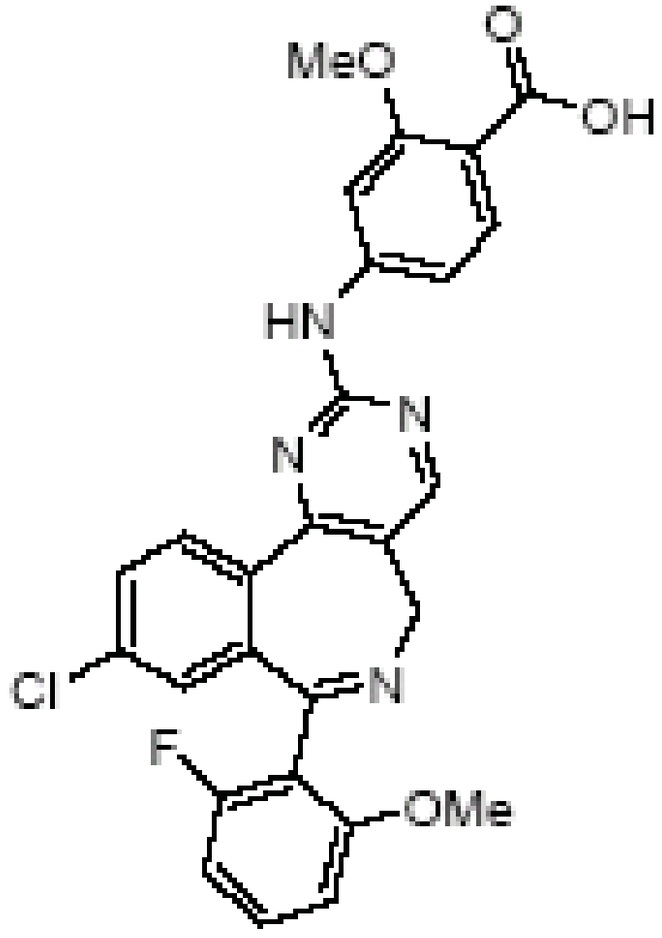
Supplementary Figure 1. MLN8237 does not induce inhibition of cell viability, but does inhibit proliferation, in PBMCs from healthy donors. Chemical structure of MLN8237 **(A)**.Peripheral blood mononuclear cells from two healthy donors were stimulated with PHA and incubated in the presence of DMSO or increasing doses of MLN8237 (0.1-4uM) for 72 hours. Inhibition of cell proliferation was determined by 3[H]thymidine incorporation assay **(B)**, and inhibition of cell viability was determined by MTT assay **(C)** in healthy PBMCs**.** Data represent mean±SD of triplicate cultures.

Supplementary Figure 2. MLN8237 in combination with other anti-MM agents. OPM1 cells were treated with MLN8237 (0.125-0.5uM) for 72 hours with conventional anti-MM agents Melphalan (2.5-5uM), Dexamethasone (50-100nM), or Doxorubucin (50-100nM); and with novel anti-MM agents Velcade (2.5-5nM) and Revlimid (0.5-1uM). Velcade was added to the culture for the last 12 hours. **A.** Following treatment, viability was assessed by MTT assay, and data are presented as per cent viability relative to control (mean±SD of triplicate cultures). Isobologram analysis using CalcuSyn software indicated that combining MLN8237 with Dexamethasone, Doxorubucin **(B)** or Velcade **(C)** induces synergistic/additive anti-MM activity against MM cell lines in vitro ($p \leq 0.05$, combination index, $CI<1$)

