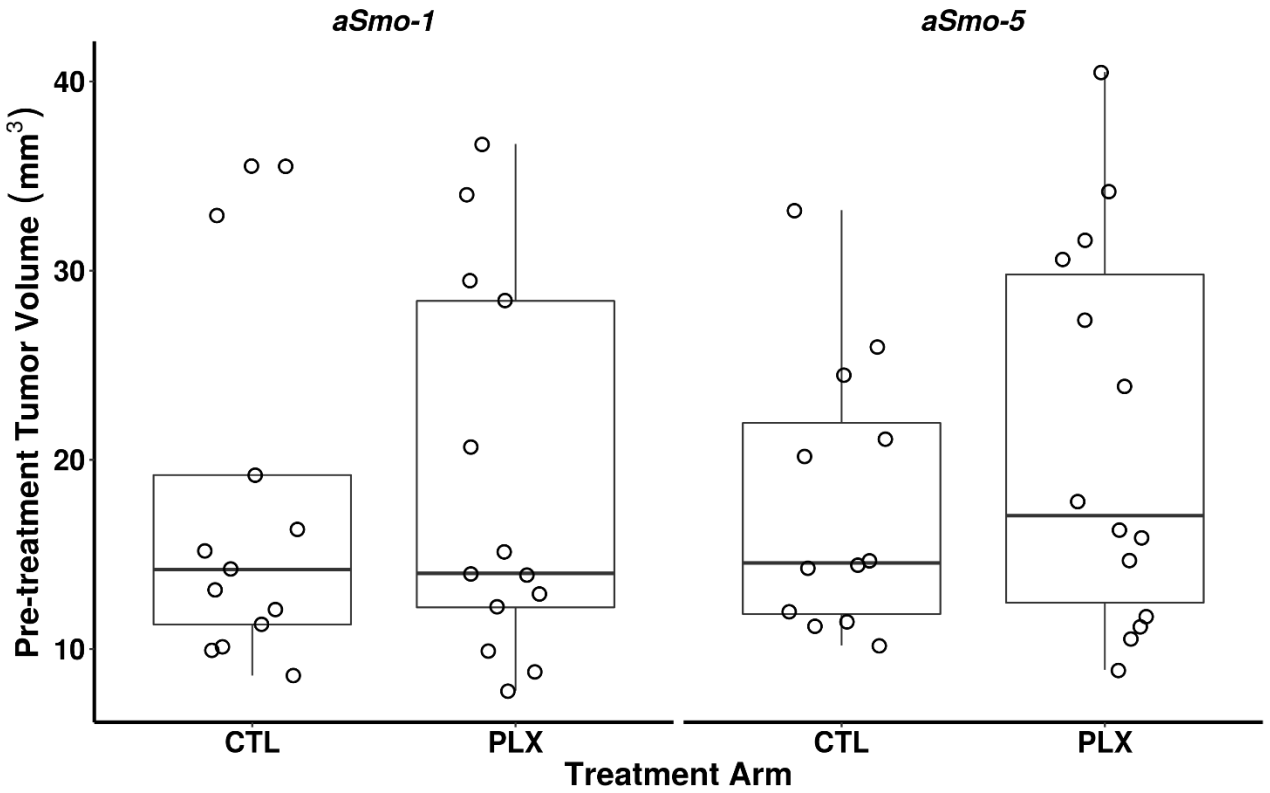
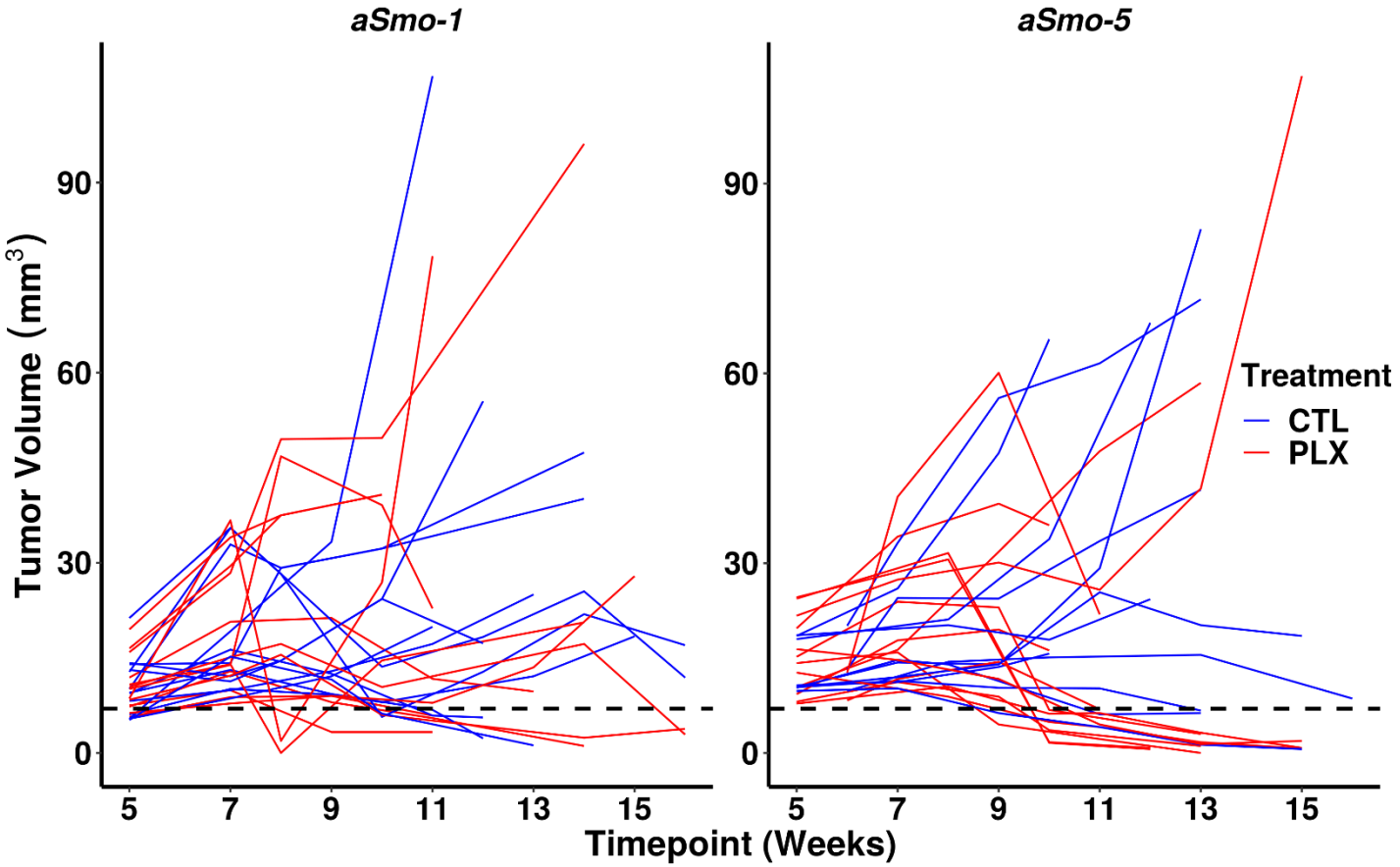
