmark$	CR*
Elderly and non-elderly AML	90%	21,380	$\checkmark$	$\checkmark$
MDS	90%	13,000	$\checkmark$	mCR <sup>#</sup>
Sarcoma	84%	12,390	$\checkmark$	PR
Peripheral T-Cell Lymphoma	90%	7,200-10,800	$\checkmark$	CR

\* Aware of third patient (off study) with response that may have qualified as a CR if observed within trial, investigator attributes response to ALRN-6924

# marrow CR observed in 2 of 3 MDS patients receiving 200mg/m<sup>2</sup> Ara-C and 4.4 mg/kg of ALRN-6924 combination therapy



### ALRN-6924 First-in-Human: IV Drug with Favorable Safety Profile

- Less than 5% of patients experienced a treatment-related SAE
- Most frequent treatment-related adverse events were G1/G2 gastrointestinal side effects, fatigue, anemia and headache
- Unlike Phase 1 all-comers trials of other MDM2 targeting agents, ALRN-6924 has not had a reported DLT due to thrombocytopenia

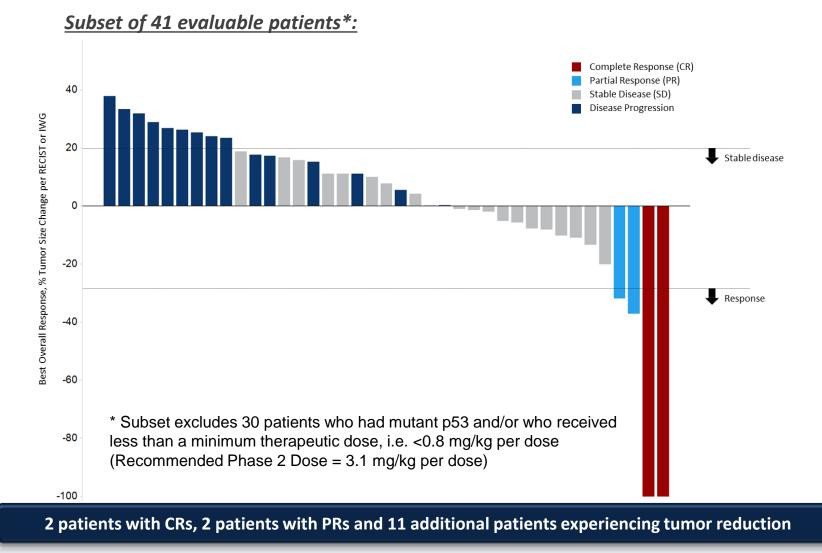
### Number and Percent of Total Patients Across All Dose Levels With A Hematological Abnormality

Grade*	1	2	3	4
Anemia	31 (43.7%)	26 (36.6%)	5 (7.0%)	0
Neutropenia	2 (2.8%)	4 (5.6%)	1 (1.4%)	2 (2.8%)
Thrombocytopenia	24 (33.8%)	1 (1.4%)	0	0

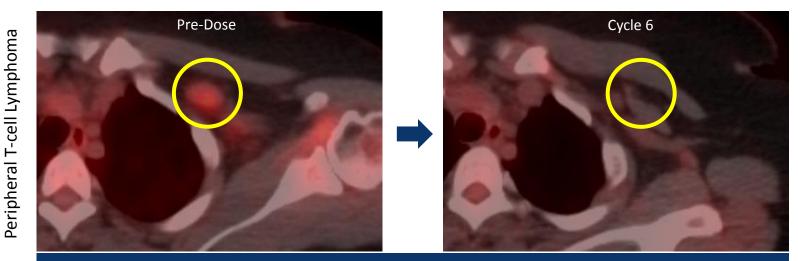
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\* Treatment-emergent hematological laboratory abnormalities

# ALRN-6924 First-in-Human: 59% Disease Control Rate - 13 Different Cancer Types



## ALRN-6924 First-in-Human: Achieved CRs in Heme and Solid Tumors



Complete Remission (CR) after 4 cycles of ALRN-6924  $\rightarrow$  2.5 years+ in treatment



