Electronic Supplementary Material (ESI) for Dalton Transactions.

A trans-Pt(II) hedgehog pathway inhibitor complex with cytotoxicity towards breast cancer stem cells and triple negative breast cancer cells.

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Supplementary Information

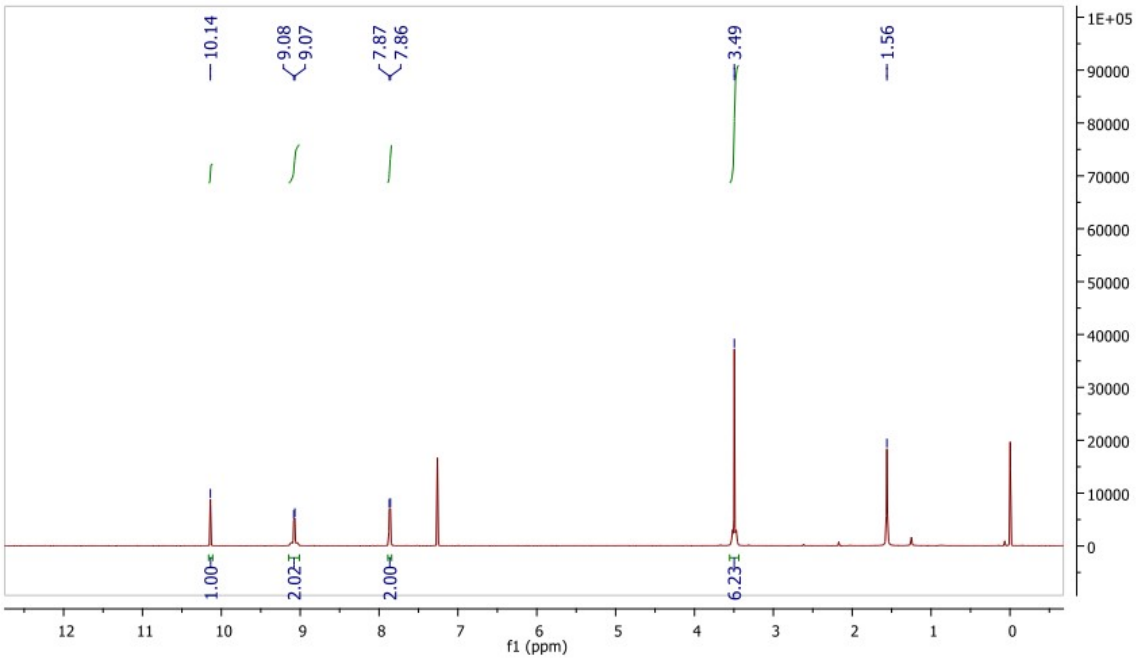


Figure S1. ^{1}H NMR spectrum of **1** in $CDCl_3$.

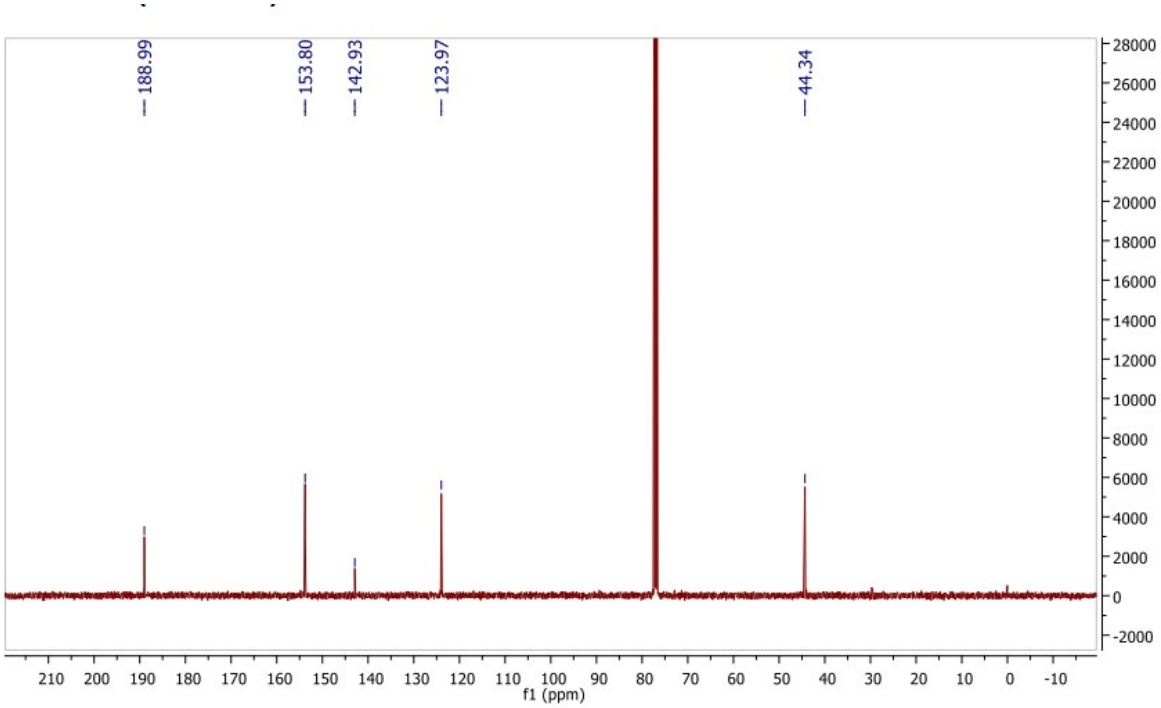


Figure S2. ^{13}C NMR spectrum of **1** in $CDCl_3$.

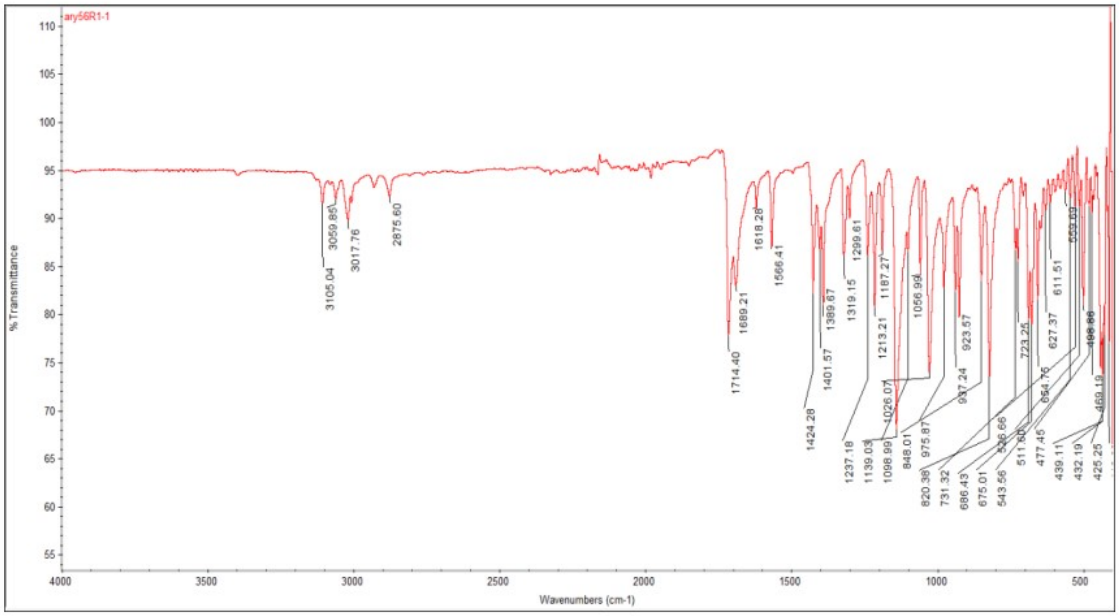


Figure S3. IR spectrum of **1**.

