Supporting Information

Synthesis and Characterization Methods

A. Materials

Oligo(ethylene glycol) methyl ether acrylate (OEGA) with M_n = 480 g mol^{-1} (denoted as OEGA$_{480}$ where relevant) was purchased from Sigma-Aldrich and deinhibited by percolating over a column of basic alumina. 3-Vinylbenzaldehyde (VBA) was purchased from Sigma-Aldrich and passed through a column of basic alumina in order to remove inhibitor. Azobisisobutyronitrile (AIBN) and diacetone acrylamide (DAAM) were purified by recrystallization from methanol before use. Triethylamine (TEA), N,N'-methylenebis(acrylamide) (MBAA) and 2,2,2-trifluoroethanol (TFE) were purchased from Sigma-Aldrich at the highest purity available and were used as received. 3-(Benzyl sulfanyl thiocarbonyl sulfanyl)-propanoic acid (BSPA) and pentafluorophenyl acrylate (PFPA) were prepared according to previously reported procedures.[1,2] Slide-A-Lyzer® MINI Dialysis Devices (3.5 kD MWCO molecular weight cut off, 0.5 mL capacity) were purchased from Thermo Fisher Scientific™. Petroleum ether (b.p. 40 - 60 °C), diethyl ether, toluene, methanol, tetrahydrofuran, chloroform and dimethyl sulfoxide were purchased from Merck Millipore and used as received. All chemicals for the rhenium tricarbonyl complex were of reagent grade quality or better, and purchased from commercial vendors, and used without further purification. All preparations were carried out using standard Schlenk techniques.

B. Synthetic Methods

B.1 Synthesis of the rhenium tricarbonyl complex (Re-NH$_3$·Cl) (see Scheme S1)

Tert-butyl 4-(bis-((quinolin-2-yl)methyl)amino)butylcarbamate (**L**) and [NEt$_4$]$_2$[Re(CO)$_3$Br$_3$] were synthesized following previously reported procedures.[3-5] Re-NH$_3$·Cl complex was synthesized by using a modified literature procedure.[3] To a stirred suspension of [NEt$_4$]$_2$[Re(CO)$_3$Br$_3$] (600 mg, 0.78 mmol) in 30 mL of degassed methanol, L (305 mg, 0.64 mmol) was added and the mixture was refluxed at 70 °C for 4 h under N$_2$ atmosphere. The reaction mixture was evaporated to dryness. Et$_2$O (15 mL) was added to the residue and the mixture sonicated using an ultrasonic bath (5 min). The mixture was then centrifuged and the ether layer was decanted off. The procedure was repeated two more times and then the solid obtained was loaded on a silica column. Column chromatography using DCM/MeOH 10:1 as an eluent afforded the desired complex Re-NHBoc as light brown solid (yield: 362 mg, 69 %). The characterization data were in agreement with the literature report.[3] To a stirred solution of Re-NHBoc (300 mg, 0.36 mmol) in 20 mL MeOH, HCl in Et$_2$O (2 M, 20 mL) was added

slowly and the mixture was stirred for 12 h at room temperature. The solvent was removed, the resulted residue was washed with Et_2O (2 x 20 mL). The powder obtained was dissolved in the minimum amount of MeOH (ca. 2 mL) and precipitated using Et_2O (ca. 12 mL). The solid precipitation was isolated by centrifugation. This procedure was repeated two more times and the title compound $Re-NH_3 \cdot Cl$ was obtained as white solid (yield: 130 mg, 50 %). The characterization data were in agreement with the literature report.[3] The purity of the batch was confirmed by elemental analysis.   Anal. Calcd for $C_{27}H_{27}BrN_4ClO_3Re \cdot (HCl)_{1.5}$: C 39.93; H 3.54; N 6.90. Found: C 39.87; H 3.33, N 6.87.

B.2 Synthesis of POEGA (10K arm polymer)

The synthesis of POEGA was carried out using the following stoichiometry: $[BSPA]_0$:$[OEGA_{480}]_0$:$[AIBN]_0$=1:20:0.1. Briefly, $OEGA_{480}$ (4.00 g, 8.33 $\times$ 10^{-3} mol), CPBD RAFT agent (0.112 g, 4.11 $\times$ 10^{-4} mol), AIBN (6.75 mg, 4.11 $\times$ 10^{-5} mol) and toluene (8 mL) were placed in a glass vial equipped with a magnetic stirrer bar and capped with a rubber septum. The reaction mixture was deoxygenated for 25 min at 0 °C by sparging with N_2. The deoxygenated and sealed reaction vessel was placed into a pre-heated oil bath at 70 °C and the polymerization was run with stirring for 6 h. The resulting mixture was then allowed to cool to 0 °C for about 15 min to quench polymerization. The monomer conversion was determined by ^1H NMR. The polymer was purified of unreacted monomer by precipitating into diethyl ether three times. The product was then placed in a vacuum oven overnight to remove remaining solvent. The final product was analysed by ^1H NMR and GPC. The molecular weight and average chain length calculated from ^1H NMR were determined to be 9551 g mol^{-1} and 19 units of OEGA, respectively. The polydispersity index (determined by GPC) was 1.10

B.3 Synthesis of Star polymer POEGA-Star -VBA

The synthesis of star polymer POEGA-Star-VBA was carried out using the following stoichiometry: $[POEGA]_0$:$[MBAA]_0$:$[VBA]_0$:$[AIBN]_0$=1:8:10:0.3. POEGA (0.50 g, 5.24 $\times$ 10^{-5} mol), MBAA (0.06 g, 4.18 $\times$ 10^{-4} mol), AIBN (2.57 mg, 1.56 $\times$ 10^{-5} mol), VBA (0.06 g, 5.22$\times$ 10^{-4} mol) and toluene (5 mL) were added to a glass vial equipped with a magnetic stirrer bar and capped with a rubber septum. The reaction mixture was deoxygenated for 30 min by sparging with N_2. The deoxygenated and sealed reaction vessel was placed into a pre-heated oil bath at 70 °C and the polymerisation was run with stirring for 24 h. The resulting mixture was then allowed to cool to 0 °C for about 15 min to halt polymerisation. The polymer was purified via three precipitation and centrifugation steps (using a mixture of petroleum ether (bp

40-60 °C) and tetrahydrofuran as the precipitant) to remove any traces of unreacted cross-linker, arm polymer and VBA monomer. The product was then placed in a vacuum oven overnight to remove residual solvent. The final composition of the product was analysed by ^{1}H NMR, giving 23.5/76.5 mol % in VBA and OEGA respectively. The polydispersity index determined by GPC was 1.14.

B.4 Synthesis of Star polymer POEGA-Star-DAAM

The synthesis of Star polymer POEGA-Star-DAAM was carried out using the following stoichiometry: $[POEGA]_0:[MBAA]_0:[DAAM]_0:[AIBN]_0=1:8:10:0.3$. POEGA (0.50 g, 5.24 × 10^{-5} mol), MBAA (0.06 g, 4.18 × 10^{-4} mol), AIBN (2.57 mg, 1.56 × 10^{-5} mol), DAAM (0.10 g, 5.84× 10^{-4} mol) and toluene (5 mL) were added to a glass vial equipped with a magnetic stirrer bar and capped with a rubber septum. The reaction mixture was deoxygenated for 30 min by sparging with N_2. The deoxygenated and sealed reaction vessel was placed into a pre-heated oil bath at 70 °C and the polymerisation was run with stirring for 24 h. The resulting mixture was then allowed to cool to 0 °C for about 15 min to halt polymerisation. The polymer was purified via three precipitation and centrifugation steps (using a mixture of petroleum ether (bp 40-60 °C) and tetrahydrofuran as the precipitant) to remove any traces of unreacted cross-linker, arm polymer and DAAM monomer. The product was then placed in a vacuum oven overnight to remove residual solvent. The final composition of the product was analysed by ^{1}H NMR, giving 37.4/62.6 mol % in DAAM and OEGA respectively. The polydispersity index determined by GPC was 1.15.

