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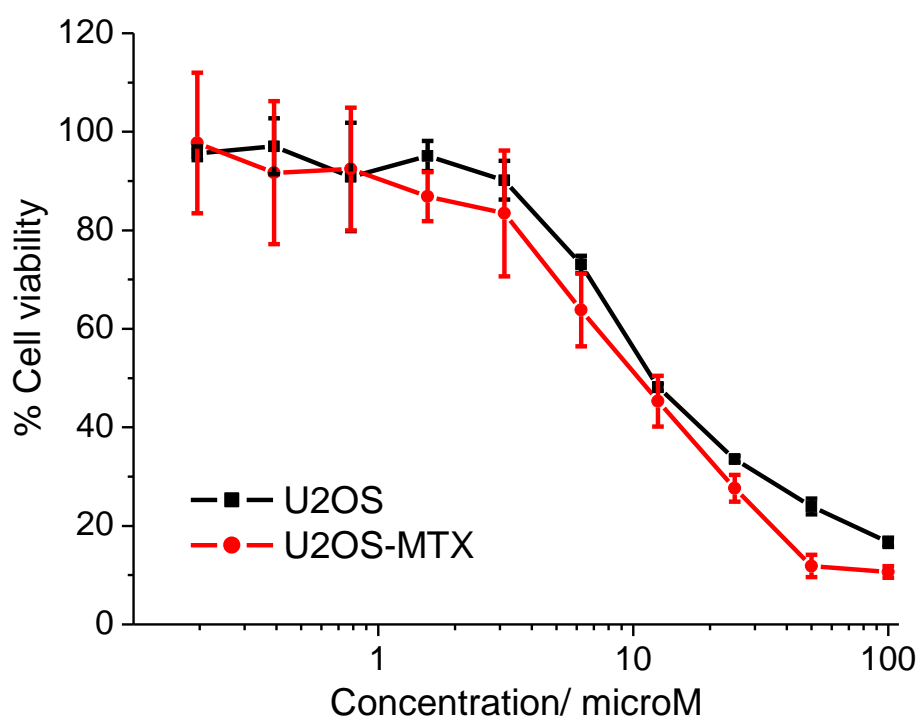


Figure S1. Representative dose-response curves for the treatment of U2OS and U2OS-MTX cells with **1** after 72 h incubation.

