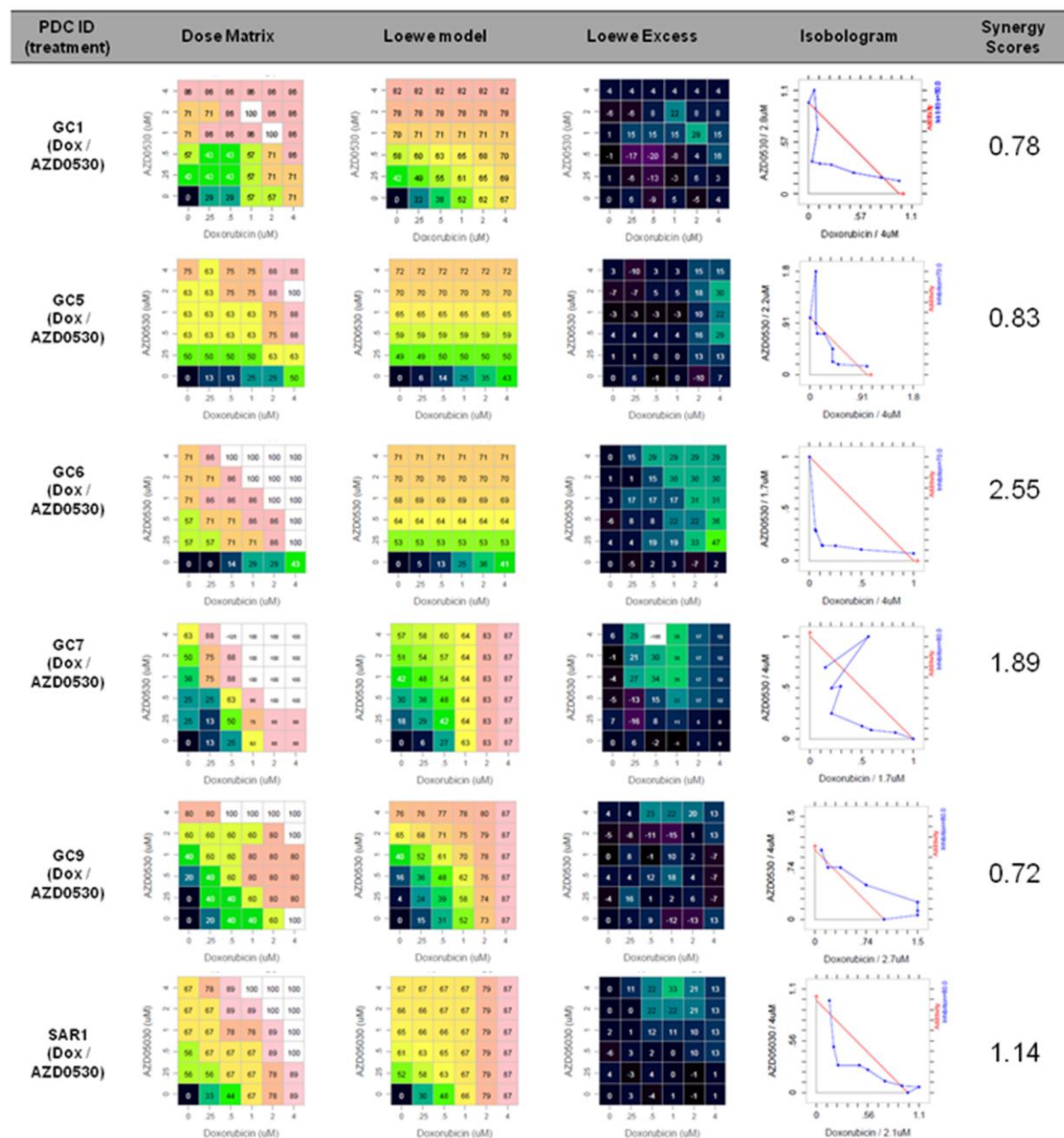


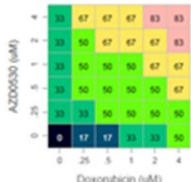
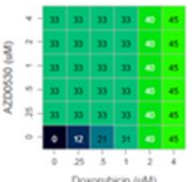
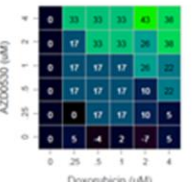
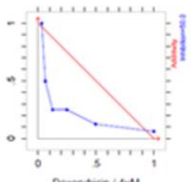
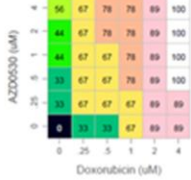
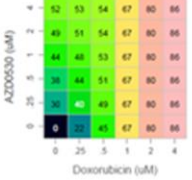
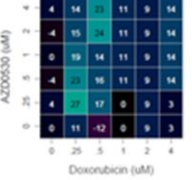
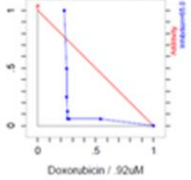
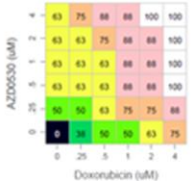
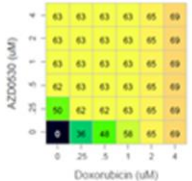
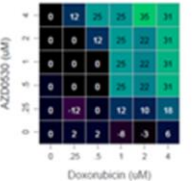
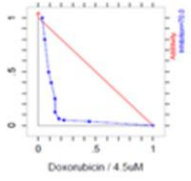
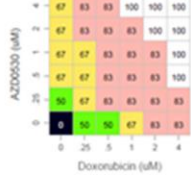
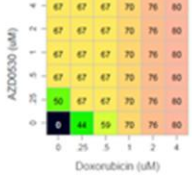
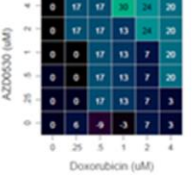
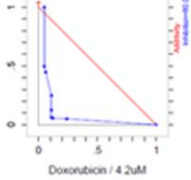
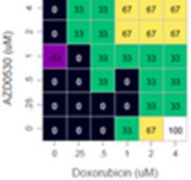
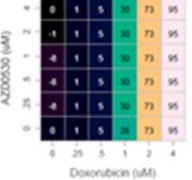
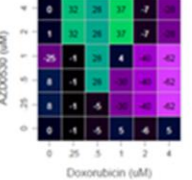
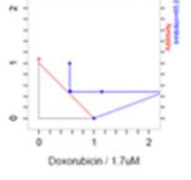
# Supplemental Figure S1. Dose response matrices, synergy scores and isobologram of PDCs

Patient derived cancer cells were treated with concentrations of Dox (0, 0.25, 0.5, 1, 2, 4  $\mu$ M), AZD0530 (0, 0.25, 0.5, 1, 2, 4  $\mu$ M), respectively or the combination of Dox and AZD0530 in dose response matrix. After treatment for 24hr, cell viability was measured by MTT assay. And the synergy scores were calculated by the Loewe dose-additivity model.



| PDC ID (treatment)        | Dose Matrix | Loewe model | Loewe Excess | Isobologram | Synergy Scores |
|---------------------------|-------------|-------------|--------------|-------------|----------------|
| SAR2 (Dox / AZD0530)      |             |             |              |             | 0.47           |
| SAR5 (Dox / AZD0530)      |             |             |              |             | 1.51           |
| SAR#6 (Dox / AZD0530)     |             |             |              |             | 0.35           |
| OS-SAR-16 (Dox / AZD0530) |             |             |              |             | 1.69           |
| OS-SAR-22 (Dox / AZD0530) |             |             |              |             | 1.18           |