B.5 Synthesis of Star polymer POEGA-Star-PFPA

The synthesis of Star polymer POEGA-Star-PFPA was carried out using the following stoichiometry: $[POEGA]_0:[MBAA]_0:[PFPA]_0:[AIBN]_0=1:8:10:0.3$. POEGA (0.50 g, 5.24 × 10^{-5} mol), MBAA (0.06 g, 4.18 × 10^{-4} mol), AIBN (2.57 mg, 1.56 × 10^{-5} mol), PFPA (0.12 g, 5.23 × 10^{-4} mol) and toluene (5 mL) were added to a glass vial equipped with a magnetic stirrer bar and capped with a rubber septum. The reaction mixture was deoxygenated for 30 min by sparging with N_2. The deoxygenated and sealed reaction vessel was placed into a pre-heated oil bath at 70 °C and the polymerisation was run with stirring for 24 h. The resulting mixture was then allowed to cool to 0 °C for about 15 min to halt polymerisation. The polymer was purified via three precipitation and centrifugation steps (using a mixture of petroleum ether (bp 40-60 °C) and chloroform as the precipitant) to remove any traces of unreacted cross-linker, arm polymer and PFPA monomer. The product was then placed in a vacuum oven overnight

to remove residual solvent. The final composition of the product determined by ^{1}H NMR and ^{19}F NMR is equal to 31.0/69.0 mol % in PFPA and OEGA using TFE as a reference peak, which calculation was reported in previous paper.[6] The polydispersity index determined by GPC was 1.13

B.6 Post-modification of POEGA-Star-VBA with Re-NH$_3$·Cl (Star 1)

POEGA-Star-VBA prepared as above (B.3) (0.01 g,) was dissolved in DMSO (500 μL). Re-NH$_3$·Cl (14.7 mg, 2.06×10^{-5} mol) and triethylamine (3.16 μL, 2.27×10^{-5} mol) were added into the solution with stirring and allowed to react at room temperature for 72 h. The purification process was conducted overnight to ensure removal of the excess amount of Re-NH$_3$·Cl and TEA by dialysis against water (pH 8-9), and the resulting polymer was dried under air and in vacuo, and then analysed by ^{1}H NMR spectroscopy to confirm the purity. The final Re concentration in the conjugates was determined using ICP-MS (Inductively coupled plasma mass spectrometry), giving 7.41 wt % (Expected value is 7.73 wt %).

B.7 Post-modification of POEGA-Star-DAAM with Re-NH$_3$·Cl (Star 2)

POEGA-Star-DAAM prepared as above (B.4) (0.01 g,) was dissolved in DMSO (500 μL). Re-NH$_3$·Cl (25.6 mg, 3.59×10^{-5} mol) and triethylamine (5.5 μL, 3.95×10^{-5} mol) were added into the solution with stirring and allowed to react at room temperature for 96 h. The purification process was conducted overnight to ensure removal of the excess amount of Re-NH$_3$·Cl and TEA by dialysis against water (pH 8-9), and the resulting polymer was dried under air and in vacuo, and then analysed by ^{1}H NMR spectroscopy to confirm the purity. The final Re concentration in the conjugates was determined using ICP-MS (Inductively coupled plasma mass spectrometry), giving 11.80 wt % (Expected value is 11.03 wt %).

B.8 Post-modification of POEGA-Star-PFPA) with Re-NH$_3$·Cl (Star 3)

POEGA-Star-PFPA) prepared as above (B.5) (0.01 g,) was dissolved in DMSO (500 μL). Re-NH$_3$·Cl (19.1 mg, 2.68×10^{-5} mol) and triethylamine (4.11 μL, 2.95×10^{-5} mol) were added into the solution with stirring and allowed to react at room temperature for 72 h. The purification process was conducted overnight to ensure removal of the excess amount of Re-NH$_3$·Cl, TEA and side products by dialysis against water, and the resulting polymer was dried under air and in vacuo, and then analysed by ^{1}H NMR and ^{19}F NMR spectroscopy to confirm the purity. The final Re concentration in the conjugates was determined using ICP-MS

(Inductively coupled plasma mass spectrometry), giving 9.78 wt % (Expected value is 9.21 wt %).

C. Analysis Methods

C.1 ^1H, ^{13}C and ^{19}F Nuclear Magnetic Resonance Spectroscopy

^1H, ^{13}C and ^{19}F NMR spectra were recorded at 400 and 500 MHz on a Bruker UltraShield 7 running Bruker Topspin, version 1.3. Spectra were recorded in C_2D_6SO and $CDCl_3$.

C.2 Elemental microanalyses and Mass spectrometry

Elemental microanalyses were obtained on a LecoCHNS-932 elemental analyser. Mass spectra was measured using a Bruker Daltonics HCT 6000 mass spectrometer.

C.3 Gel Permeation Chromatography (GPC)

GPC was performed using a Shimadzu modular system comprised of a SIL-20AD automatic injector, a RID-10A differential refractive-index detector and a 50 × 7.8 mm guard column followed by three KF-805L columns (300 × 8 mm, bead size: 10 μm, pore size maximum: 5000 Å). N,N'-Dimethylacetamide (DMAc, HPLC grade, 0.03% w/v LiBr) at 50 °C was used for the analysis with a flow rate of 1 mL min-1 . Samples were filtered through 0.45 μm PTFE filters before injection. The GPC calibration was performed with narrow-polydispersity polystyrene standards ranging from 500 to $2 × 10^6$ g mol^{-1}.

C.4 Dynamic Light Scattering (DLS)

DLS measurements were carried out on a Malvern Zetasizer Nano ZS Series running DTS software (laser, 4 mW, λ = 633 nm; angle 173°). The polydispersity index (PDI), used to describe the average diameters and size distribution of prepared micelles, was determined via a cumulants analysis of the measured intensity autocorrelation function using the DTS software. Samples were filtered using 0.45 μm PTFE syringe filter to remove contaminants / dust prior to measurement.

C.5 Inductively coupled plasma mass spectrometry (ICP-MS)

Rhenium content in the star polymer conjugates was determined by inductively coupled plasma mass spectrometry (ICP-MS) using a Perkin-Elmer OPTIMA 7300 spectrometer. For cellular uptake, the rhenium content was measured using an Agilent QQQ 8800 Triple quad ICP-MS

spectrometer (Agilent Technologies) with an ASX200 autosampler (Agilent Technologies), equipped with standard nickel cones and a "micro-mist" quartz nebulizer fed with 0.3 ml/min analytic flow.

C.6 Transmission Electron Microscopy (TEM)

The core cross linked star polymers were observed by transmission electron microscopy (TEM), taking micrographs on a Tecnai F20 electron microscope (Advanced Microscopy Facility at the Bio21 Advanced Microscopy Facility, The University of Melbourne) at an accelerating voltage of 200 kV at ambient temperature. An aliquot (5 µL) of 0.5 wt% star polymer solution (in MiliQ water) was placed on a Formvar coated copper grid (GSCu100F-50, Proscitech) and dried in air at ambient temperature overnight before TEM imaging.

C.7 UV-vis spectrophotometry

UV-Vis spectra were acquired on a Shimadzu UV-3600 UV-VIS-NIR spectrophotometer using quartz cuvettes with 10 mm path length.

C.8 Release profile (%) of Re-NH_2 from the star polymers in different pH conditions (pH 7.4 and 5).

Release profile (%) of Re-NH_2 from the star polymers was examined in different pH conditions (pH 7.4 and 5), using UV-visible spectrophotometry. 3.05 mg of Re-NH_2 conjugated POEGA-Star-VBA (Star **1**) was dissolved in PBS (0.5 mL) pH 7.4 and 5.0 respectively. 0.5 mL of each PBS solution was then placed in the cap of Slide-A-Lyzer MINI Dialysis Device 15 mL, 3.5K MWCO (0.5 mL capacity), which then added into the conical tube of the dialysis device containg 14 mL PBS pH 7.4 or5.0 respectively. The mixture was shaken in the incubator at 37 °C. The release study was performed under sink conditions. At defined time points, 0.5 mL of the soultion in the conical tube of the dialysis device was taken out and measured by UV-vis (320 nm). To keep constant the total volume of solution, 0.5 mL of the measured solution was back added into the sample. The total amount of releasable Re-NH_2 was determined by adjusting the pH to between pH 0-1.

3.8 mg of Re-NH_2 conjugated POEGA-Star-DAAM (Star **2**) was dissolved in PBS (0.5 mL) at pH 7.4 or 5.0. 0.5 mL of each PBS solution was then placed in the cap of Slide-A-Lyzer MINI Dialysis Device 15 mL, 3.5K MWCO (0.5 mL capacity), which was then added into the conical tube of the dialysis device containing 14 mL PBS pH at 7.4 or 5.0as appropriate. The mixture

was shaken in the incubator at 37 ℃. The release study was performed under sink conditions. At defined time points, 0.5 mL of the soultion in the conical tube of the dialysis device was taken out and measured by UV-vis (320 nm). To keep constant the total volume of solution, 0.5 mL of the measured solution was added back into the sample. The total amount of releasable Re-NH$_2$ complex was determined by adjusting the pH to between pH 0-1.

4.5 mg of Re-NH$_2$ conjugated POEGA-Star-PFPA (Star **3**) was dissolved in PBS (0.5 mL) at pH 7.4 or 5.0. 0.5 mL of each PBS solution was then placed in the cap of Slide-A-Lyzer MINI Dialysis Device 15 mL, 3.5K MWCO (0.5 mL capacity), which was then added into the conical tube of the dialysis device containg 14 mL PBS at pH 7.4 5.0 respectively. The mixture was shaken in the incubator at 37 ℃. The release study was performed under sink conditions. At defined time points, 0.5 mL of the solution in the conical tube of the dialysis device was taken out and measured by UV-vis (320 nm). To keep constant the total volume of solution, 0.5 mL of the measured solution was back added into the sample.