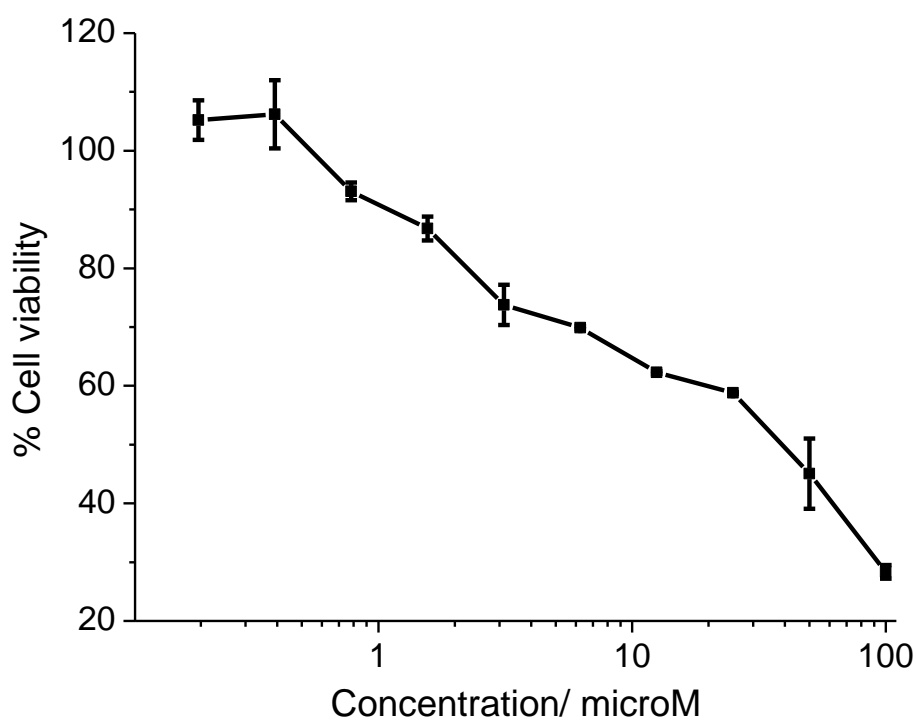


Figure S2. Representative dose-response curve for the treatment of HEK 293T cells with **1** after 72 h incubation.

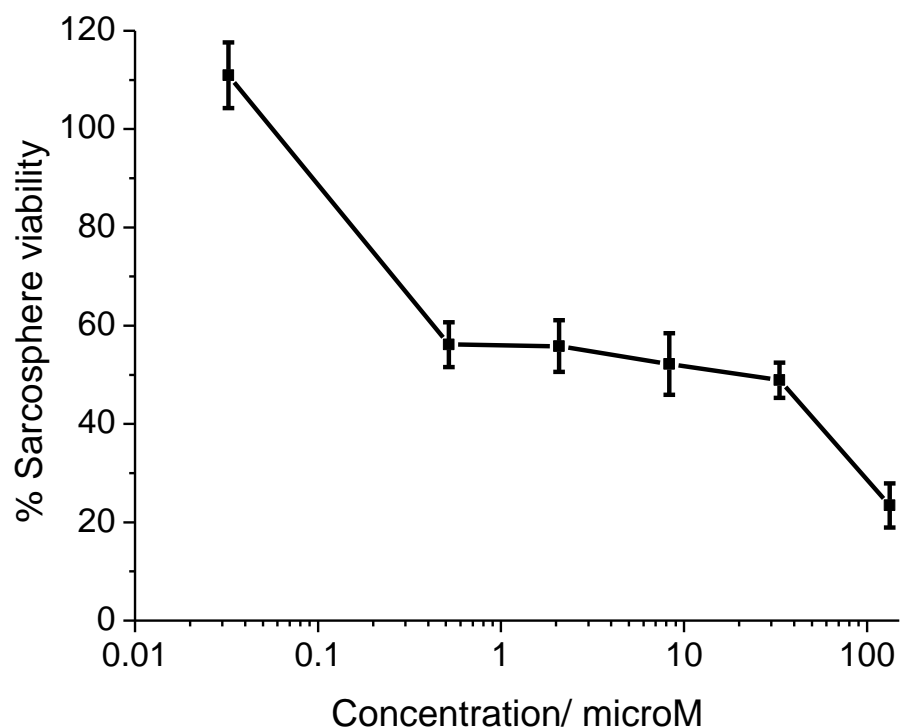


Figure S3. Representative dose-response curve for the treatment of U2OS-MTX sarcospheres with **1** after 10 days incubation.