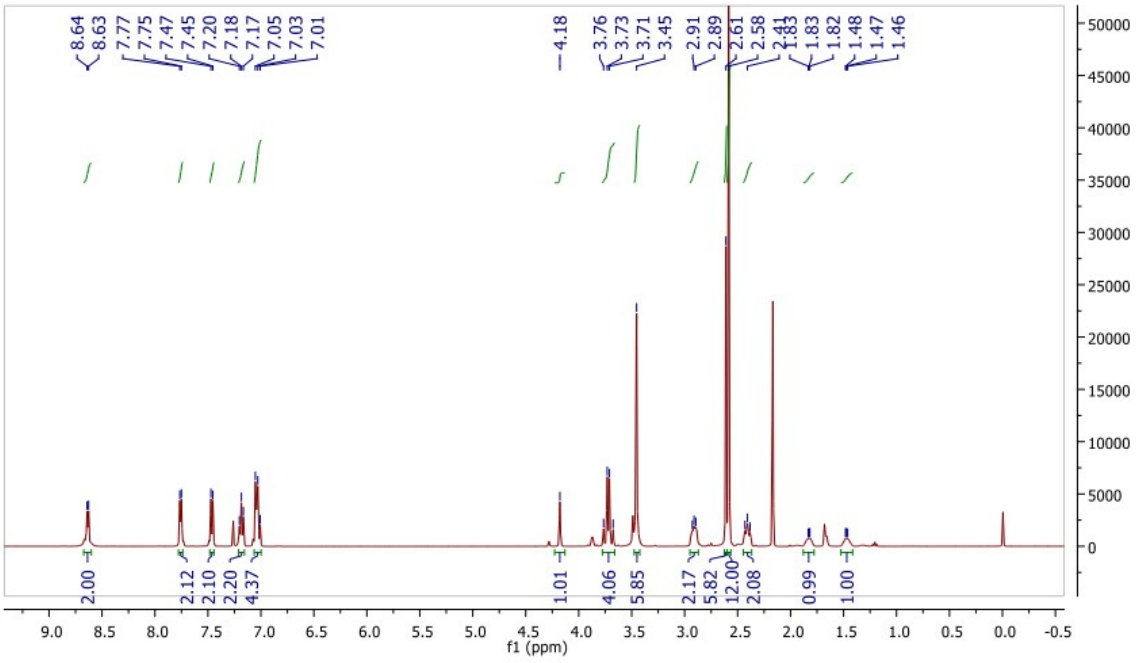


Figure S4. ^{1}H NMR spectrum of **2** in $CDCl_3$.

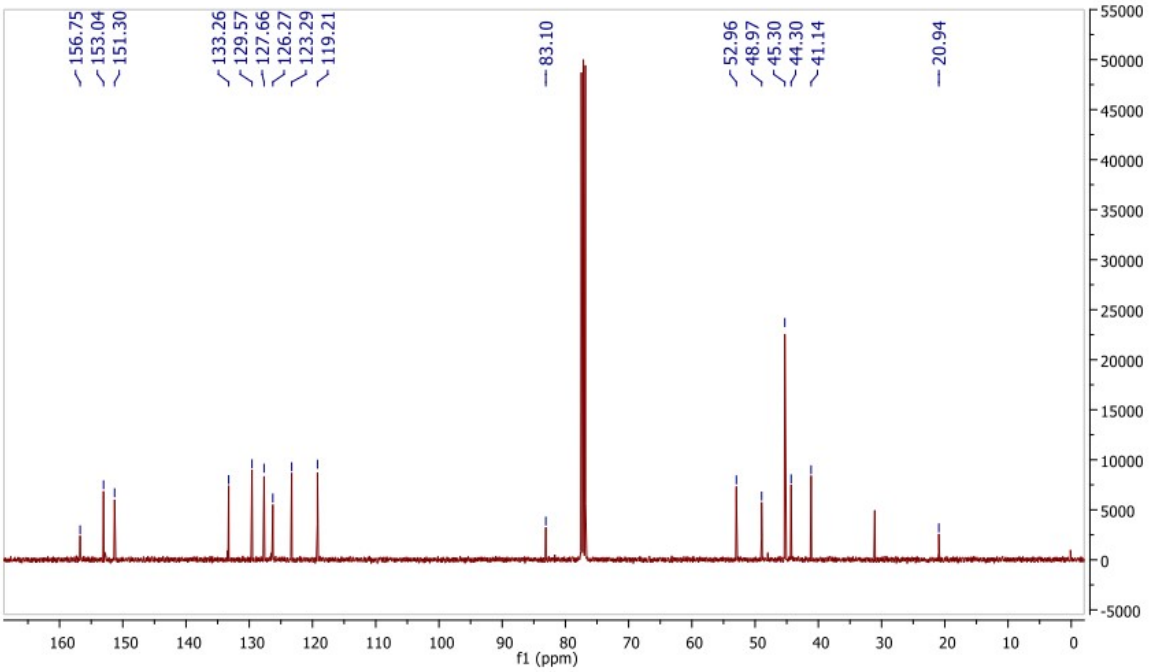


Figure S5. ^{13}C NMR spectrum of **2** in $CDCl_3$.

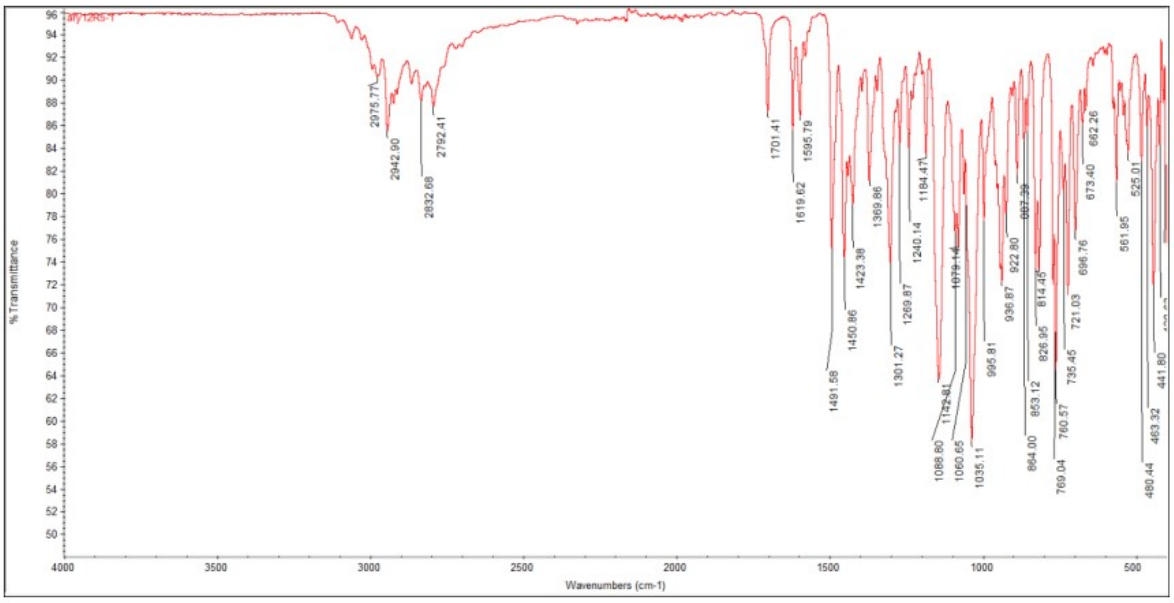


Figure S6. IR spectrum of **2**.