C.9 Cell lines and cell culture conditions

HeLa (human cervical cancer) cells were grown in DMEM (Gibco) supplemented with 10% fetal bovine serum (FBS, Gibco) and 1% penicillin/streptomycin. MRC5 (non-cancerous lung fibroblast) cells were maintained in F-10 medium (Gibco) supplemented with 10% FBS (Gibco) and 1% penicillin/streptomycin. All cells were cultured at 37 ℃ in a humidified atmosphere containing 5% CO$_2$.

C.10 Cell culture irradiation,

Cells were irradiated with a Rayonet RPR-200 photochemical reactor with 6 bulbs (14 W each) with maximum intensity output at 350 nm.

C.11 Cytotoxicity and phototoxicity assays

The cytotoxicity of Re-NH$_2$ conjugated star polymers (Star **1**, Star **2** and Star **3**) against HeLa and MRC-5 cells in the presence or absence of UV irradiation was measured using a resazurin-based fluorometric cell viability assay (Promocell GmbH) . In 96-well plates, Hela cells (at a density of 4 x 10^3 cells per well) and MRC-5 cells (at a density of 7 x 10^3 cells per well) were seeded in triplicate in 100 µL medium 24 h prior to treatment. The following day, cells were treated with increasing concentrations of compounds. For this purpose, freshly prepared stocks (suspensions of 5 mM in PBS) of the Re-NH$_3$·Cl and Re-NH$_2$ conjugated star polymers (Star

1, Star **2** and Star **3**) were diluted using the respective cell culture media and 100 µL was added to each well (total volume 200 µL/well).

For evaluation of cytotoxicity, cells were incubated with Re-NH$_3$·Cl or the stars for 48 h before the medium was replaced by 100 µL complete medium containing resazurin (0.2 mg/mL). After 4 h of incubation, fluorescence of the highly fluorescent resorufin metabolite at 580 nm emission was quantified using a SpectraMax M5 microplate reader (Molecular Devices, LLC.) with an excitation wavelength of 540 nm.

To assess phototoxicity, cells were treated with increasing concentrations of Re-NH$_3$·Cl and the stars for 4 h only. After that, the medium was removed and replaced by fresh complete medium and either kept in the dark or irradiated for 10 min with 350 nm UVA (2.58 J cm^{-2}). Cells were then returned to the incubator for an additional 44 h. After incubation, the viability was quantified using the resazurin assay as described above. The resorufin fluorescence intensities were normalized to untreated control wells and plotted as concentration of test compound versus % cell viability. IC$_{50}$ values were interpolated from the resulting dose-dependence curves. The reported IC$_{50}$ values are the average from at least three independent experiments.

C.12 Fluorescence microscopy imaging

Cellular uptake as well as intracellular localization of Re-NH$_3$·Cl and the Re-NH$_3$·Cl conjugated star polymers (Star **1**, Star **2** and Star **3**) were assessed using fluorescence microscopy. HeLa cells were seeded in 1 mL medium on Menzelgläser coverslips at a density of 1 x 10^5 cells per mL and incubated for 24 h. The next day, the media was replaced with 1 mL fresh media containing 50 µM of Re-NH$_3$·Cl or the stars (50 µM with respect to Re), and incubated for 9 h. Media was then aspirated, and the cells were washed with 1 mL (x 3) with PBS. Cells were then fixed by treatment with 4% formaldehyde solution in PBS for 5 min at room temperature. The coverslips were mounted on slides for viewing by confocal microscopy on a CLSM Leica SP5 microscope. The rhenium complexes were excited at 405 nm, and the emission between 450 and 550 nm was recorded.

C.13 Cellular uptake quantification using ICP-MS

Treatment and subcellular fractionation of cells.

HeLa cells (0.5 million in 12 mL medium) were seeded on 100 mm x 20 mm petri dishes and incubated for 48 h at 37 ^{0}C. When the cells reached ca. 70-80% confluency, the medium was aspirated and 10 mL of fresh medium containing 30 µM of Re-NH$_3$·Cl and the Re-NH$_2$ conjuated star polymers (Star **1**, Star **2** and Star **3**) was added and incubated for 4 h at 37 ^{0}C. The medium was removed, cells were washed with PBS (3 x 8 mL), harvested by trypsinization (0.8 mL), collected and counted using a hemocytometer. Cells were then spun down (2000 rpm, 7 min) and the pellet was resuspended in 1.5 mL PBS and transferred to a 2 mL eppendorf tube and centrifuged (2000 rpm, 7 min) and supernatant was aspirated. The pellet was used for cytosolic and nuclear fractionation of cells following a previously reported REAP protocol.[7,8] Briefly, 1 mL of ice cold 0.1% NP40 in PBS was added to the cell pellet (on ice) and triturated using a p1000 micropipette for 5 times. An aliquot (300 µL) was removed as "whole cell lysate" which was used for quantifying whole cell uptake. The remaining lysate was centrifuged at maximum speed 14800 rpm for 1 min at 4 °C. 300 µL of supernatant was collected in a new Eppendorf tube as the "cytosolic fraction" and the rest aspirated carefully. The pellet was resuspended in 1 mL of ice cold 0.1% NP40 in PBS and centrifuged at maximum speed for 1 min at 4 °C. The supernatant was decanted and the pellet was kept as the "nuclear fraction". The experiment was performed in triplicate.

Sample preparation and ICP-MS measurements.

For digestion, 300 µL of 60% ICP-MS grade HNO$_3$ was added to the whole cell lysate, cytosolic fraction and nuclear fraction and kept at room temperature for 5 days. The solutions were then diluted to a final volume of 3.3 mL using MilliQ water, and filtered using a 0.4 µm syringe filter. The rhenium content in each fraction was measured using an Agilent QQQ 8800 Triple quad ICP-MS spectrometer (Agilent Technologies) with an ASX200 autosampler (Agilent Technologies), equipped with standard nickel cones and a "micro-mist" quartz nebulizer fed with 0.3 ml/min analytic flow. The amount of Re was normalized to number of cells in the pellet.
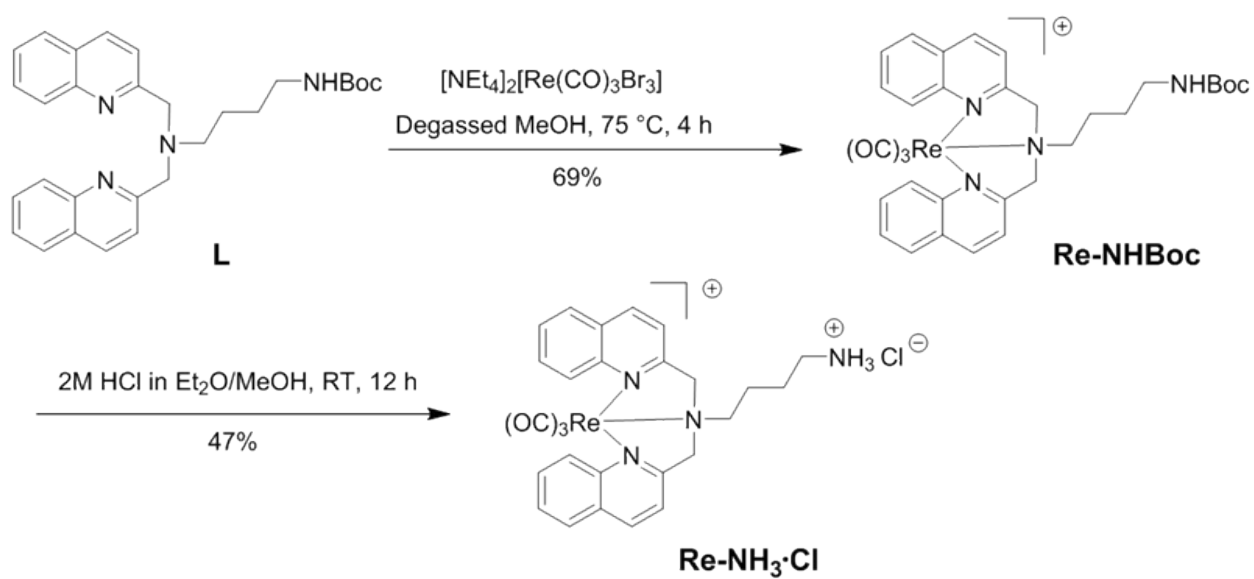
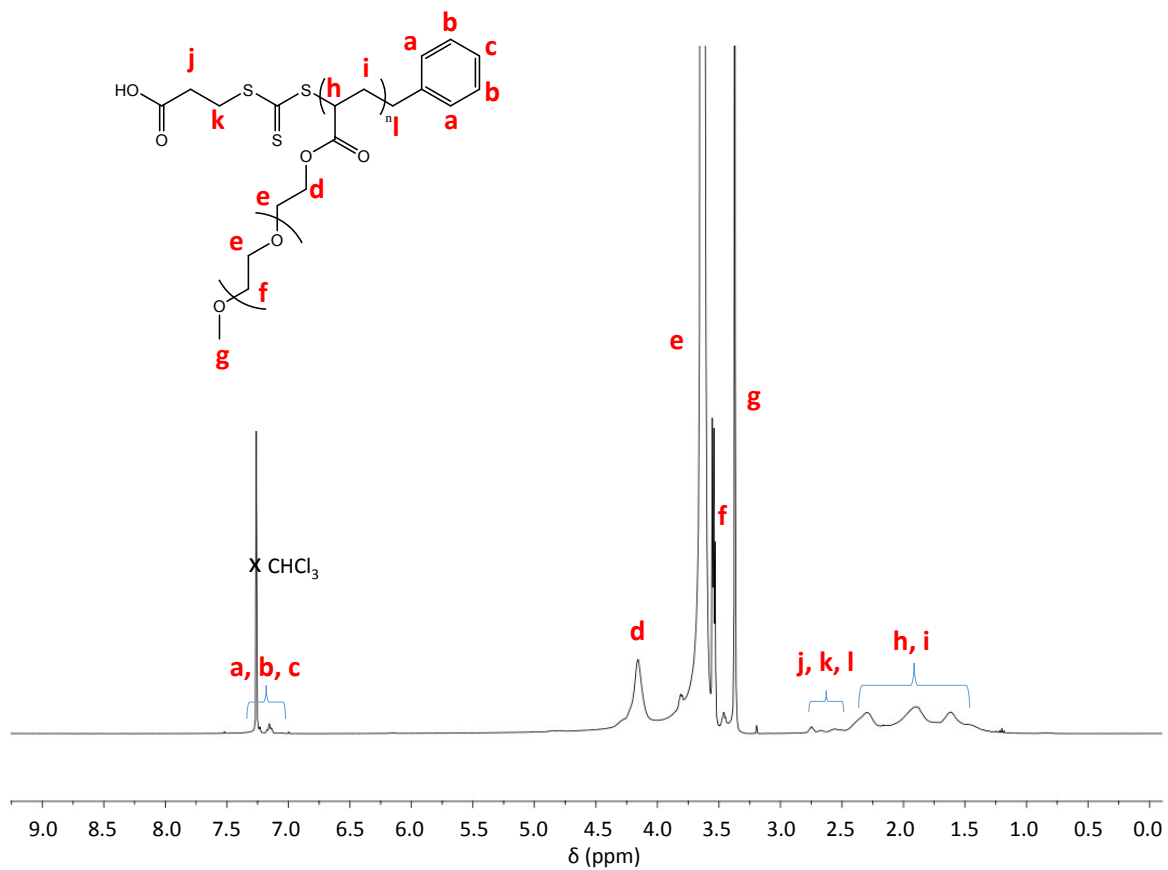Scheme S1. Synthesis of the rhenium tricarbonyl complex (Re-NH$_3$·Cl).

