ARRY-520 is a potent, selective inhibitor of the kinesin 5 motor protein K5CIP1. 

- Kinesin 5-α is restricted to proliferating cells.
- ARRY-520 preferentially targets McI-1–sensitized cells.
- Precisely hematopoietic cells and tumors, and some solid tumors.

ARRY-520 safety profile is restricted by target expression and biology.

Transient, non-cumulative myelosuppression.

- Neutrophils: Granulocytes 10x lower with dose
- Neutropenia: 12% with 0.75 mg/m2 ARRY-520 + 1.3 mg/m2 bortezomib.

- Neutropenia and thrombocytopenia have been reversible and not cumulative.

- Rapidly reversible, non-cumulative neutropenia was the most common toxicity.

- All hematologic toxicity was the most commonly observed adverse effect.

- Rapidly reversible, non-cumulative neutropenia was the most common toxicity.

- 15 patients treated with ARRY-520 at doses of ≤1.0 mg/m2 with full dose bortezomib (1:1 ratio).

- Dose escalation is continuing with the addition of low-dose dexamethasone.

- An alternative schedule of ARRY-520 on Days 1, 15 with bortezomib and low-dose dexamethasone is also open for enrollment.

- Dose escalation is continuing with the addition of low-dose dexamethasone.

- The combination of ARRY-520 and bortezomib is well-tolerated with prophylactic G-CSF.

- ARRY-520 + weekly bortezomib has been administered to patients at each of their respective doses

ARRY-520 + bortezomib demonstrated an acceptable safety profile at the maximum planned dose.

- Hematologic toxicity was the most commonly observed adverse effect.

- Grade 4 neuropathy in 4/30 pts treated without prophylactic G-CSF, regardless of ARRY-520 dose.

- G-CSF adequately manages neutropenia (2/30 Grade 4 neutropenia in patients with prophylactic G-CSF).

- Neutropenia and thrombocytopenia have been reversible and not cumulative.

- Low incidence of Grade 3/4 non-hematologic toxicity.

- 336 (5%) patients experienced neuropathy, all Grade 1, with full dose bortezomib.

- 336 (5%) patients required a dose reduction due to an adverse event, regardless of causality only.

- Anorexia, neuropathy.

- 4/36 (11%) patients discontinued treatment due to an adverse event, regardless of causality.

- 232 (35%) patients experienced any SAE, regardless of causality or grade.

- 5 related SAEs (2 Grade 3 pneumonia, 2 Grade 7 bronchitis, Grade 4 pseudomyceliosis, Grade 4 subdural hematoma).

**Summary**

- ARRY-520 is a weekly bortezomib has been administered to patients at each of their respective maximum single-agent doses.

- ARRY-520 1.5 mg/m2/d on Days 1, 15, 18 + 1.3 mg/m2/d bortezomib on Days 1, 8, 15 with prophylactic G-CSF.

- The combination of ARRY-520 and bortezomib is well-tolerated with prophylactic G-CSF.

- Rapidly reversible, non-cumulative neutropenia was the most common toxicity.

- G-CSF adequately manages neutropenia allowing for dose escalation to maximum planned dose of ARRY-520 with full bortezomib dose.

- Low incidence of non-hematologic AEs are predominantly Grade 1/2.

- Low incidence of neuropathy.

- The combination of ARRY-520 and bortezomib has promising activity in heavily pretreated patients with multiple myeloma, including in disease refractory to bortezomib.

- Dose escalation is continuing with the addition of low-dose dexamethasone.

- An alternative schedule of ARRY-520 on Days 1, 15 with bortezomib and low-dose dexamethasone is also open for enrollment.

- The role of the axon protein 1 (axonal glycoprotein (AGP) as a potential selection biomarker has been explored in another study.

- Expansion cohort will commence at completion of dose escalation cohorts.

- In multiple myeloma patients with 1-3 prior therapies; bortezomib-refractory patients excluded.