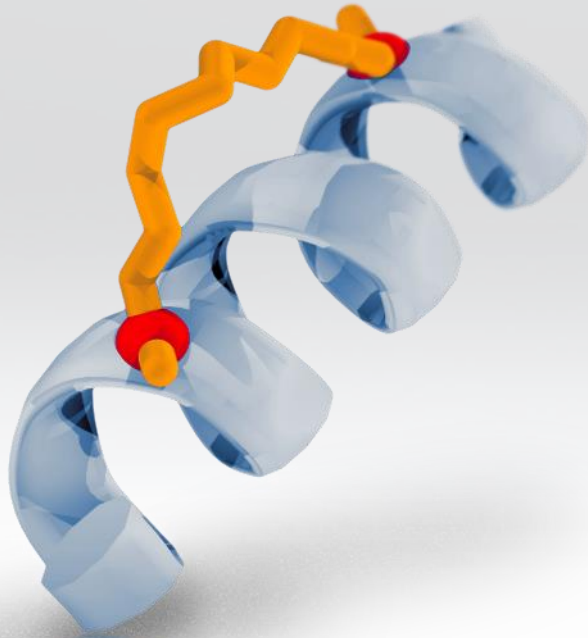
AILERON THERAPEUTICS

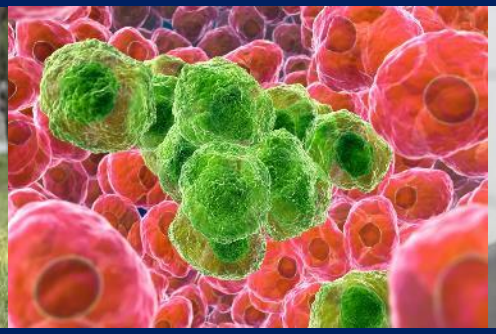


Jefferies 2018 Healthcare Conference
June 5th

Manuel Aivado, M.D., Ph.D.
SVP, Chief Medical and Chief Scientific Officer

Donald Dougherty, CFA, CPA
SVP, Chief Financial Officer



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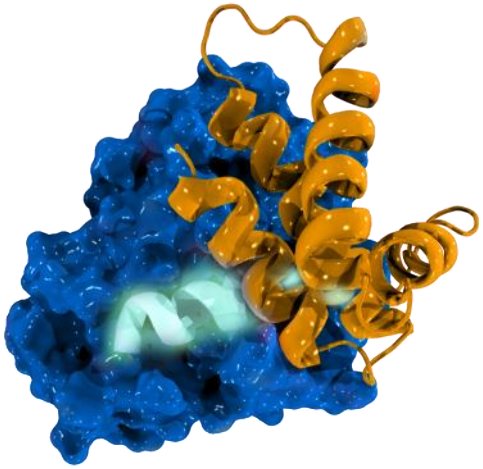
This presentation also contains market data and other statistical information that are based on independent industry publications, reports by market research firms or published independent sources. Some market data and statistical information are also based on the Company's good faith estimates, which 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 quarterly report on Form 10-Q.

Aileron - Corporate Highlights

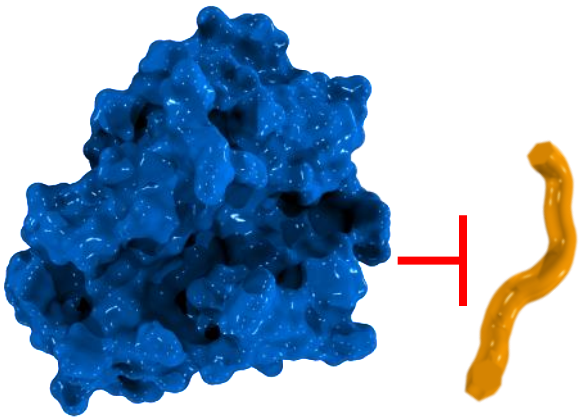
- Clinical-stage **leader in stapled peptide therapeutics** for cancer and other diseases
- **Clinical proof-of-concept with multiple complete and partial remissions** showing that stapled peptides successfully engage with intracellular targets
- Clinical compound ALRN-6924
  - has potential to be **best-in-class p53-activating** therapy, and
  - is the **only** dual MDMX/MDM2 inhibitor in clinical development
- 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

Stapled Peptides Overcome Historical Constraints of Peptide Drugs and Limitations of Small Molecules

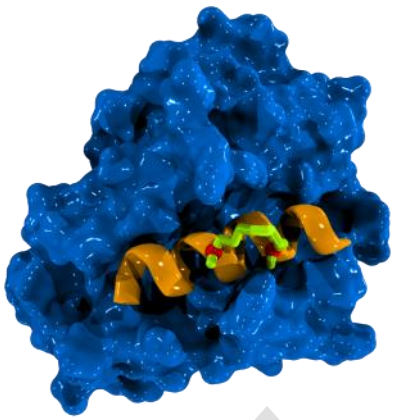
Natural protein-protein helical peptide interface



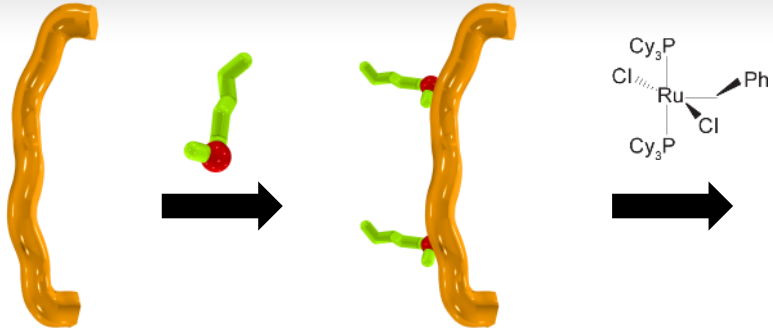
Removal of full protein context destabilizes interface helix



