**Phase 1b Study of the Stapled Peptide ALRN-6924, a Dual Inhibitor of MDMX and MDM2, as Monotherapy or in Combination for the Treatment of Relapsed/Refractory AML and Advanced MDS with TP53 Wild-Type**

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### Background

**Figure 1: The Cell-Permeating c-helical Peptide, ALRN-6924, is a First-in-Class Dual Inhibitor of MDMX and MDM2**

- Peptide Linkers
- MDMX
- p53
- MDM2
- p53 Suppression
- Nucleus
- Cytoplasm
- Key Inclusion Criteria
- ALRN-6924 QW and TIW monotherapy and in combination in cytarabine have acceptable safety profiles
- Conclusions and Study Statistics
- ALRN-6924 in combination with low-dose Ara-C has shown preliminary clinical activity in MDS patients, including marrow CRs and hematological improvement, with one patient bridged to transplant. An accrual to the ALRN-6924 + Ara-C combination cohort and the TP53-mutated MDS cohort continues.

### Primary Objectives

- **Evaluate the safety and tolerability of ALRN-6924 alone and in combination with cytarabine (Ara-C) in adult patients with acute myeloid leukemia (AML) or advanced myelodysplastic syndrome (MDS) with wild-type (WT) TP53 who are relapsed/refractory to or intolerant of standard therapy, or for whom no standard therapy exists.**
- **Determine the dose limiting toxicities (DLTs) and the maximum tolerated dose (MTD) of ALRN-6924 alone and in combination with cytarabine in adult patients with AML or advanced MDS.**

### Methods

- **ALRN-6924 is being evaluated alone and in combination with low-dose cytarabine, using a 3+3 dose escalation design.**
- **Adverse events (AEs) are assessed per CTCAE V4.03.**
- **Responses are evaluated by the investigator according to IWG (Cheson 2016) and AML Response Criteria (Dohner 2010), for MDS and AML, respectively.**

### Key Inclusion Criteria

- **AML: Relapsed or refractory acute myeloid leukemia according to WHO criteria.**
- **MDS: Diagnosis of MDS according to WHO criteria not responsive to, intolerant to, or progression after hypomethylating agents.**
- **ECOG performance status 0-2.**

### Table 1: Patient Characteristics

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Monotherapy TIW</th>
<th>1.0 mg/kg QW</th>
<th>3.1 mg/kg TIW</th>
<th>5.8 mg/kg QW</th>
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</thead>
<tbody>
<tr>
<td>DLT</td>
<td>0</td>
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<td>2</td>
<td>1</td>
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</table>

### Table 2: Patient Disposition

<table>
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<tr>
<th>Days on Treatment</th>
<th>QW monotherapy</th>
<th>TIW monotherapy</th>
<th>QW combo</th>
<th>TIW combo</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1</td>
<td>5</td>
<td>12</td>
<td>11</td>
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</tr>
<tr>
<td>2</td>
<td>8</td>
<td>14</td>
<td>13</td>
<td>12</td>
</tr>
</tbody>
</table>

### Table 3: Related TEAE (% in All Patients)

<table>
<thead>
<tr>
<th>Cohort</th>
<th>Monotherapy TIW</th>
<th>1.0 mg/kg QW</th>
<th>3.1 mg/kg TIW</th>
<th>5.8 mg/kg QW</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>23.1%</td>
<td>9.5%</td>
<td>15.4%</td>
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</tr>
<tr>
<td>Vomiting</td>
<td>46.2%</td>
<td>14.3%</td>
<td>7.7%</td>
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</tr>
</tbody>
</table>

### Table 4: Related SAEs

- **Conclusions and Study Statistics**
- **ALRN-6924 in combination with low-dose Ara-C has shown preliminary clinical activity in MDS patients, including marrow CRs and hematological improvement, with one patient bridged to transplant. An accrual to the ALRN-6924 + Ara-C combination cohort and the TP53-mutated MDS cohort continues.**

### References

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