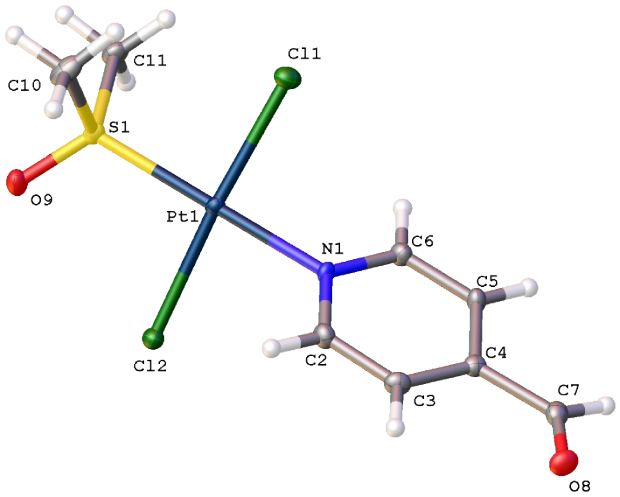


Figure S7. Fully labelled molecular structure of **1** with atomic displacement at 50% probability.

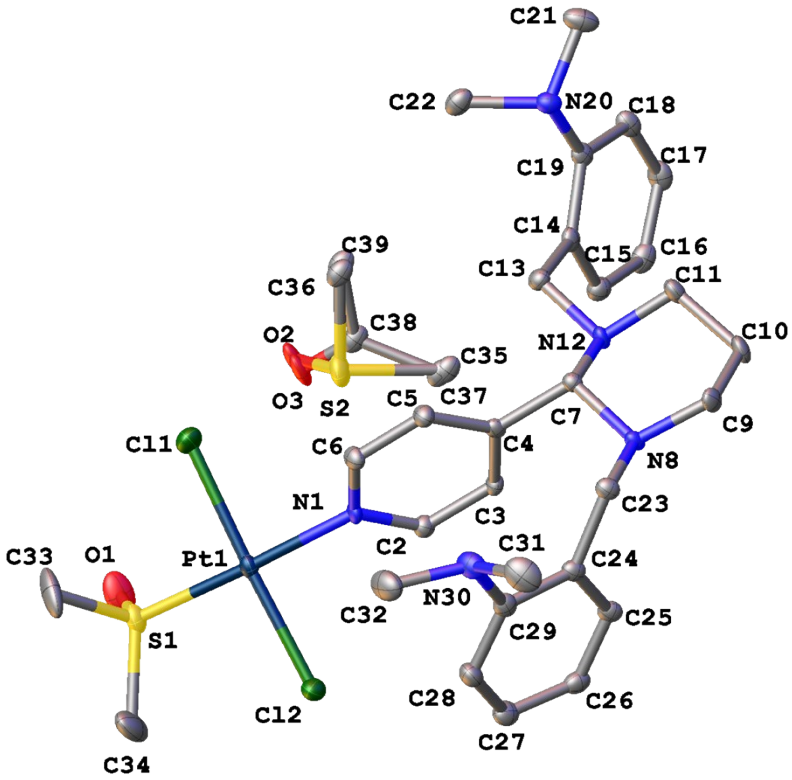


Figure S8. Fully labelled molecular structure of **2** with atomic displacement at 50% probability. Partially occupied mixed solvent DMSO/acetone shown also.

Table S1 Crystal data and structure refinement for **1** and **2**.

Identification Code	1	2
Empirical formula	$C_8H_{11}Cl_2NO_2PtS$	$C_{30.65}H_{45.5}Cl_2N_5O_{1.75}PtS_{1.6}$
M (g/mol)	451.23	829.30
T (K)	100(2)	100(2)
Crystal System	orthorhombic	triclinic
SG	$P2_12_12_1$	$P\bar{1}$
a (Å)	7.8958(4)	8.787(3)
b (Å)	8.1157(4)	9.901(2)
c (Å)	19.7202(9)	20.617(6)
α (°)	90	98.136(10)
β (°)	90	97.555(7)
γ (°)	90	94.640(8)
V (Å^3)	1263.67(11)	1751.2(8)
Z	4	2
Dcalc (g/cm^3)	2.372	1.573
μ (mm^{-1})	11.671	4.288
F(000)	840.0	832.0
Crystal size (mm^3)	0.08 × 0.07 × 0.05	0.17 × 0.14 × 0.1
Radiation	Mo Kα (λ = 0.71073)	Mo Kα (λ = 0.71073)
Reflections collected	68332	40236
Independent reflections	4231 R_{int} = 0.0487, R_{sigma} = 0.0249	8428 R_{int} = 0.0486, R_{sigma} = 0.0362
Data/restraints/parameters	4231/0/138	8428/0/392
Goodness-of-fit on F^2 (*S*)	1.092	1.050
Final R indexes [$I \geq 2\sigma(I)$]*	R_1 = 0.0163, wR_2 = 0.0269	R_1 = 0.0299, wR_2 = 0.0658
Final R indexes [all data]	R_1 = 0.0192, wR_2 = 0.0275	R_1 = 0.0390, wR_2 = 0.0692
Largest diff. peak/hole / e Å^{-3}	1.20/-1.43	1.64/-1.15
CCDC No.	2196198	2196199

*$R_1 = \sum ||F_o| - |F_c|| / \sum |F_o|$, $wR_2 = [\sum w(F_o^2 - F_c^2)^2 / \sum w(F_o^2)^2]^{1/2}$.

