**Phase 1 Trial of ARRY-520 in Relapsed/Refractory Multiple Myeloma**

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**Abstract # 8132**

**Thank You to the Patients and Their Families**

**Background:**

Kinesin spindle protein (KSP) is a novel antimitotic target. ARRY-520 is a potent and highly selective inhibitor of KSP.

**Study Design and Objectives:**

- **Key Eligibility Criteria:**
  - At least 2 prior treatment regimens which must have included both bortezomib and an IMiD, unless patients were not eligible or refused these treatments
  - Measurable disease (if lymph), light chain in urine, FLC in serum or ≥ 30% plasma cells in bone marrow
  - ECOG Performance Status 0-1
  - Age ≥ 18 years
  - Adequate hematologic, hepatic and renal function
  - No prior amyloidosis
  - No bone marrow or stem cell transplant within 3 months of first dose

**MM Patient Characteristics**

<table>
<thead>
<tr>
<th>NGS (gene)</th>
<th>49 – 78</th>
<th>46 – 63</th>
<th>44 – 77</th>
<th>38 – 78</th>
<th>44 – 79</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease high-risk status</td>
<td>30%</td>
<td>33%</td>
<td>30%</td>
<td>31%</td>
<td>35%</td>
</tr>
<tr>
<td>ECOG Performance Status</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Prior MM Therapy</td>
<td>20%</td>
<td>25%</td>
<td>10%</td>
<td>20%</td>
<td>25%</td>
</tr>
</tbody>
</table>
| **Study Design** | Open label, multicenter, dose-escalation study to assess safety, PK and PO of ARRY-520 given IV for 1 hour on Days 1 and 2 ± 2 weeks  
**Primary Objectives:**
- Determine the safety and maximum tolerated dose (MTD) of ARRY-520 without and with G-CSF support
- Assess preliminary anti-myeloma activity of ARRY-520
- Evaluate the plasma PK profile of ARRY-520

**Dose Escalation:**

<table>
<thead>
<tr>
<th>Dose (mg/m2/day)</th>
<th>1.25</th>
<th>1.6</th>
<th>≥ 2.0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Range</td>
<td>0.6 – 1.6</td>
<td>1.0 – 1.6</td>
<td>2.0 – 3.0</td>
</tr>
<tr>
<td><strong>PK Parameter</strong></td>
<td>AUCinf (hr-ng/mL)</td>
<td>T1/2 (h)</td>
<td>V1 (L/m2)</td>
</tr>
<tr>
<td>1.25 mg/m2/day</td>
<td>57.4 (36.0 – 85.6)</td>
<td>4.4 (2.2 – 8.5)</td>
<td>15.5 (181%)</td>
</tr>
<tr>
<td>1.6 mg/m2/day</td>
<td>59.0 (36.2 – 93.2)</td>
<td>3.9 (2.3 – 6.1)</td>
<td>21.6 (262%)</td>
</tr>
<tr>
<td>≥ 2.0 mg/m2/day</td>
<td>61.0 (40.2 – 91.3)</td>
<td>3.3 (2.1 – 5.9)</td>
<td>33.0 (408%)</td>
</tr>
</tbody>
</table>

**PK Summary:**

- **Cmax:** 1460 ng/mL (24 h after start of Day 1 ARRY-520 infusion)  
- **Tmax:** 4 h (Day 1)  
- **Cl:** 0.14 L/h/m2 (Day 1)  
- **V1:** 34.6 (54.0%)  
- **V2:** 86.2 (131%)

**Clinical Activity:**

- **Response:**
  - 30% plasma cells
  - 12% lumbar plasma cells
  - 3% bone marrow plasma cells

**Safety:**

- **Adverse Events:**
  - Neutropenia
  - Fatigue
  - Anemia
  - Infections
  - Thrombocytopenia
  - Leukopenia
  - Nausea

**Preliminary Anti-Myeloma Activity:**

- **Response per IMWG and EBM3 criteria (2 evaluable patients):**
  - 1 PR (1 mm/h/day)  
  - 1 SD (2 mm/h/day)

- **MTD was 1.25 mg/m2/day without G-CSF**

- **Further studies, including single agent Phase 2 study and combination trials in multiple myeloma, are planned**

**Conclusion:**

These data support the initiation of studies with ARRY-520 in multiple myeloma patients who have progressed after treatment with bortezomib and an IMiD.

**References:**


**Figures:**

- **Figure 1:** Dose-escalation study to assess safety, PK and PO of ARRY-520 given IV for 1 hour on Days 1 and 2 ± 2 weeks  
- **Figure 2:** Population PK estimates showed moderate-to-high inter-individual variability (IIV) as well as inter-occasion variability (IOV) in a two-compartment linear model.

**Tables:**

- **Table 1:** ARRY-520 Treatment
- **Table 2:** MM Patient Characteristics
- **Table 3:** Pharmacokinetics