Stapled peptides recapitulate the helical interface and restore functionality

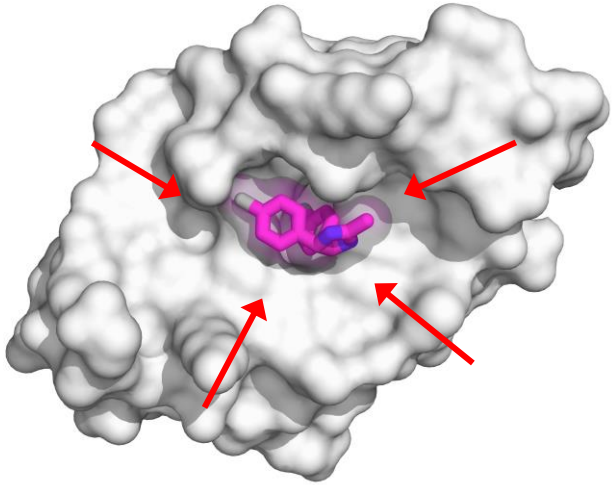


Aileron adds a chemical bridge - a “staple” - that solves the inherent liabilities of peptides including stability and cell penetrability



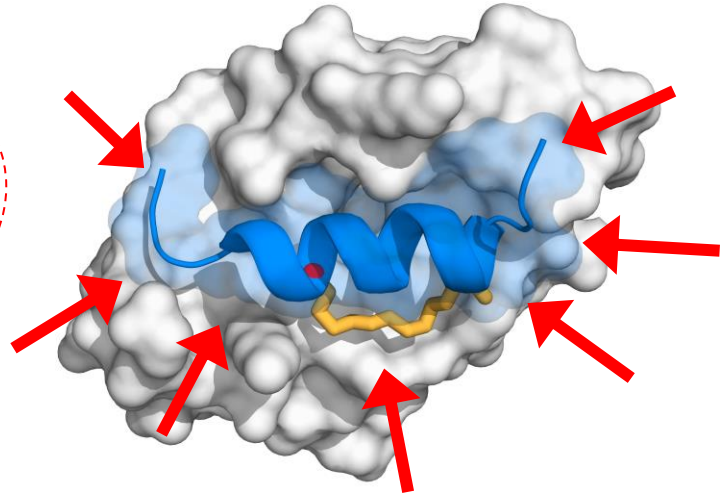
Stapled Peptides Bind the Entire Pocket

SMALL MOLECULES:
Not enough contact points to bind



KEY CONTACT POINTS

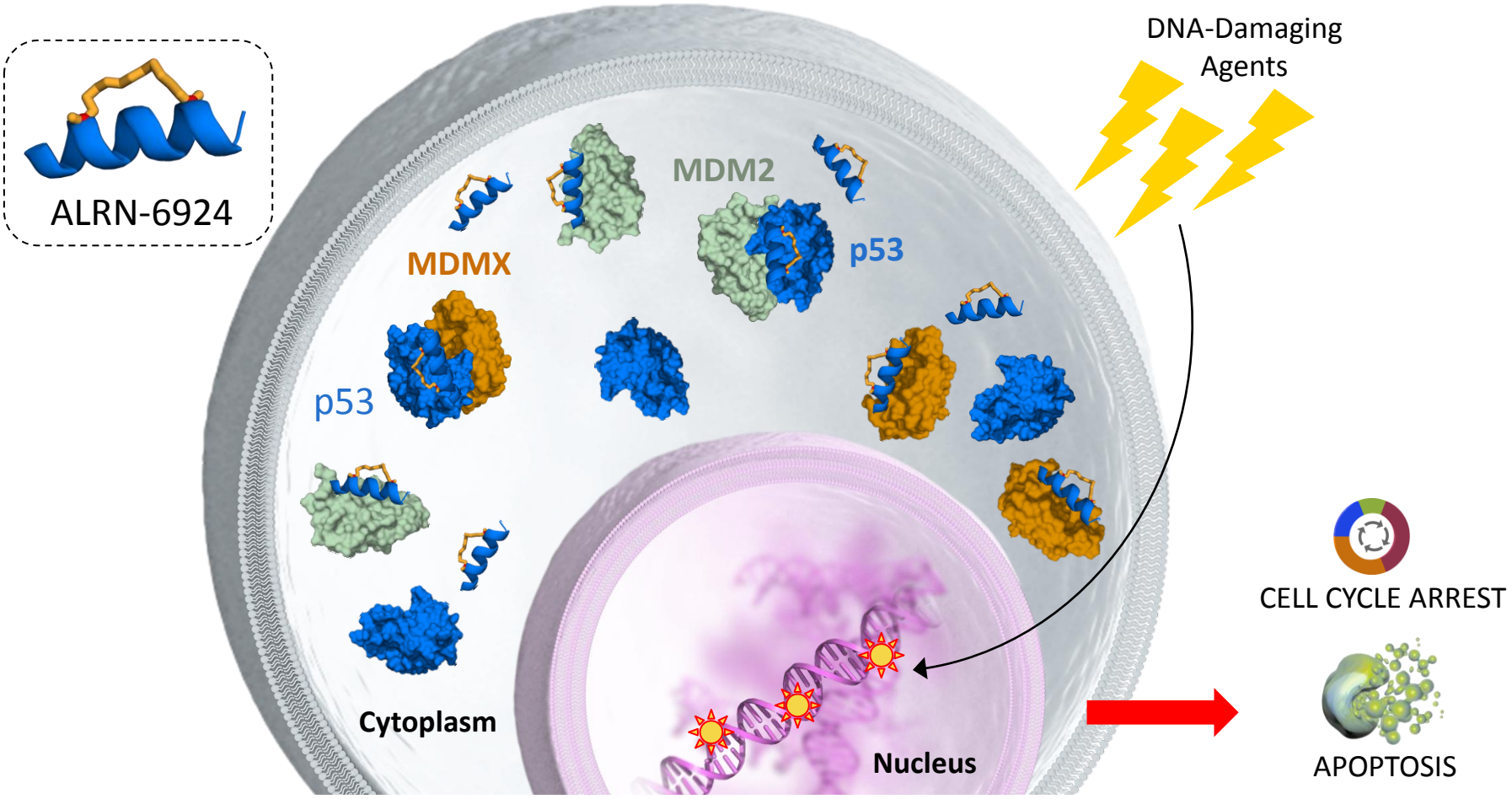
STAPLED PEPTIDES:
Able to bind entire interaction surface



