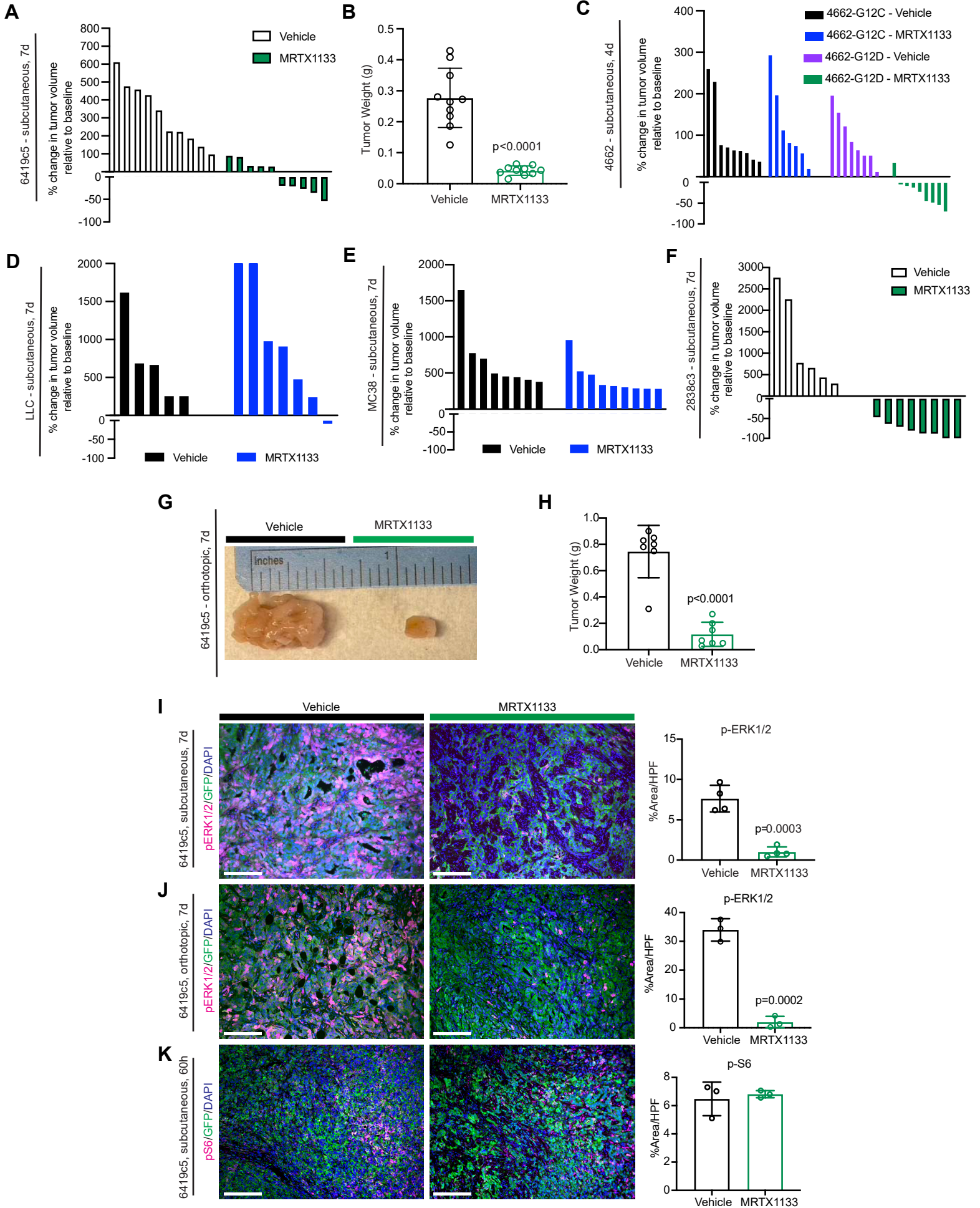


**Figure S2**



**Supplementary Figure 2. MRTX1133 is selective for KRAS<sup>G12D</sup> in immunocompetent implantation tumor models.**

**(A)** Waterfall plot of vehicle and MRTX1133 treated tumors (6419c5, subcutaneous) showing change in tumor volume after 7d of treatment compared to baseline at day 0. Each bar represents a single tumor. n=10 mice/group.

**(B)** Final tumor weights (g) from **(A)** after 7d of treatment. n=10/group. p-values were determined using Student's unpaired t-test. Error bars indicate SD.

**(C)** Waterfall plot of 4662<sup>G12C</sup> and 4662<sup>G12D</sup> subcutaneous tumors treated with vehicle or MRTX1133. Plot shows change in tumor volume after 4d of treatment. Each bar represents a single tumor. n=7-9/group.

**(D)** Waterfall plot of vehicle and MRTX1133 treated tumors (LLC, subcutaneous) showing change in tumor volume after 7d of treatment. Each bar represents a single tumor. n=5-7/group.

**(E)** Waterfall plot of vehicle and MRTX1133 treated tumors (MC38, subcutaneous) showing change in tumor volume after 7d of treatment. Each bar represents a single tumor. n=5-7/group.

**(F)** Waterfall plot of vehicle and MRTX1133 treated tumors (2838c3, subcutaneous) showing change in tumor volume after 7d of treatment. Each bar represents a single tumor. n=6-8/group.

**(G)** Representative gross images of orthotopic tumors 7d after treatment with vehicle or MRTX1133.

**(H)** Final tumor weights (g) from **(G)** after 7d of treatment. n=10/group. p-values were determined using Student's unpaired t-test. Error bars indicate SD.

**(I)** Left: Representative co-immunofluorescence images of p-ERK1/2, GFP, and DAPI in vehicle and MRTX1133 treated tumors (6419c5, subcutaneous, 7d). Scale bars, 100  $\mu$ m. Objective, 20x. Right: Quantitation of p-ERK1/2 expression as percent area per high power field (HPF) in vehicle (n= 4) and MRTX1133 treated tumors (n=4). At least 3 fields of view were averaged per tumor. p-value was determined by Student's unpaired t-test. Error bars indicate SD.

**(J)** Left: Representative co-immunofluorescence images of p-ERK1/2, GFP and DAPI in vehicle and MRTX1133 treated tumors (6419c5, orthotopic, 7d). Scale bars, 100  $\mu$ m. Objective, 20x. Right: Quantitation of p-ERK1/2 expression as percent area per high power field (HPF) in vehicle (n= 4) and MRTX1133 treated tumors (n=4). At least 3 fields of view were averaged per tumor. p-value was determined by Student's unpaired t-test. Error bars indicate SD.

**(K)** Left: Representative co-immunofluorescence images of p-S6, GFP and DAPI in vehicle and MRTX1133 treated tumors (6419c5, subcutaneous, 60h). Scale bars, 100  $\mu$ m. Objective, 20x. Right: Quantitation of p-S6 expression as percent area per high power field (HPF) in vehicle (n= 3) and MRTX1133 treated tumors (n=3). At least 3 fields of view were averaged per tumor. p-value was determined by Student's unpaired t-test. Error bars indicate SD.