Fig. 6. (A and *B*) Kit immunostaining of placebo and 7-day imatinib treated mice (40x magnification).

Fig. 7. Imatinib treatment decreases cell proliferation and increases apoptosis in tumor lesions of imatinib-treated $Kit^{V558\Delta/+}$ mice. (*A*-*D*) Ki67 immunostaining of tumor sections of placebo and imatinib-treated $Kit^{V558\Delta/+}$ mice (20x magnification). (*E*-*H*) Cleaved caspase 3 immunostaining of tumor sections of placebo and imatinib-treated mice (20x magnification). Quantification of proliferating and apoptotic cells are presented in Fig 2.

Fig. 8. Validation of microarray data by semiquantitative PCR analysis with RNA extracted from four placebo and four imatinib-treated tumors assaying indicated genes. In the microarray analysis, the maximum fold changes for Ccnd3 (cyclin D3), ifi1 (interferon-inducible protein 1) and Fkbp1a (FK506-binding protein 1a) were -2.14, -2.94, and -1.5, respectively, whereas for Cdkn2C ($p18^{ink4}$) and Tgfb1/4 (transforming growth factor beta 1-induced transcript 4), the maximum fold changes were +1.84 and +3.99, respectively.

Fig. 9. RAD001 treatment induces cell cycle arrest in GIST lesions of $Kit^{V558\Delta/+}$ mice. H&E (*A*) and Ki67 (*B*) staining of tumor sections of RAD001 (10 mg/kg) treated mice (7 days). Magnification 20x. (*C*) Quantification of proliferating cells (percent of control) in GIST lesions of placebo, RAD001 (5 mg/kg) treated for 7 days and 4 weeks and RAD001 (10 mg/kg) for 7 days. Groups were judged to differ significantly at $P < 0.05$ (Materials and Methods).

Fig. 10. Imatinib and RAD001 do not synergize in the treatment of GIST in $Kit^{V558\Delta/+}$ mice. H&E-stained tumor sections of mice treated for 7 days with imatinib (45 mg/kg) plus RAD001 (10 mg/kg). Eight mice were treated with varied responses from mild (*A*) to moderate (*B*).

Fig. 11. Imatinib treatment for 7 days reduces ribosomal S6 protein phosphorylation. P-S6 protein immunostaining of tumor sections of placebo (*A*) and imatinib-treated $Kit^{V558\Delta/+}$ mice (*B* and *C*) for 7 days (20x magnification). The reduction in S6 protein phosphorylation upon imatinib treatment seems to be independent of the degree of the histological response (*B*, minimal response: *C*, mild response; moderate response not shown) and indicates a consistent down-regulation of the translational response in GIST from 7-day imatinib-treated $Kit^{V558\Delta/+}$ mice (see Table 1).