Figure S1. ^{1}H NMR spectrum of POEGA ($M_n = 9551$ g mol^{-1}, 19 units of OEGA), recorded in CDCl$_3$ (400 MHz).
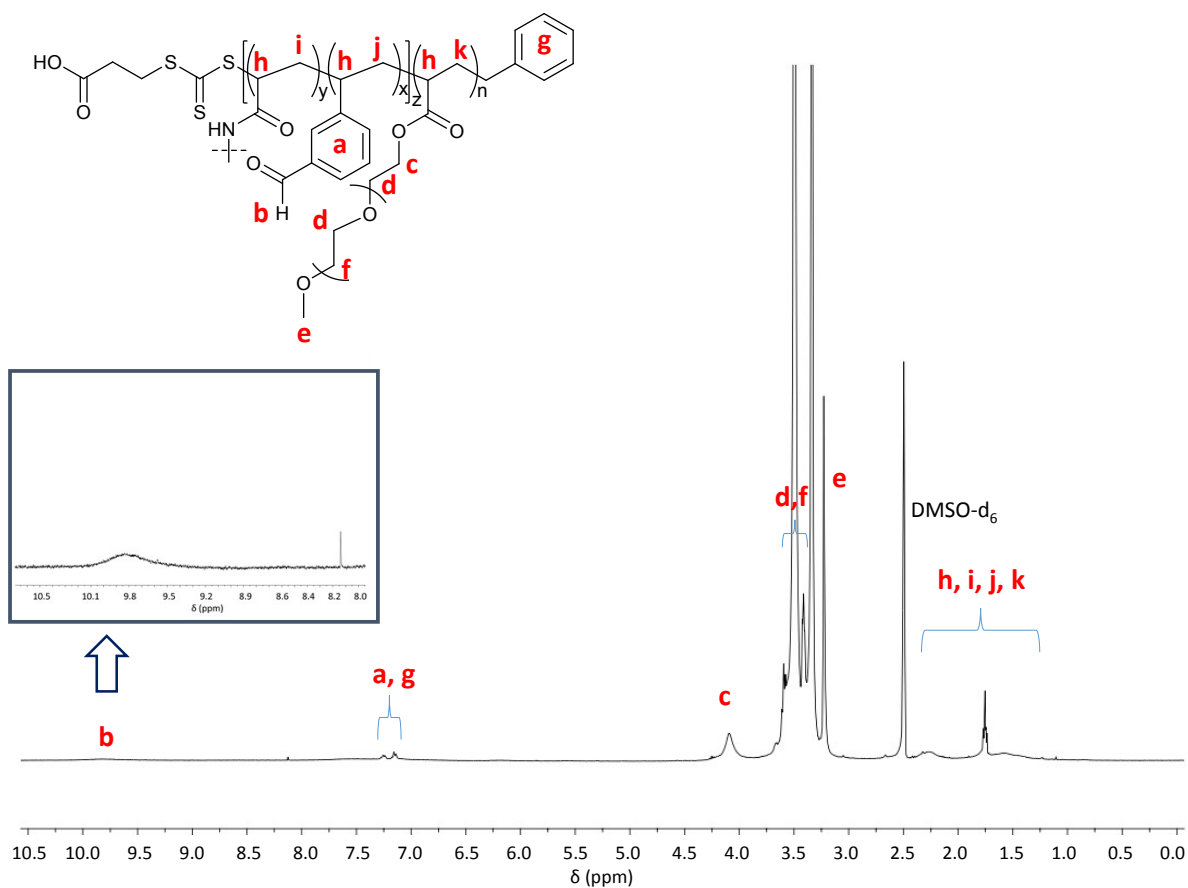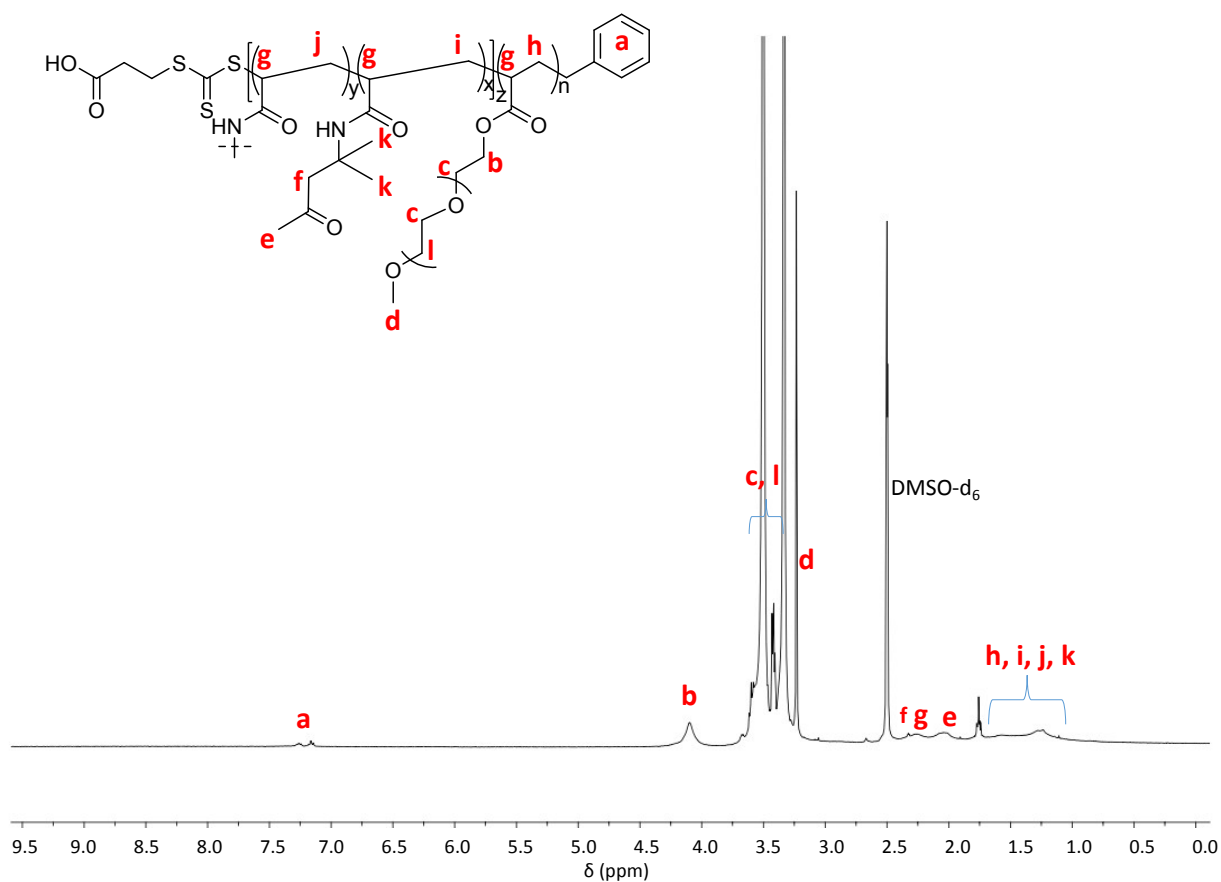
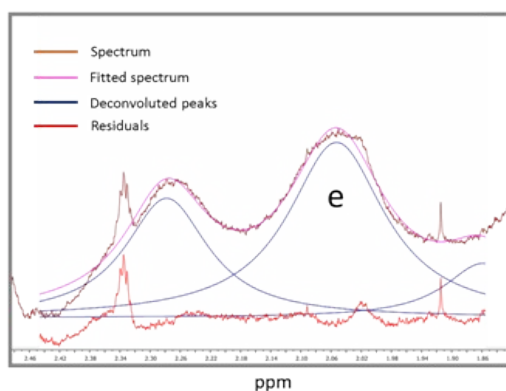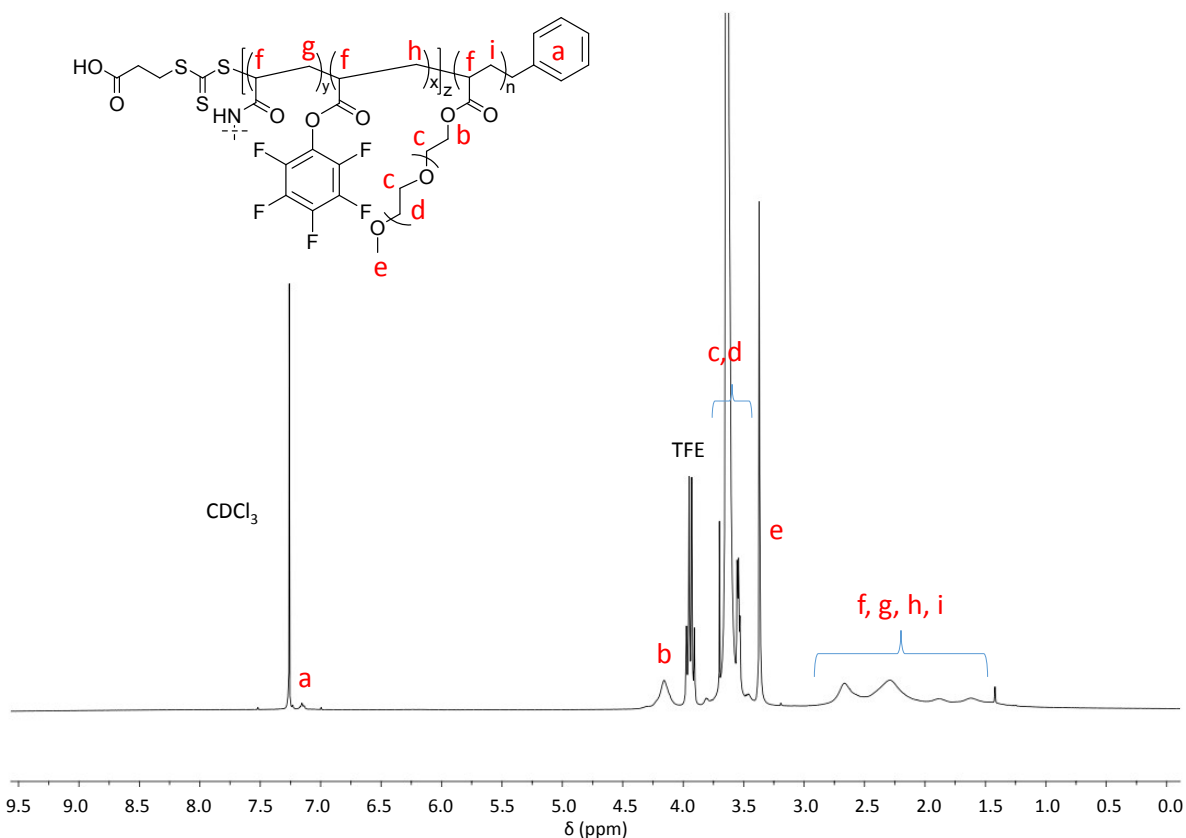Figure S2. ^{1}H NMR spectrum of POEGA-Star-VBA containing VBA in the core, recorded in DMSO-d$_6$ (400 MHz).