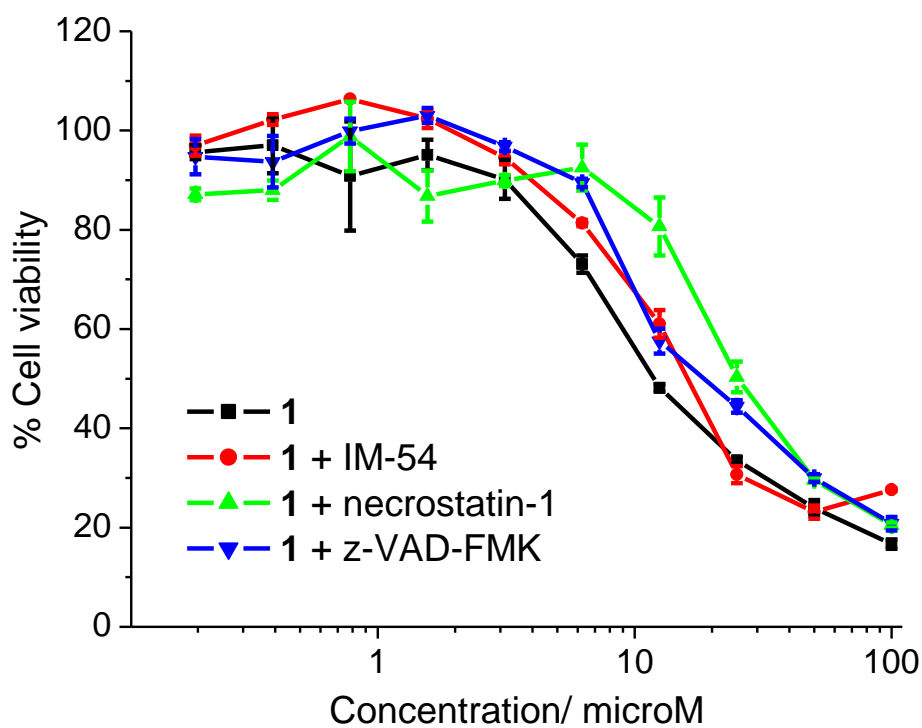


Figure S4. Representative dose-response curves for the treatment of U2OS cells with **1** after 72 h incubation in the absence and presence of IM-54 (10 μ M), necrostatin-1 (20 μ M), or z-VAD-FMK (5 μ M).

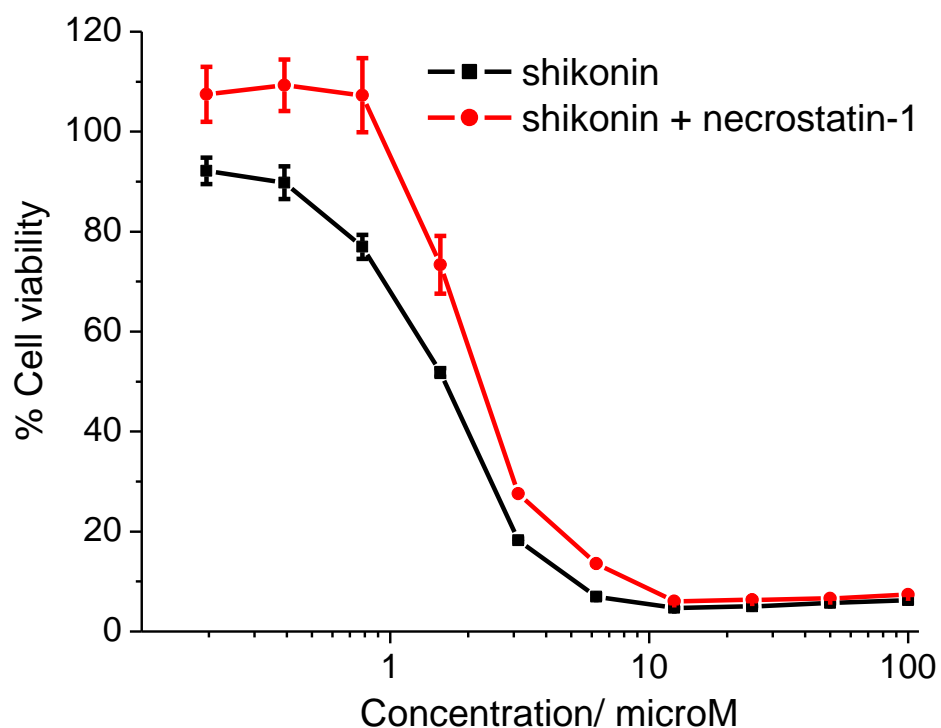


Figure S5. Representative dose-response curves for the treatment of U2OS cells with shikonin after 72 h incubation in the absence and presence of necrostatin-1 (20 μ M).

