**Supplementary information:**

**DZ-2384 has a superior pre-clinical profile to taxanes for the treatment of triple-negative breast cancer and is synergistic with anti-CTLA-4 immunotherapy**

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**Supplementary Figure 1. Body weight changes in murine PDX mammary fat pad models following administration of DZ-2384 or paclitaxel.** Percentage body weight change relative to weights at randomization corresponding to GCRC-1945 (A) and GCRC-2076 (B) models. Treatment days are indicated by arrows, doses in mg/kg are indicated in brackets. All body weights are plotted as the mean +/- SEM.

**Supplementary Figure 2.** **Body weight changes in murine MDA-MB231LM2 lung metastatic model following administration of DZ-2384 or docetaxel.** Percentage body weight change relative to weights at randomization corresponding to DZ-2384 (A) or docetaxel (B) treatments as indicated. Treatment days are indicated by arrows. All body weights are plotted as the mean +/- SEM.

**Supplementary Figure 3.** **Anti-tumor activity of DZ-2384 and paclitaxel in brain metastatic GCRC-1945 and MDA-MB-231BrM2 TNBC models.**

(A) Mice bearing intra-cranially transplanted GCRC-1945 PDX brain metastases were treated biweekly for two weeks with DZ-2384 or paclitaxel (treatment days indicated by arrows at the dose shown in mg/kg in brackets in the legend). Graph represents mean bioluminescence signal +/- SEM measured weekly. A tumor free animal was imaged to represent the background signal. (B) Kaplan-Meier curve depicting survival for the GCRC-1945 brain metastatic model. Statistical differences with vehicle control are indicated to the left of the legend and were determined by student’s t-test for bioluminescence and Log-rank (Mantel-Cox) test for survival curves. Asterisks on the left of the legend represent differences with vehicle control, on the right differences between groups. \* P<0.05 and ns, not significant. (C, D) Percentage body weight change relative to weights at randomization corresponding to DZ-2384 or paclitaxel treatments as indicated. Treatment days are indicated by arrows. All body weights are plotted as the mean +/- SEM.

**Supplementary Table 1. The pharmacokinetic parameters of DZ-2384 and paclitaxel in plasma and tissues.**

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| --- | --- | --- | --- | --- | --- | --- |
| Parameter | **DZ-2384** | | | **Paclitaxel** | | |
| AUC0-t  (ng/mL\*h) | Cmax (ng/mL) | t1/2 terminal (h) (4-24h) | AUC0-t (ng/mL\*h) | Cmax (ng/mL) | t1/2 terminal (h) (4-24h) |
| Plasma | 1858 | 1580 | 5.8 | 55557 | 29400 | 2.3 |
| Brain | 284 | 47 | 17.4 | 6544 | 349 | 36.0 |
| Heart | 1206 | 1305 | 0.8 | 60870 | 30150 | 1.8 |
| Lung | 2894 | 2144 | 7.0 | 193024 | 40095 | 2.8 |
| Tumor | 34504 | 2048 | 29.3 | 164336 | 13785 | 19.1 |