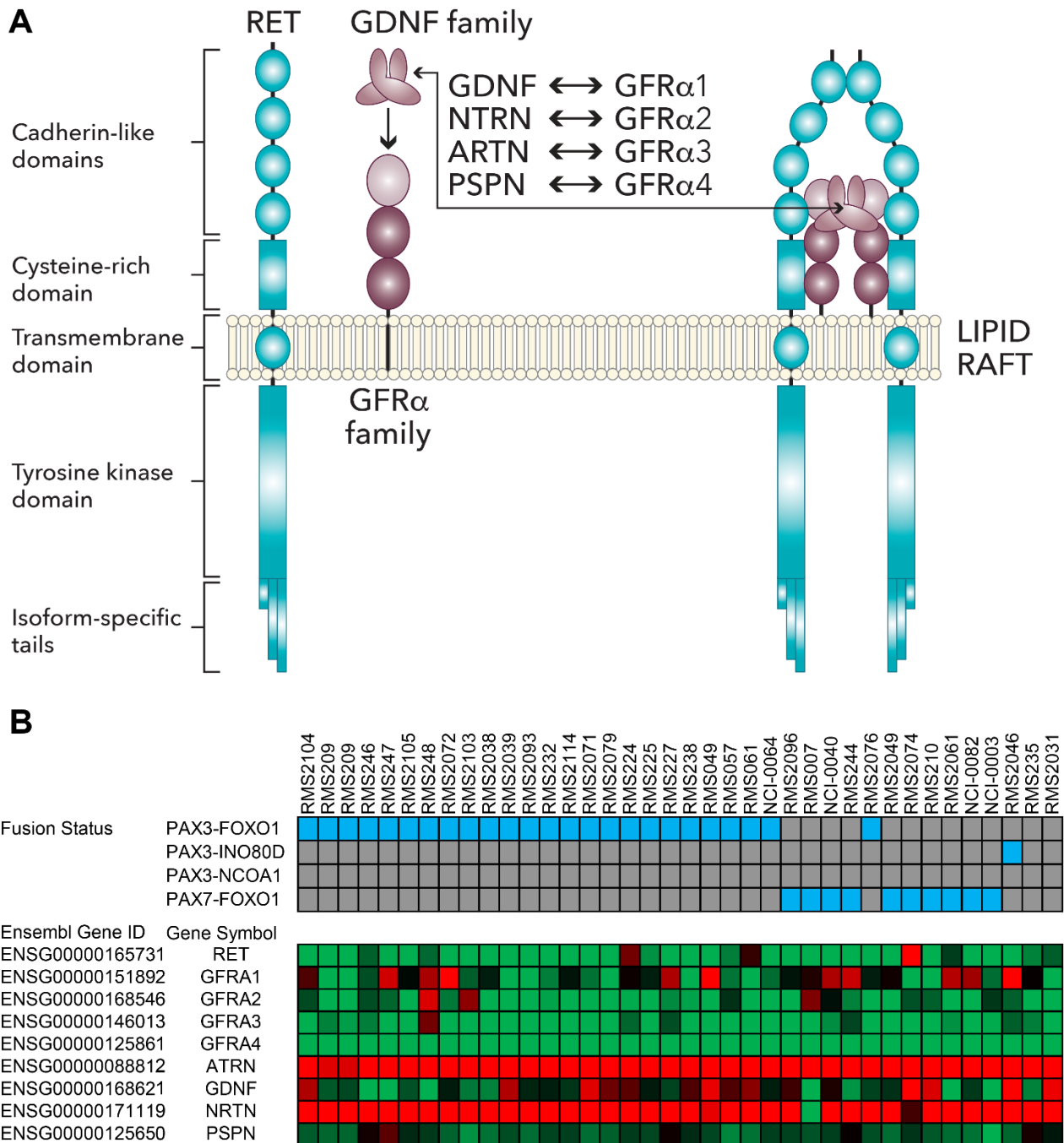**Supplemental Figure 1. Canonical RET signaling and heatmap of RET signaling components in alveolar rhabdomyosarcoma.**

A) Diagram of canonical RET signaling. A member of the glial cell line-derived-neurotrophic factor (GDNF) ligand family (GDNF, NTRN, ARTN, PSPN) binds with the corresponding GFRα family receptor (GFRα1, GFRα2, GFRα3, GFRα4 respectively). All GFRα family receptors are three globular proteins, except the two globular

receptor GFRα4. The GDNF family ligand/GFRα family receptor complex then associate in a two to two ratio with membrane-bound RET to form a complete GFL-RET signaling complex. Figure adapted from a previous publication(Mulligan 2014).

B) Expression of genes involved in canonical RET signaling, including the GDNF factor receptor family and its ligands.

Supplemental Tables

Supplemental Table 1. Table of sequencing data used in endotype analysis.

Supplemental Table 2. Quantified gene expression values used in endotype analysis, and statistical comparison between disease cohorts.

Supplemental Table 3. Drug screen results for U31314 and CF-00001X. Cell viability of the two most endotypically-similar cell models following treatment by 60 monotherapy agents, as well as the U31431 screen supplemented with ARTN. Values shown are IC$_{50}$ values in nM units. Heatmap colors indicate sensitive of agents. The heatmap key is provided to the right of the table.

Supplemental Table 4. Complete set of drug manifolds and combination index values from null plasmid and RET C364F monotherapy and cabozantinib-focused combination therapy experiments.