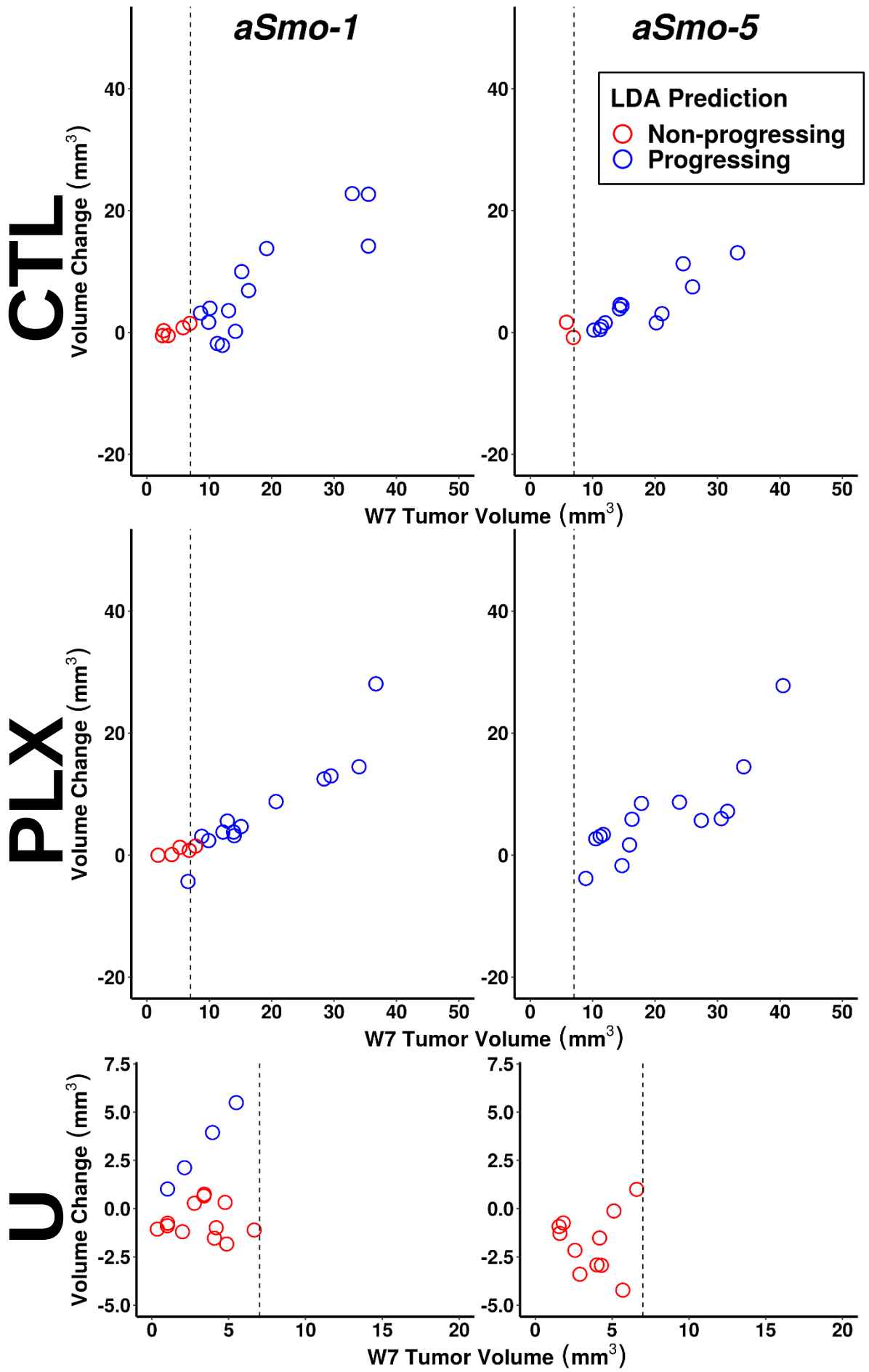


