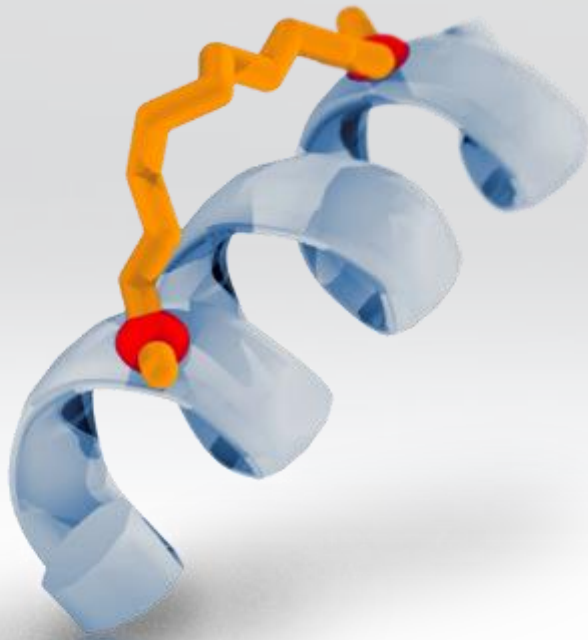
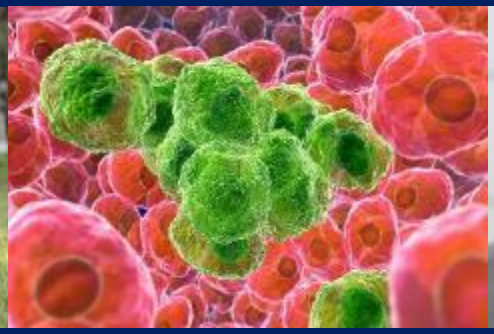
AILERON THERAPEUTICS



Corporate Presentation

November, 2018






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 quarterly report on Form 10-Q for the period ended September 30, 2018 filed with the SEC on November 7, 2018, 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 quarterly report on Form 10-Q.

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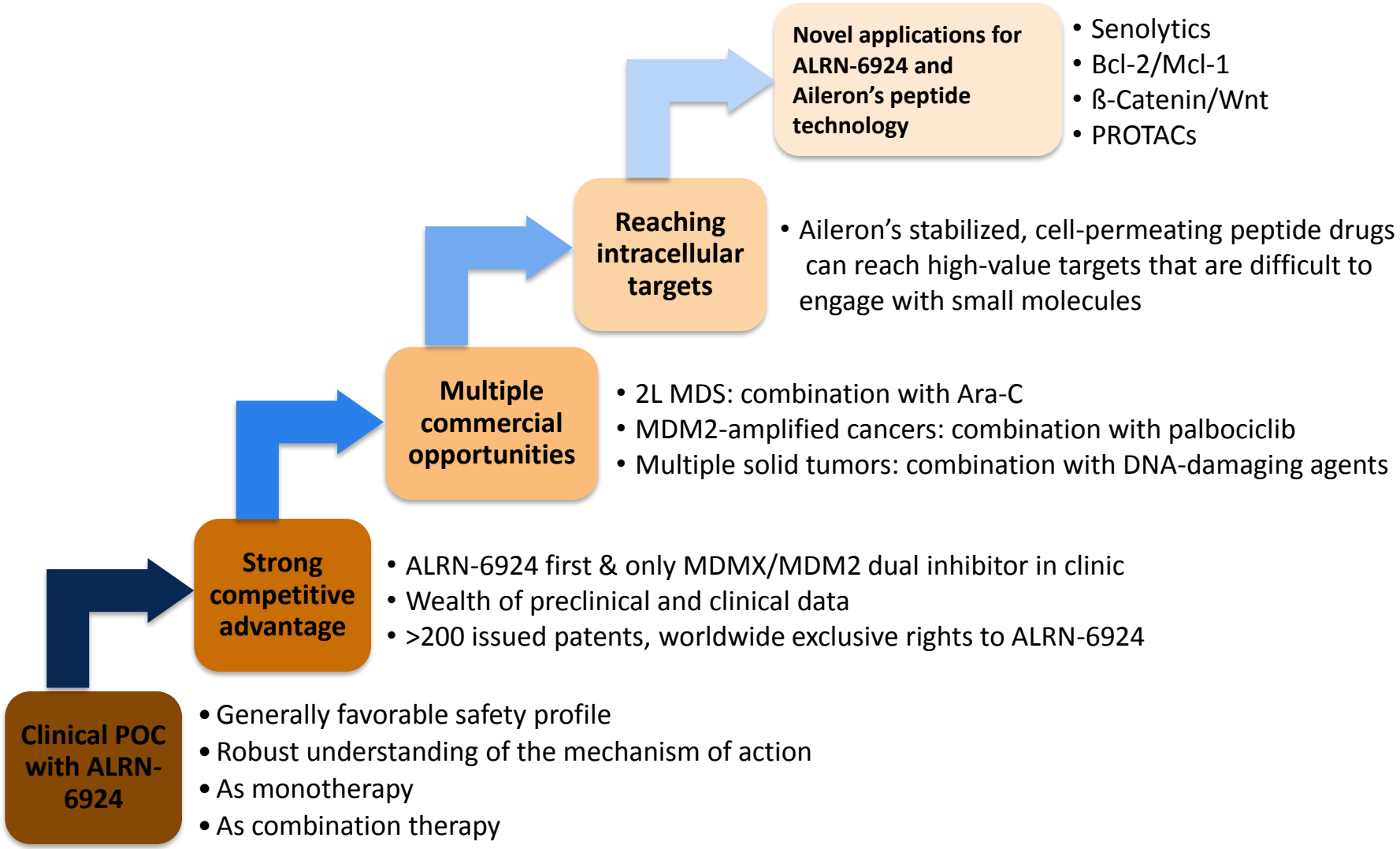
Investment Thesis