The final composition of the product was analysed by ^{1}H NMR, giving 23.5/76.5 mol % in VBA and OEGA respectively.

In the ^{1}H NMR

$FVBA:FOEGA = (I_{9.75ppm}/1):(I_{4.1ppm}/2)$

Figure S3. ^{1}H NMR spectrum of POEGA-Star-DAAM containing DAAM in the core, recorded in DMSO-d_6 (400 MHz).

The final composition of the product was analysed by ^{1}H NMR, giving 37.4/62.6 mol % in DAAM and OEGA respectively.

Briefly:

In the ^{1}H NMR

$$FDAAM:FOEGA = (I_{2.06ppm}/3):(I_{4.1ppm}/2)$$

$I_{2.06ppm}$ was estimated from a spectral deconvalution performed via MestReNova software package as per the below:

Figure S4. ^{1}H NMR spectrum of POEGA-Star-PFPA containing PFPA in the core, recorded in CDCl$_3$ (400 MHz).

The final composition of the product determined by ^{1}H NMR and ^{19}F NMR is equal to 31.0/69.0 mol % in PFPA and OEGA using TFE as a reference peak, which calculation was reported in previous paper and shown in Figure S5 below.[6,9]
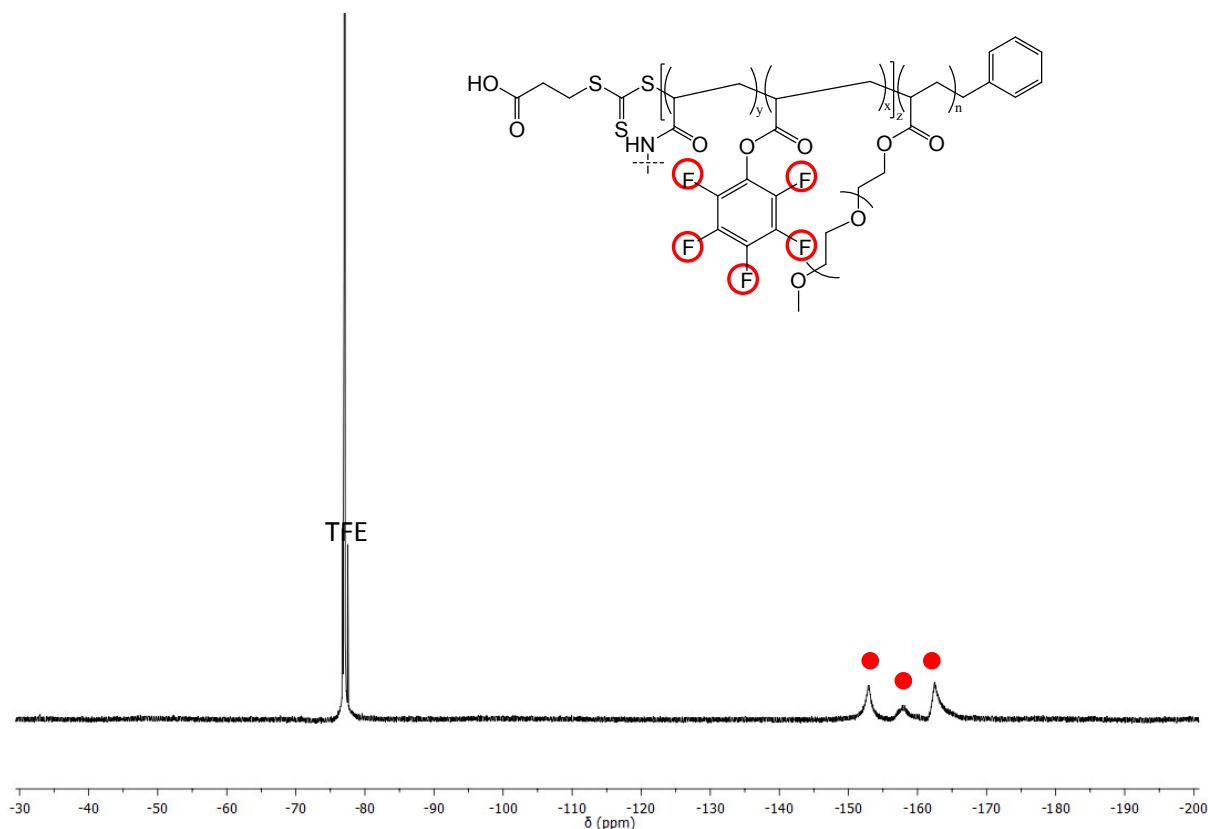
Figure S5. ^{19}F NMR spectrum of POEGA-Star-PFPA containing PFPA in the core, recorded in CDCl$_3$ (400 MHz).