Supporting Information Figure S1.
After preliminary classification, for outcome prediction before entry into the PLX5622 preclinical trial, tumors were randomly assigned into the treatment (PLX) or control (CTL) arms of the study. Tukey's HSD test of the W7 tumor volumes showed no significant differences between treatment arms nor across tumor models.



Supporting Information Figure S2.

Raw progression *aSmo* tumor progression data from the PLX5622 preclinical trial. From these data, it was apparent there was substantial heterogeneity in response to therapy. In the *aSmo-1* model, there are no apparent differences in progression between PLX (red) or CTL (blue) treated tumors. However, there appears to be a trend towards tumor volume reduction after treatment with PLX in the *aSmo-5* model.



Supporting Information Figure S3.

In an effort to reduce the number of false 'Progressing' tumors entered into the drug trial, the pre-treatment time point data were re-analyzed using the trained LDA classifier. The early time point data from tumors not meeting the empirical classification criteria (dashed line; which included sub-threshold tumors in animals with a second tumor that met the volume threshold criteria) were added to these retrospective analyses (10 *aSmo*-1 and 2 *aSmo-5* tumors). It is apparent that LDA reclassification produced results very similar to those of the empirical classifier. After LDA reclassification, 5 *aSmo-1* and 2 *aSmo-5* MBs were removed from the CTL arm and 5 *aSmo*-1 tumors were removed from the PLX arm of the study. The statistically significant, positive effect of pre-treatment tumor volume on post-treatment tumor volume persisted after LDA reclassification (effect size = 1.43, p = 0.002). Also, the positive, statistically insignificant effects of CTL chow on post-treatment tumor volume remained in both the *aSmo-1* (effect size = 2.5, p = 0.826) and *aSmo-5* MBs (effect size = 8.33, p = 0.475). After LDA reclassification, a negative effect of PLX on post-treatment *aSmo-1* tumor volume was observed (effect size = -1.16, p = .921), and a similar effect was observed in the *aSmo-5* MBs (effect size = -11.88, p = 0.338). The effect of treatment nominally increased after LDA when compared to the results after empirical classification (Cohen's d = 0.31), although the effect remained small. Also, the TMX dose-specific effects were relatively unchanged for both the *aSmo-1* (Cohen's d = 0.09) and *aSmo-5* (Cohen's d = 0.52) MBs. Retrospective LDA of early time point data from tumors excluded from the preclinical trial (U) suggests that 4 *aSmo-1* tumors were in fact 'Progressing'. This process did not change the classification for *aSmo-5* tumors.