Executive Team

Manuel Aivado, MD, PhD
President and CEO

Taiho Oncology,
GlaxoSmithKline,
Beth Israel Deaconess/
Harvard Medical School

Don Dougherty, CFA, CPA
Chief Financial Officer

CCGrowth, Essex
Investment Management,
Putnam Investments,
KPMG

Vojo Vukovic, MD, PhD
Chief Medical Officer

Taiho Oncology,
Synta Pharmaceuticals,
Pfizer, Ilex Oncology

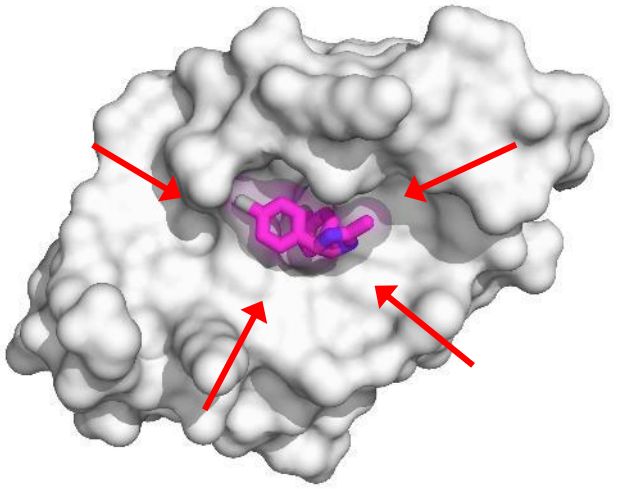
Allen Annis, PhD
SVP, Research

Schering-Plough
Research Institute,
NeoGenesis
Pharmaceuticals

Prior Experience

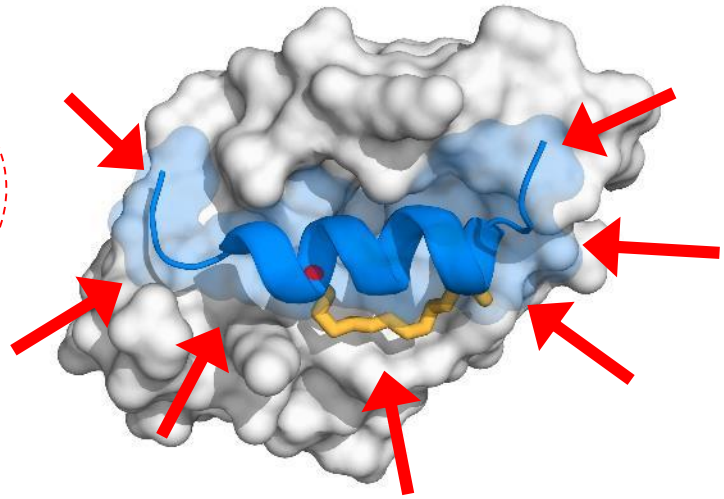
Aileron's peptides are designed to surpass binding properties of small molecules and interact effectively with "difficult" intracellular targets

Small Molecules:
Not enough contact points to bind



KEY CONTACT POINTS

Aileron's Peptides:
Bind entire interaction surface



Advantages of 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: Aileron's peptides largely replicate natural peptide sequences

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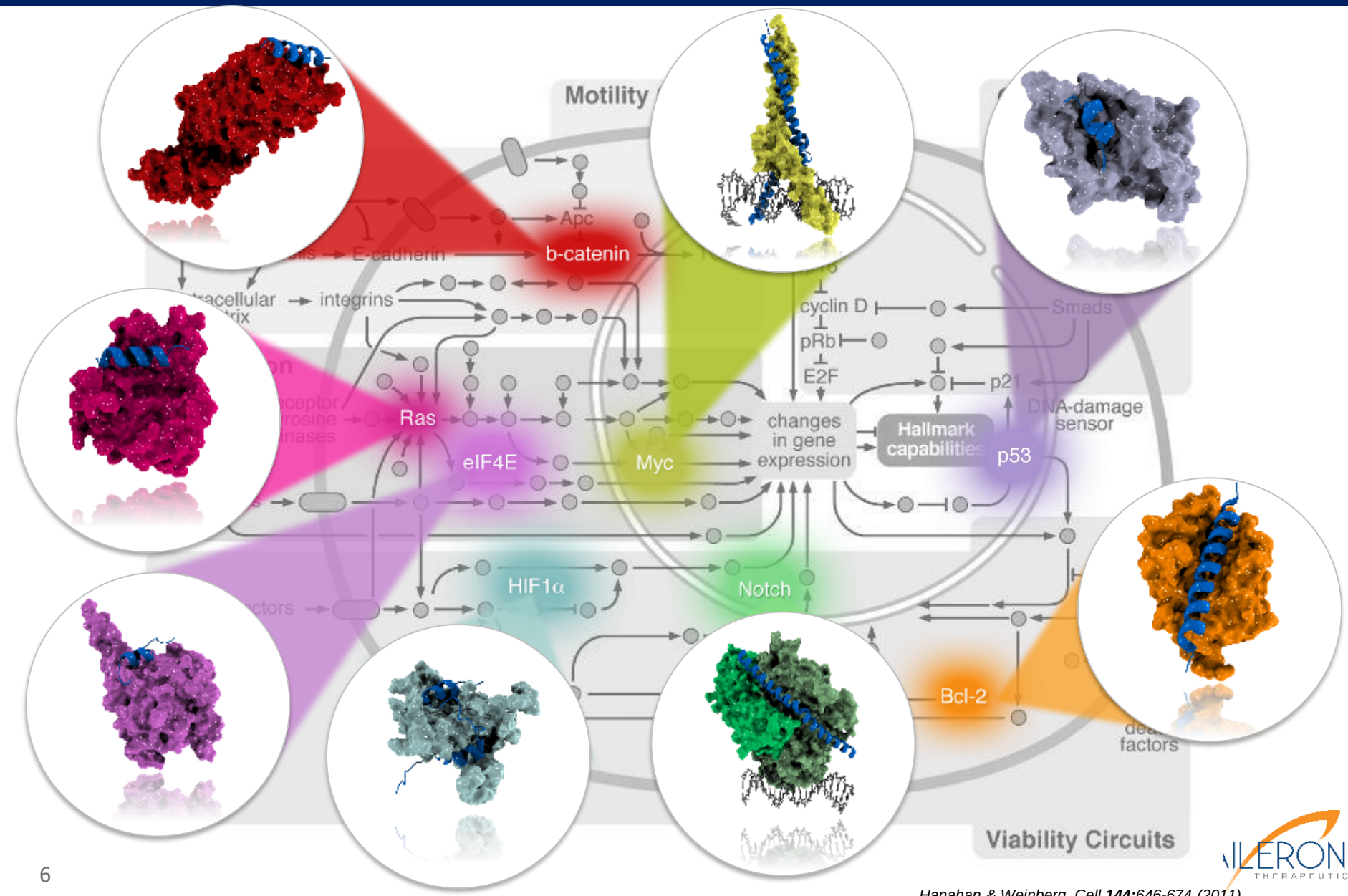
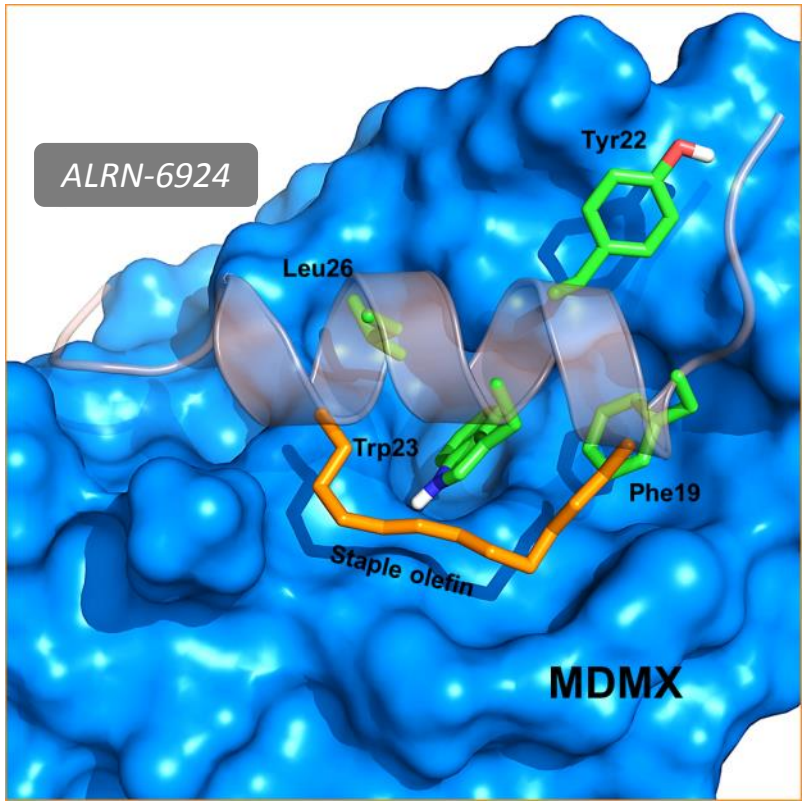
Aileron's peptides may address highly valuable intracellular targets