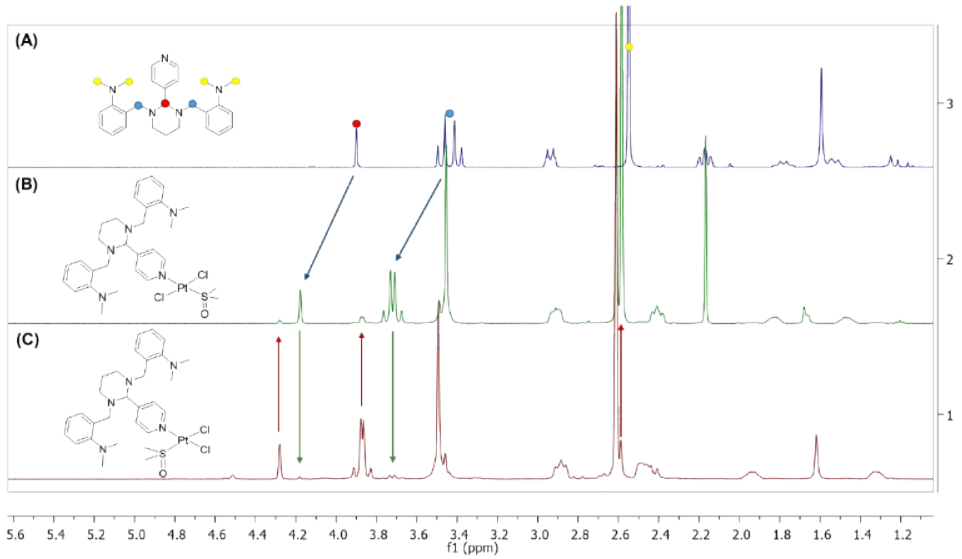
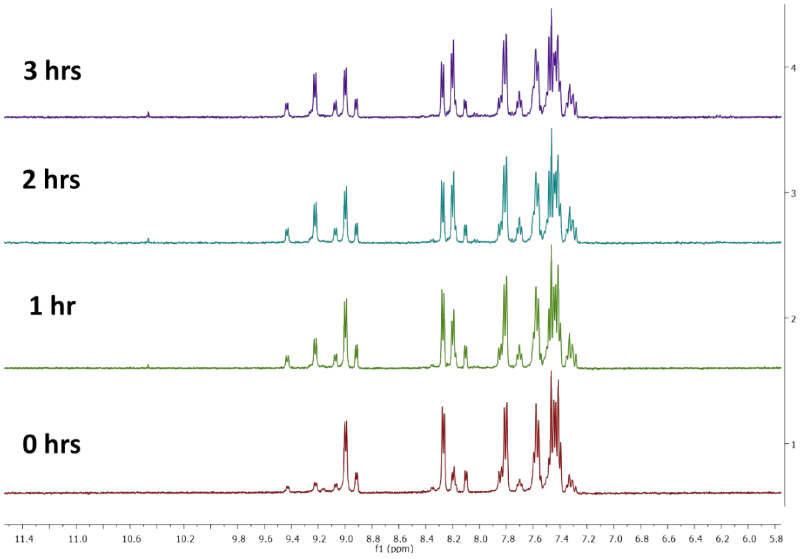


Figure S9. ^{1}H NMR ($CDCl_3$) of the aliphatic region (5.4 – 2.4 ppm) of (A) GANT61, (B) *trans*-[Pt(II)Cl_2(dmso)(GANT61)] 22 and (C) *cis*-[Pt(II)Cl_2(dmso)(GANT61)] 21, highlighting key chemical shifts associated with *trans* to *cis* isomerisation.

A.



B.

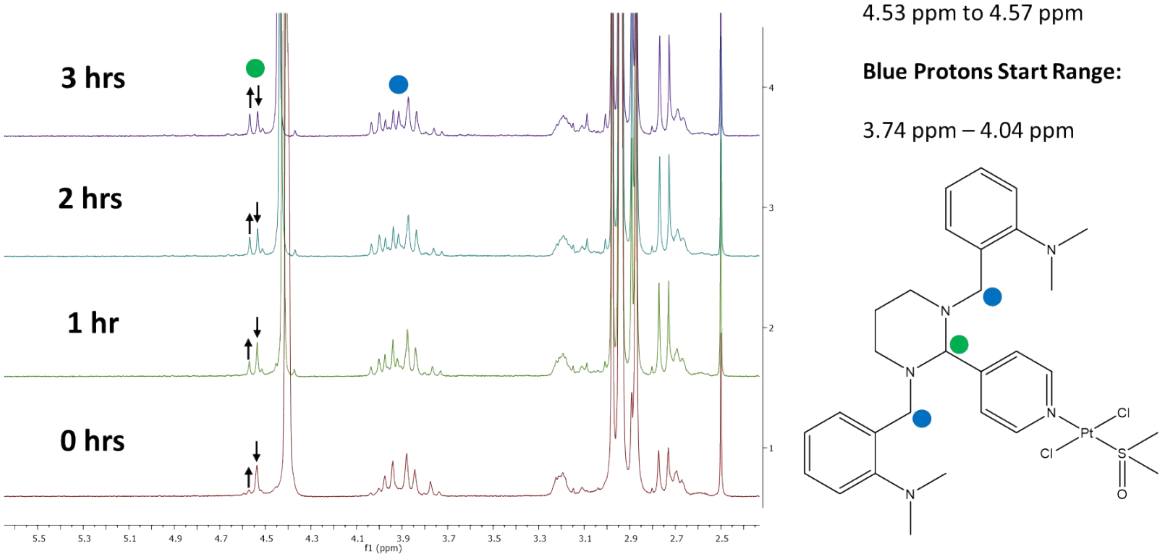


Figure S10. ^{1}H NMR study of **2** in D6-DMSO: D_2O (90:10) over 3 hours at RT. A. Aromatic region and B. Aliphatic region of the ^{1}H NMR spectrum.

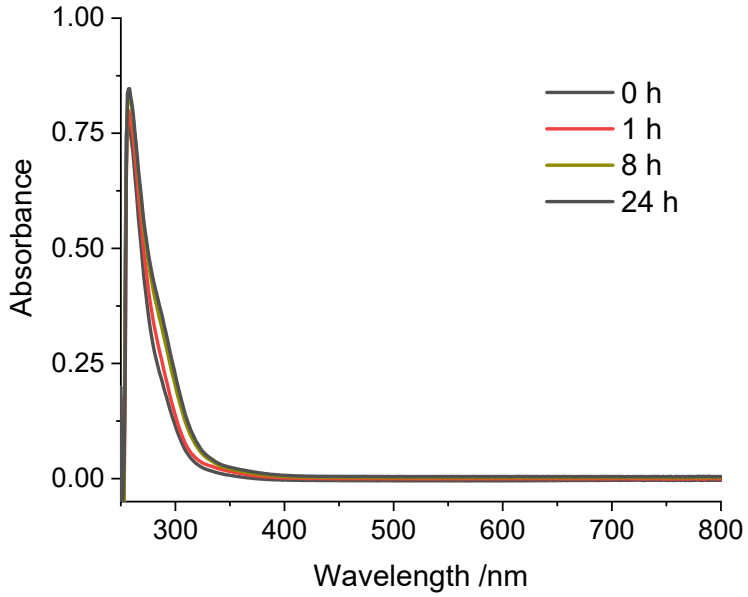


Figure S11. UV-Vis spectrum of **2** (50 µM) in DMSO over the course of 24 h at 37 °C.

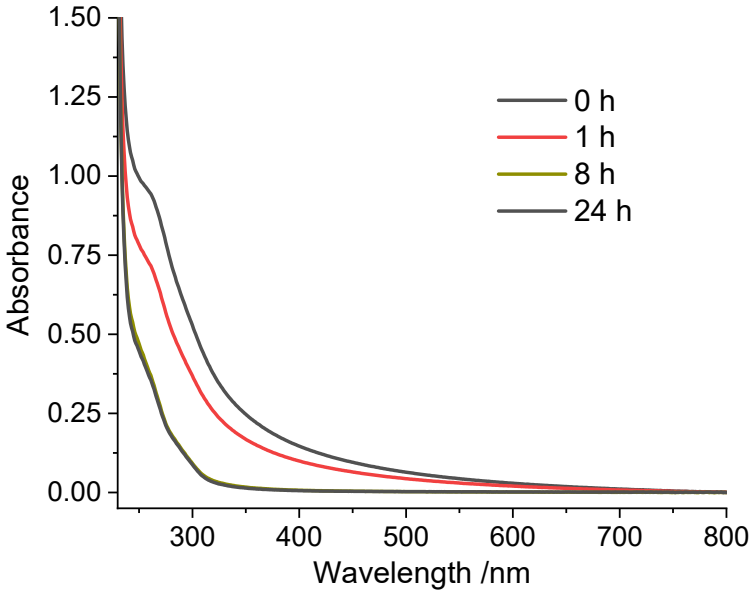


Figure S12. UV-Vis spectrum of **2** (50 µM) in PBS:DMSO (200:1) over the course of 24 h at 37 °C.

