Legal Matters

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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.
Clinical POC with ALRN-6924

- Generally favorable safety profile
- Robust understanding of the mechanism of action
- As monotherapy
- As combination therapy

Strong competitive advantage

- ALRN-6924 first & only MDMX/MDM2 dual inhibitor in clinic
- Wealth of preclinical and clinical data
- >200 issued patents, worldwide exclusive rights to ALRN-6924

Multiple commercial opportunities

- 2L MDS: combination with Ara-C
- MDM2-amplified cancers: combination with palbociclib
- Multiple solid tumors: combination with DNA-damaging agents

Reaching intracellular targets

- Aileron’s stabilized, cell-permeating peptide drugs can reach high-value targets that are difficult to engage with small molecules

Novel applications for ALRN-6924 and Aileron’s peptide technology

- Senolytics
- Bcl-2/Mcl-1
- ß-Catenin/Wnt
- PROTACs
Executive Team

Manuel Aivado, MD, PhD
President and CEO

Don Dougherty, CFA, CPA
Chief Financial Officer

Vojo Vukovic, MD, PhD
Chief Medical Officer

Allen Annis, PhD
SVP, Research

Prior Experience

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

CCGrowth, Essex Investment Management, Putnam Investments, KPMG

Taiho Oncology, Synta Pharmaceuticals, Pfizer, Ilex Oncology

Schering-Plough Research Institute, NeoGenesis Pharmaceuticals
Aileron’s peptides are designed to surpass binding properties of small molecules and interact effectively with “difficult” intracellular targets.

**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
Aileron’s peptides may address highly valuable intracellular targets
ALRN-6924: the only clinical MDMX/MDM2 dual inhibitor

ALRN-6924 replicates native p53 binding contacts
Staple linker contributes to binding affinity

<table>
<thead>
<tr>
<th></th>
<th>Binding Affinity</th>
</tr>
</thead>
<tbody>
<tr>
<td>$K_d$, nM</td>
<td>MDM2</td>
</tr>
<tr>
<td>Native p53</td>
<td>770</td>
</tr>
<tr>
<td>ALRN-6924</td>
<td>13.7</td>
</tr>
<tr>
<td>RG7388</td>
<td>9.8</td>
</tr>
</tbody>
</table>

RG7388 = selective MDM2-inhibitor (Roche)
Superior binding kinetics of ALRN-6924 over small molecules

MDM2

Load\text{ } wash

ALRN-6924 binding is sustained during wash-off from MDM2-coated surface\n$t_{1/2} = 85$ minutes

RG7388 washes off from MDM2 surface\n$t_{1/2} 2-3$ min

MDMX

Load\text{ } wash

ALRN-6924 binds MDMX, $t_{1/2} = 5$ minutes

RG7388 No binding to MDMX

Ref: “Dual Inhibition of MDMX and MDM2 as a Therapeutic Strategy in Leukemia” Sci Transl Med 2018
ALRN-6924: a first-in-class p53 activator that acts by inhibition of both MDMX and MDM2

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

**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*
## Presentations and Awards

<table>
<thead>
<tr>
<th>Conference</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCO 2017</td>
<td>Oral presentation and selected for “Best of ASCO”</td>
</tr>
<tr>
<td>ISEH 2017</td>
<td>Oral presentation and gold medal investigator award</td>
</tr>
<tr>
<td>ASH 2017</td>
<td>Two oral presentations</td>
</tr>
</tbody>
</table>

## Editorial Highlights

**Clinical Cancer Advances 2018**

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

**Constrained peptides’ time to shine?**

*Chris Morrison, Nature Reviews Drug Discovery, July 2018*

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

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

<table>
<thead>
<tr>
<th>First-in-Human Phase 1 Trial</th>
<th># pts</th>
<th>Dose range</th>
<th># CR</th>
<th># PR</th>
<th># SD</th>
<th>Thrombocytopenia Grade ≥ 3</th>
<th>Neutropenia Grade ≥ 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>AILERON THERAPEUTICS ALRN-6924</td>
<td>71</td>
<td>28x</td>
<td>2</td>
<td>2</td>
<td>21</td>
<td>0%</td>
<td>3%</td>
</tr>
<tr>
<td>AMGEN AMG 232</td>
<td>39</td>
<td>32x</td>
<td>0</td>
<td>0</td>
<td>30</td>
<td>33%</td>
<td>21%</td>
</tr>
<tr>
<td>Daiichi-Sankyo DS-3032b</td>
<td>103</td>
<td>22x</td>
<td>0</td>
<td>3</td>
<td>52</td>
<td>19%</td>
<td>12%</td>
</tr>
<tr>
<td>NOVARTIS HDM201</td>
<td>107</td>
<td>28x</td>
<td>0</td>
<td>2</td>
<td>31</td>
<td>24%</td>
<td>23%</td>
</tr>
<tr>
<td>Roche RO6839921</td>
<td>41</td>
<td>8x</td>
<td>0</td>
<td>0</td>
<td>17</td>
<td>15%</td>
<td>20%</td>
</tr>
<tr>
<td>Roche RG7388</td>
<td>95</td>
<td>16x</td>
<td>0</td>
<td>0</td>
<td>20</td>
<td>33%</td>
<td>21%</td>
</tr>
<tr>
<td>MERCK MK-8242</td>
<td>47</td>
<td>8x</td>
<td>0</td>
<td>3</td>
<td>31</td>
<td>15%</td>
<td>19%</td>
</tr>
</tbody>
</table>
Phase 2 dose optimization trial in PTCL patients shows single-agent activity