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. Single compound can engage with ≥2 targets, e.g. MDMX + MDM2 or Bcl-2 + Mcl-1
3. Design Benefits: Stapled peptides largely replicate natural peptide sequences

OPPORTUNITY: Reactivating p53, the “Guardian of the Genome”



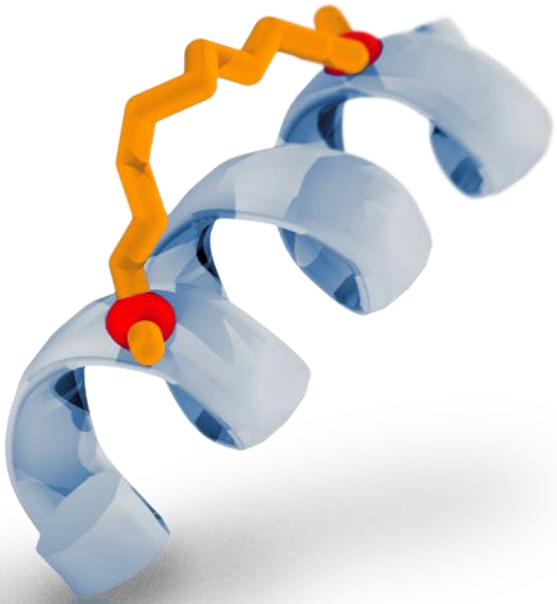
ALRN-6924 is a decoy that mimics p53 and selectively binds to MDMX + MDM2, releasing and reactivating p53 to induce cell cycle arrest and apoptosis

Aileron Pipeline

Program	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3
ALRN-6924 **Reactivating p53**	All-comers solid tumors & lymphomas				Enrollment completed 1Q2017; patients ongoing	
	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

ALRN-6924: a First-in-Class p53 Reactivating Stapled Peptide



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ALRN-6924 Collaborative Research – Two high-profile papers in 2018

April 2018

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

CANCER

Dual inhibition of MDMX and MDM2 as a therapeutic strategy in leukemia

Luis A. Carvajal,[1] Daniela Ben Neriah,[1] Adrien Senecal,[2] Lumie Benard,[1] Victor Thiruthuvananathan

May 2018

Targetable vulnerabilities in T-and NK-cell lymphomas identified through preclinical models

Samuel Y. Ng et al.[#]

AILERON THERAPEUTICS

ALRN-6924: Externally Recognized & Validated Science

Presentations and Awards

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 as 2018 Oncology Highlight

JOURNAL OF CLINICAL ONCOLOGY

Clinical Cancer Advances 2018:

Heymach et al., JCO 2018 Apr 1;36(10):1040

AILERON THERAPEUTICS

ALRN-6924: total of 118 cancer pts in clinical trials, an active treatment, generally well tolerated

Phase 1 FIH dose-escalation in all-comers:	• Efficacy (41 pts*): 2 CRs, 2 PRs, and 20 SDs for a DCR of 59% (24/41 pts) • 55% of SD pts experienced tumor shrinkage • 5 pts still on therapy, average time on therapy 685 days (incl. 3 responding pts) • Some of the responses showed delayed-onset
Ph2a expansion cohort in PTCL:	• 15 evaluable pts: 27% ORR, incl. 1 CR, 3 PRs, 3 SDs (all 3 w/ tumor shrinkage) • 3 pts showed PET/CT flare yet continued on treatment: → 2 pts achieved PR, 1 patient achieved SD
Phase 1/1b dose-escalation in AML & advanced MDS:	• Monotherapy and combination with low-dose Ara-C • Ongoing dose-escalation, thus far: 2 marrow CRs , 3 pts w/ ≈50% BM blast ↓

* CR – Complete Response, PR – Partial Response, SD – Stable Disease, DCR – Disease Control Rate, ORR – Overall Response Rate, BM – Bone Marrow, Efficacy subset defined on slide 13

(Data as of February 26, 2018)