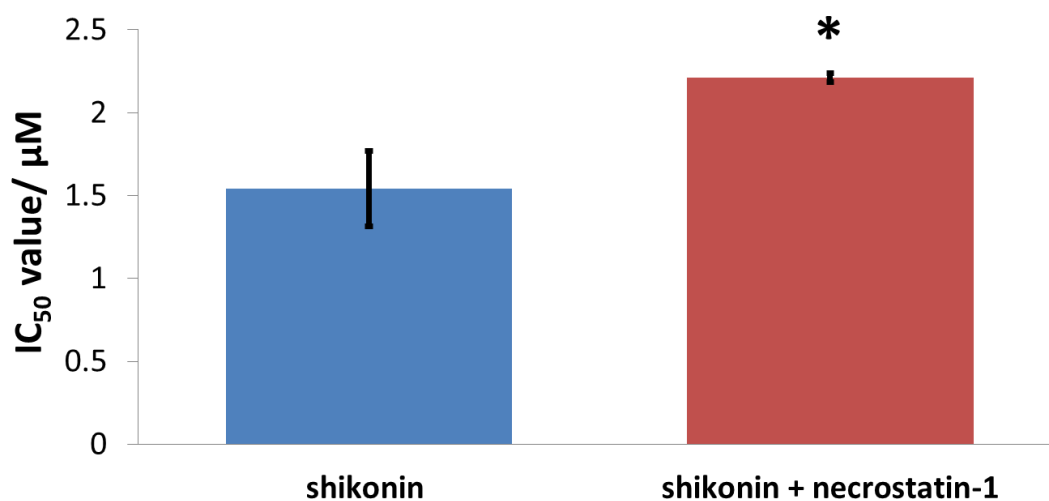


Figure S6. Graphical representation of the IC₅₀ values of shikonin against U2OS cells in the absence and presence of necrostatin-1 (20 μ M). Error bars represent standard deviations and Student t-test, * = $p < 0.05$.

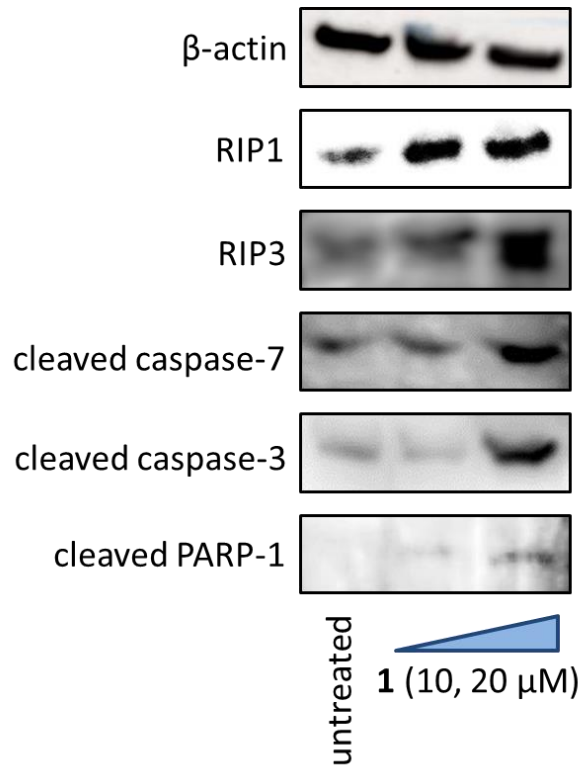


Figure S7. Immunoblotting analysis of proteins related to the necroptosis and apoptosis pathway. Protein expression in U2OS cells following treatment with **1** (10 - 20 μ M) after 72 h incubation. Whole cell lysates were resolved by SDS-PAGE and analysed by immunoblotting against cleaved caspase 3, cleaved caspase 7, cleaved PARP-1, RIP1, RIP3, and β -actin (loading control).