*Hanahan & Weinberg, Cell **144:**646-674 (2011)*

ALRN-6924: the only clinical MDMX/MDM2 dual inhibitor



	Binding Affinity	
K_d, nM	MDM2	MDMX
Native p53	770	480
ALRN-6924	13.7	8.9
RG7388	9.8	> 3000

RG7388 = selective MDM2-inhibitor (Roche)

ALRN-6924 replicates native p53 binding contacts

Staple linker contributes to binding affinity

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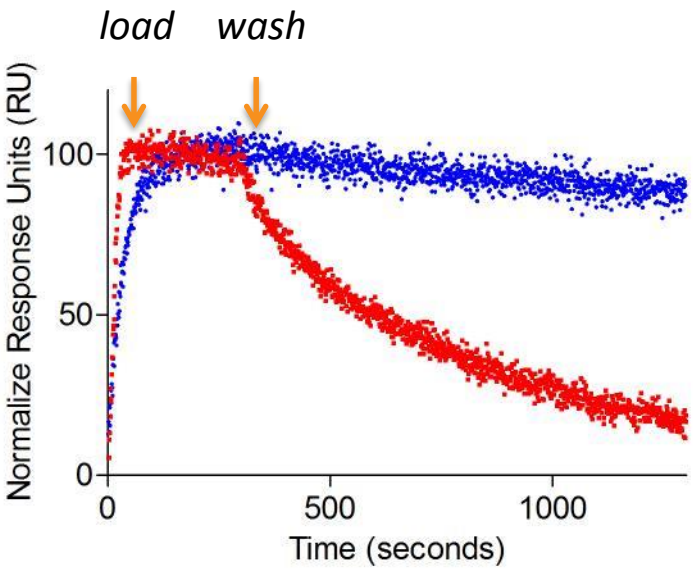
Superior binding kinetics of ALRN-6924 over small molecules

MDM2



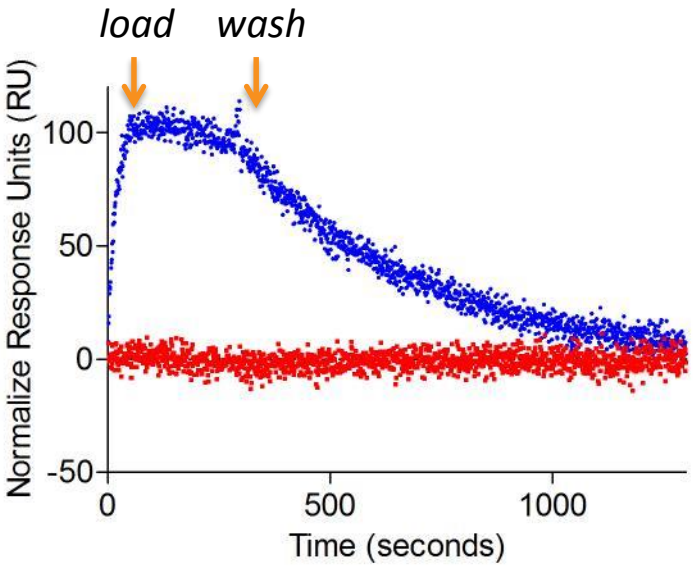
ALRN-6924

binding is sustained during wash-off from MDM2-coated surface
$t_{½}$ = 85 minutes

RG7388

washes off from MDM2 surface
$t_{½}$ 2-3 min

MDMX



ALRN-6924

binds MDMX, $t_{½}$ = 5 minutes

RG7388

No binding to MDMX

Ref: "Dual Inhibition of MDMX and MDM2 as a Therapeutic Strategy in Leukemia" *Sci Transl Med* **2018**

