### Introduction

- Kinesin Spindle Protein (KSP) is a novel antimitotic target.
- ARRY-520 is highly active in preclinical models of leukemia and other hematological cancers.
- Preclinical data suggest acute leukemias are a good target for KSP inhibition.

### Study Design and Objectives

- **Primary Objective**: Determine the safety and maximum tolerated dose (MTD) of ARRY-520.
- **Secondary Objectives**:
  2. Assess markers of PD activity.

### Key Eligibility Criteria

- Acute myeloid leukemia (AML) (including RAEB-2).
- AML, CMML, M0-M7 allowed but not enrolled.
- Relapsed or refractory disease or confirmed diagnosis in patients who are not eligible for, or refuse, recommended or standard of care treatment.
- Normal or corrected baseline renal function.
- Normal or corrected baseline hepatic function.

### Patient Characteristics

<table>
<thead>
<tr>
<th>Gender (Male:Female)</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>3/1</td>
<td>12</td>
</tr>
</tbody>
</table>

### Schedule 1

**Number of Patients**: N = 15

<table>
<thead>
<tr>
<th>Dose (mg/m²)</th>
<th>Median (mos)</th>
<th>Range (mos)</th>
<th>Prior BMT</th>
<th>Number of Dose Modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>12</td>
<td>6 – 108</td>
<td>2</td>
<td>1360</td>
</tr>
<tr>
<td>3</td>
<td>12</td>
<td>6 – 108</td>
<td>2</td>
<td>1360</td>
</tr>
<tr>
<td>4</td>
<td>11</td>
<td>0 – 45</td>
<td>1</td>
<td>1360</td>
</tr>
</tbody>
</table>

### Schedule 2

**Number of Patients**: N = 15

<table>
<thead>
<tr>
<th>Dose (mg/m²)</th>
<th>Median (mos)</th>
<th>Range (mos)</th>
<th>Prior BMT</th>
<th>Number of Dose Modifications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>13</td>
<td>0 – 160</td>
<td>2</td>
<td>1360</td>
</tr>
</tbody>
</table>

### Disease History

- **Gender (male:female)**: 3/1
- **Median age (years)**: 64
- **Median Performance Status**: 0

### Dose-Limiting Toxics

<table>
<thead>
<tr>
<th>Dose Limiting Toxicity</th>
<th>N = 18</th>
<th>Grade 3–4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucositis</td>
<td>11</td>
<td>100%</td>
</tr>
<tr>
<td>Nausea</td>
<td>3</td>
<td>16.7%</td>
</tr>
<tr>
<td>Vomiting</td>
<td>2</td>
<td>11.1%</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>1</td>
<td>5.6%</td>
</tr>
</tbody>
</table>

### Treatment-Related Adverse Events* at the MTD (4.5 mg/m²)

**Number of Patients**: N = 15

- **Any event assessed as treatment-related by Investigator/Sponsor that occurred in > 1 patient overall**
- **Any grade mucositis**: 3/1
- **Grade 3 mucositis**: 1/2
- **Grade 4 mucositis**: 1/2

### Summary

- The clinical observations for the two schedules of administration for ARRY-520 are comparable.
- The study demonstrated an acceptable safety profile in both schedules at dose levels up to the MTD (4.5 mg/m²), with no significant difference in the toxicity observed between the two schedules.
- Overall, the most common DLT was mucositis, with additional AEs of hand-foot syndrome and bilirubinemia observed in Schedule 2 at the nondose-dense level.
- Despite the fact that patients were heavily pretreated, encouraging preliminary efficacy was observed for both schedules.
- No differences were observed in PK exposure between Schedule 1 and Schedule 2.
- An expansion cohort in patients with minimally pretreated advanced myelodysplastic syndrome (MDS) is ongoing with the Days 1, 3 and 5 dosing.

---

* Significance of **any event assessed as treatment-related by Investigator/Sponsor that occurred in > 1 patient overall**.

**IA**: Investigational Agent

**NA**: Not applicable

**%**: Percent of patients

**Pts**: Patients

**Median time to onset**: Median time to onset

**Median duration**: Median duration

**Median ARRY-520 Plasma Concentrations**: Median ARRY-520 Plasma Concentrations

**Median (Range) Pharmacokinetic Parameters by Schedule and Total Dose per Cycle**

**Phase 1 Dose-Escalation Study of the Novel KSP Inhibitor ARRY-520 in Advanced Leukemias**

Guillermo Garcia-Manero, MD

A Thank You to the Patients and Their Families

Available at www.arraybiopharma.com

1Department of Leukemia, MD Anderson Cancer Center, Houston, TX; 2Department of Hematology and Medical Oncology, Emory University, Atlanta, GA; 3Array BioPharma, Boulder, CO