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

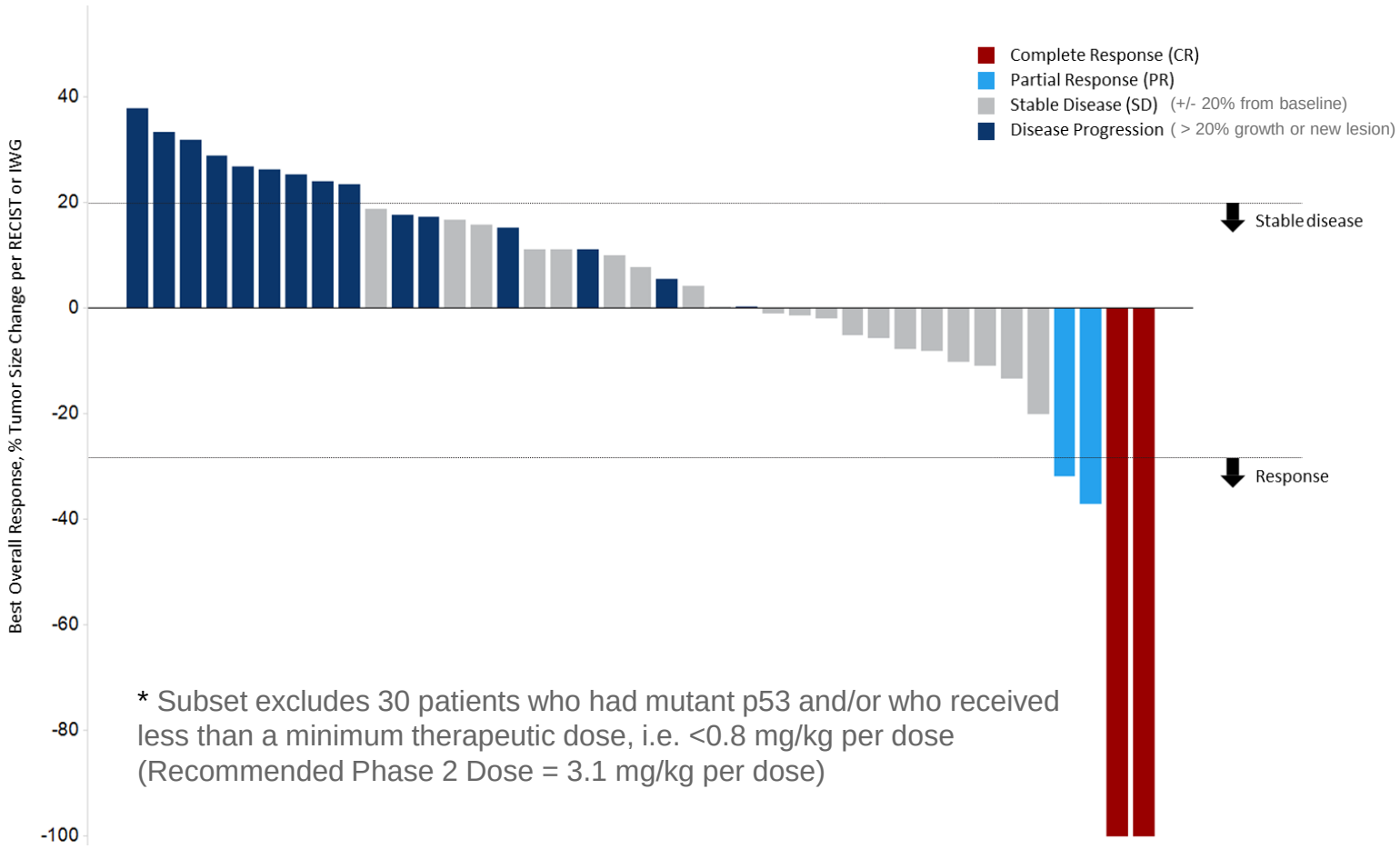
NUMBER AND PERCENT OF TOTAL PATIENTS ACROSS ALL DOSE LEVELS WITH A HEMATOLOGICAL ABNORMALITY

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**

(Data as of February 26, 2018)

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

Subset of 41 evaluable patients*:



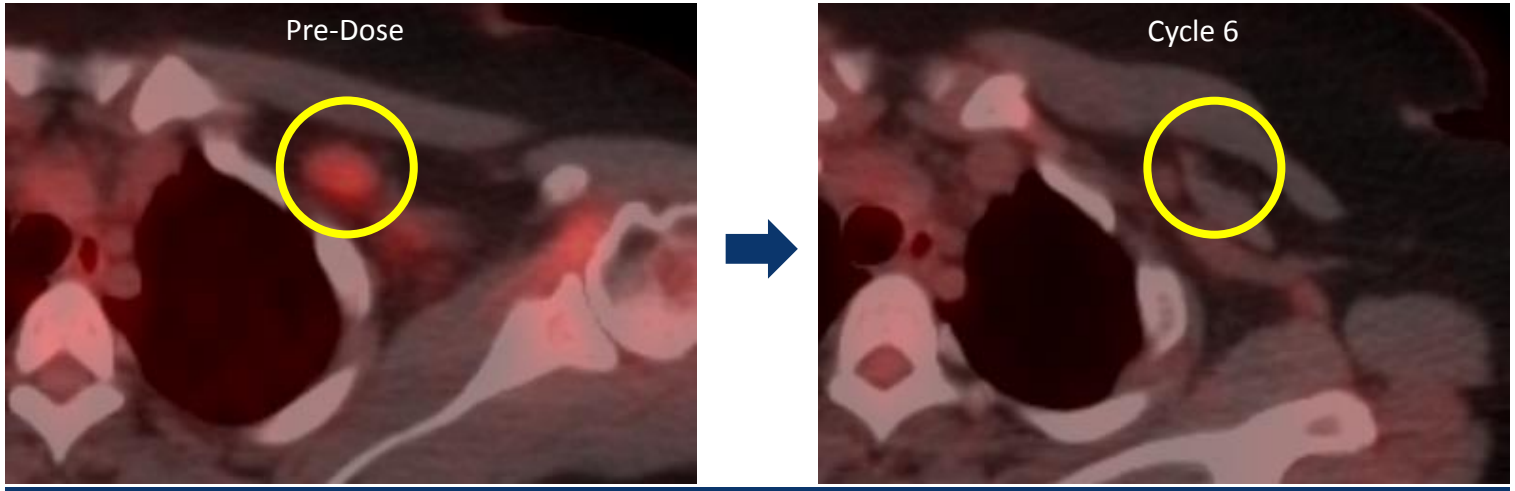
* Subset excludes 30 patients who had mutant p53 and/or who received less than a minimum therapeutic dose, i.e. <0.8 mg/kg per dose (Recommended Phase 2 Dose = 3.1 mg/kg per dose)