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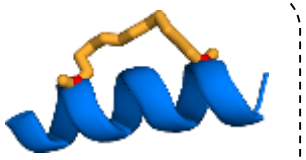
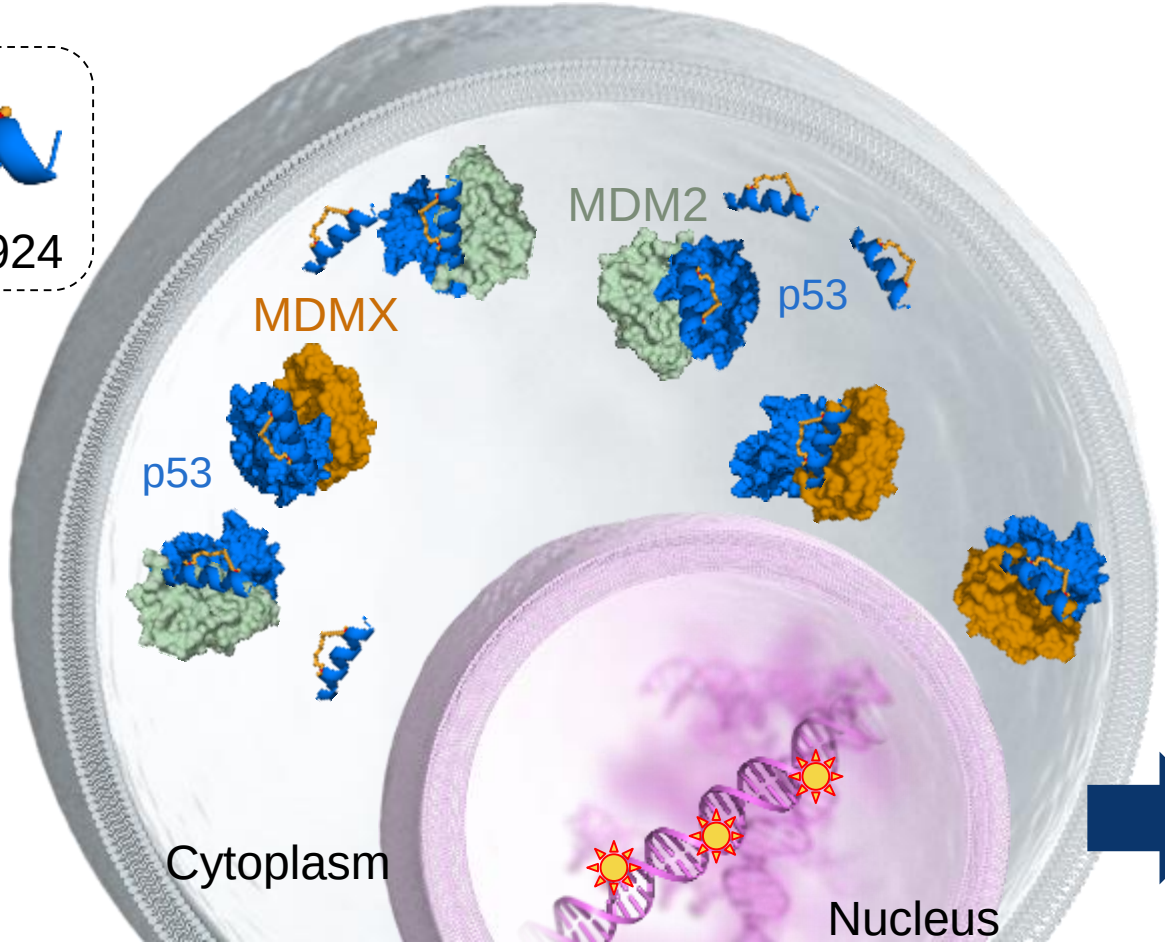
ALRN-6924: a first-in-class p53 activator that acts by inhibition of both MDMX and MDM2



ALRN-6924



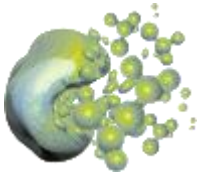
MDM2-only Inhibitors:

- **RG7388 (Roche)**
- HDM201 (Novartis)
- DS-3032 (Daiichi)
- AMG 232 (Amgen)

as well as Sanofi, Merck, Boehringer, Unity Bio

No MDMX-Inhibition!

Cell Cycle Arrest
DNA Repair



Apoptosis

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 Collaborative Research: Two seminal 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 et al

May 2018

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

Samuel Y. Ng et al

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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

Editorial Highlights

Journal of Clinical Oncology

Clinical Cancer Advances 2018

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

nature reviews DRUG DISCOVERY

Constrained peptides' time to shine?

Chris Morrison, Nature Reviews Drug Discovery, July 2018

The Hematologist
ASH NEWS AND REPORTS®

New Means to Reactivate p53 in Leukemia:
A Stapled Peptide Inhibitor of MDMX & MDM2

Omar Abdel-Wahab, MD, The Hematologist, July 2018

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A cancer patient who failed standard chemotherapy as well as high-dose chemotherapy with autologous stem cell transplantation … shown here after 6 cycles of single agent therapy with ALRN-6924

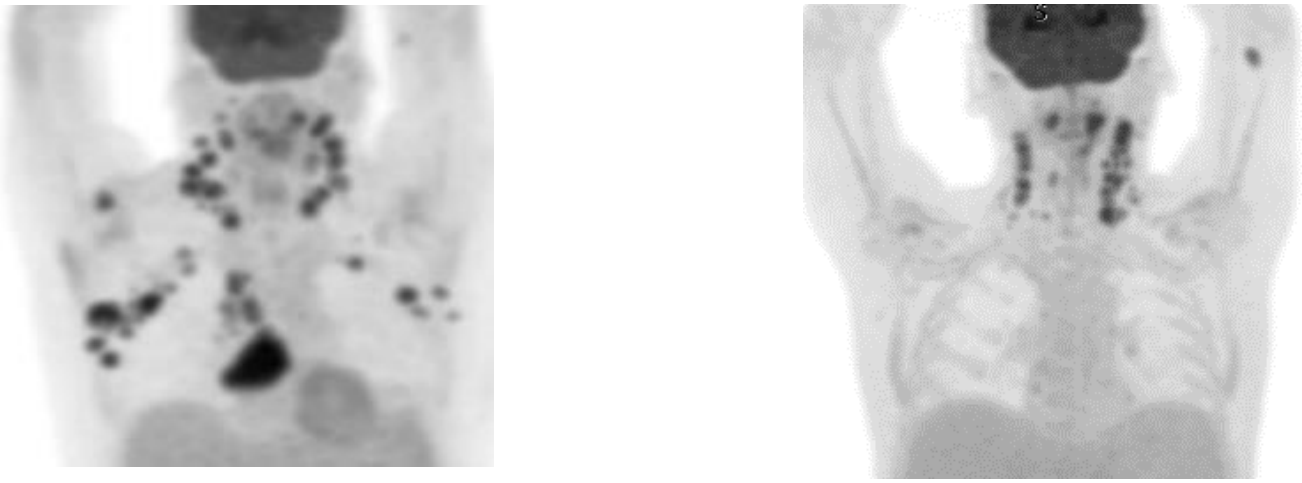
ALRN-6924 Program Accomplishments

- ✓ 150+ cancer patients treated
- ✓ Dose-dependent pharmacokinetics
- ✓ Pharmacodynamic biomarker shows clinical proof of mechanism
- ✓ Favorable safety profile established
- ✓ Single-agent activity with multiple CRs and PRs
- ✓ Clinical activity demonstrated in first combination therapy trial
- ✓ Understanding of dose and dose regimen developed
- ✓ Commercial CMC manufacturing process developed

P53-reactivating MDM2-Inhibitors: Phase 1 'All-comers' Trials

			Efficacy			*Heme Tox*	
First-in-Human Phase 1 Trial	**# pts**	**Dose range**	**# CR**	**# PR**	**# SD**	**Thrombo-cytopenia Grade ≥ 3**	**Neutropenia Grade ≥ 3**
ALRN-6924	**71**	**28x**	**2**	**2**	**21**	**0%**	**3%**
AMG 232	39	32x	0	0	30	33%	21%
DS-3032b	103	22x	0	3	52	19%	12%
HDM201	107	28x	0	2	31	24%	23%
RO6839921	41	8x	0	0	17	15%	20%
RG7388	95	16x	0	0	20	33%	21%
MK-8242	47	8x	0	3	31	15%	19%

Phase 2 dose optimization trial in PTCL patients shows single-agent activity



Baseline → Post Cycle 6

- Relapsed/refractory PTCL pts received single agent treatment in QW and TIW regimens, interim results to be presented at ASH, December 2018.
- Preliminary QW analysis suggests a range of 21-27% ORR, with more convenient administration than available therapies and with a favorable safety profile
- Enrollment expected to complete by year-end 2018, future development path for PTCL to be decided based on data. No Aileron-sponsored pivotal trial planned for strategic reasons.

