Figure S1.  $^{177}$ Lu-DOTATATE uptake following treatment with onalespib. (A) Uptake of  $^{177}$ Lu-DOTATATE in the BON and NCI-H727 cells. Cells were either untreated (black bars) or treated with 25 nM onalespib (grey bars) 24 h prior to the addition of  $^{177}$ Lu-DOTATATE. Graph displays uptake normalized to untreated (means  $\pm$  standard deviation, n=8). (B) Western blot analysis of SSTR5 in untreated spheroids or 24 h after no treatment or treatment with 25 nM onalespib, 5 kBq  $^{177}$ Lu-DOTATATE or the combination of the two. Graph displays signal normalized to untreated (means  $\pm$  standard deviation, n=4).  $^{177}$ Lu-DOT,  $^{177}$ Lu-DOTATATE; n.s, not significant.

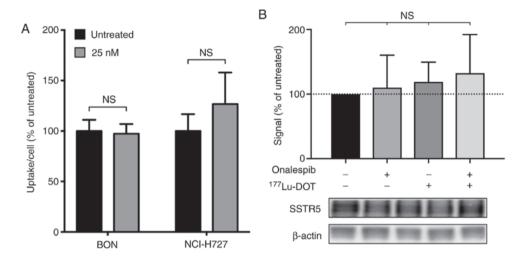


Figure S2. Spheroid size with representative spheroid images at last time point following treatment with DMSO or unlabeled DOTATATE. (A) BON cells; (B) NCI-H727 cells; (C) NCI-H460 cells. Graphs display volume (means  $\pm$  standard deviation, n $\geq$ 4). Scale bar, 500  $\mu$ m. DOT, DOTATATE; n.s, not significant.

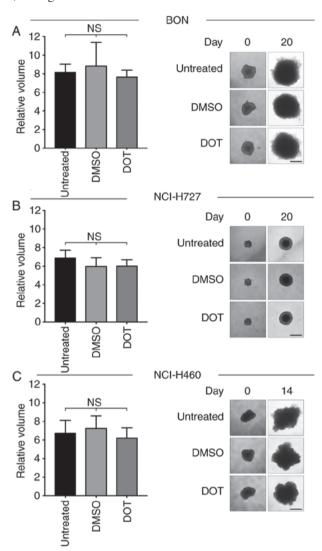


Figure S3. Combination treatments of spheroids. Spheroids were either untreated or treated with onalespib,  $^{177}$ Lu-DOTATATE or the combination of the two. (A) BON, (B) NCI-H727 and (C) NCI-H460 cells. Spheroids were treated with a daily dose indicated in the graphs. Graphs display size normalized to untreated (means  $\pm$  standard deviation,  $n \ge 4$ ).  $^*P \le 0.05$ ,  $^{**}P \le 0.01$ ,  $^{***}P \le 0.001$  and  $^{****}P \le 0.0001$ ; n.s, not significant.

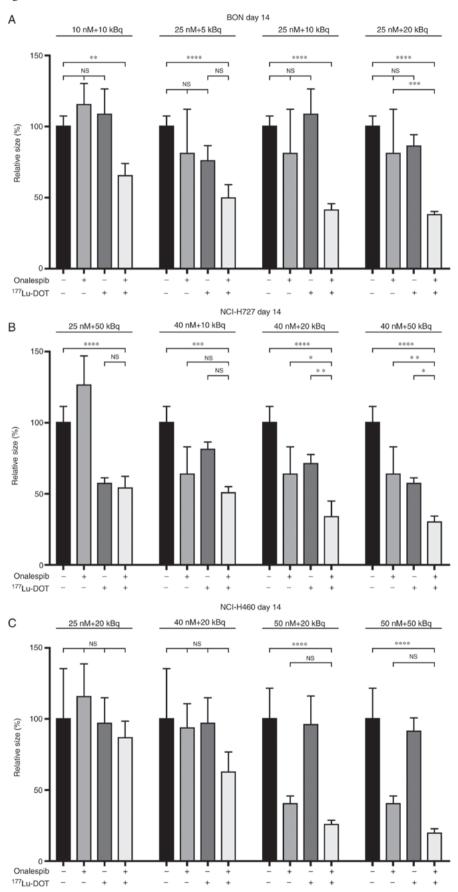


Figure S4. Representative images of flow cytometric analysis of caspase 3 and 7 activity in BON spheroids. Live/dead staining (y-axis) and caspase activity (x-axis) of untreated control (A), 25 nM onalespib (B), 5 kBq <sup>177</sup>Lu-DOTATATE (C) and combination treated spheroids (D).