| OS-SAR-25 (Dox / AZD0530) |             |             |              |             | 1.03           |
| OS-SAR-27 (Dox / AZD0530) |             |             |              |             | 1.42           |

| PDC ID (treatment)        | Dose Matrix | Loewe model | Loewe Excess | Isobologram | Synergy Scores |
|---------------------------|-------------|-------------|--------------|-------------|----------------|
| OS-LC-1 (Dox / AZD0530)   |             |             |              |             | 0.02           |
| OS-LC-2 (Dox / AZD0530)   |             |             |              |             | 0.4            |
| OS-27 (Dox / AZD0530)     |             |             |              |             | 2.16           |
| OS-SAR-41 (Dox / AZD0530) |             |             |              |             | 1.01           |
| OS-SAR-32 (Dox / AZD0530) |             |             |              |             | 0.88           |
| OS-SAR-35 (Dox / AZD0530) |             |             |              |             | 0.61           |
| OS-SAR-39 (Dox / AZD0530) |             |             |              |             | 0.89           |

| PDC ID (treatment)      | Dose Matrix                                                                         | Loewe model                                                                         | Loewe Excess                                                                         | Isobologram                                                                           | Synergy Scores |
|-------------------------|-------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|----------------|
| OS-BC-1 (Dox / AZD0530) |    |    |    |    | 1.75           |
| SAR12 (Dox / AZD0530)   |    |    |    |    | 1.28           |
| SAR13 (Dox / AZD0530)   |    |    |    |    | 1.82           |
| GC10 (Dox / AZD0530)    |   |   |   |   | 1.55           |
| 061T (Dox / AZD0530)    |  |  |  |  | 0.53           |