The final composition of the product determined by ^{1}H NMR and ^{19}F NMR is equal to 31.0/69.0 mol % in PFPA and OEGA using TFE as a reference peak. The calculation used was reported in a previous paper[6,9], briefly:

In the ^{1}H NMR

FOEGA:FTFE= $(I_{3.3ppm}/3):(I_{3.8-4.0ppm}/2)$

In the ^{19}F NMR

FPFPA:FTFE= $[(I_{-152ppm} + I_{-158ppm} + I_{-163ppm})/5]:(I_{-78ppm}/3)$

Therefore, by using this reference peak TFE, these two monomers, PFPA and OEGA can be compared. The molar composition can be calculated as follows;

[FPFPA:FTFE/(FOEGA:FTFE + FOEGA:FTFE)] : [FOEGA:FTFE/(FOEGA:FTFE + FOEGA:FTFE)]

= 31.0 : 69.0 mol % in PFPA and OEGA .
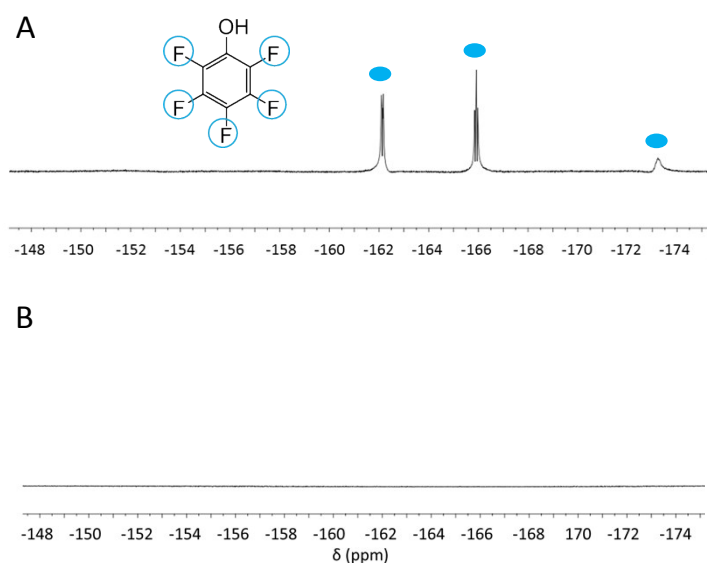
Figure S6. ^{19}F NMR spectra of A) POEGA-Star-PFPA star polymer after attachment of Re-NH$_2$ and B) Purified Re-NH$_2$ conjugated POEGA-Star-PFPA star polymer (Star **3**) after the reaction, recorded in DMSO-d$_6$

Note: ^{19}F NMR analysis confirmed that the reaction between Re-NH$_2$ and PFP group was selective and quantitative; Once the reaction was occurred, the side product, pentafluorophenol was released, which was confirmed by ^{19}F NMR. The three signals from PFPA in star polymer (Figure S5) were shifted to -162, -166 and -174 ppm, corresponding to pentafluorophenol (A). This also confirmed that all reaction was fully completed. After purification, no more side product pentafluorophenol was observed, which was also confirmed from ^{19}F NMR spectrum (no more peaks observed) (B).
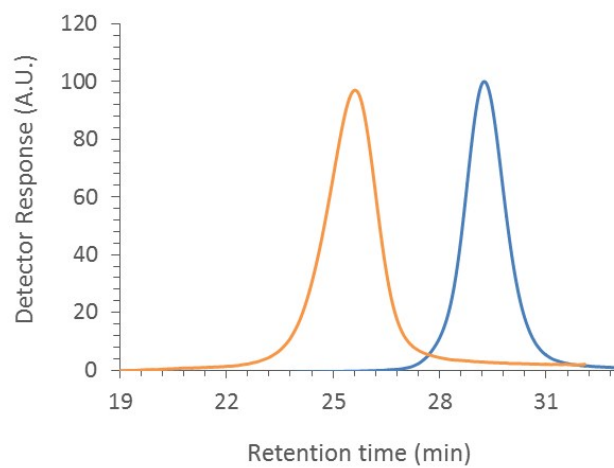
Figure S7. GPC chromatograms for POEGA (10K arm polymer) (blue line) and POEGA-Star-VBA (orange line).
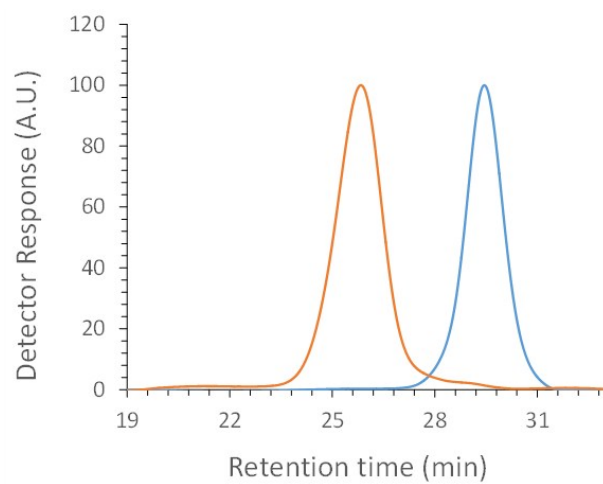
Figure S8. GPC chromatograms for POEGA (10K arm polymer) (blue line) and POEGA-Star-DAAM (orange line).
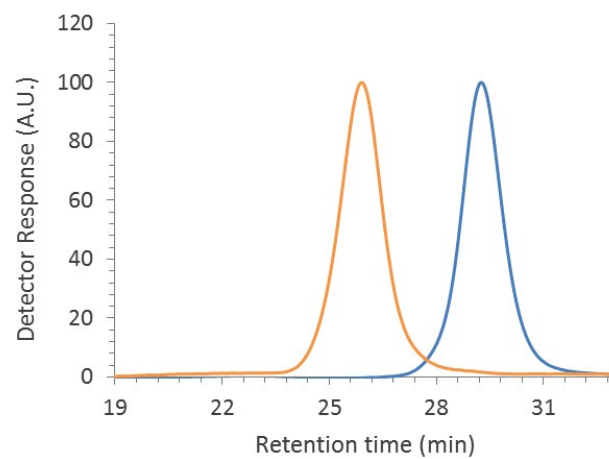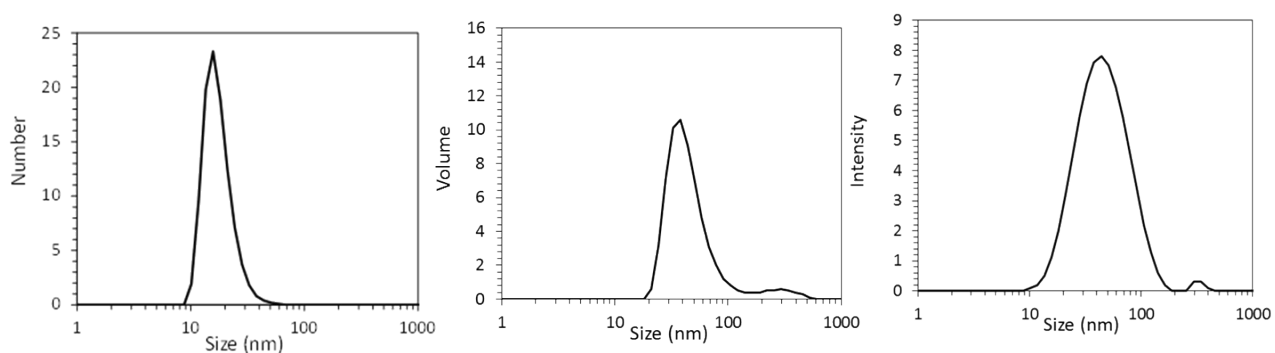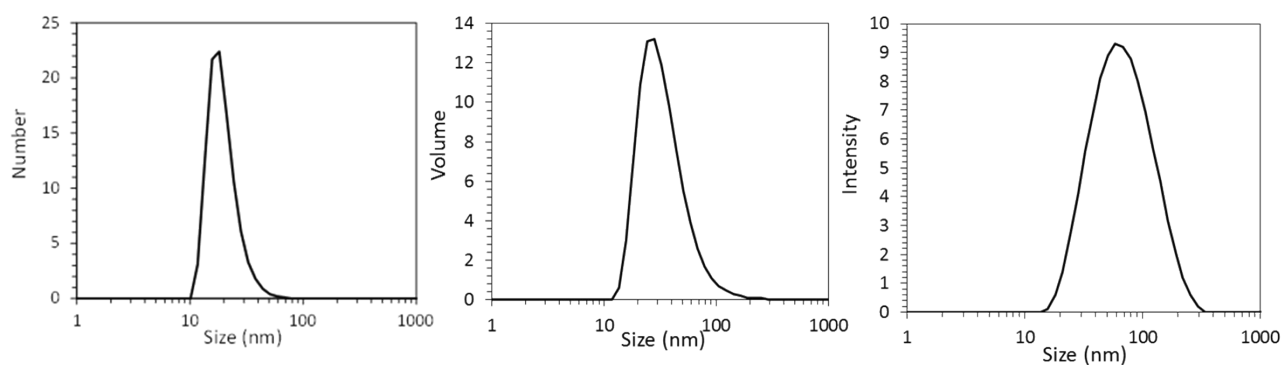
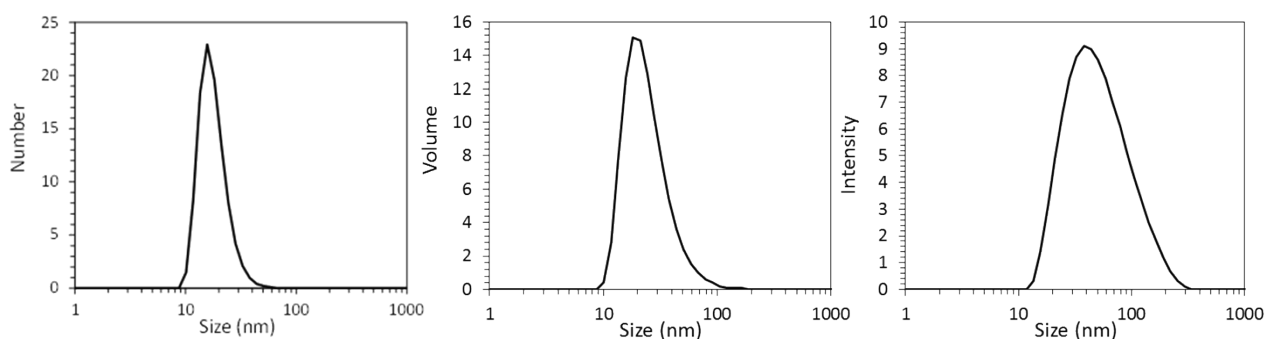Figure S9. GPC chromatograms for POEGA (10K arm polymer) (blue line) and POEGA-Star-PFPA (orange line).

