## Supplementary Methods

### Wound healing assay

H3122 and H3122 CR1 cells were grown to confluence on 6-well plates before scraping to generate linear wounds. Cells were incubated at 37$^{o}$C/5% $CO_2$ during the imaging time intervals, and plates were photographed at 0, 8, 24, 48 and 72 h. To examine the effects on ganetespib treatment on this process, H3122 CR1 cells were cultured in the presence or absence of 12.5 and 25 nM ganetespib and cells photographed at 0, 24 and 48 h.

### Reverse phase protein array analysis

Cellular lysates from H3122 and crizotinib-resistant H3122 CR1 cells were prepared as recommended by the Reverse Phase Protein Analysis Core Facility at MD Anderson Cancer Center (Houston, TX). Serial diluted lysates were arrayed on nitrocellulose-coated FAST slides (Whatman) and probed for a standard list of antibodies as previously described (1,2).

1. Tibes R, Qiu Y, Lu Y, Hennessy B, Andreeff M, Mills GB, et al. Reverse phase protein array: validation of a novel proteomic technology and utility for analysis of primary leukemia specimens and hematopoietic stem cells. Mol Cancer Ther 2006;5:2512-21.

2. Iadevaia S, Lu Y, Morales FC, Mills GB, Ram PT. Identification of optimal drug combinations targeting cellular networks: integrating phospho-proteomics and computational network analysis. Cancer Res 2010;70:6704-14.

## Supplementary Figure Legends

**Figure S1.** Chemical structures of ganetespib and crizotinib.

**Figure S2.** Ganetespib and crizotinib are similarly efficacious in H3122 xenograft tumors implanted in nude mice. **A,** Nude mice bearing H3122 xenografts (n=7/group) were i.v. dosed with 150 mg/kg ganetespib once weekly, or p.o. dosed with 200 mg/kg crizotinib 5X/week over a 5 week cycle as indicated. % T/C values are indicated to the right of each growth curve and the error bars are the SEM.

**Figure S3.** The addition of ganetespib to crizotinib does not result in added toxicity in H3122 xenografts. Mice bearing established H3122 xenografts (n=7/group) were i.v. dosed with 25 mg/kg ganetespib once weekly, 100 mg/kg crizotinib 5x/week p.o., or the combination, as indicated. Body weights were measured 5 times per week. Mean values are plotted against vehicle controls.

**Figure S4.** Crizotinib-resistant H3122 CR1 cells express an EMT phenotype. **A,** Fold-changes in protein expression following ganetespib treatment in H3122 and H3122 CR1 cells using reverse phase protein array analysis. **B,** Whole cell lysates from H3122 and H3122 CR1 cells were immunoblotted with the indicated antibodies. Lysates derived from the NIH-3T3 mouse fibroblast cell line were included as a control for mesenchymal marker expression. **C,** Confluent cultures of H3122 and H3122 CR1 cells were scraped to generate linear wounds. After wounding, cells were maintained in culture medium and images collected at 0, 8, 24, 48 and 72 h to determine the comparative degrees of cellular migration. **D,** Effect of ganetespib on migratory capacity of H3122 CR1 cells. H3122 and H3122 CR1 cells were seeded in the wound healing assay. H3122 CR1 cells were also cultured in the presence of increasing concentrations (12.5 and 25 nM) of ganetespib and images collected at 0, 24 and 48 h.