**Supplementary Table1.** Patient derived cancer cells used for the experiments

| #  | PDC ID    | Tumor type                          | TP53 Status | IARC definition (Transcriptional Activity) | Synergy Scores     |                         |
|----|-----------|-------------------------------------|-------------|--------------------------------------------|--------------------|-------------------------|
|    |           |                                     |             |                                            | Dox/AZD0530        | Mean $\pm$ S.D.         |
| 1  | GC1       | Advanced Gastric Cancer             | WT          | Functional                                 | 0.78               | 1.138<br>$\pm$<br>0.620 |
| 2  | GC5       | Advanced Gastric Cancer             |             | Functional                                 | 0.83               |                         |
| 3  | GC6       | Advanced Gastric Cancer             |             | Functional                                 | <b><u>2.55</u></b> |                         |
| 4  | GC7       | Advanced Gastric Cancer             |             | Functional                                 | <b><u>1.89</u></b> |                         |
| 5  | GC9       | Advanced Gastric Cancer             |             | Functional                                 | 0.72               |                         |
| 6  | SAR1      | Leiomyosarcoma                      |             | Functional                                 | 1.14               |                         |
| 7  | SAR2      | Angiosarcoma                        |             | Functional                                 | 0.47               |                         |
| 8  | SAR5      | Ewing                               |             | Functional                                 | <b><u>1.51</u></b> |                         |
| 9  | SAR6      | Rhabdomyosarcoma                    |             | Functional                                 | 0.35               |                         |
| 10 | OS-SAR-16 | osteosarcoma                        |             | Functional                                 | <b><u>1.69</u></b> |                         |
| 11 | OS-SAR-22 | osteosarcoma                        |             | Functional                                 | 1.18               |                         |
| 12 | OS-SAR-25 | leiomyosarcoma                      |             | Functional                                 | 1.03               |                         |
| 13 | OS-SAR-27 | myxofibro sarcoma                   |             | Functional                                 | 1.42               |                         |
| 14 | OS-LC-1   | lung cancer                         |             | Functional                                 | 0.02               |                         |
| 15 | OS-LC-2   | NSC lung cancer                     |             | Functional                                 | 0.4                |                         |
| 16 | OS-27     | Metastatic Adenoid Cystic Carcinoma |             | Functional                                 | <b><u>2.16</u></b> |                         |
| 17 | OS-SAR-41 | Synovial sarcoma                    |             | Functional                                 | 1.01               |                         |
| 18 | OS-SAR-32 | Osteosarcoma                        |             | Functional                                 | 0.88               |                         |
| 19 | OS-SAR-35 | Chondrosarcoma                      |             | Functional                                 | 0.61               |                         |
| 20 | OS-SAR-39 | Synovial sarcoma                    |             | Functional                                 | 0.89               |                         |
| 21 | OS-BC-1   | Breast cancer                       |             | Functional                                 | <b><u>1.75</u></b> |                         |
| 22 | SAR12     | Leiomyosarcoma                      |             | Functional                                 | 1.28               |                         |
| 23 | SAR13     | Ewing                               |             | Functional                                 | <b><u>1.82</u></b> |                         |
| 24 | GC10      | Advance Gastric cancer              |             | Functional                                 | <b><u>1.55</u></b> |                         |
| 25 | 061T      | Breast cancer                       |             | Functional                                 | 0.53               |                         |
| 26 | GC24      | Advanced Gastric Cancer             | R248Q       | non-functional                             | <u>2.9</u>         | 2.882<br>$\pm$<br>0.736 |
| 27 | GC26      | Advanced Gastric Cancer             | C176F       | partially functional                       | <u>2.15</u>        |                         |
| 28 | GC16      | Advanced Gastric Cancer             | Q104X       | No data available                          | <u>1.79</u>        |                         |
| 29 | GC20      | Advanced Gastric Cancer             | I195T       | non-functional                             | <u>2.04</u>        |                         |
| 30 | GC25      | Advanced Gastric Cancer             | A189V       | functional                                 | <u>3.19</u>        |                         |
| 31 | GC14      | Advanced Gastric Cancer             | R342X       | No data available                          | <u>3.53</u>        |                         |
| 32 | OS-SAR-42 | Leiomyosarcoma                      | Null        | non-functional                             | <u>3.18</u>        |                         |
| 33 | GC28      | Advanced Gastric Cancer             | W91X        | No data available                          | <u>3.21</u>        |                         |
| 34 | GC32      | Advanced Gastric Cancer             | R248W       | non-functional                             | <u>3.94</u>        |                         |
| 35 | GC18      | Advanced Gastric Cancer             | Y236C       | non-functional                             | <u>2.13</u>        |                         |
| 36 | GC33      | Advanced Gastric Cancer             | Del         | non-functional                             | <u>3.65</u>        |                         |

**Supplementary Table2.** The coding sequence of target genes and siRNA duplex sequence

| Gene   | Forward                                    | Reverse                                     |
|--------|--------------------------------------------|---------------------------------------------|
| p53    | 5'-AAGAAGCTTATGGAGGAGCCGCGAGTCAGATCCTAG-3' | 5'-CAGAAATTCAGTCTGAGTCAGGCCCTTCTGTCTT-3'    |
| CA-Src | 5'-AAGAAGCTTATGGGTAGCAACAAGAGCAAGCCCAA-3'  | 5'-CAGAATTCCTAGAGGTTCTCCCCGGGCTGGAAGTGGG-3' |

| siRNA | Sense                           | Antisense                       |
|-------|---------------------------------|---------------------------------|
| p53   | 5'-CACUACAACUACAUGUGUA(dTdT)-3' | 5'-UACACAUGUAGUUGUAGUG(dTdT)-3' |
| STAT3 | 5'-GGAGCAGCACCUUCAUUU(dTdT)-3'  | 5'-AAAUGAAGGUGCUGCUCC(dTdT)-3'. |