2 patients with CRs, 2 patients with PRs and 11 additional patients experiencing tumor reduction

(Data as of February 26, 2018)

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

Peripheral T-cell Lymphoma

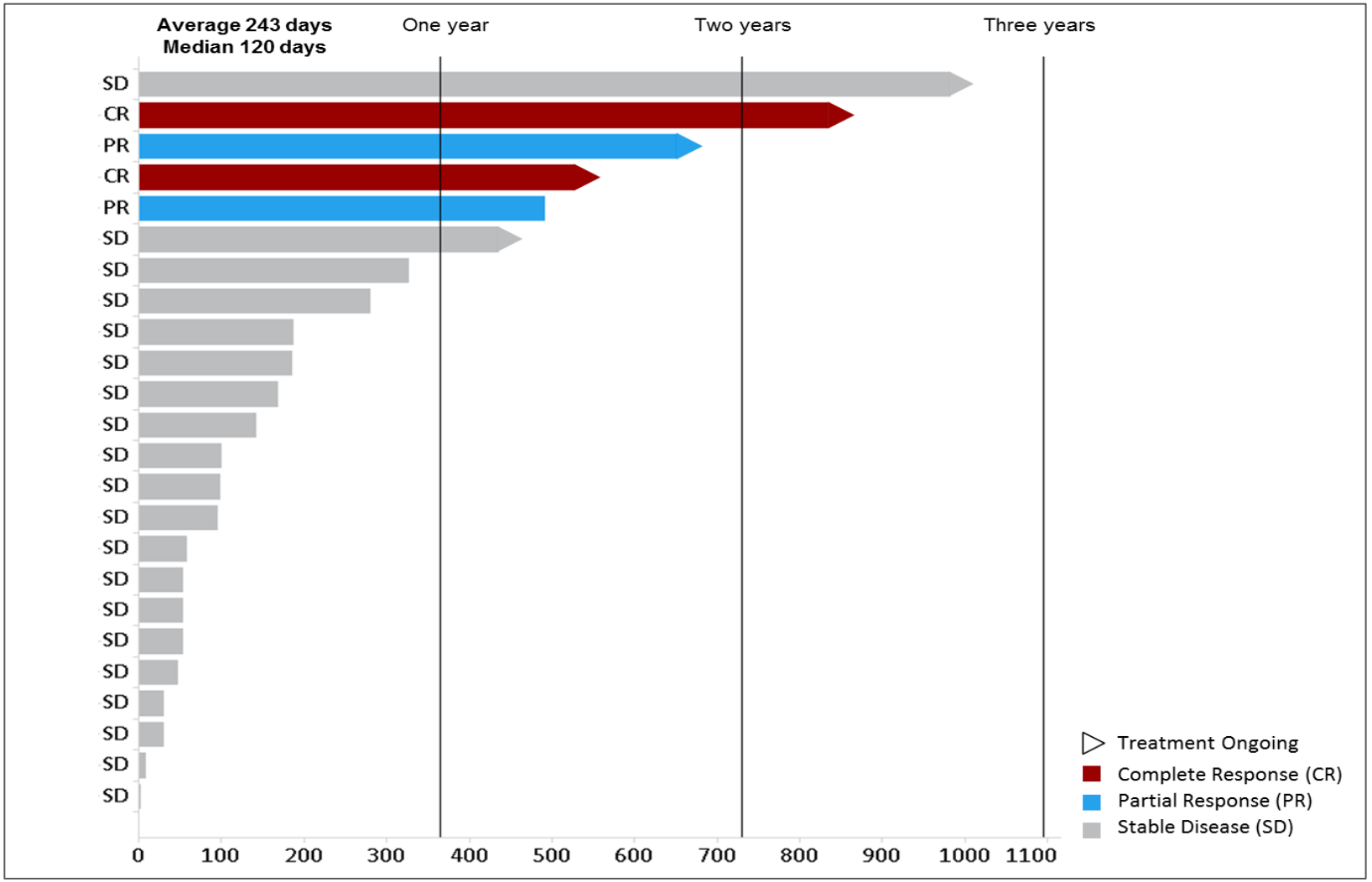


Complete Remission (CR) after 4 cycles of ALRN-6924 → 2.5 years+ in treatment

Merkel Cell Carcinoma

Response during 1st cycle of ALRN-6924, CR after 6 cycles → 1.5 years+ in treatment

ALRN-6924 First-in-Human:
Durable Disease Control - 10 patients treated 6-32+ months



