# Supplementary Information

# Image-Guided Nanodelivery of Pt(IV) Prodrugs to GRP-Receptor Positive Tumors

Francisco Silva[1,*], Carolina Mendes[1], Alice D'Onofrio[1], Maria Paula Cabral Campello[1,2], Fernanda Marques[1,2], Teresa Pinheiro[2,3], Kyle Gonçalves[1], Sérgio Figueiredo[4,5], Lurdes Gano[1,2], Mauro Ravera[6], António Paulo[1,2*]

## Index

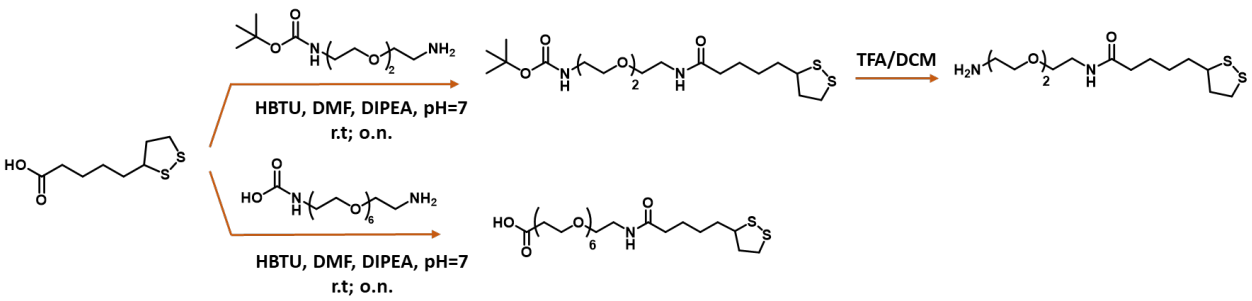



**Figure S 1.** Schematic synthesis of the pegylated thioctic acid precursors.

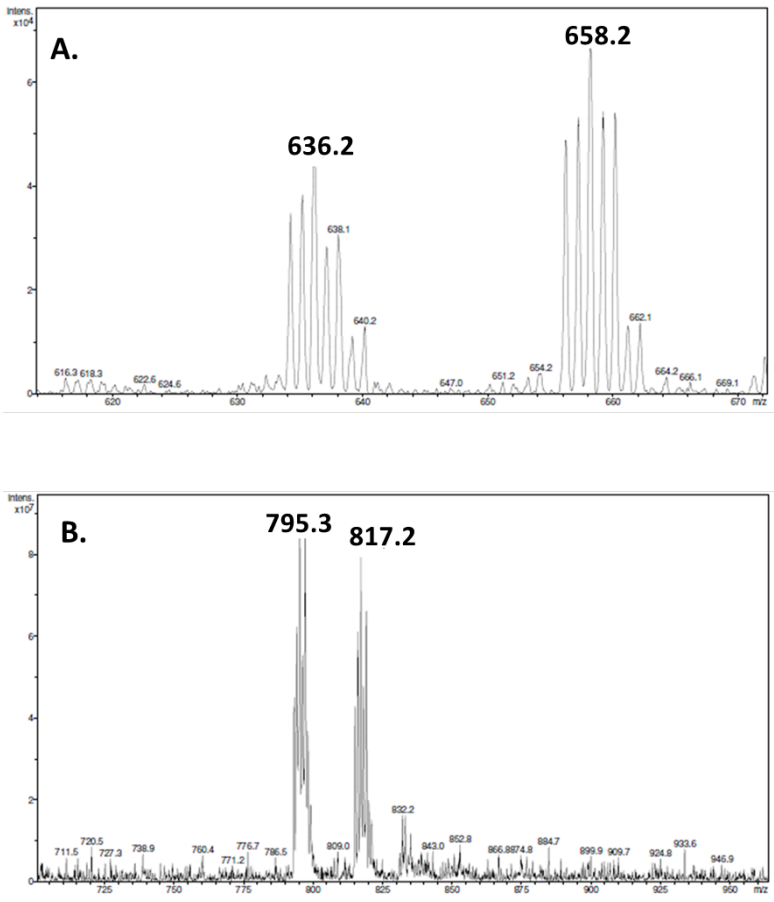
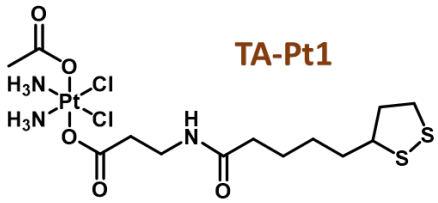



**Figure S 2. A. TA-Pt1**: m/z $[C_{13}H_{27}Cl_2N_3O_5PtS_2H]^+$: calc. = 636.0; found = 636.2, $[C_{13}H_{27}Cl_2N_3O_5PtS_2$-$Na]^+$: calc. = 658.0; found = 658.2. **B. TA-Pt2**: m/z: $[C_{20}H_{40}PtCl_2N_4O_8S_2H]^+$ calc. = 795.1; found = 795.3 $[C_{20}H_{40}PtCl_2N_4O_8S_2Na]^+$ calc. = 817.1; found = 817.2.