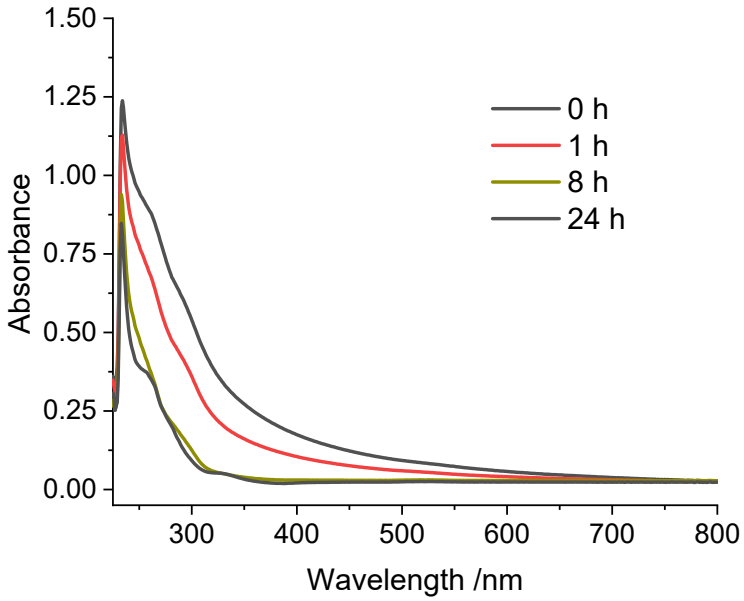
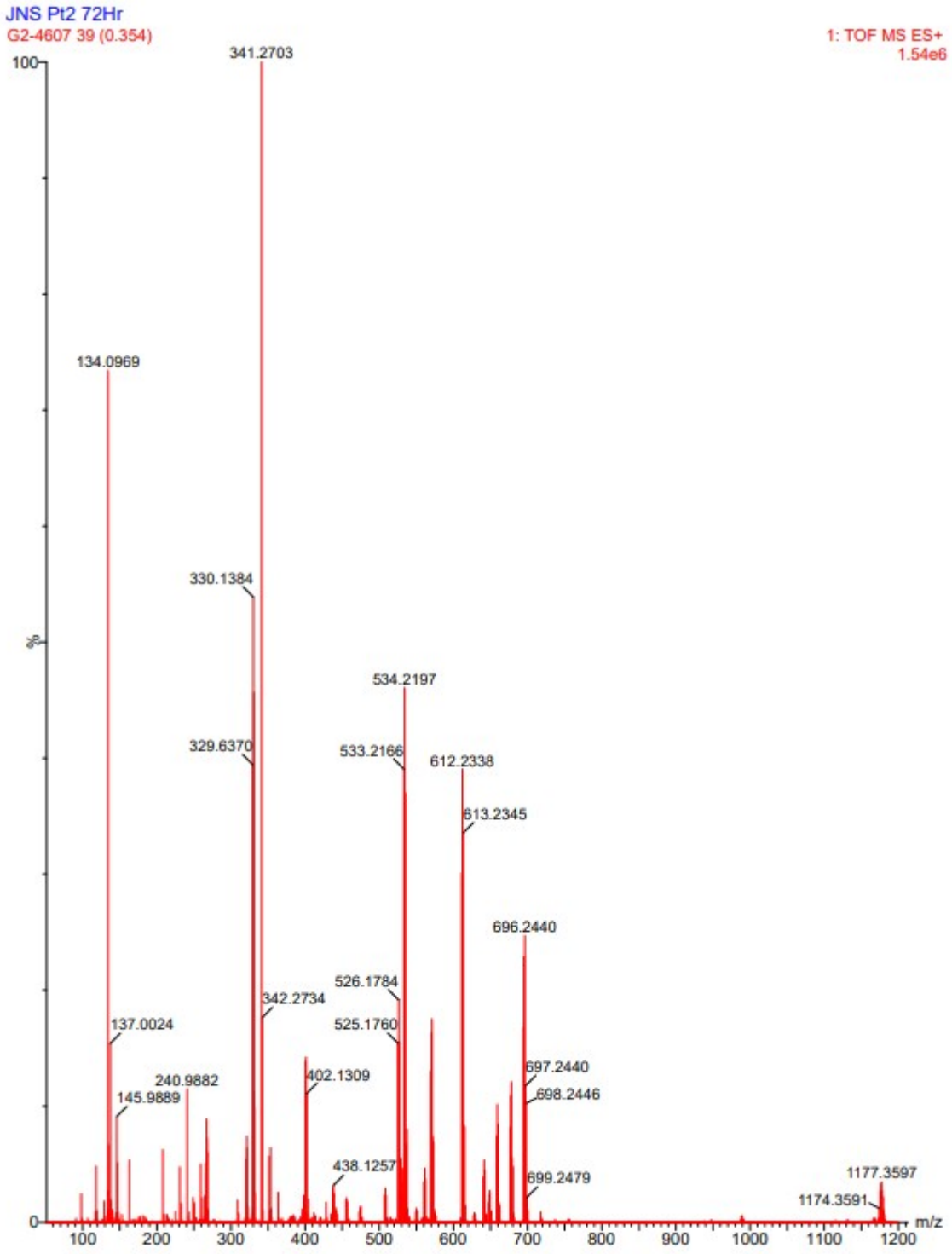


Figure S13. UV-Vis spectrum of **2** (50 µM) in DMEM:DMSO (200:1) over the course of 24 h at 37 °C.