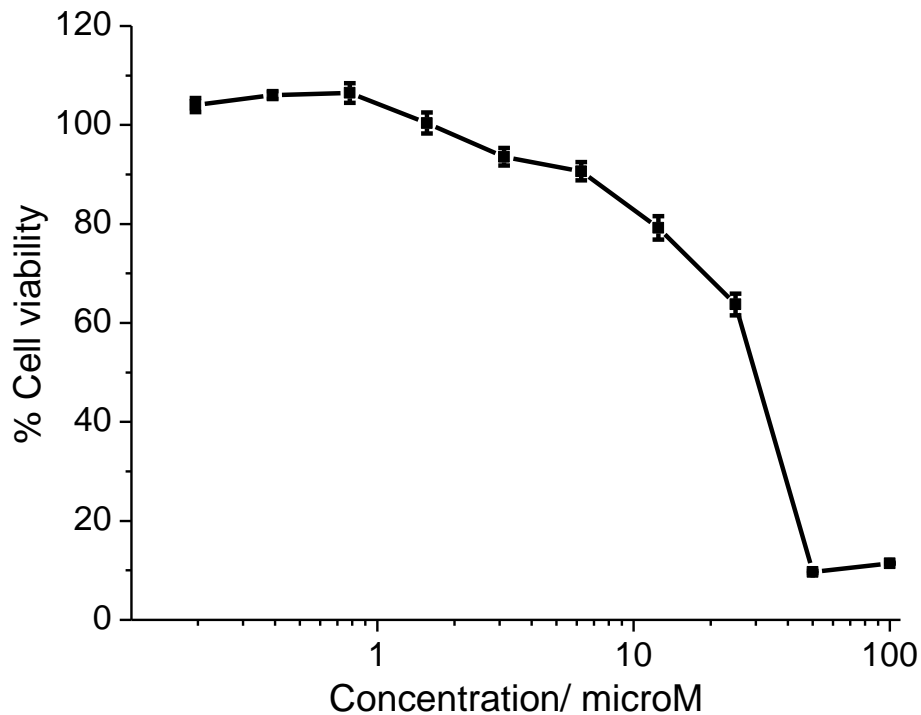


Figure S8. Representative dose-response curve for the treatment of U2OS cells with cisplatin after 72 h incubation in the presence of z-VAD-FMK (5 μ M).

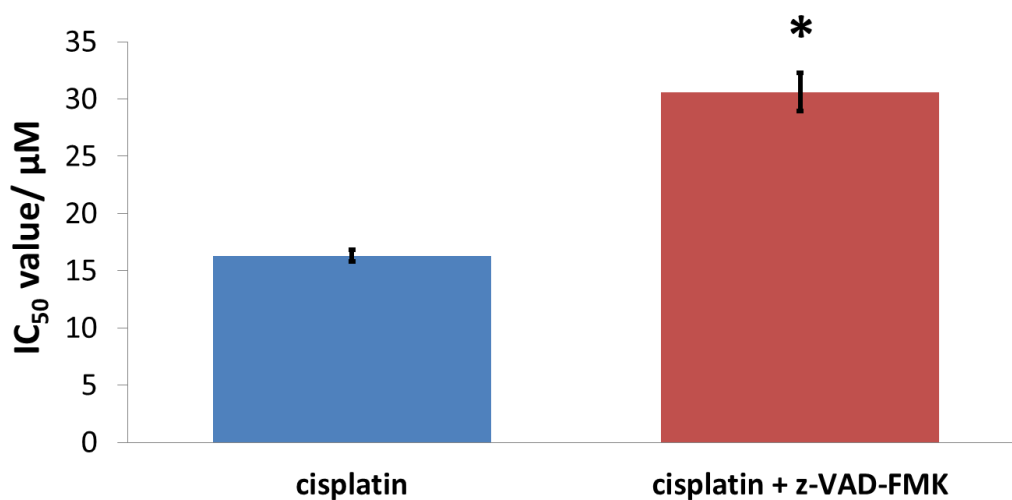


Figure S9. Graphical representation of the IC₅₀ values of cisplatin against U2OS cells in the absence and presence of z-VAD-FMK (5 μM). Error bars represent standard deviations and Student t-test, * = $p < 0.05$.