Response during 1<sup>st</sup> cycle of ALRN-6924, CR after 6 cycles  $\rightarrow$  <u>1.5 years+ in treatment</u>



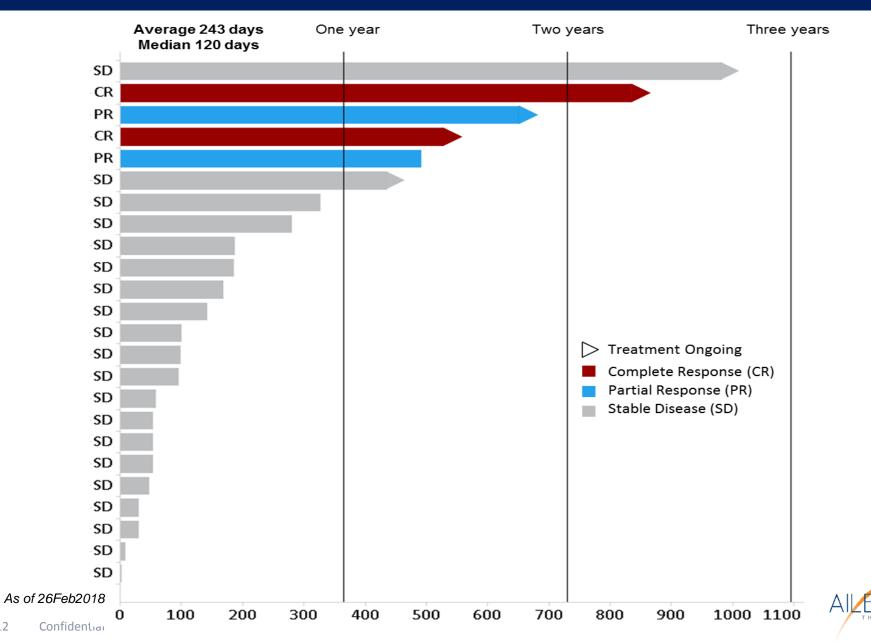
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**Merkel Cell Carcinoma** 

### ALRN-6924 First-in-Human:

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### Durable Disease Control - 10 patients treated 6-32+ months



### PTCL: Significant Unmet Need Exists in 2L PTCL

#### Market Opportunity

- 10-15% of all NHL are Peripheral T-cell Lymphoma (PTCL)
- PTCL: approx. 7,200 10,800 cases (US annually)
- 5-year survival in most common subtypes of PTCL is estimated to be only 32%

#### **Rationale for Pursuing PTCL**

Unmet medical need	$\checkmark$
Fast-to-market regulatory potential	$\checkmark$
Own preclinical & clinical data	$\checkmark$

#### Status

- Two phase 2a expansion cohorts relapsed/refractory PTCL pts with WT p53:
  - 1<sup>st</sup> cohort: 3.1 mg/kg QW x3, every 28d
  - 2<sup>nd</sup> cohort: 3.1 mg/kg TIW x1, every 21d
- Interim data 1<sup>st</sup> PTCL cohort:
  - 21% ORR and 43% DCR (14 evaluable pts) "Cheson et al. 2014"
  - 27% ORR and 47% DCR (15 evaluable pts) "Modified Cheson et al. 2007"
  - Pseudoprogression: 3 pts meeting disease progression criteria continued on treatment to achieve 2 PRs and 1 SD (based on *modified Cheson 2007 criteria*) => inflammatory / immune mechanism?
- 2<sup>nd</sup> cohort interim data expected 2H 2018



### AML/MDS: Significant Unmet Need in 25K+ Elderly Patients

#### Market Opportunity

- ≈ 33,000 new cases of AML and MDS estimated to be diagnosed in the U.S. annually, vast majority are elderly patients, (ACS & NIH SEER database)
- Elderly AML: 5-year survival rate is 6%
- MDS relapsed/refractory to hypomethylating agents: 4 months median overall survival