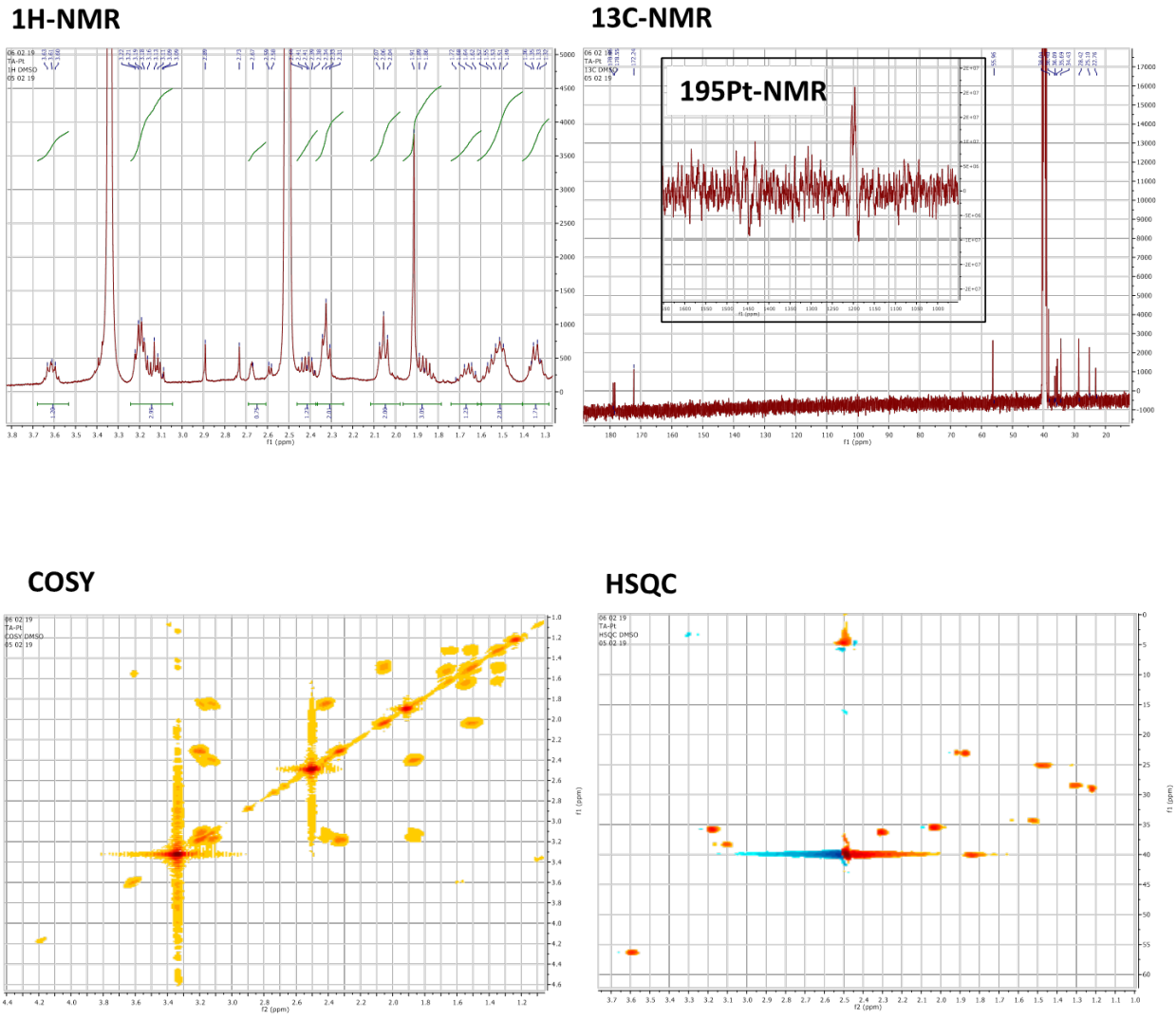




**Figure S 3.** Characterization of the thioctic acid-containing Pt(IV) prodrug **TA-Pt1** by multinuclear $^{1}H$, $^{13}C$ and $^{195}Pt$ NMR analysis in DMSO-$d_6$.

