PYK2/FAK inhibitors reverse hypoxia-induced drug resistance in multiple myeloma

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Supplementary Figure 1 Hypoxia induces pPYK2 expression in H929 cells. Expression of intracellular pPYK2 in H929 cell line untreated or treated with 100 µM CoCl2 in normoxia for 24 hours demonstrated as a fold change of expression (relative to untreated) (Ai) and histogram (Aii) using flow cytometry.
**Supplementary Figure 2**

**Ai**

**Aii**

Supplementary Figure 2. VS-4718 and VS-6063 combined with bortezomib (BTZ) overcome hypoxia-induced drug resistance in MM cells *in vitro*. Absorbance readout (Ab 590nm) of MTT assay performed on MM.1S (Ai) and H929 (Aii) treated with VS-4718 (2.5 µM) or VS-6063 (2.5 µM) and in combination with bortezomib (5nM). Results are shown as average ± standard deviation (SD) performed in penta-replicates and repeated minimum in three separate experiments.
Supplementary Figure 3 VS-4718 and VS-6063 combined with carfilzomib (CFZ) overcome hypoxia-induced drug resistance in MM cells *in vitro*. Survival of MM.1S cells treated with VS-4718 (2.5 µM) or VS-6063 (2.5 µM) and in combination with carfilzomib (5 nM) (Ai); and H929 cells treated with VS-4718 (2.5 µM) or VS-6063 (2.5 µM) and in combination with carfilzomib (2 nM) (Aii), cultured for 24 hours in normoxic and hypoxic conditions based on a survival/cytotoxic MTT assay. Absorbance readout of MTT assay performed on MM.1S (Bi) and H929 (Bii) treated with either VS-4718 and VS-6063 and combined with carfilzomib. Results are shown as average ± standard deviation (SD) performed in penta-replicates and repeated minimum in three separate experiments; the statistical significance was assessed by student t-test (*** p<0.001).