

Supplementary Figure Legends

Supplementary Figure S1. UCSC Genome Browser images of Infinium Human Methylation 450 BeadChip (Illumina) probes that overlap the BCL-2 gene (A), the BCL-2 promoter region (B) and exon 2 (C).

Supplementary Figure S2. BCL-2 methylation vs mRNA expression for all 42 methylation probes that span the BCL-2 gene. Highlighted dot-plots are those for probes that overlap exon 2 i.e. probes 9 to 15. Those probes that overlap the exon 2 CpG island (i.e. probes 11 to 13) are enclosed by the dashed green lines.

Supplementary Figure S3. BCL-2 Methylation in tumour vs normal samples for all 42 methylation probes that span the BCL-2 gene. Highlighted box-plots are those for probes that overlap exon 2 i.e. probes 9 to 15. Those probes that overlap the exon 2 CpG island (i.e. probes 11 to 13) are enclosed by the dashed green lines.

Supplementary Figure S4. BCL-2 Methylation vs disease specific survival for all 42 methylation probes that span the BCL-2 gene. Highlighted term-plots are those for probes that overlap exon 2 i.e. probes 9 to 15. Those probes that overlap the exon 2 CpG island (i.e. probes 11 to 13) are enclosed by the dashed green lines.

Supplementary Figure S5. A: The association between Plk1 expression and relapse-free survival in endocrine treated ER-positive breast cancer patients (n=287) using multiple quantiles (green – high expression, red – low expression). **B:** TCGA RNA-Seq data (n=774) was used to show a positive correlation between ER and BCL-2 expression ($\rho= 0.61$) (top left panel) and a negative correlation between ER and PLK1 ($\rho= -0.35$) (top right panel) and BCL-2 and PLK1 expression ($\rho= -0.43$) (bottom left panel) (Spearman's rank correlation test; red line = line of best fit). The association between BCL-2 methylation and PLK1 expression was assessed using TCGA samples with both RNASeq and methylation data present (n=485) (bottom right panel). The red dashed line represents the 95th percentile of BCL-2 methylation in the normal samples. The dashed blue line represents an arbitrary cut-off for PLK1 expression (i.e. >5).

Supplementary Figure S6. A representation of the effect of BI2536 in endocrine-sensitive and endocrine-resistant breast cancer cells.