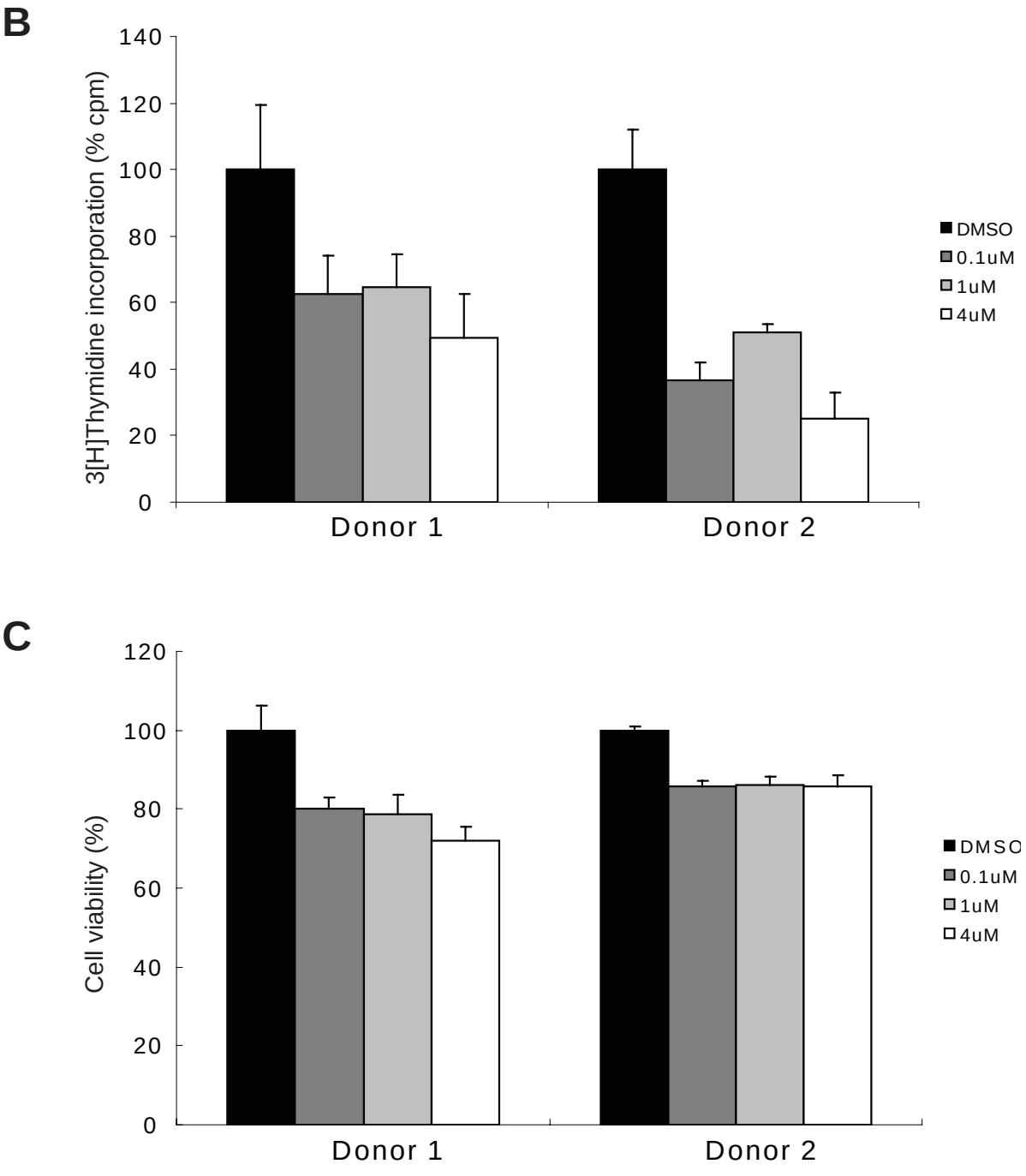
Supplementary Figure 1

A

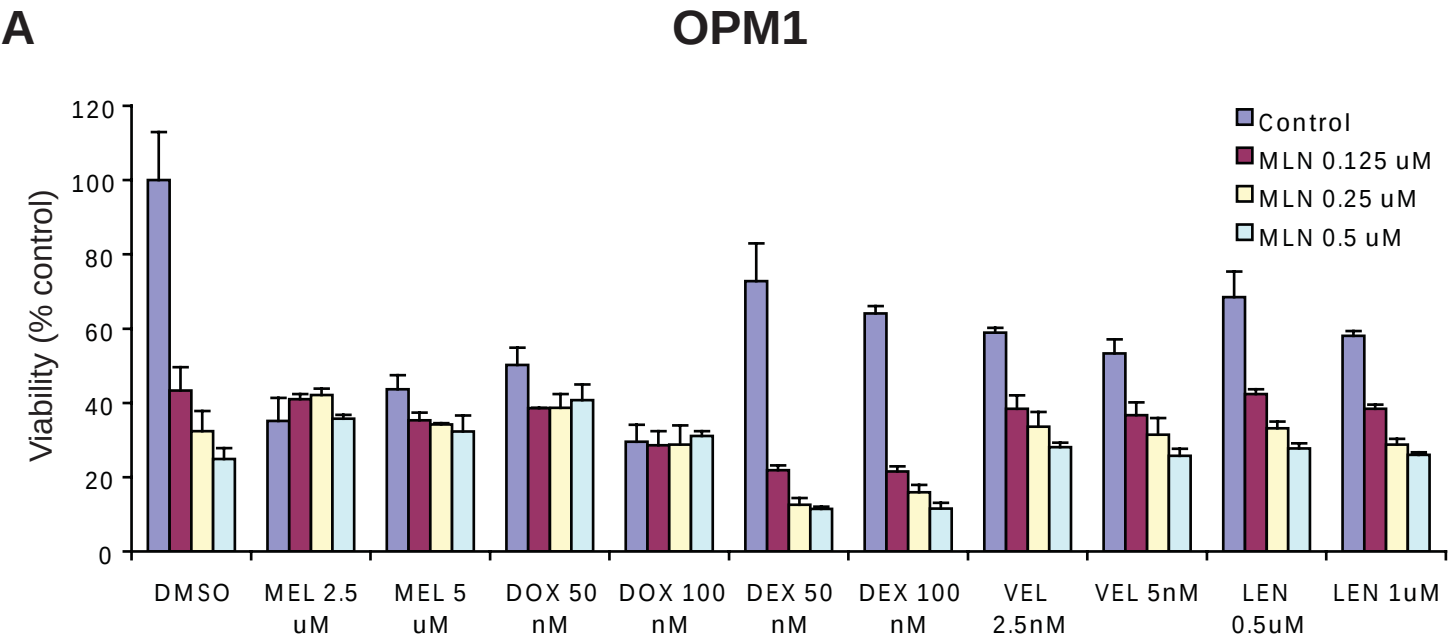


MLN8237, 4-{[9-chloro-7-(2-fluoro-6-methoxyphenyl)-5Hpyrimido[5,4-d][2]benzazepin-2-yl]amino}-2-methoxybenzoic acid.

Supplementary Figure 1

