

**Supplementary Table 6. The synergistic antiproliferative effect of Palbociclib and Telaglenastat combined treatment is conserved *ex vivo*.** Cells obtained from tumors from mice that have been administered with Palbociclib and Telaglenastat combination were treated for 96 h at the indicated concentrations ( $\mu\text{M}$ ) of Palbociclib and Telaglenastat in a constant ratio (1:10). The combination index (CI) results obtained with CompuSyn software revealed a synergy ( $\text{CI}<1$ ) in the antiproliferative effects of Palbociclib and Telaglenastat at each dose combination tested.

Combination Index (CI) equation of Chou and Talalay and CompuSyn software

| CI value  | Agonistic effect                 |
|-----------|----------------------------------|
| <0.10     | Very strong synergism            |
| 0.10–0.30 | Strong synergism                 |
| 0.30–0.70 | Synergism                        |
| 0.70–0.90 | Moderate to slight synergism     |
| 0.90–1.10 | Nearly additive                  |
| 1.10–1.45 | Slight to moderate antagonism    |
| 1.45–3.30 | Antagonism                       |
| >3.30     | Strong to very strong antagonism |

|                                |                                  | Cell line 1 derived from tumor 1 treated with Combination |     |              | Cell line 2 derived from tumor 2 treated with Combination |     |              | Cell line 3 derived from tumor 3 treated with Combination |     |              |
|--------------------------------|----------------------------------|-----------------------------------------------------------|-----|--------------|-----------------------------------------------------------|-----|--------------|-----------------------------------------------------------|-----|--------------|
| [Palbociclib]<br>$\mu\text{M}$ | [Telaglenastat]<br>$\mu\text{M}$ | Viability                                                 | SD  | CI Value     | Viability                                                 | SD  | CI Value     | Viability                                                 | SD  | CI Value     |
| 0.04                           | 0.4                              | 80.9                                                      | 1.5 | <b>0.450</b> | 76.8                                                      | 1.0 | <b>0.615</b> | 78.6                                                      | 1.9 | <b>0.662</b> |
| 0.08                           | 0.8                              | 71.0                                                      | 2.3 | <b>0.398</b> | 64.7                                                      | 5.6 | <b>0.386</b> | 67.0                                                      | 2.7 | <b>0.400</b> |
| 0.15                           | 1.5                              | 59.7                                                      | 3.3 | <b>0.367</b> | 55.6                                                      | 2.0 | <b>0.379</b> | 57.2                                                      | 1.3 | <b>0.350</b> |
| 0.3                            | 3                                | 52.2                                                      | 2.0 | <b>0.486</b> | 48.9                                                      | 5.2 | <b>0.514</b> | 48.9                                                      | 4.8 | <b>0.404</b> |
| 0.5                            | 5                                | 50.7                                                      | 5.4 | <b>0.749</b> | 47.9                                                      | 3.0 | <b>0.813</b> | 48.1                                                      | 1.1 | <b>0.641</b> |
| 0.65                           | 6.5                              | 49.0                                                      | 2.4 | <b>0.891</b> | 43.9                                                      | 2.5 | <b>0.869</b> | 43.5                                                      | 0.8 | <b>0.632</b> |
| 0.8                            | 8                                | 42.8                                                      | 1.5 | <b>0.797</b> | 41.0                                                      | 5.0 | <b>0.940</b> | 41.8                                                      | 3.3 | <b>0.704</b> |
| 0.9                            | 9                                | 37.9                                                      | 3.5 | <b>0.698</b> | 35.0                                                      | 2.6 | <b>0.834</b> | 37.7                                                      | 3.6 | <b>0.627</b> |
| 1.1                            | 11                               | 27.0                                                      | 1.6 | <b>0.476</b> | 26.3                                                      | 1.8 | <b>0.764</b> | 17.7                                                      | 1.0 | <b>0.238</b> |
| 1.4                            | 14                               | 13.5                                                      | 2.1 | <b>0.245</b> | 11.1                                                      | 2.4 | <b>0.616</b> | 8.6                                                       | 1.7 | <b>0.140</b> |