Supplementary Figure Legends

Figure S1. Integrated display of FGFR kinase alterations in the 178 lung squamous cell carcinomas reported by the TCGA Network. Tumor samples are represented by columns and the presence of FGFR1 amplification or FGFR2 or FGFR3 mutation is depicted by the shading. For each FGFR isoform relative expression is displayed. Transcript isoform usage is displayed for FGFR2 and FGFR3, with higher values (pink shading) favoring expression of the IIIB isoforms. Expression subtypes as previously described (27) are shown as the bottom track.

Figure S2. Tumors were dissected from xenograft models as in Figure 2 for visual inspection comparing treatment with vehicle or drug. Top panel FGFR2-K660N tumors; bottom panel, FGFR2-WT.

Figures S3. Mutations in the extracellular domains of FGFR2 and FGFR3 form covalent dimers in the absence of ligand, but retain sensitivity to ligand stimulation. (A) & (B) NIH-3T3 cells expressing the indicated mutations were serum starved and stimulated with PBS or FGF1 and heparin for 8 hours, or with FGF1 and heparin for 30 minutes, washed, and then stimulated with PBS for 7.5 hours. Unreduced and reduced lysates were probed for the formation of covalently bonded receptor-dimers. Dimers were formed in cells expressing FGFR2 (A) and FGFR3 (B) (30). (C) Cells from (A) & (B) were seeded into Select agar as in Figure 2A in the presence of PBS, heparin alone, or FGF1 and heparin and colonies were counted after three weeks.

Figure S4. Anchorage independent colony formation is abrogated in the presence of anti-FGFR inhibitors. (A) NIH-3T3 cells expressing FGFR2 WT lose FGFR and ERK phosphorylation when exposed to BG398. (B) NIH-3T3 cells expressing transforming mutations were seeded into Select agar as in Figure 2, in the presence of increasing concentrations of dovitinib (left panel) or pazopanib (right panel), and resulting colonies were quantified. (C) & (D) Cells were serum starved and exposed to indicated concentrations of dovitinib (C) or pazopanib (D) for four hours and then ligand stimulated for 30 minutes with FGF1, after which cells were lysed and probed for known downstream phosphorylated signaling molecules via immunoblot.

Figure S5. Ba/F3 cells transformed with FGFR2 and FGFR3 mutations are sensitive to FGFR inhibitors. (A-F) Ba/F3 cells expressing each mutation construct were seeded into 96-well plates in the presence of increasing concentrations of the indicated drugs. After four days, proliferation was measured with Cell Titer Glo. IC\textsubscript{50} values were calculated for each mutation.

Figure S6. FGFR2-P253R is transforming in anchorage independent growth assays and Ba/F3 assays. (A) NIH-3T3 cells stably expressing FGFR2-P253R, FGFR2 wild type, or EGFR insNPG, were seeded into Select agar as in Figure 2A and subsequent colonies were counted. (B) Anchorage independent colony formation driven by
P253R is inhibited in the presence of anti-FGFR inhibitors BGJ398 or AP24534. (C) Ba/F3 cells expressing FGFR2-P253R, EGFR insNPG, or parental cells respond to BGJ398 (left panel) or AP24534 (right panel). Individual IC$_{50}$ values were calculated for each mutation.