JNS Pt2 72Hr
G2-4607 39 (0.354)
1: TOF MS ES+
1.54e6
100
%
0
341.2703
134.0969
330.1384
534.2197
329.6370
533.2166
612.2338
613.2345
696.2440
526.1784
342.2734
137.0024
525.1760
697.2440
240.9882
402.1309
145.9889
698.2446
438.1257
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1100
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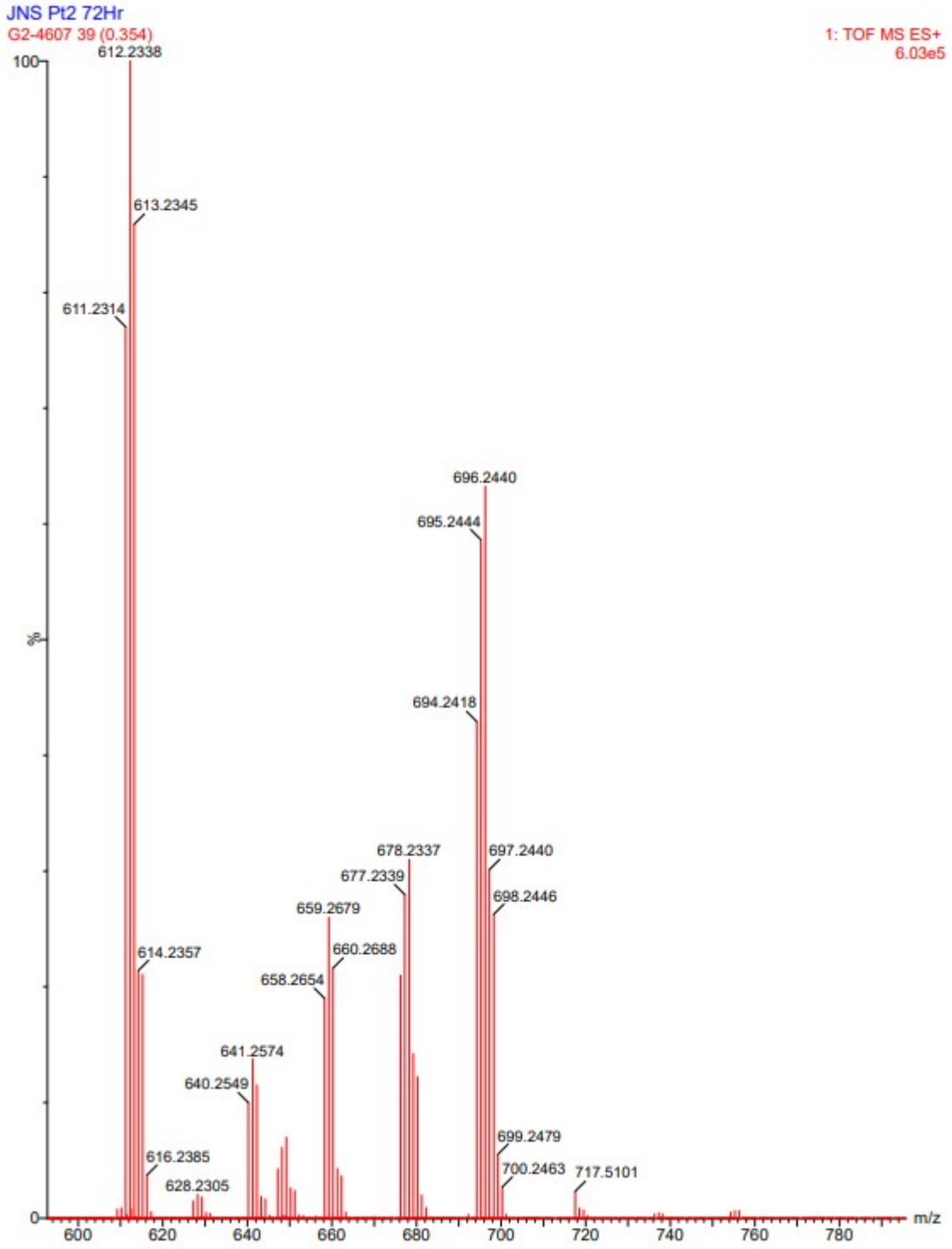
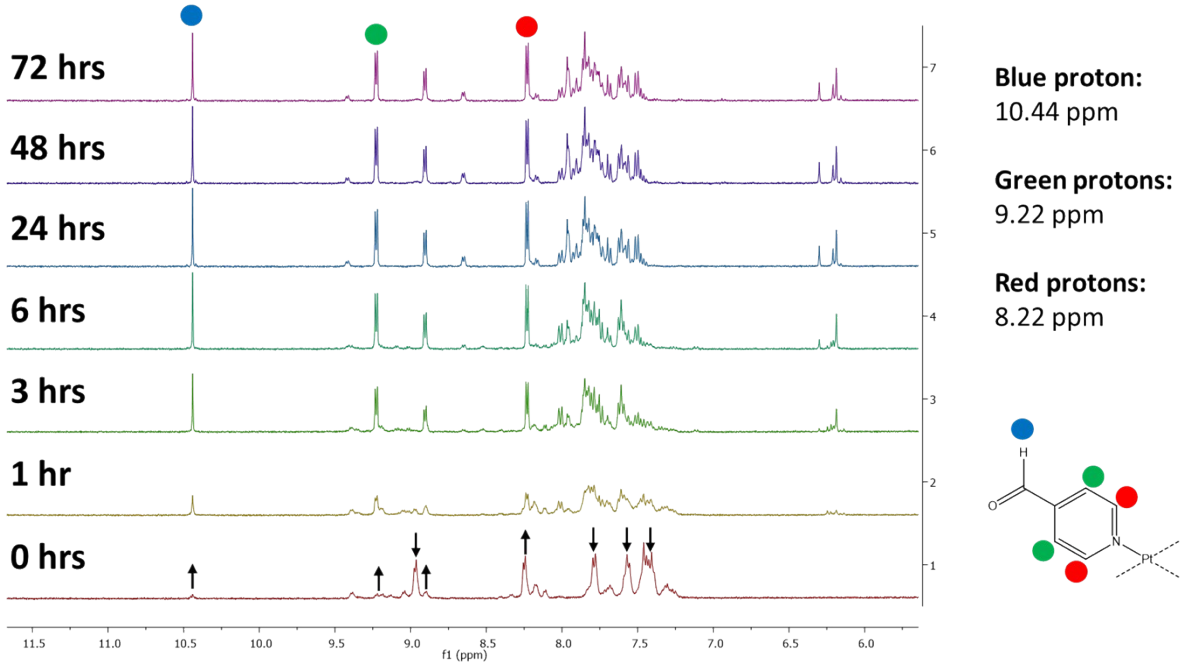


Figure S14. HR MS spectra (top is full spectrum and bottom zoomed in spectrum) of **2** (500 μM) in H_2O:DMSO (10:1) post 72 h incubation at 37 °C.

A.



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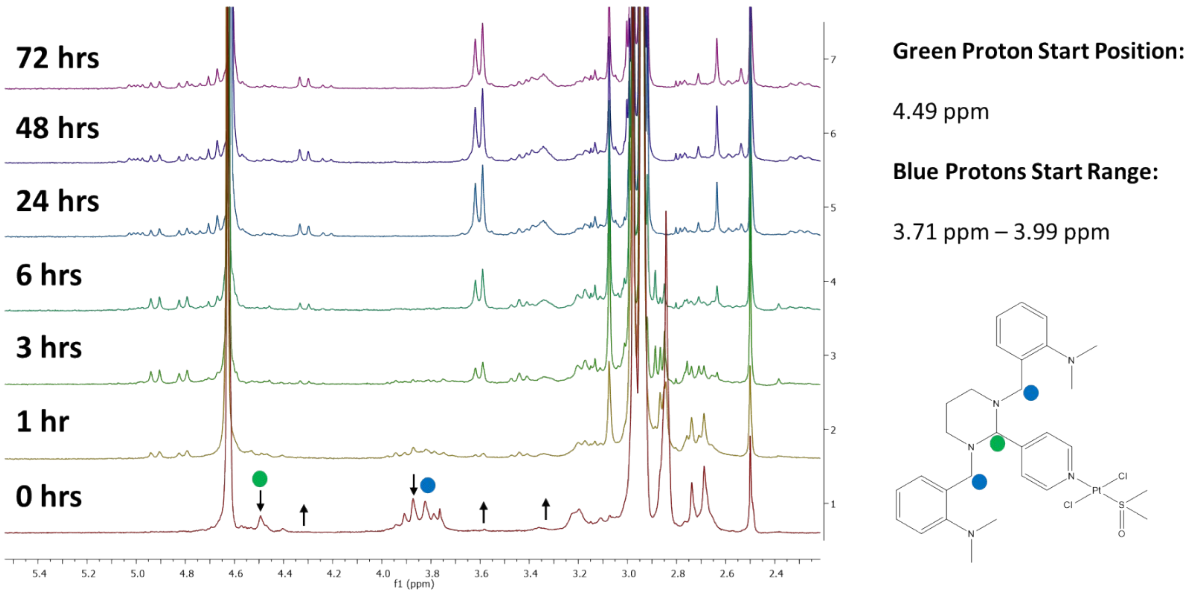

Figure S15. ^{1}H NMR study of **2** in D6-DMSO: D_2O (90:10) over 72 hours at 37°C. A. Aromatic region and B. Aliphatic region of the ^{1}H NMR spectrum.