Rationale for Pursuing AML/MDS		
Unmet medical need	$\checkmark$	
Third party clinical data	$\checkmark$	
Own preclinical & clinical data	$\checkmark$	

#### Status

Dose-escalation phase 1/1b enrolling AML and MDS patients with WT p53:

#### 1. Monotherapy:

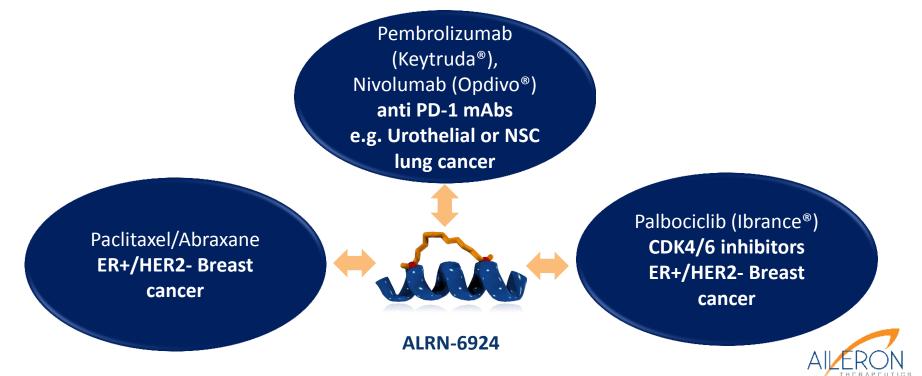
•Completed: up to 5.8 mg/kg, QWx3, every 28d •Ongoing: 2.7 mg/kg, TIWx2, every 21d

- Combination therapy (Ara-C 100-200mg/m<sup>2</sup>):
  •Completed: up to 4.4 mg/kg, QWx3, every 28d
  •Ongoing: 4.4 mg/kg QWx3, every 28d
- Expect to report in 2H 2018: efficacy from doseescalation cohorts, dosing strategy and plans for Phase 2
- FDA granted orphan drug designation to ALRN-6924 for AML



## Combination Therapy Opportunities for Solid Tumors

- Combination opportunities addressing a market with aggregate sales of \$13B in 2017:
  - Immune checkpoint inhibitors (e.g. Keytruda + Opdivo \$9B)
  - CDK4/6-inhibitors (e.g. Palbociclib \$3B)
  - Chemotherapeutic agents (e.g. Abraxane \$1B)
- <u>Rationale:</u>
  - p53 activation mechanistically important for efficacy
  - Favorable safety profile of ALRN-6924
  - Strong preclinical combination therapy data



### Key Developmental Milestones:

- PTCL 2nd cohort interim data expected 2H 2018
- AML/MDS mono- and combination data expected 2H 2018
- In-vivo combination data for solid tumors expected 2H 2018
- Clinical combination trial for solid tumors expected 1Q 2019

### 2<sup>nd</sup> Half 2018 – Targeted Scientific Communications:

- MDM2 World Conference (St. Petersburg, FL, Nov 4-7)
- SITC (Society for Immunotherapy of Cancer Wash. DC, Nov 7-11)
- AACR-NCI-EORTC Triple Conference (Dublin/Ireland, Nov 13-16)
- American Society of Hematology (San Diego, Dec 1-4)
- San Antonio Breast Cancer Conference (Dec 4-8)



### Aileron - Corporate Summary

- Phase 1 proof-of-concept with multiple complete and partial remissions in both our First-in-Human and PTCL trials, showing that stapled peptides successfully engage with intracellular targets
- Preclinical data and clinical safety profile enable opportunities for combination therapies with immune checkpoint inhibitors, kinase inhibitors and chemotherapeutics addressing large oncology markets in which p53 modulation plays an important role
- \$43m in cash, cash equivalents and investments as of March 31, 2018. Cash runway into 2H 2019.



# Appendix



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