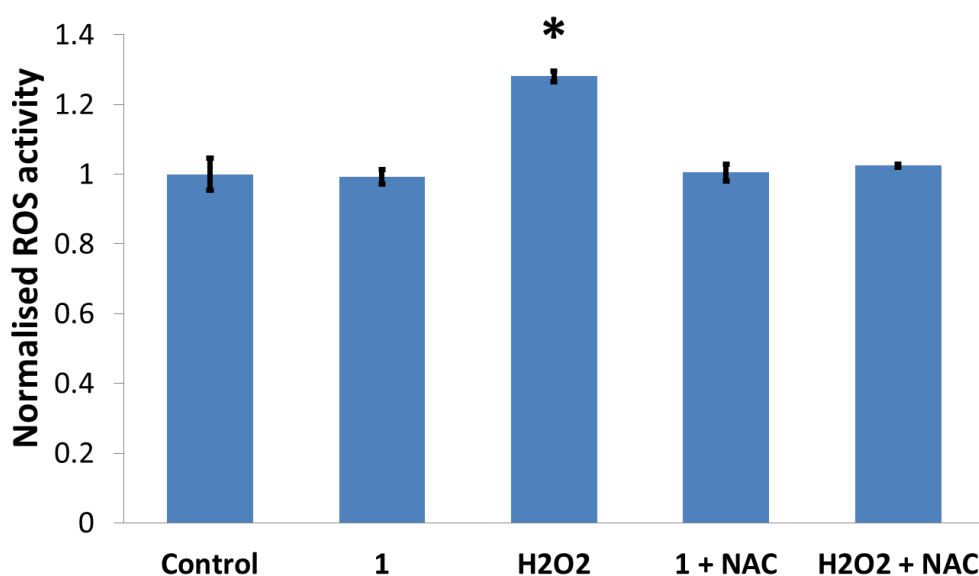


Figure S10. Normalised ROS activity in untreated U2OS cells (control) and U2OS cells treated with **1** (20 μM for 48 h), H₂O₂ (6 μM for 48 h); co-treated with **1** (20 μM for 48 h) and *N*-acetylcysteine (1.5 mM for 48 h), and H₂O₂ (6 μM for 48 h) and *N*-acetylcysteine (1.5 mM for 48 h). Error bars represent standard deviations and Student t test, * = $p < 0.05$.