PTCL: Peripheral T-cell Lymphoma, ASH: American Society of Hematology, QW: once-weekly, TIW: three-times-a-week
Data as of 26-Feb-2018: 21% per investigator-reported IWG 2014 criteria or 27% per independent radiology review by modified Cheson 2007 criteria

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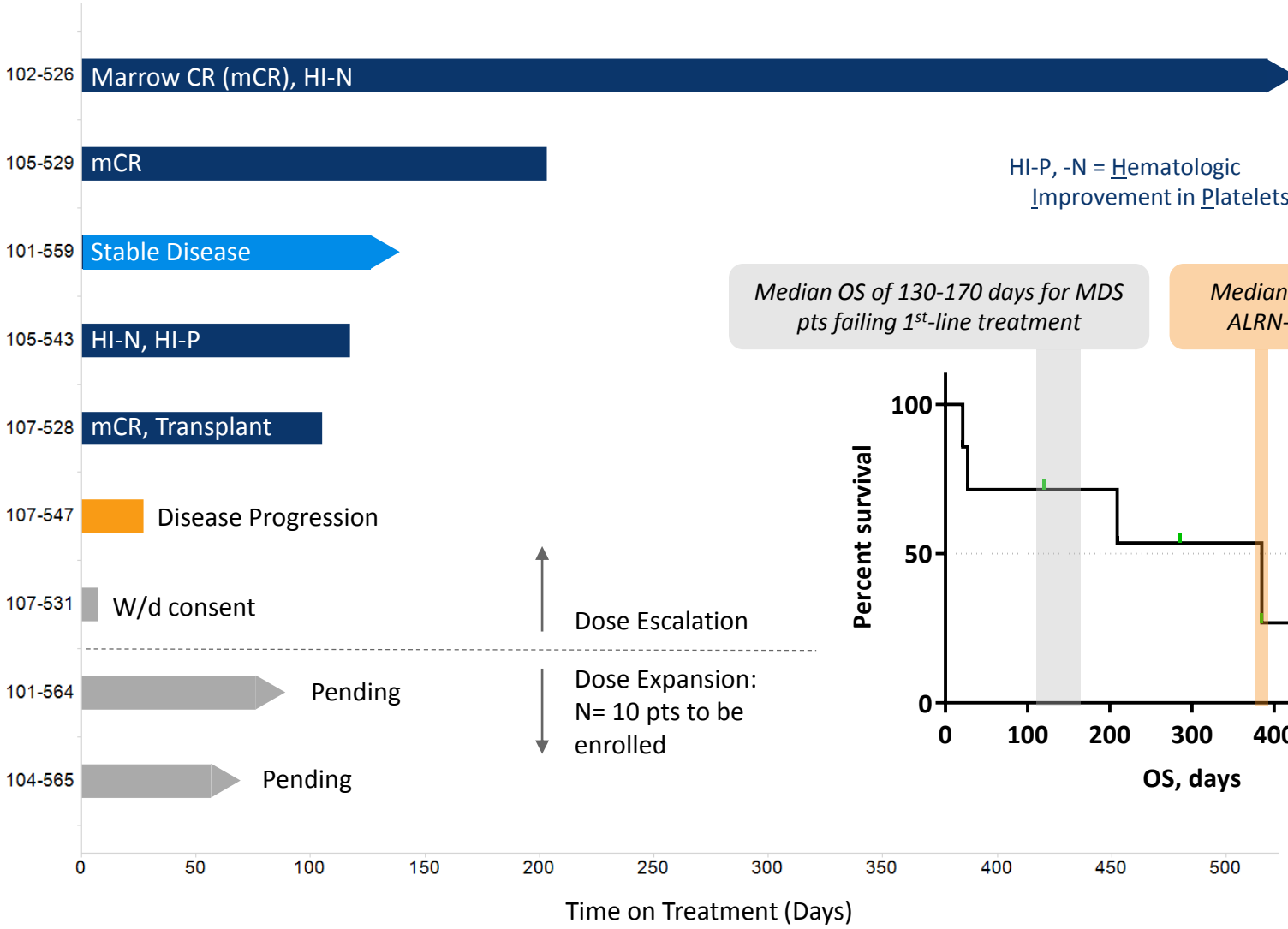
2nd line MDS: 5/6 evaluable pts at 4.4 mg/kg ALRN-6924 + low-dose Ara-C show anti-cancer activity, expansion underway



HI-P, -N = Hematologic Improvement in Platelets or Neutrophils

Median OS of 130-170 days for MDS pts failing 1st-line treatment

Median OS of 385 days for ALRN-6924-treated pts

Data as of 31-Oct-2018

Possible registration pathway for ALRN-6924 + low-dose Ara-C in MDS patients who failed a hypomethylating agent

- If data from expansion cohort are positive, the Company would seek meeting with FDA to discuss registration pathway
- Potential pivotal study design based on pivotal study of Azacitidine in MDS patients

Patient background	High-risk MDS patients who failed treatment with a hypomethylating agent (i.e., azacitidine, decitabine)
Design	Phase 3, randomized, controlled study of ALRN-6924 + Ara-C vs. Best Supportive Care
Endpoint	Overall survival
Rationale	ALRN-6924 potentiates Ara-C efficacy

Projected trials in 2019

Program	Indication	Preclinical	Phase 1	Phase 2	Phase 3
ALRN-6924 **Dual MDMX- and MDM2 Inhibitor**	+ Ara-C in 2L MDS ●	Ongoing			
	+ Azacitidine in 1L MDS ●	Planned			
	+ Palbociclib in MDM2↑ tumors	In Start-up			
	+ Topotecan in 2L SCLC + Carboplatin/Pemetrexed in 1L MPM + MEKi in 4L CRC + Capecitabine in 2L/3L Breast Cancer	Planned		*Umbrella Trial*	
	+ Paclitaxel in Breast cancer	In Start-up			
	+ Ara-C in Pediatric Leukemias	Ongoing			
	+ anti-PD-L1 in Solid tumors	Planned			
	Peripheral T-cell Lymphoma	Ongoing			
	Acute Myeloid Leukemia ●	Ongoing			
	Myelofibrosis	Planned			
	Pediatric solid tumors	Ongoing			

