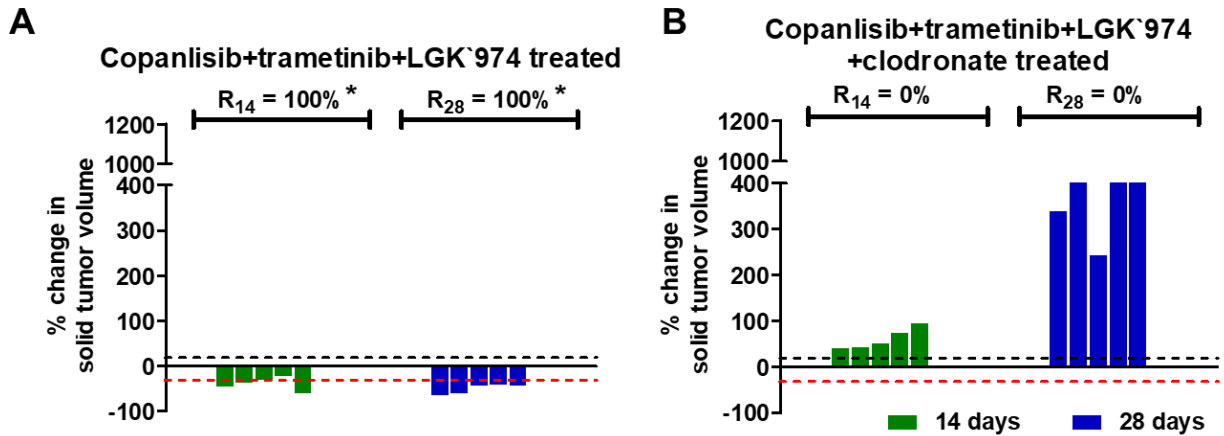


## Supplementary Figure S8



**Supplementary Figure S8. PI3Ki + MEKi + PORCNI combination therapy elicits a 100% response rate in PTEN/p53-deficient GEMMs via TAM activation.** (A-B) Pb-Cre;PTEN<sup>fl/fl</sup>Trp53<sup>fl/fl</sup> mice with established tumors were treated with copanlisib (14 mg/kg, *iv*, every alternate day) + trametinib (3 mg/kg, *po*, every day) + LGK`974 (3 mg/kg, *po*, every day) -/+ clodronate (200  $\mu$ g/mouse, *ip*, every week). Tumor volumes were non-invasively monitored by MRI and % response rate at days 14 ( $R_{14}$ ) and 28 ( $R_{28}$ ) were determined as described in Methods. The % change in solid tumor volume are represented by waterfall plot for copanlisib + trametinib + LGK`974 (A) and copanlisib + trametinib + LGK`974 + clodronate (B) treated groups. n=5 mice per group (experimental male mice with the correct genotype were obtained following screening of 28 littermates derived from 4 breeding pairs and randomized until the indicated number of mice were achieved in each group). Significances/p-values were calculated by Chi-square test and indicated as follows, \* $p < 0.05$ , relative to untreated.