Figure S10. Size distribution (by number, volume and intensity) for star polymers in water, as determined by dynamic light scattering; (A) Re-NH$_2$ conjugated POEGA-Star-VBA (Star **1**) (B) Re-NH$_2$ conjugated POEGA-Star-DAAM (Star **2**); (C) Re-NH$_2$ conjugated POEGA-Star-PFPA (Star **3**).
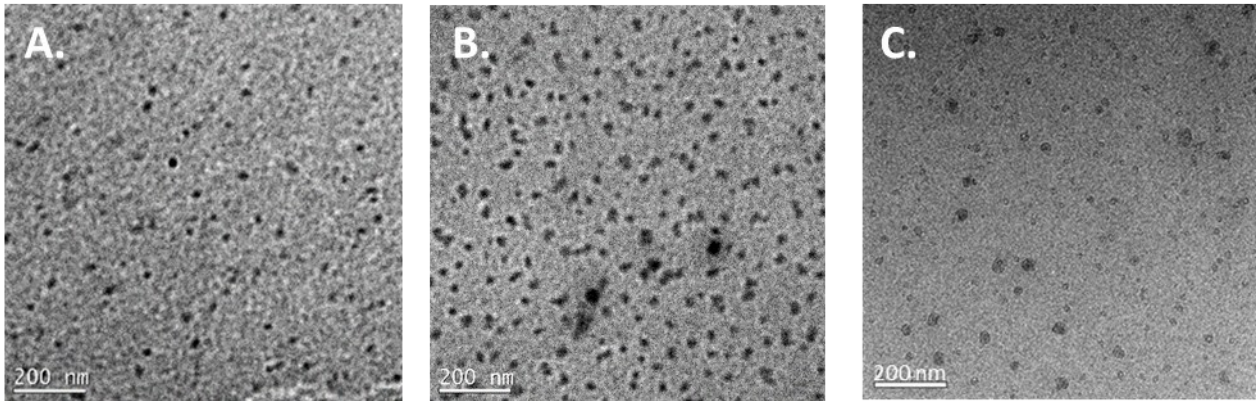
Figure S11. TEM images and size analysis of (A) Re-NH$_2$ conjuated POEGA-Star-VBA (Star 1: diameter = 19.2 nm, SD = 1.5 nm); (B) Re-NH$_2$ conjugated POEGA-Star-DAAM (Star 2: diameter = 19.8 nm, SD = 1.1); (C) Re-NH$_2$ conjugated POEGA-Star-PFPA (Star 3: diameter = 20.9 nm , SD = 1.2). Scale bar, 200 nm.
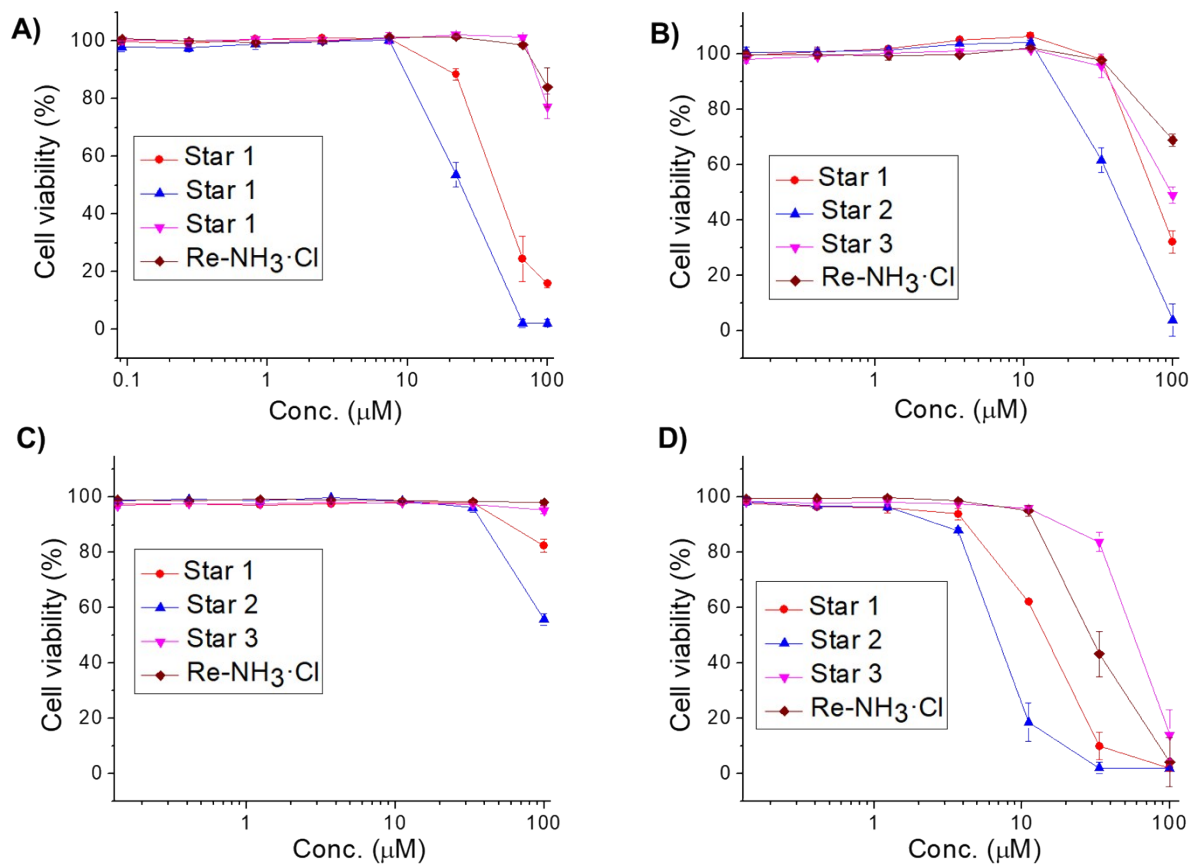
Figure S12. Dose-response curves of Star 1, Star 2, Star 3 and Re-NH$_3$·Cl. A) HeLa cells treated with compounds for 48 h in the dark. B) MRC5 cells treated with compounds for 48 h in the dark. C) HeLa cells treated with compounds for 4 h in the dark followed by 44 h with fresh media in the dark. D) HeLa cells treated with compounds for 4 h, media replaced with fresh media, irradiated with 350 nm light for 10 min and then incubated in the dark for 44 h.
