Selinexor: First-in-Class, Oral Selective Inhibitor of Nuclear Export Reactivates Tumor Suppressor Proteins and is Synergistic with IMiDs

Exportin 1 (XPO1) is a critical nuclear export protein: • Tumor suppressor proteins (TSPs, e.g., p53, MDM2, and FOXO1a,1) • RNA-bound circRNA mRNAs (e.g., miR-155, let-7d, miR-150).2

XPO1 is overexpressed in MM: • High XPO1 levels enable cancer cells to escape TSP-mediated cell cycle arrest and apoptosis.2,3 • XPO1 levels correlate with poor prognosis and drug resistance.2

Selinexor is an oral selective XPO1 inhibitor; preclinical data supports that selinexor: • Reactivates multiple TSPs by preventing nuclear export and suppresses NFκB activity1,2,4 • Inhibits circRNA export2 • Reactivates glucocorticoid receptor (GR) signals in presence of selinexor1

Selinexor demonstrated synergistic activity in combination with lenalidomide in vivo2

STOMP: Selinexor + Pomalidomide + Dexamethasone (XPD) Selinexor and Backbone Treatments Of Multiple Myeloma Patients

Objectives:
- Primary endpoint: OS
- Maximum Tolerated Dose (MTD) + Recommended Phase 2 Dose (RP2D)
- Overall Response Rate (ORR)
- Secondary endpoints:
  - Safety and Tolerability per CTCAE
  - Progression Free Survival (PFS)
  - Overall Survival (OS)

Key eligibility criteria:
- ANC ≥ 1,000/mm3, Hb ≥ 8.0 g/dL, Platelet count ≥ 75,000/mm3
- Progressing or refractory to a previous regimen
- Previously undergone treatment with ≥2 cycles of lenalidomide and a proteasome inhibitor (in combination or separately)
- Prior pomalidomide-treatment is allowed, pomalidomide-resistant only allowed in the dose escalation phase
- Smoldering MM, non-secretory MM, active plasma cell leukemia are excluded

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