(Data as of February 26, 2018)

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)
- Prognosis: post 1L treatment, median overall survival of relapsed/refractory pts ≈ 5.5 months

Rationale for Pursuing PTCL

Unmet medical need ✓
- Significant percentage of 2nd-line pts pursue experimental options

Fast-to-market regulatory potential ✓
- Single arm study, relatively low patient number precedent

Aileron preclinical & clinical data ✓

(Data as of February 26, 2018)

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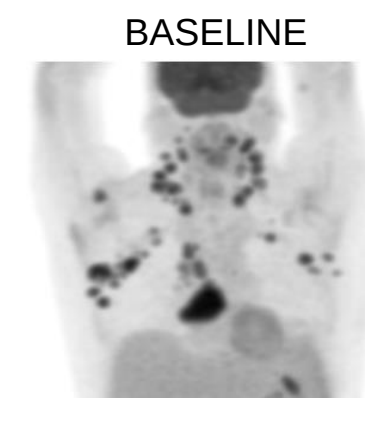
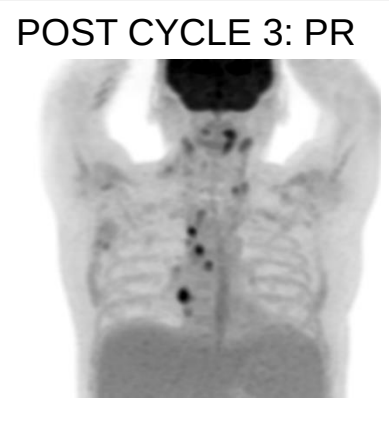
ALRN-6924 in the 2nd Line Treatment of PTCL

- **Interim data 1st 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*"

- **2nd cohort interim data expected 2H 2018**
  - Assessing dosing frequency

- **Pseudoprogression:** 3 pts initially meeting disease progression criteria continued on treatment to achieve 2 PRs and 1 SD
  (based on *modified Cheson 2007 criteria*) => inflammatory / immune mechanism?



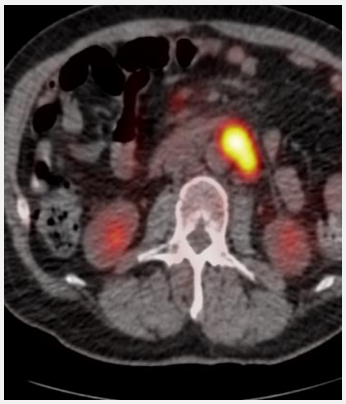


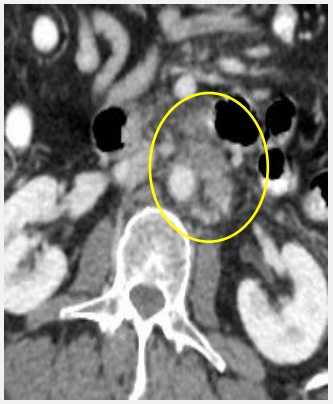
(Data as of February 26, 2018)

Mechanisms of resistance/progression

Pseudo-progression in PTCL patient after 1st TIW cycle:

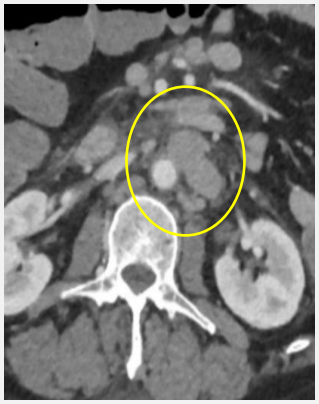
Baseline PET-CT





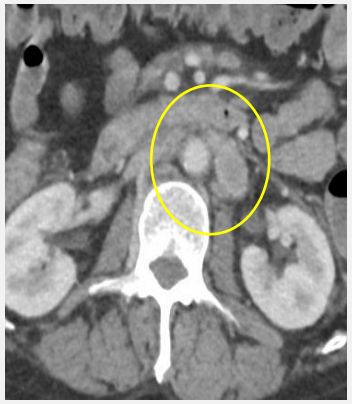
33 x 17 mm = 561 mm^2

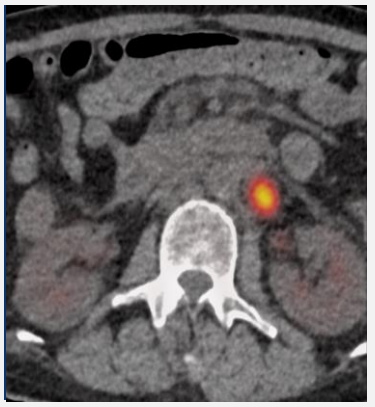
Day 11 CT-only



39 x 21 mm = 819 mm2

Post Cycle 3 PET-CT





25 x17 mm = 425 mm2

- Early progression (i.e. within < 2 cycles) suggesting pseudo-progression:
  - PTCL phase 2a expansion: 5/8 TP53-wt patients progressing early
  - Solid tumors phase 1 dose-escalation: 6/17 patients progressing early
- Tumor biopsies from 5 patients post-progression reveal that **TP53 remains WT**

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

Market Opportunity

- ≈ 33,000 new cases of AML and MDS (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 ✓
- *Limited Options for elderly pts*

Third party clinical data ✓
- *Several MDM2- only inhibitors show efficacy (but toxicity an issue)*

Aileron preclinical & clinical data ✓
- *As presented at ASH (Oral), marrow CRs, reduction in bone marrow blasts*

(Data as of February 26, 2018)