• 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.

Data as of 26-Feb-2018: 21% per investigator-reported IWG 2014 criteria or 27% per independent radiology review by modified Cheson 2007 criteria*
2nd line MDS: 5/6 evaluable pts at 4.4 mg/kg ALRN-6924 + low-dose Ara-C show anti-cancer activity, expansion underway

Marrow CR (mCR), HI-N
mCR
Stable Disease
HI-N, HI-P
mCR, Transplant
Disease Progression
W/d consent
Pending
Pending

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

<table>
<thead>
<tr>
<th>Patient background</th>
<th>High-risk MDS patients who failed treatment with a hypomethylating agent (i.e., azacitidine, decitabine)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Design</td>
<td>Phase 3, randomized, controlled study of ALRN-6924 + Ara-C vs. Best Supportive Care</td>
</tr>
<tr>
<td>Endpoint</td>
<td>Overall survival</td>
</tr>
<tr>
<td>Rationale</td>
<td>ALRN-6924 potentiates Ara-C efficacy</td>
</tr>
</tbody>
</table>
### Projected trials in 2019

<table>
<thead>
<tr>
<th>Program</th>
<th>Indication</th>
<th>Preclinical</th>
<th>Phase 1</th>
<th>Phase 2</th>
<th>Phase 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ALRN-6924</strong></td>
<td><strong>Dual MDMX- and MDM2 Inhibitor</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>+ Ara-C in 2L MDS</td>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>+ Azacitidine in 1L MDS</td>
<td>Planned</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>+ Palbociclib in MDM2↑ tumors</td>
<td>In Start-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>+ Topotecan in 2L SCLC + Carboblatin/Pemetrexed in 1L MPM + MEKi in 4L CRC + Capecitabine in 2L/3L Breast Cancer</td>
<td>Planned</td>
<td></td>
<td></td>
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</tr>
<tr>
<td></td>
<td>+ Paclitaxel in Breast cancer</td>
<td>In Start-up</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>+ Ara-C in Pediatric Leukemias</td>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>+ anti-PD-L1 in Solid tumors</td>
<td>Planned</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Peripheral T-cell Lymphoma</td>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Acute Myeloid Leukemia</td>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Myelofibrosis</td>
<td>Planned</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pediatric solid tumors</td>
<td>Ongoing</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Ongoing**: Data readouts within 12 months from initiation
- **Planned**: Investigator-sponsored trial
- **Umbrella Trial**: In Start-up

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)
Synergistic Combination Therapies with ALRN-6924
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
### 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

<table>
<thead>
<tr>
<th>Combination therapy and indications</th>
<th>ALRN-6924 + Capecitabine in 2L/3L Breast Cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ALRN-6924 + MEKi in 4L Colorectal Cancer</td>
</tr>
<tr>
<td></td>
<td>ALRN-6924 + Topotecan in 2L Small Cell Lung Cancer</td>
</tr>
<tr>
<td></td>
<td>ALRN-6924 + Pemetrexed/Carboplatin in 1L Mesothelioma</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Endpoints</th>
<th>1° Objective Response Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2° Progression-free Survival, Overall Survival</td>
</tr>
</tbody>
</table>

| Response Assessments                | Imaging every 6 weeks                           |

<table>
<thead>
<tr>
<th>Data</th>
<th>Interim data: 2H-2019</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Final data 2H-2020</td>
</tr>
</tbody>
</table>

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

**Oncology**
- Bcl-2 family: MCL-1, Bcl-XL, Bcl-2
- β-Catenin/Wnt
- Myelopreservation for chemo-induced cytopenias in p53-mutant cancers

**Senolytics**
- Therapeutics that eliminate senescent (aging) cells
- First drug now in trials: Unity Bio’s MDM2 inhibitor

**PROTACs**
- Proteolysis targeting chimeras
- Linking Aileron’s peptides with ubiquitinase attractants
- Proof-of-Concept: ALRN-6924 as “bait” to degrade MDM2
## Key Upcoming and Projected Milestones

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

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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
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
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- As combination therapy

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