**Supplementary Figure 1. A:** Pathways targeted by the Dana-Farber Targeted Therapy Collection. **B.** Clinical development status of agents in the Dana-Farber Targeted Therapy Collection.

**Supplementary Figure 2:** Comparison of compound libraries reported in ROS1 kinase screens

**Supplementary Figure 3: A:** Inhibition of Ba/F3 *CD74-ROS1* proliferation by 1 M drug, expressed as % viability of Ba/F3 cells - Ba/F3 *CD74-ROS1*. Cabozantinib is shown in red, crizotinib in green, and foretinib in blue. Drugs are displayed for the multiple targets that they inhibit. **B:** Inhibition of Ba/F3 transformed with *CD74-NTRK1* proliferation by 1 M drug, expressed as % viability of Ba/F3 cells - Ba/F3 *CD74-NTRK1*. Dovitinib is shown in red, BMS-5369924 in green.

**Supplementary Figure 4:** Chemical structures of lead compounds.

**Supplementary Figure 5:** Inhibition of ROS1 signaling in Ba/F3 cells by PF-06463922 and entrectinib.

**Supplementary Figure 6:** Inhibition of ROS1 signaling in UMG-118 glioblastoma cells that express the FIG-ROS1 fusion protein.

**Supplementary Figure 7:** *RNPC3-ROS1* fusion; the *ROS1* sequence is shown in bold.

**Supplementary File 1: A:** Contents of the Dana-Farber Targeted Therapy Library. **B:** IC50

values for compounds inhibiting ROS1 kinase. **C:** IC50 values for compounds inhibiting NTRK1 kinase.