

577 **Supplementary table 1. List of compound used in drug screening.**

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579 **Supplementary table 2. IC₅₀ values to test the synergism between hits and**
580 **mTOR inhibitors.**

581 Note: MPNST cells were treated with indicated drug in combination with mTOR
582 inhibitors (at 25% of IC₅₀) and cell proliferation was analyzed by alamarBlue
583 assay 72 hours after drug exposure.

584

585 **Supplementary table 2. Bortezomib decreased mTOR inhibitors IC₅₀ values.**

586 Note: MPNST cells were treated with nine different concentrations of mTOR
587 inhibitors in combination with bortezomib (at 25% of IC₅₀) and cell proliferation
588 was analyzed by alamarBlue assay 72 hours after drug exposure.

589

590 **Supplementary table 3. Overall results of drug combination analysis.**

591 Note: Combination index (CI) values and fraction of cells affected (FA) by drug
592 treatment were calculated using the Chou-Talalay method. MPNST cells were
593 treated with the indicated drug combination and cell proliferation was performed
594 72 hours after drug exposure. CI<1 indicates synergism, CI=1 indicates additive
595 effect, and antagonism CI>1 indicates antagonism. Rapa: rapamycin; Eve:
596 everolimus; Borte: bortezomib.

597

598 **Supplementary figure 1. Bortezomib inhibits proteasome activity in MPNST**
599 **cells.** MPNST cells were treated with indicated concentrations of bortezomib and

600 5 hours after treatment chymotrypsin-like activity of the 20S proteasome was
601 measured by a fluorescence cell-based assay.

602

603 **Supplementary figure 2. Radiation inhibits proliferation in MPNST cells. (A)**

604 Human MPNST cells were subjected to different doses of radiation Gammacell
605 1000 (2.24 Gy/min; radiation source: Caesium¹³⁷), seeded (1000 cells/well) in
606 quadruplicate in 96-well plate. Cell proliferation was assessed by alamarBlue
607 assay overtime.

608

609 **Supplementary figure 3. Anti-proliferative effects of mTOR inhibitors and**

610 **radiation in MPNST cell lines.** Human MPNST cells were subjected to radiation
611 (12 Gy) (Gammacell 1000; 2.24 Gy/min; radiation source: Caesium¹³⁷), seeded
612 (1000 cells/well) in quadruplicate in 96-well plate, and treated with rapamycin
613 (25% of IC₅₀) or Everolimus (25% of IC₅₀) and cell growth was assessed by
614 alamarBlue assay. * $p < 0.05$ vs control; ** $p < 0.01$ vs control; *** $p < 0.001$ vs
615 control; # $p < 0.05$ vs 12 Gy; ## $p < 0.01$ vs 12 Gy; ### $p < 0.001$ vs 12 Gy.

616

617 **Supplementary figure 4. Anti-proliferative effects of mTOR gene silencing**

618 **plus radiation in MPNST cell lines. (A)** Human MPNST cells were transfected
619 with siGFP, simTOR#13, or simTOR#19 (10 nM), subjected to radiation (12 Gy)
620 (Gammacell 1000; 2.24 Gy/min; radiation source: Caesium¹³⁷), seeded (1000
621 cells/well) in quadruplicate in 96-well plate, and cell growth was assessed by
622 alamarBlue assay. ** $p < 0.01$ vs Control; *** $p < 0.001$ vs Control; ## $p < 0.01$ vs 12

623 Gy; ### $p < 0.001$ vs 12 Gy. **(B)** Total protein lysates (50 μ g) from MPNST cells
624 were separated by SDS-PAGE and analyzed by Western blotting for mTOR and
625 GAPDH 96 hours after MPNST cells transfection.

626

627 **Supplementary figure 5. The effect of drug combination in mice body mass.**

628 Female nude mice (5 to 6 weeks old) were randomized in four groups and
629 Everolimus (1.5 mg/kg, orally 5 days a week) and bortezomib (0.65; 0.95, and
630 1.3 mg/m², intraperitoneal, 2 days a week) were administered. Body mass was
631 measured three times per week.