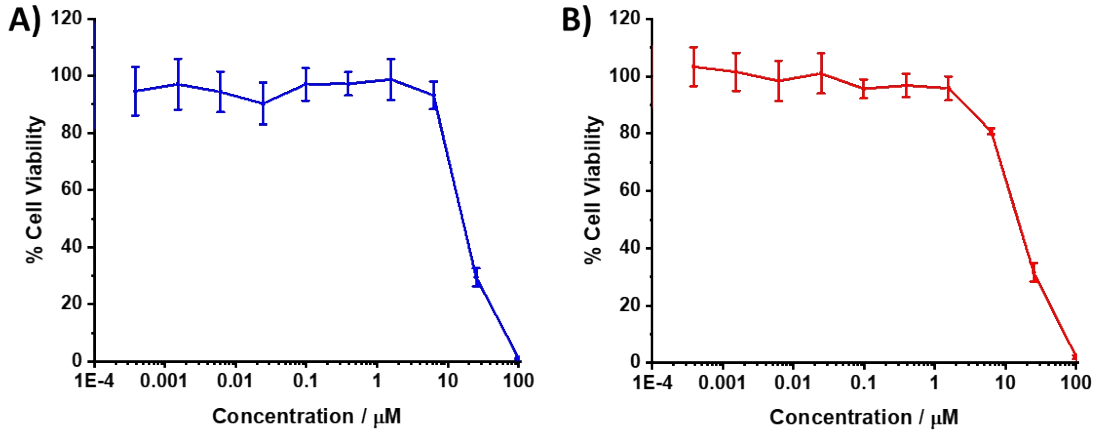

Figure S16. Representative dose-response curves for the treatment of (A) HMLER and (B) HMLER-shEcad cells with GANT61 after 72 h incubation.

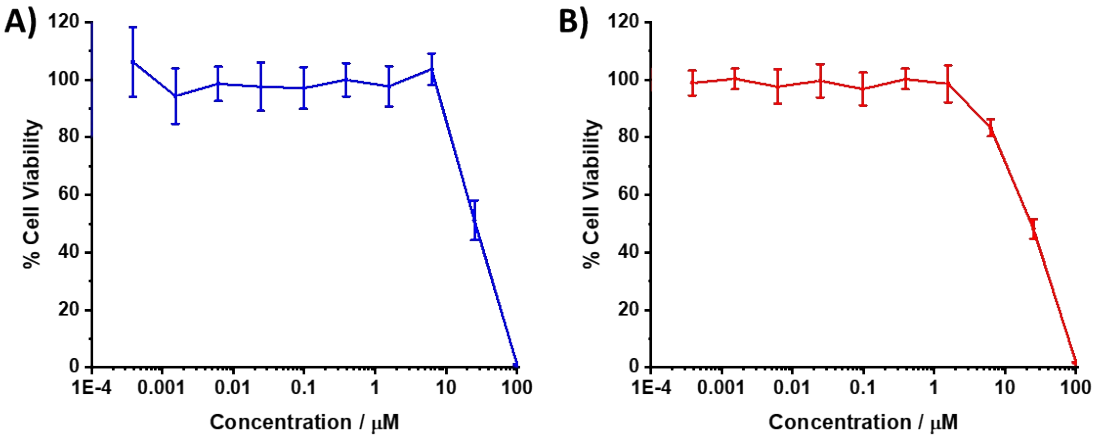

Figure S17. Representative dose-response curves for the treatment of (A) HMLER and (B) HMLER-shEcad cells with GANT61-D after 72 h incubation.

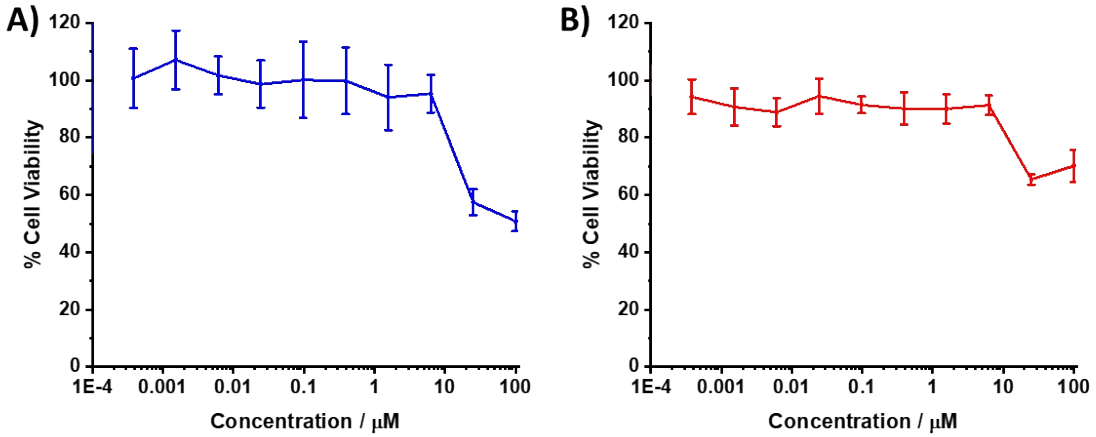

Figure S18. Representative dose-response curves for the treatment of (A) HMLER and (B) HMLER-shEcad cells with 4-PCA after 72 h incubation.

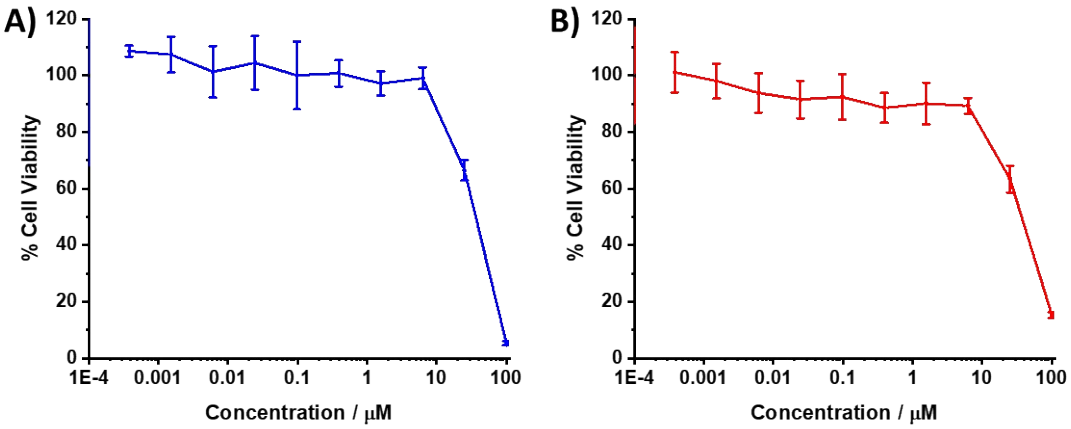

Figure S19. Representative dose-response curves for the treatment of (A) HMLER and (B) HMLER-shEcad cells with **1** after 72 h incubation.