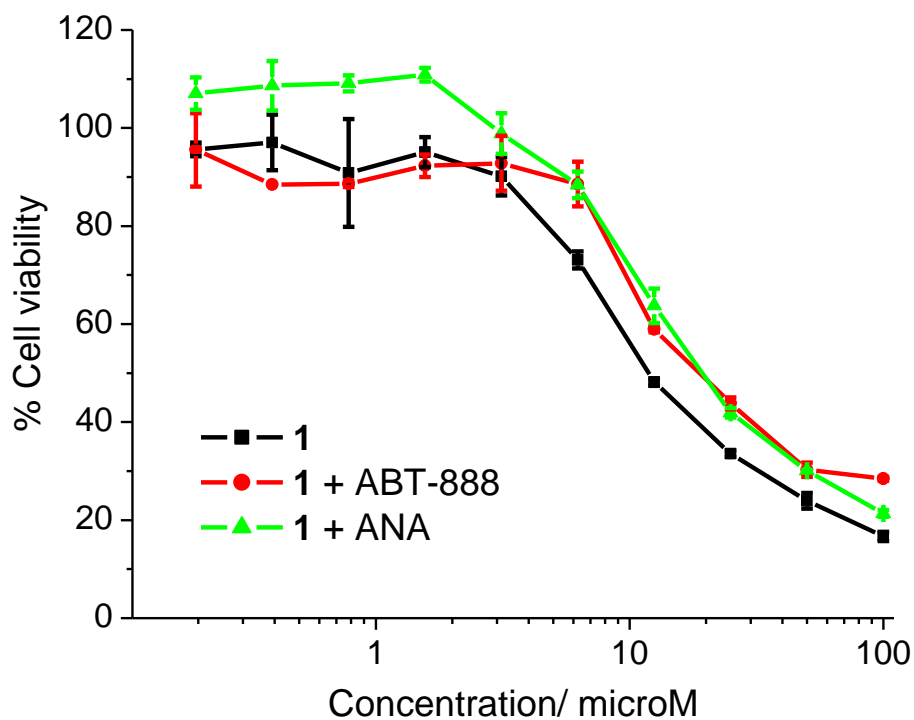


Figure S11. Representative dose-response curves for the treatment of U2OS cells with **1** after 72 h incubation in the absence and presence of veliparib (ABT-888, 10 μ M) or 4-amino-1,8-naphthalimide (ANA, 10 μ M).

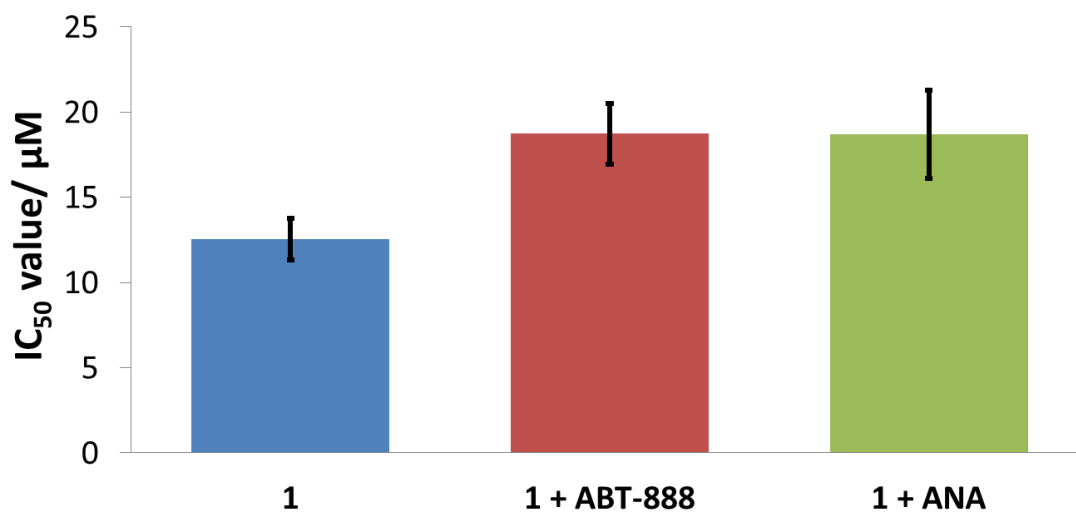


Figure S12. Graphical representation of the IC_{50} values of **1** against U2OS cells in the absence and presence of veliparib (ABT-888, 10 μ M) or 4-amino-1,8-naphthalimide (ANA, 10 μ M).