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ALRN-6924 in the Treatment of relapsed/refractory AML or advanced MDS: Dose-escalation phase 1/1b

Monotherapy:	• Completed: up to 5.8 mg/kg, QWx3, every 28d • Ongoing: 2.7 mg/kg, TIWx2, every 21d
Combination therapy (with Ara-C 100-200 mg/m^2):	• Completed: up to 4.4 mg/kg + 100, QWx3, every 28d • Ongoing: 4.4 mg/kg + 200 QWx3, every 28d
Reporting	• Expect to report in 2H 2018: efficacy from dose-escalation cohorts, dosing strategy and plans for Phase 2a expansion cohorts
Orphan Drug designation	• FDA granted orphan drug designation to ALRN-6924 for AML

(Data as of February 26, 2018)

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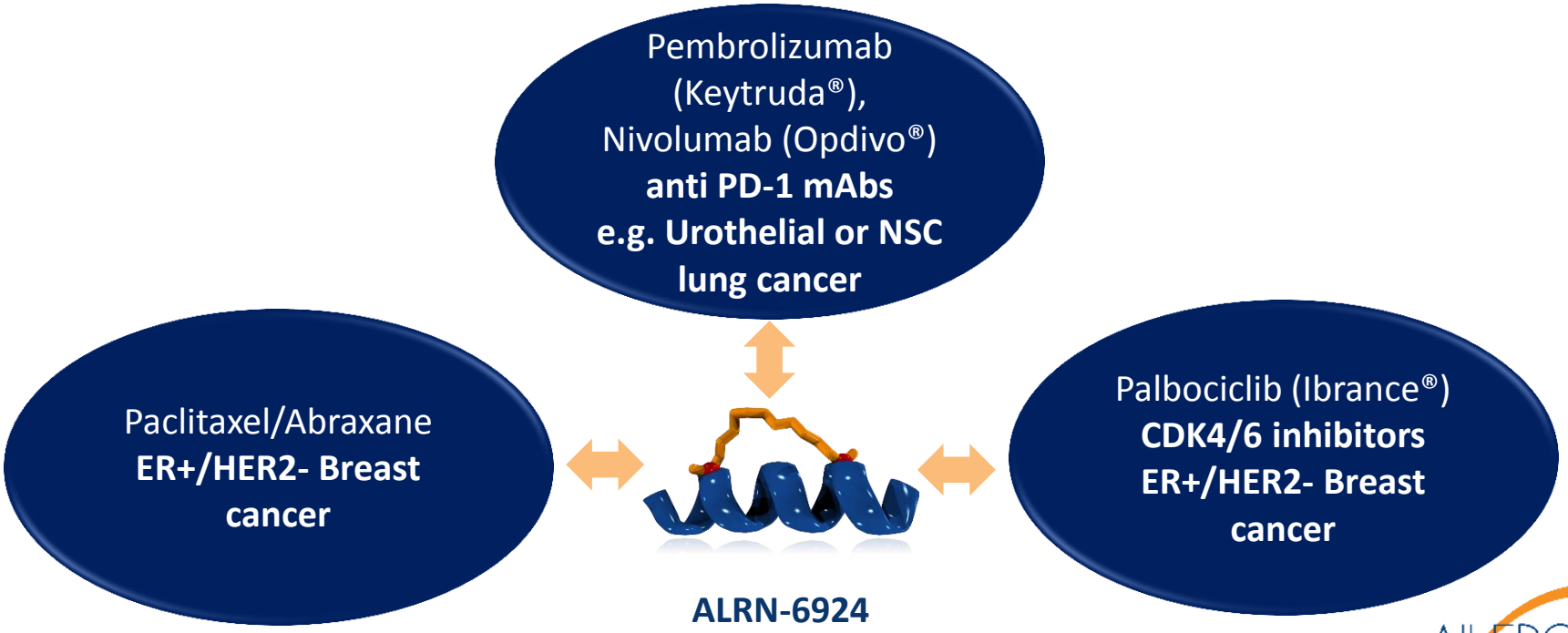
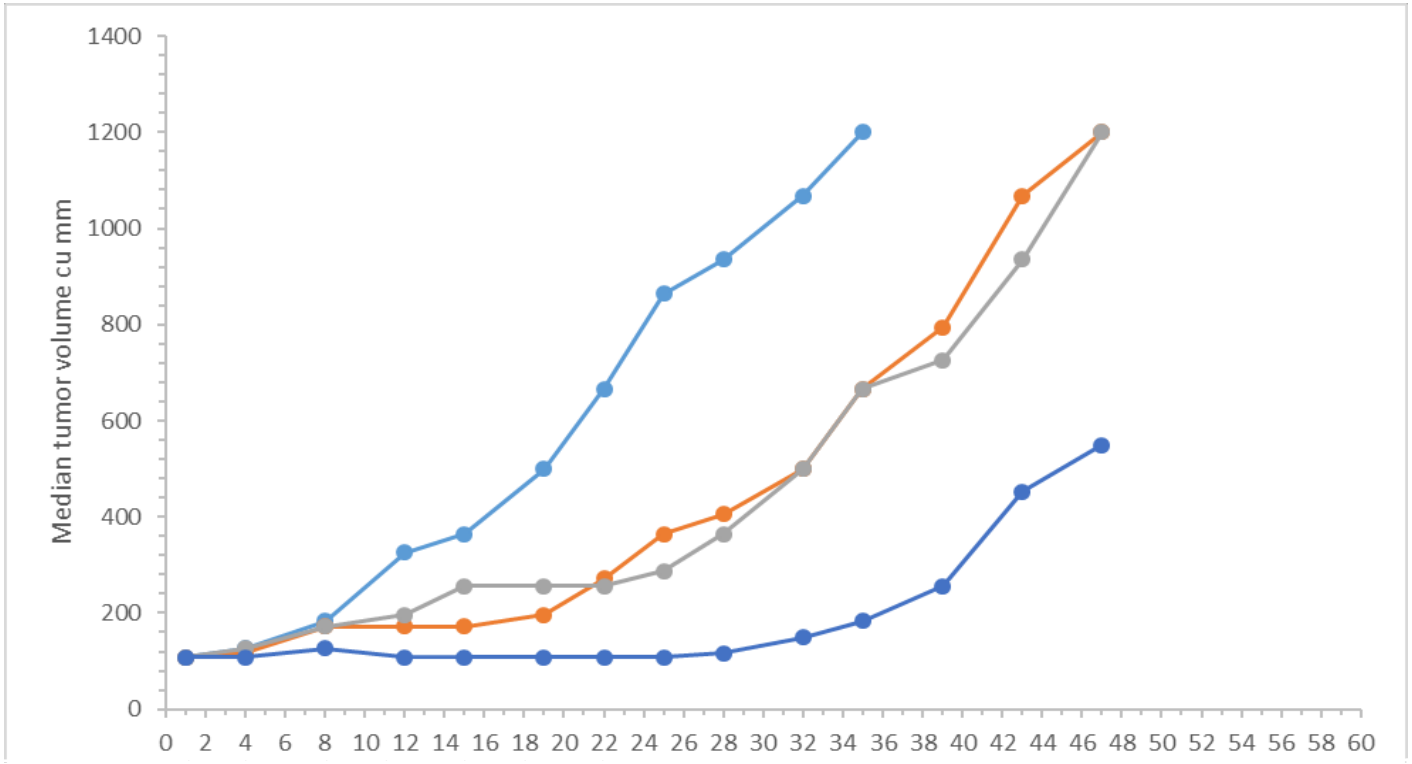
Combination Therapy Opportunities for Solid Tumors