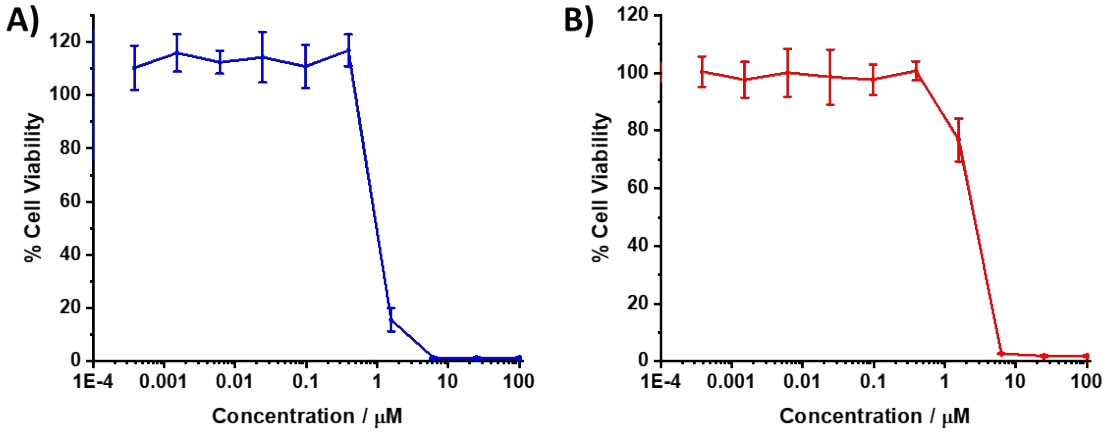

Figure S20. Representative dose-response curves for the treatment of (A) HMLER and (B) HMLER-shEcad cells with **2** after 72 h incubation.

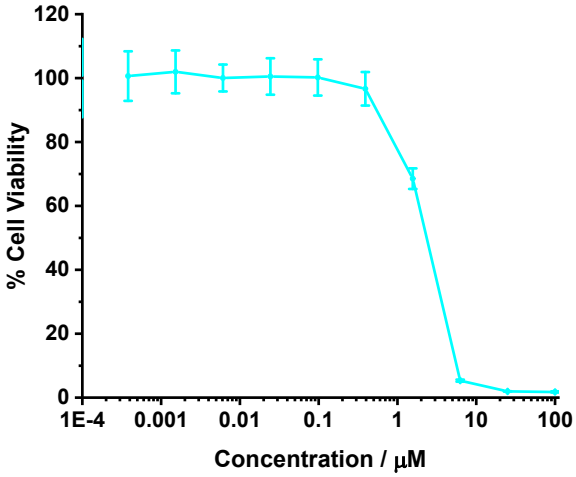

Figure S21. Representative dose-response curves for the treatment of MCF10A cells with **2** after 72 h incubation.

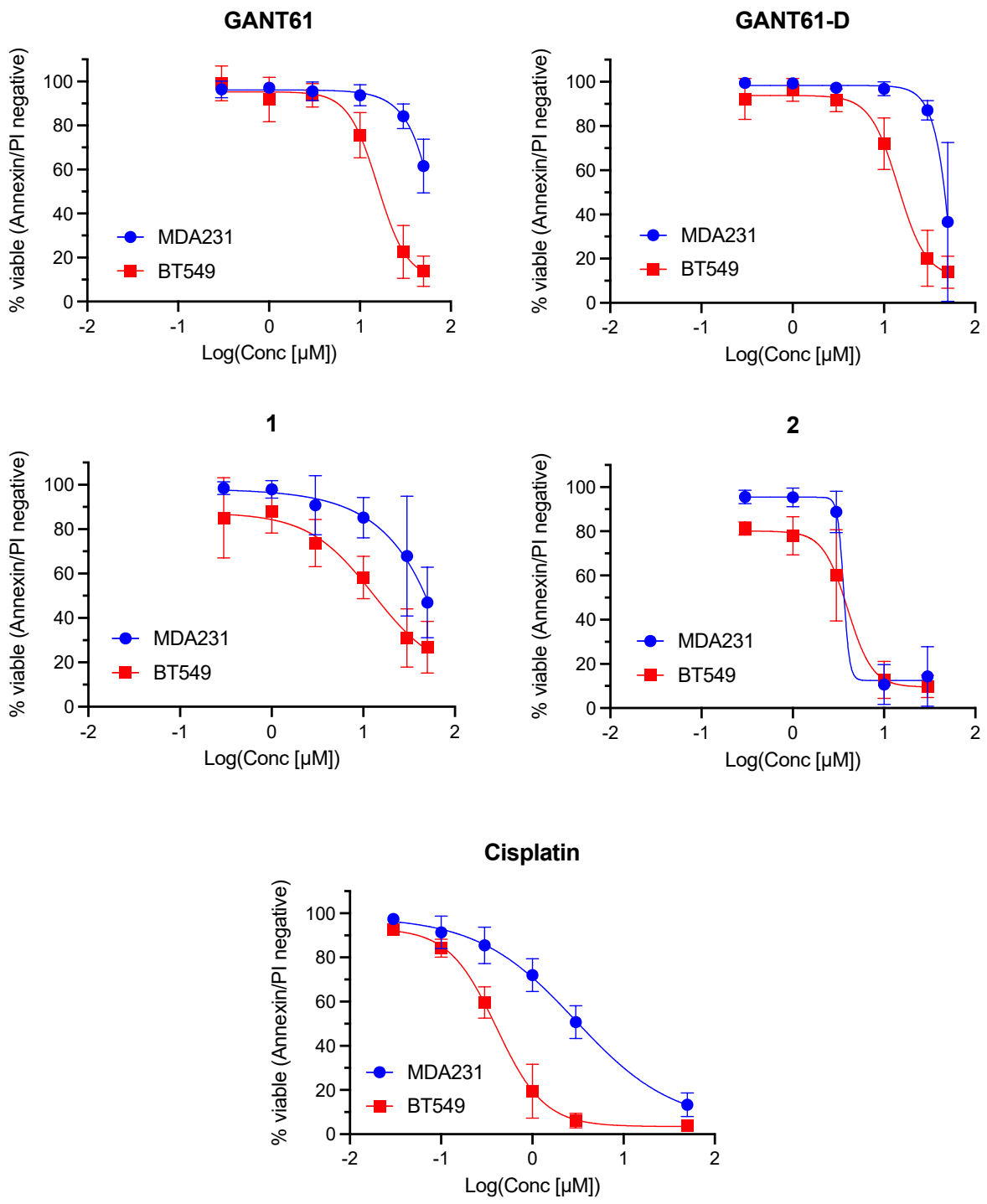

Figure S22. Annexin V-PI cell viability dose-response curves for the treatment of MDA231 (blue) and BT549 (red) cells with GANT61, GANT61-D, **1**, **2**, or cisplatin after 48 h incubation normalized to DMSO control. Data show mean ± SD (*n* = 3).