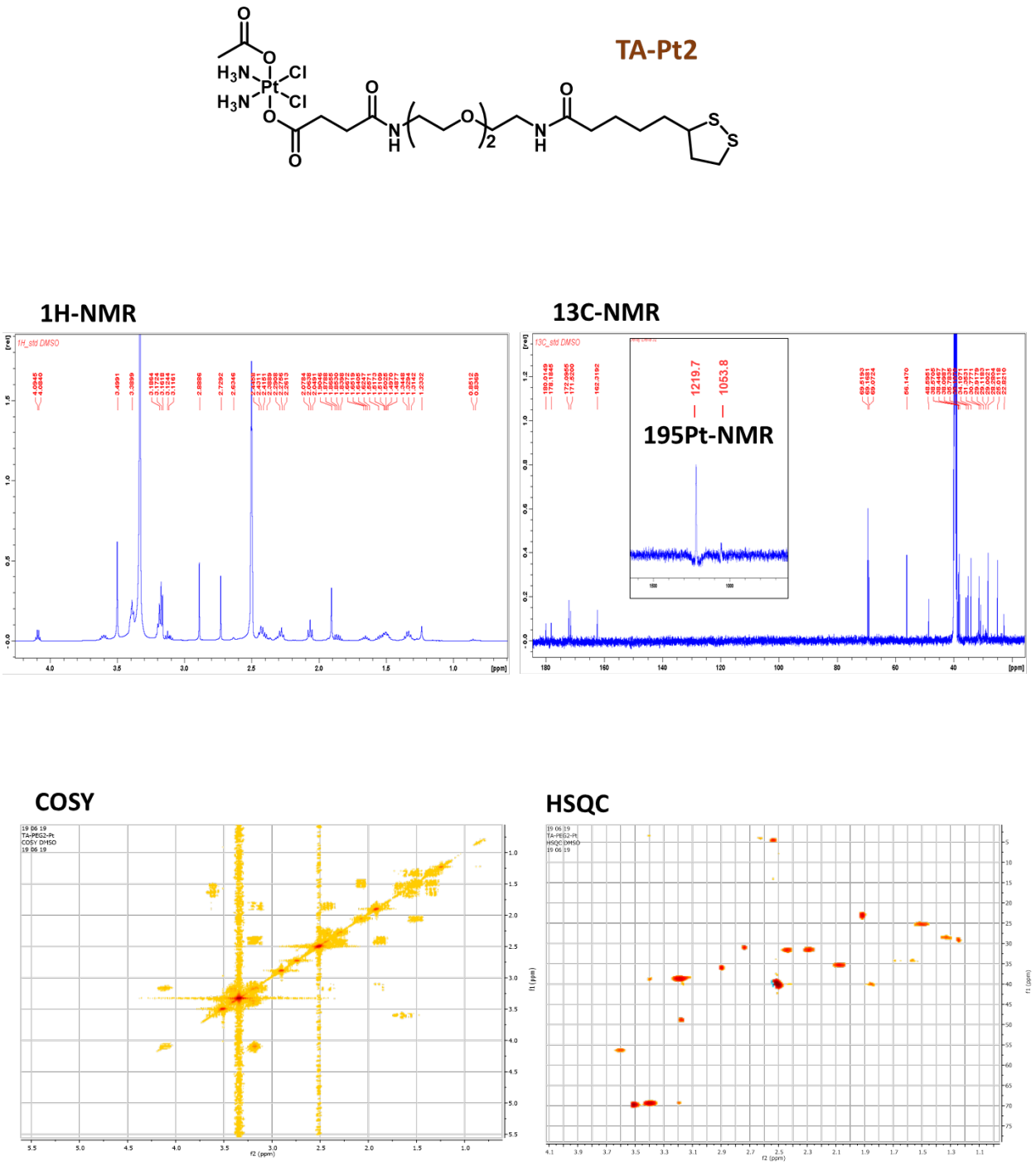



**Figure S 4.** Characterization of theathioctic acid-containing Pt(IV) prodrug **TA-Pt2** by multinuclear $^{1}H$, $^{13}C$ and $^{195}Pt$ NMR analysis in DMSO-$d_6$.