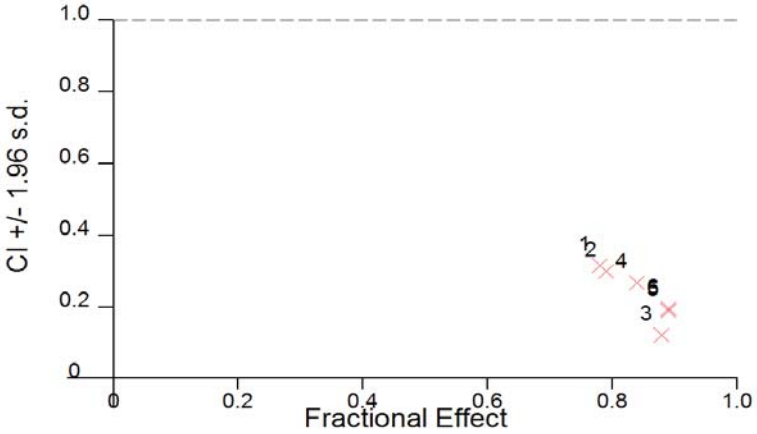


Supplementary Figure 2

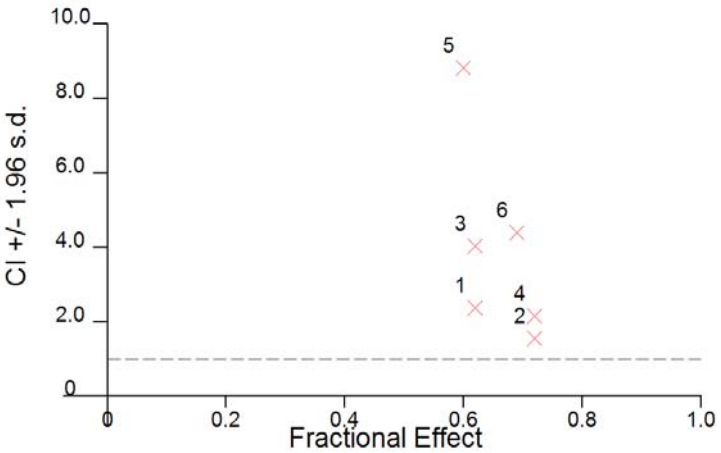


B

Combination of MLN8237 and Dexamethasone



Combination of MLN8237 and Doxorubucin



C

Combination of MLN8237 and Velcade