**Supplementary Figure Legends**

**Supplementary Figure S1. Study schema**. Diagram showing administration schedule for study drug and sampling schedule for pharmacokinetic (PK) and pharmacodynamic (PD) evaluations. Irinotecan was administered on days 1 and 8 of each cycle. Veliparib was administered Day 3 through Day 14 of Cycle 1 and from Day -1 through Day 14 (half dose on Day -1 of Cycle 2 only) on subsequent cycles. Tumor collection for PD assays occurred at two times: 28 hours after chemotherapy alone (Day 2) and 28 hours after the combination of veliparib and irinotecan (Day 9). Single–dose PK sampling of irinotecan was obtained up to 48h starting on Day 1. Single–dose PK sampling of veliparib was obtained up to 28 h starting on Day -1 of cycle 2. The first dose of veliparib administered on Day 8 of Cycle 2 was taken at the time of the start of irinotecan infusion, so PK sampling up to 48 h could be lined up for both drugs in combination.

**Supplementary Figure S2. Dose-exposure relationships.** (A and B) Relationships between veliparib dose and the maximum plasma concentration (Cmax) or area under the plasma concentration time curve from time 0 to the last sampling time point (AUClast) of veliparib. (C and D) Relationships between veliparib dose and the Cmax and AUClast of A-925088.

**Supplementary Figure S3. pNBS1 staining post-combination treatment is limited to tumor cells.**  Liver biopsy images from patient 13 (see Figure 3B) at 40x showing DAPI staining, pNBS1 staining and merged images that reconstruct the dual staining. The DAPI staining demonstrates that normal hepatocytes are present in the pNBS1-negative region.

**Supplementary Figure S4. Assessment of pNBS1 in the exploratory multiplex immunofluorescence assay.**  Multiplex immunofluourescence microscopy with Definiens image analysis was used to assess expression of pNBS (red signal) after irinotecan alone and after combined veliparib/irinotecan. H&E panels and the “a” panels demonstrate cytology and pharmacodynamic response of adjacent sections. The “b” and “c” panels demonstrate representative staining patterns of other fields in the series of sections prepared from each biopsy specimen. (Upper panels) Sections from biopsies from patient 7 (ovarian cancer; best response SD). (Lower panels) Sections from biopsies from patient 2 (breast cancer; best response PD). In contrast to patient 13 (Figure 3), no increases in pNBS1 staining were detected after combination treatment compared to irinotecan alone in patient 7, and only background was detectable in patient 2.