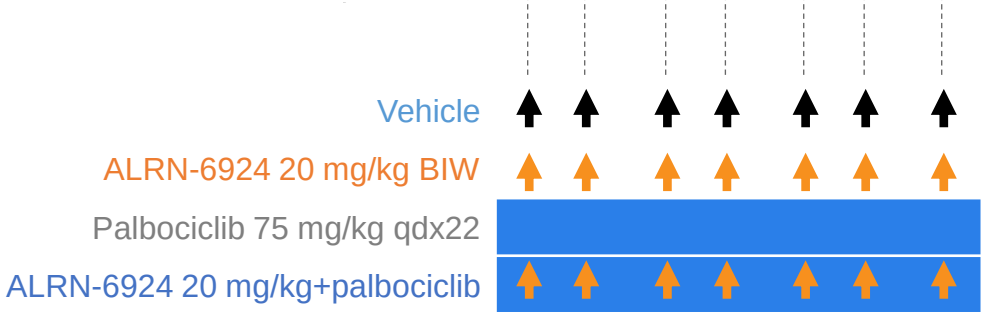
- **Combination opportunities** addressing a market with aggregate sales of $13B in 2017:
  - Immune checkpoint inhibitors (e.g. Keytruda + Opdivo $9B)
  - CDK4/6-inhibitors (e.g. Palbociclib $3B)
  - Chemotherapeutic agents (e.g. Abraxane $1B)

- **Rationale**:
  - p53 activation mechanistically important for efficacy
  - Favorable safety profile of ALRN-6924
  - Strong preclinical combination therapy data



ALRN-6924 in combination with palbociclib yields better MCF-7 tumor growth inhibition and PFS than either single agent alone





	%TGI (±SEM) on d22	Median days to >500 mm^3	Median days to >1000 mm^3
Vehicle	---	20	29
ALRN-6924 20 mg/kg BIW	65 (5)	31	44
Palbociclib 75 mg/kg qdx22	80 (3)	32	45
ALRN-6924 20 mg/kg+palbociclib	94 (2)	42	*Not reached*

ALRN-6924: Developmental Milestones & Scientific Communications 2018/2019

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

2nd Half 2018 – Targeted Scientific Communications:

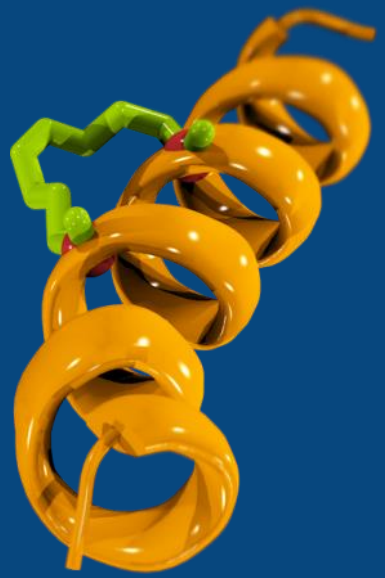
- MDM2 World Conference (St. Petersburg, FL, Nov 4-7)
- SITC (Society for Immunotherapy of Cancer – Wash. DC, Nov 7-11)
- AACR-NCI-EORTC Triple Conference (Dublin/Ireland, Nov 13-16)
- American Society of Hematology (San Diego, Dec 1-4)
- San Antonio Breast Cancer Conference (Dec 4-8)

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 and provide clinical benefit.

- 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.



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