Data readouts within 12 months from initiation

↑ Combinations

↓ Monotherapy

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Investigator sponsored trial

● Separate cohorts in a single protocol

(Company does not intend to initiate "Planned Trials" unless and until it obtains cash resources needed to fund them)

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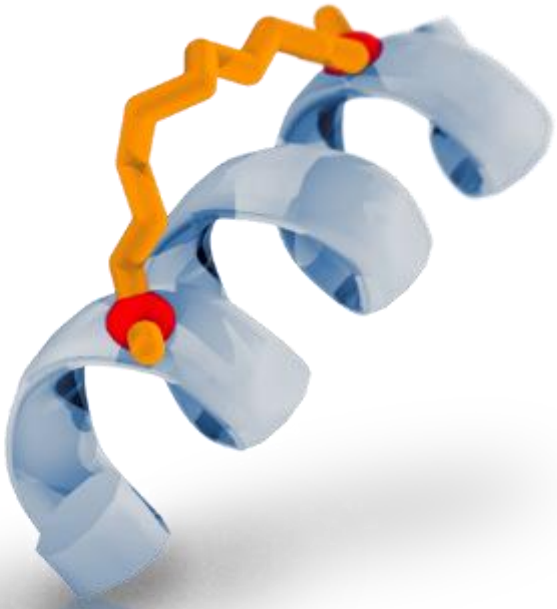
Synergistic Combination Therapies with ALRN-6924



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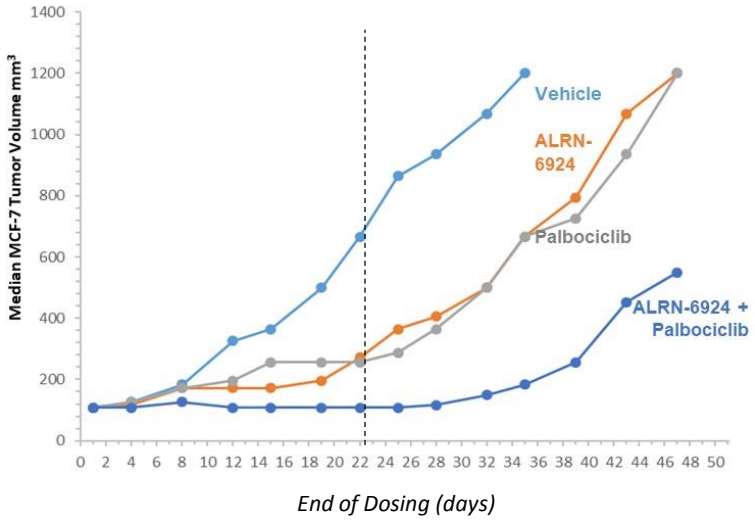
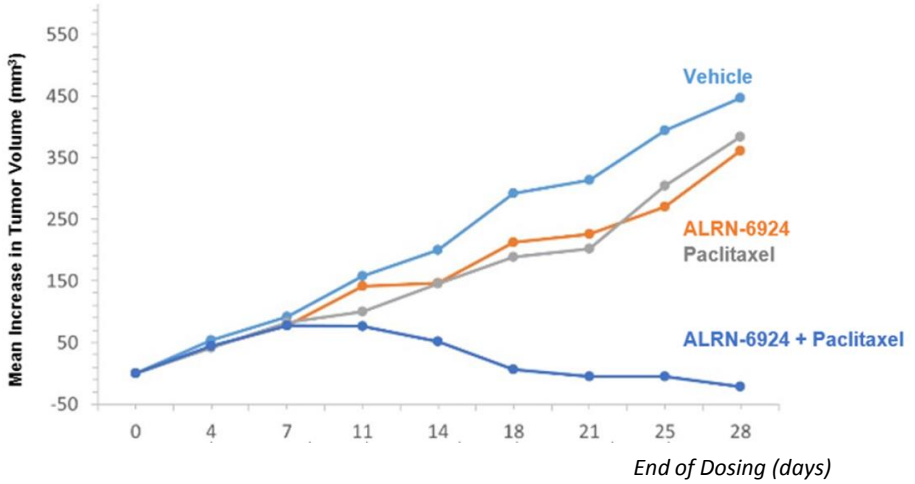
Double duties of cell cycle arrest and apoptosis with the right combination agent

ALRN-6924 induces cell cycle arrest in combination with a CDK4/6 inhibitor in-vivo



ALRN-6924 induces apoptosis in combination with chemotherapy in-vivo



Palbociclib combination trial anticipated Q1-2019

- Precision Medicine: combination will be evaluated in patients with tumor MDM2 amplification or MDM2/CDK4 co-amplification
- Tumor types include breast and lung cancers, sarcomas, glioblastomas, etc.
- Interim data readout 2H2019

Paclitaxel combination trial anticipated Q4-2018

- Paclitaxel is indicated for breast, lung, prostate, esophageal and other cancers
- Positions ALRN-6924 as a combination partner that increases paclitaxel efficacy
- Trial sponsor: MD Anderson Cancer Center

Additional combination trials: umbrella design with three chemotherapies and a targeted agent

Phase 1b/2a Trial size	**Simon-Two-Stage Optimal Design 4 cohorts of: ≈15 pts/cohort in stage 1 and ≈25 pts/cohort in stage 2**
Combination therapy and indications	ALRN-6924 + Capecitabine in 2L/3L Breast Cancer ALRN-6924 + MEKi in 4L Colorectal Cancer ALRN-6924 + Topotecan in 2L Small Cell Lung Cancer ALRN-6924 + Pemetrexed/Carboplatin in 1L Mesothelioma
Endpoints	1° Objective Response Rate 2° Progression-free Survival, Overall Survival
Response Assessments	Imaging every 6 weeks
Data	Interim data: 2H-2019 Final data 2H-2020

(Company does not intend to initiate cohorts unless and until it obtains the necessary cash resources. Anticipated timelines for disclosure of data assume the initiation of cohorts in 1Q 2019)

ALRN-6924 in MDS patients in combination with azacitidine

Phase 1b/2a Trial size	**Simon-Two-Stage Optimal Design ≈15 pts in stage 1 and ≈30 pts in stage 2**
Patient background	Patients with advanced high risk MDS with p53 wild-type who are azacitidine-naïve
Endpoints	Complete and Partial Remission by IWG Criteria
Rationale	ALRN-6924 in combination with azacitidine has additive/synergistic activity in-vitro
Data	Preliminary data: 2H-2019 Final data 2H-2020