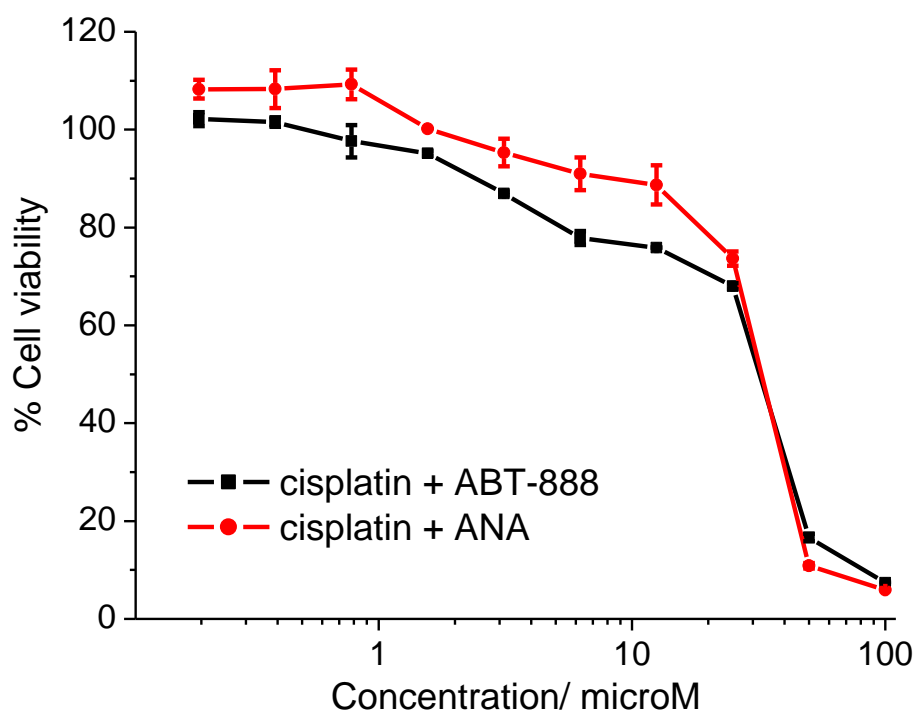


Figure S13. Representative dose-response curves for the treatment of U2OS cells with cisplatin after 72 h incubation in the presence of veliparib (ABT-888, 10 μ M) or 4-amino-1,8-naphthalimide (ANA, 10 μ M).

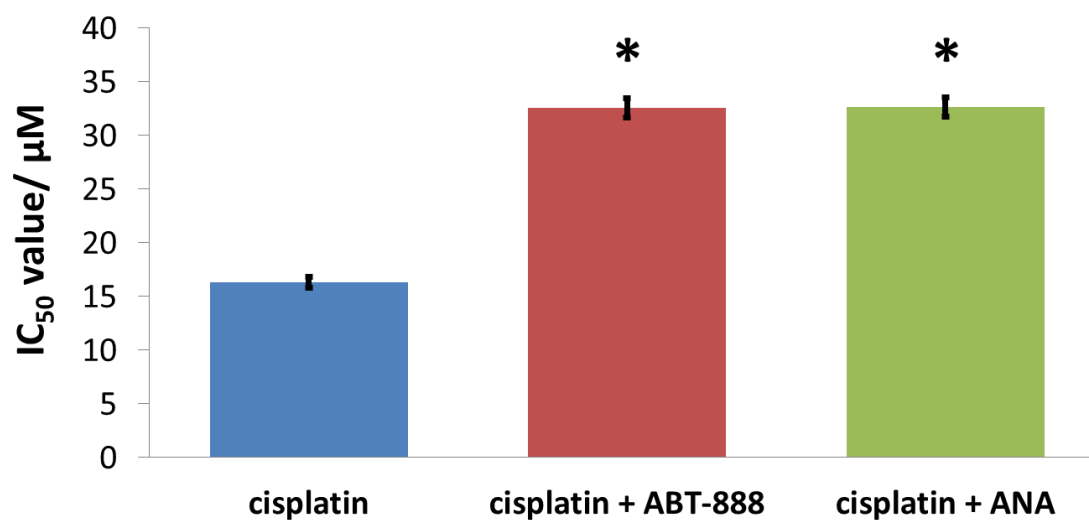


Figure S14. Graphical representation of the IC₅₀ values of cisplatin against U2OS cells in the absence and presence of veliparib (ABT-888, 10 μ M) or 4-amino-1,8-naphthalimide (ANA, 10 μ M). Error bars represent standard deviations and Student t-test, * = $p < 0.05$.