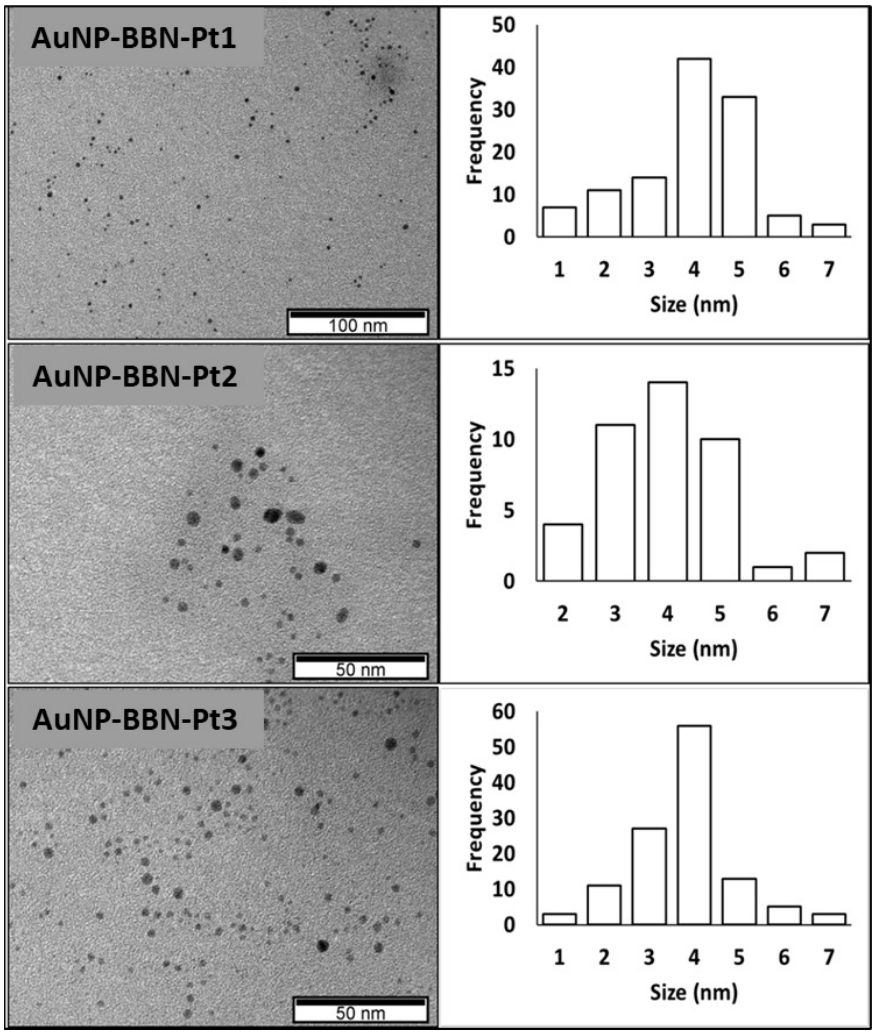



**Figure S 5.** TEM imaging of the Pt(IV) prodrug-containing AuNPs.

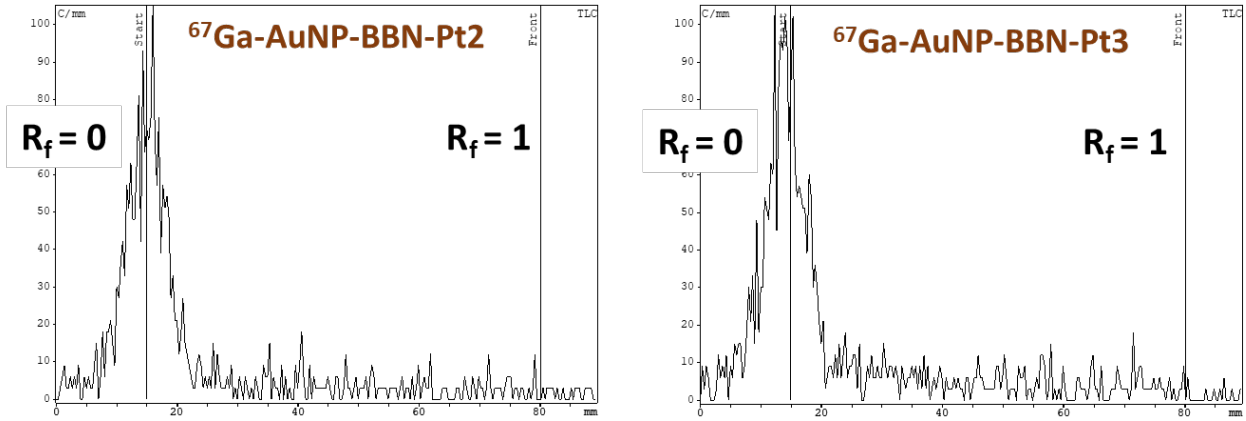
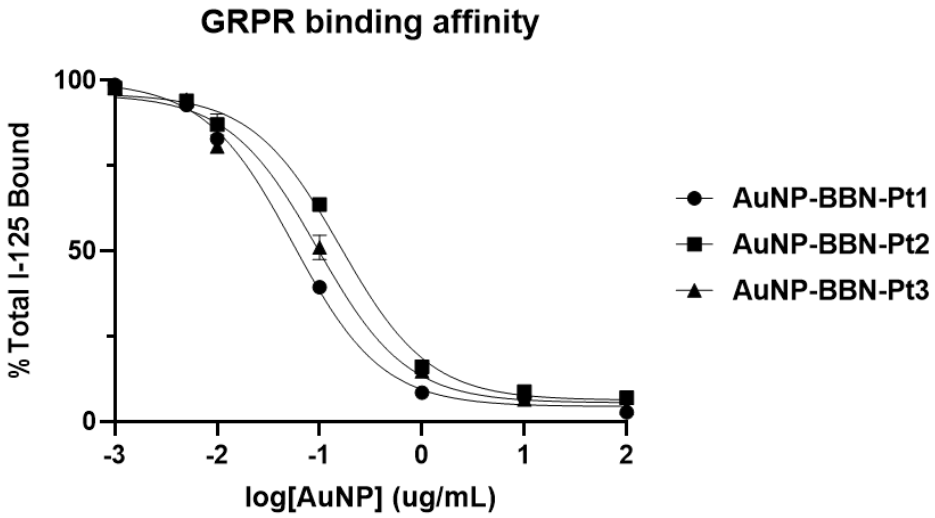



**Figure S 6.** iTLC radiochromatograms of **$^{67}$Ga-AuNP-BBN-Pt2** and **$^{67}$Ga-AuNP-BBN-Pt3**.




| Compound | $IC_{50}$ |
|---|---|
| **AuNP-BBN-Pt1** | 0.055 ± 0.005 µg/mL |
| **AuNP-BBN-Pt2** | 0.160 ± 0.022 µg/mL |
| **AuNP-BBN-Pt3** | 0.096 ± 0.019 µg/mL |

**Figure S 7.** Binding Affinity curves and $IC_{50}$ values of the Pt(IV) prodrug-containing AuNPs obtained by competitive binding assay using PC3 cells and [$^{125}$I-Tyr4]BBN as the GRPR-specific radioligand.

**Table S 1.** Biodistribution data of **$^{67}$Ga-AuNP-BBN-Pt1** in PC3 xenograft model, upon bolus intratumoral administration, performed at 1, 24 and 72 h post-administration.

| Organ | % Injected Dose/organ | | |