(Company does not intend to initiate trial unless and until it obtains cash resources needed to fund trial. Anticipated timelines for disclosure of data assume the trial is company-sponsored and initiated 1Q 2019. Trial may be conducted by the Company or as an investigator-sponsored study)

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Additional Investigator-initiated ALRN-6924 trials under consideration

- Myelofibrosis (myeloproliferative neoplasm)
  - Published scientific basis and clinical results for MDM2 inhibition in a JAK2-mutant setting
  - Two arms: Ruxolitinib naïve (ALRN-6924 monotherapy) and Ruxolitinib failure (ALRN-6924 combination with Ruxolitinib)
- Anti-PD-L1 immune checkpoint inhibitor combination
  - Supported by Aileron's nonclinical results presented at Society for Immunotherapy of Cancer (SITC) 2018 Annual Conference

(Company does not intend to initiate trials unless and until it obtains cash resources needed to fund trials)

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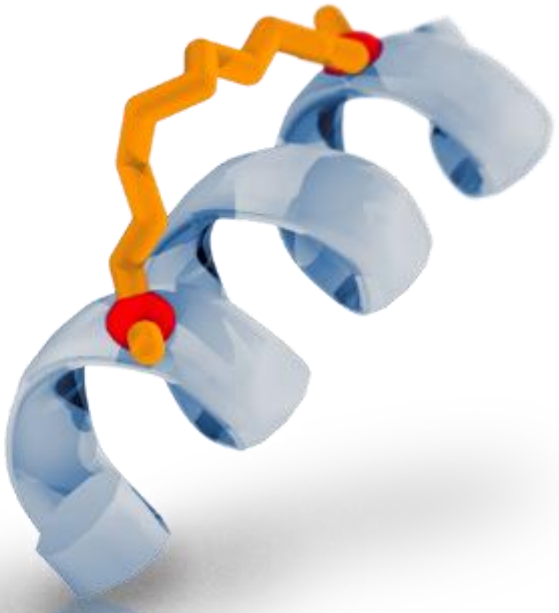
Combination Therapies - Summary

- Aileron-owned and investigator-initiated trials testing ALRN-6924 plus
  - 5 different chemotherapies
  - 5 different targeted therapies

- Combinations are based on strong mechanistic rationales and supported by *in vitro* and *in vivo* data
  - p53 pathway activation complements chemotherapies and response to DNA-damaging (and related) agents like capecitabine, carboplatin, Ara-C, azacitidine, paclitaxel, topotecan…
  - The p53 pathway intersects with nearly all signaling pathways for targeted therapies, like the Rb pathway for CDK4/6i's, the Ras pathway for MEK, etc.
  - Synergy with IO therapy: p53 is key to immune signaling in cancer cells and tumor stroma, including expression of PD-L1 on cancer cells

Outlook



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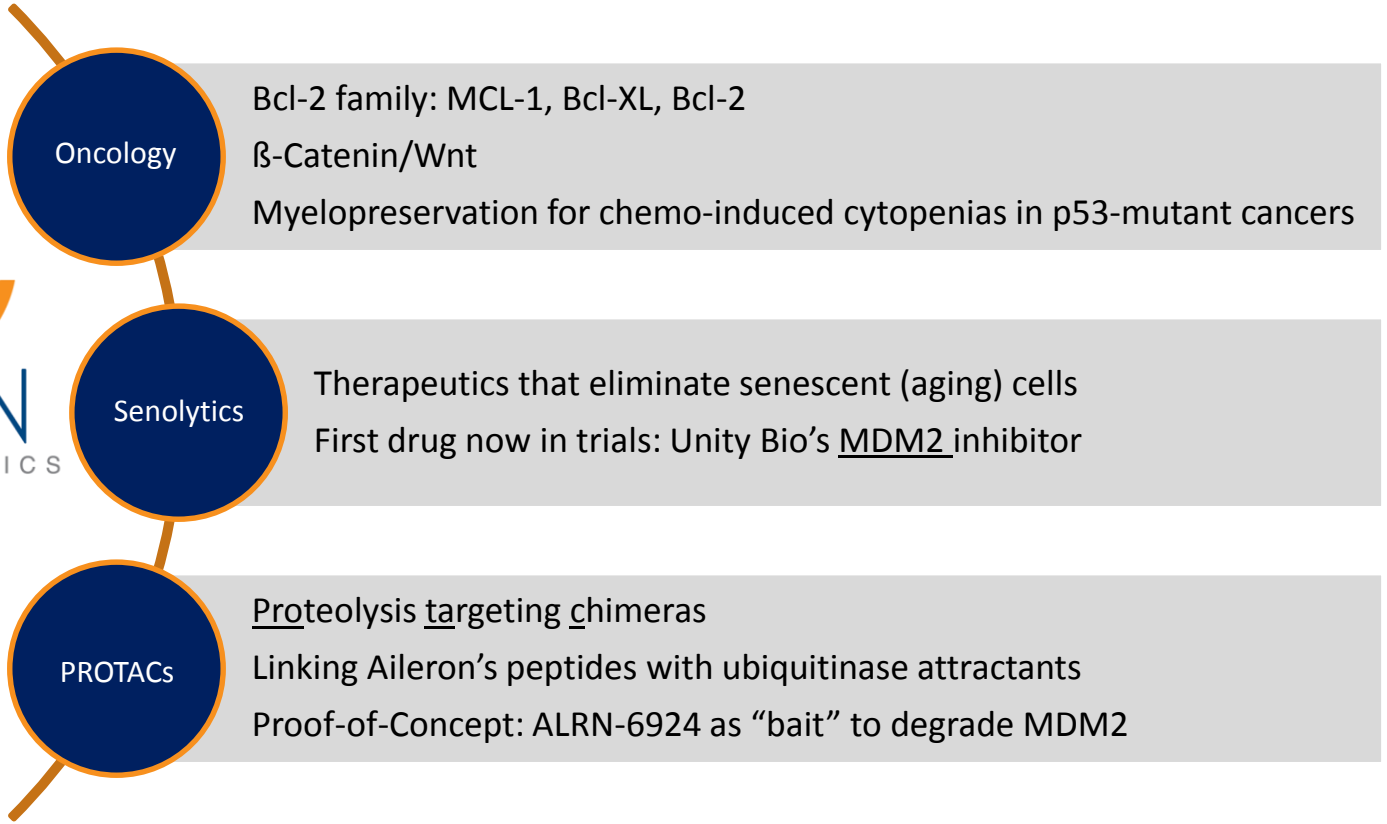
New indications and targets in discovery stage to maximize the value of cell-permeating peptides: ongoing research



