

S1. Absorbed dose-rates of analyzed organs and correlation between SPECT and biodistribution. (A) SPECT/MRI images of [¹⁷⁷Lu]Lu-DOTA-TATE injected mice at different time points p.i. (B) The absorbed dose-rates of different analyzed organs, depicted in mGy per hour. (C) Pearson's correlation for BioD-SPECT data of kidneys.



S2. Histopathological overviews of tumors of [177Lu]Lu-DOTA-TATE treated mice. Representative overview images of NCI-H69 tumors on different time points p.i. of [¹⁷⁷Lu]Lu-DOTA-TATE.



S3. All independent foci quantifications and average in NCI-H69 cells. (A) 53BP1 foci quantification over time in NT versus [¹⁷⁷Lu]Lu-DOTA-TATE treated NCI-H69 cells. Error bars indicate 95% confidence interval, *p < 0.05, **p < 0.01, ****p < 0.0001. (B) γ H2AX foci quantification over time in non-treated- versus [¹⁷⁷Lu]Lu-DOTA-TATE treated NCI-H69 cells. Error bars indicate 95% confidence interval, *p < 0.05, **p < 0.01, ****p < 0.0001.



S4. [¹⁷⁷Lu]Lu-DOTA-TATE uptake in SST₂^{high} and SST₂^{low} NCI-H69 cells. (A) lutetium-177 uptake measured by γ -counts in NCI-H69 and CA20948 cells after 4 hours of incubation (experiment n = 3). **p < 0.01 (B) Representative IF images of SST₂ after [¹⁷⁷Lu]Lu-DOTA-TATE treatment. Arrows indicate internalization and accumulation of SST₂.



S5. Additional foci quantifications in SST_2^{high} and SST_2^{low} cells. γ H2AX foci quantification in SST_2^{high} and SST_2^{low} NCI-H69 cells 2 days after [¹⁷⁷Lu]Lu-DOTA-TATE treatment. Error bars indicate 95% CI. *p < 0.05, ****p < 0.0001.



S6. [¹⁷⁷Lu]Lu-DOTA-TATE uptake in NCI-H69 and CA20498 tumors measured 2 d and 4 d p.i. Depicted is the percentage of the injected dose per gram (%ID/g) (n = 4). Error bars indicate standard deviation.



S7. Different degrees of SST_2 heterogeneity in patient NET samples. Representative images of SST_2 stainings on resected pancreatic NETs from different patients.