Figure S1. TP53 and MDM2 dependency and IHC quantification in samples from patients with ATRT. (A) TP53 and MDM2 dependency was analyzed using the Dependency Map portal. TP53 was shown to be a key dependency in BT16 ATRT. The DepMap score for CRISPR demonstrates high dependency of ATRT from MDM2. (B) Quantification of TP53 and MDM2 expression from IHC in samples from patients with ATRT and different subgroups. IHC, immunohistochemistry; ATRT, atypical teratoid rhabdoid tumor.



Figure S2. Original uncropped western blots showing MDM2 and TP52 protein expression in BT16 and CHB-ATRT1 cell lines following transfection with TP53 or MDM2 shRNAs and with overexpression of TP53. ATRT, atypical teratoid rhabdoid tumor; sh, short hairpin; Ov, overexpression.



Figure S3. Quantification from western blot analysis to analyze MDM2 and TP52 protein expression in BT16 and CHB-ATRT1 cell lines following transfection with TP53 or MDM2 shRNAs and with overexpression of TP53. ATRT, atypical teratoid rhab-doid tumor; sh, short hairpin; Ov, overexpression.











Figure S4. MDM2 chemical inhibition suppresses ATRT growth *in vitro*. Nutlin3 inhibits colony formation ability in the (A) BT16 and (B) MAF737 cell lines. Idasanutlin inhibits colony formation ability in the (C) BT16 and (D) MAF737 ATRT cell lines. ATRT, atypical teratoid rhabdoid tumor.



Figure S5. IVIS signal and the weight of the mice during treatment with idasanutlin. (A) IVIS signal for each mouse during treatment. (B) Weight of the mice during treatment with idasanutlin, showing that idasanutlin was not toxic and did not lead to any weight lost as compared with that in the vehicle control group.



Figure S6. Original uncropped western blots showing the expression level of different pro-apoptotic proteins in the BT16 ATRT cells following treatment with idasanutlin for $24 h (IC_{50}, 30 nM)$ in combination with radiation (2, 4 and 6 Gy). ATRT, atypical teratoid rhabdoid tumor.



Figure S7. Quantification from western blot analysis to analyze the expression level of different pro-apoptotic proteins in the BT16 ATRT cells following treatment with idasanutlin for 24 h (IC₅₀, 30 nM) in combination with radiation (2, 4 and 6 Gy). ATRT, atypical teratoid rhabdoid tumor.