Key Upcoming and Projected Milestones

Programs	4Q 2018	1H 2019	2H 2019
ALRN-6924 + Ara-C in 2L MDS	Interim results at ASH 2018	Interim results	Final results
ALRN-6924 Combination Therapies	Investigator trials initiated in: Breast cancer (+ Paclitaxel) *MD Anderson* Pediatric leukemias (+ Ara-C) *Dana-Farber Cancer Institute*	Initiate ALRN phase 1b/2a's: Umbrella[1,2] *+ Pem/Carbo in 1L MPM* *+ Topotecan in 2L SCLC* *+ MEKi in 4L CRC* *+ Capecitabine in 2L/3L Breast* + Palbociclib in MDM2↑ + Azacitidine in 1L MDS[1,2]	Phase 1b/2a **Interim data readout**
ALRN-6924 Monotherapy	Initial results in AML, interim results in PTCL at ASH 2018 Investigator trial initiated in pediatric solid tumors *Dana-Farber Cancer Institute*	Investigator-sponsored trial initiated in myelofibrosis[1,2,3]	Preliminary data on myelofibrosis
Myelopreservation with ALRN-6924	Non-clinical studies		Initiate phase 1
Bcl-2/Mcl-1	Optimization of cell-permeating dual inhibitor		Candidate selection

1. Company does not intend to initiate trial unless and until it obtains cash resources needed to fund trial
2. Anticipated timelines for disclosure of data assume initiation of trial 1Q 2019
3. Trial may be conducted by Company or as investigator-sponsored trial

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Corporate highlights

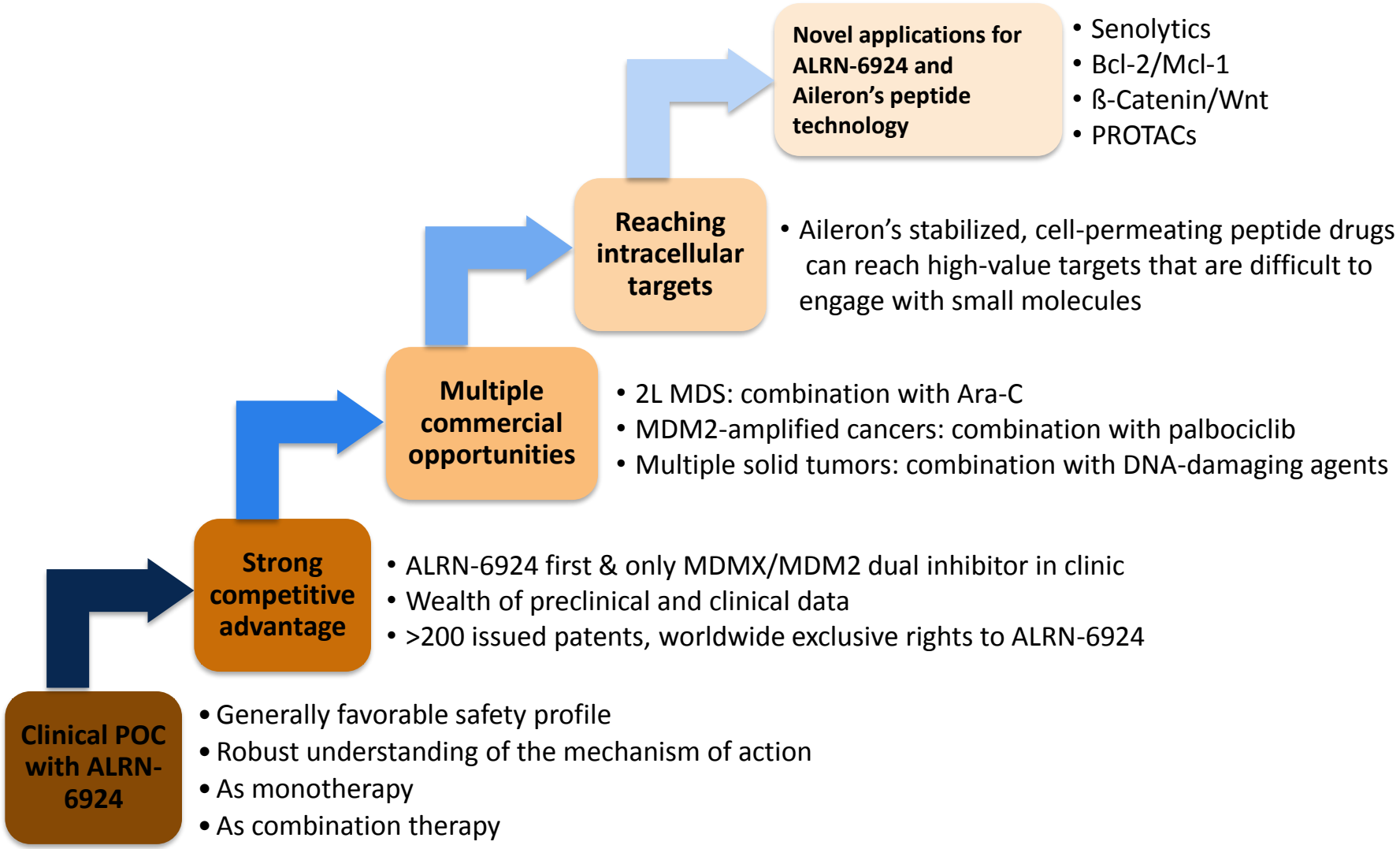
Operational highlight

- 23 employees (60% R&D)
- New location in Watertown: 18,600 sq. ft. lab + office
- 150+ patients enrolled to date

Financial highlight

- $28M in cash and equivalents as of Sept 30, 2018. Expected cash runway into 3Q 2019
- Cash burn in Q3 was $7.4 million
  - R&D: $4.9 million
  - SG&A: $2.5 million

Investment Thesis



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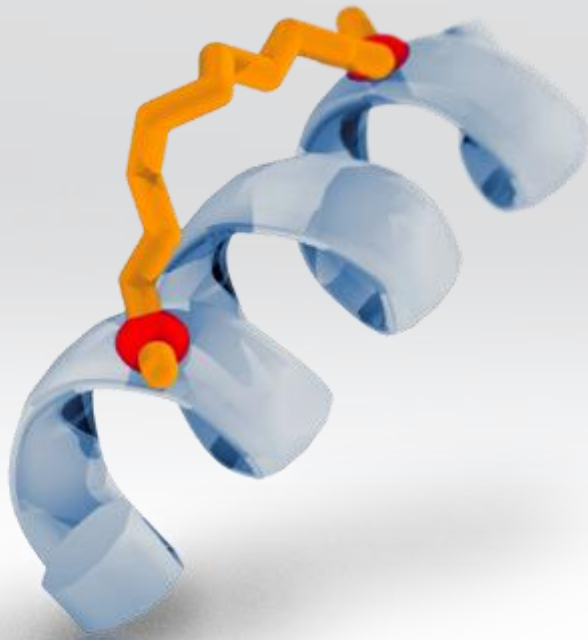

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