|---|---|---|---|
| | **1 h** | **24 h** | **72 h** |
| **Blood** | 3.4 ± 0.7 | 1.29 ± 0.02 | 0.43 ± 0.08 |
| **Liver** | 0.7 ± 0.3 | 7.0 ± 0.9 | 4.7 ± 0.6 |
| **Intestine** | 0.9 ± 0.4 | 3.1 ± 0.2 | 2.3 ± 0.2 |
| **Spleen** | 0.04 ± 0.01 | 0.43 ± 0.01 | 0.17 ± 0.02 |
| **Heart** | 0.14 ± 0.01 | 0.05 ± 0.01 | 0.06 ± 0.01 |
| **Lung** | 0.16 ± 0.07 | 1.1 ± 0.2 | 0.20 ± 0.07 |
| **Kidney** | 0.3 ± 0.1 | 1.1 ± 0.1 | 1.3 ± 0.1 |
| **Muscle** | 2.3 ± 1.0 | 2.2 ± 0.1 | 2.5 ± 0.3 |
| **Bone** | 0.9 ± 0.3 | 4.6 ± 0.7 | 8.3 ± 1.0 |
| **Stomach** | 0.13 ± 0.05 | 0.28 ± 0.03 | 0.25 ± 0.02 |
| **Pancreas** | 0.08 ± 0.02 | 0.19 ± 0.06 | 0.22 ± 0.09 |
| **Brain** | 0.03 ± 0.01 | 0.05 ± 0.01 | 0.04 ± 0.01 |
| **Tumor** | 77.5 ± 0.7 | 34.3 ± 1.6 | 25.6 ± 10.6 |
| **Excretion** | 2.2 ± 1.0 | 34.5 ± 0.8 | 40.7 ± 2.6 |