

Supplementary Table S5: Antitumor Activity of MRTX0902 and Avutometinib in Human KRAS-MAPK Pathway Mutant Tumor Cell line-derived Xenograft Models

Model	Tumor Type	MRTX0902 Treatment	Avutometinib Treatment	% Growth Inhibition ¹ / Regression ² (Day)	Response
LN229	GBM	50 mg/kg BID	n/a	34% (32)	TGI
		n/a	0.3 mg/kg BID Q2D	80% (32) ³	TGI
		50 mg/kg BID	0.3 mg/kg BID Q2D	99% (32) ^{3,4}	TGI
NCI-H1435	NSCLC	50 mg/kg BID	n/a	73% (27) ³	TGI
		n/a	0.3 mg/kg BID Q2D	80% (27) ³	TGI
		50 mg/kg BID	0.3 mg/kg BID Q2D	99% (27) ^{3,4}	TGI

Abbreviations: BID = twice daily dosing; QD = once daily; NA = not applicable; NSCLC = non-small cell lung cancer; GBM = glioblastoma; TGI = tumor growth inhibition

MRTX0902 was administered daily via oral gavage at 50 mg/kg BID (to mice bearing established tumor cell-derived xenografts (n = 5) with average starting volumes of ~150 mm³. MRTX0902 was formulated in a suspension of 0.5% methylcellulose (4000 cps) + 0.2% Tween 80 in water.

Avutometinib was administered BID Q2D via oral gavage at 0.3 mg/kg to mice bearing established tumor cell-derived xenografts (n = 5) with average starting volumes of ~150 mm³. Avutometinib was formulated as a solution in 5% DMSO/10% HPCD in H₂O.

¹ Tumor growth inhibition (TGI) was calculated using the following equation: $100\% \times ((\text{Final vehicle tumor volume}) - (\text{Final treated tumor volume})) / ((\text{Final vehicle tumor volume}) - (\text{Initial Drug Treated Tumor Volume}))$. **Note:** TGI values are positive.

² Tumor regression was calculated when the average tumor volume of final treated tumors was less than initial treated tumor volume using the following equation: $(-100\%) \times (1 - ((\text{Final treated tumor volume}) / (\text{Initial treated tumor volume})))$.

³ indicates drug treated-tumor volumes are significantly different compared to vehicle-treated cohorts on the study day at which % TGI or Regression was calculated by the two-tailed Student's *t* test (*p*-value <0.05).

⁴ indicates drug treated-tumor volumes are significantly different compared to the avutometinib (monotherapy)-treated cohorts on the study day at which % TGI or Regression was calculated by the two-tailed Student's *t* test (*p*-value <0.05).