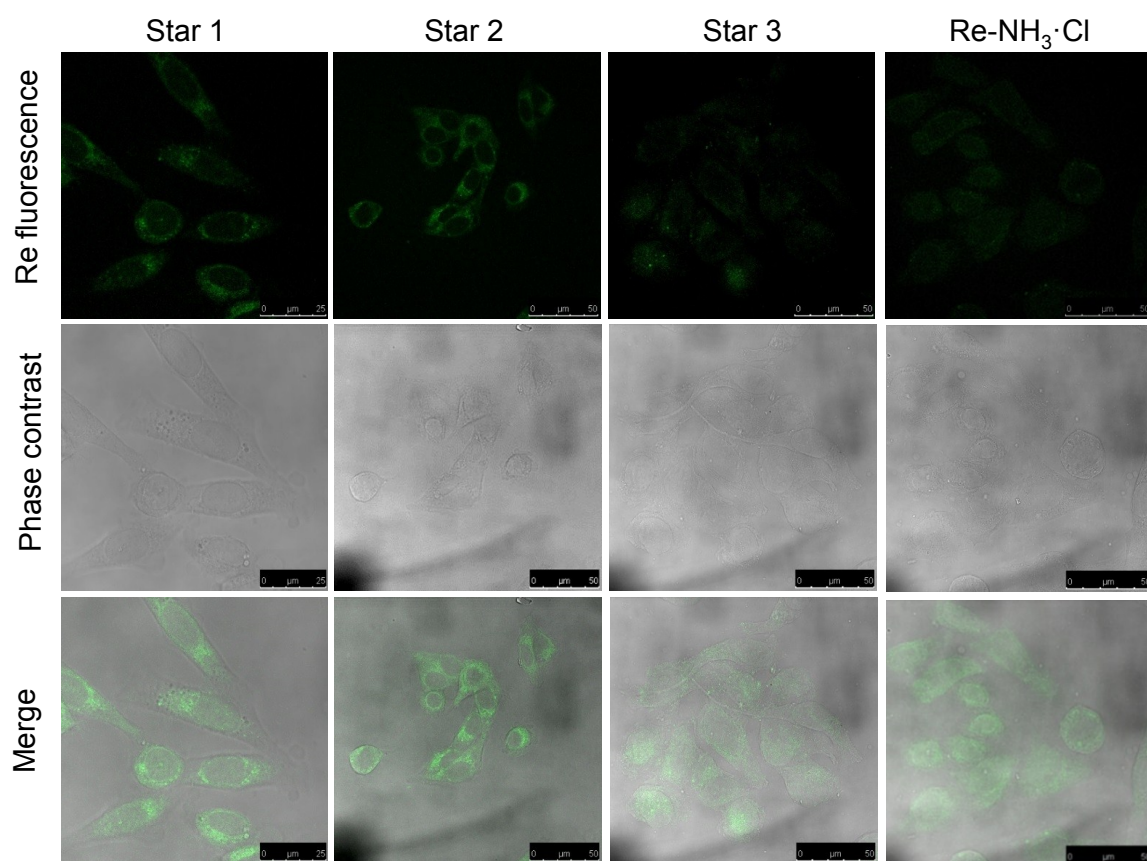
Figure S13. Fluorescence microscopy images of HeLa cells treated with Re-NH$_3$·Cl and its star polymer nanoparticle conjugates, Star 1, Star 2 and Star 3 (50 µM, 9 h). Scale bar, 50 µm.
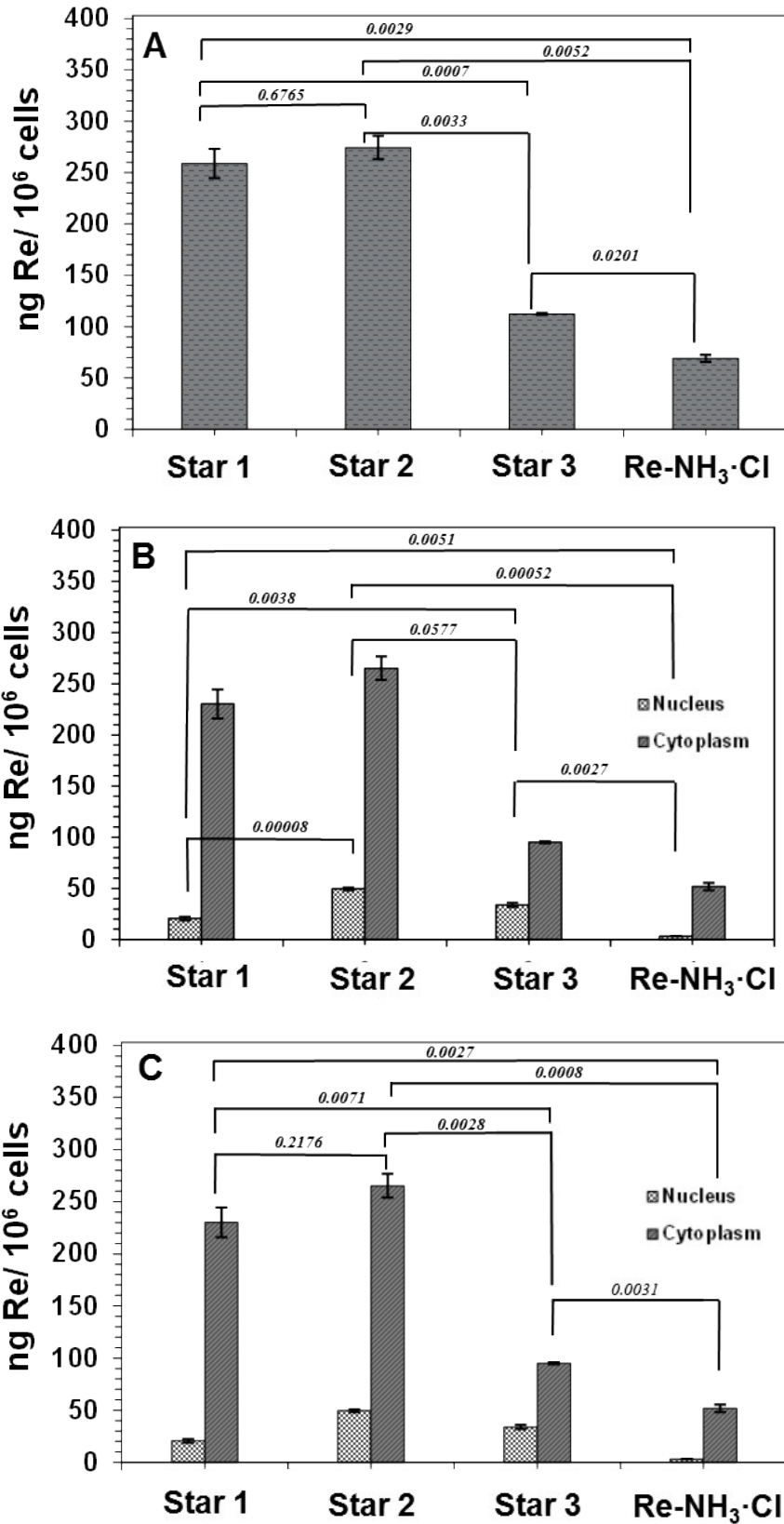
Figure S14 : ρ values determined by t-test analysis of the Re content (ng/10^6 cells) in **A.** whole cell, **B.** nuclear compartments and **C.** cytoplasmic compartments of HeLa cells, determined by ICP-MS after treatment of Re-NH$_3$·Cl and its polymer conjugates (error = SD, n = 3).

Reference

1. Stenzel, M. H.; Davis, T. P. *J. Polym. Sci. Part A Polym. Chem*. **2002**, 40, 4498.

2. Eberhardt, M.; Mruk, R.; Zentel, R.; Théato, P. *Eur. Polym. J.* **2005**, 41, 1569.

3. Viola-Villegas, N.; Rabideau, A. E.; Bartholomä, M.; Zubieta, J.; Doyle, R. P. *J. Med. Chem.* **2009**, *52*, 5253.

4. Alberto, R.; Egli, A.; Abram, U.; Hegetschweiler, K.; Gramlich, V.; Schubiger, P. A. *J. Chem. Soc., Dalton Trans.* **1994**, 2815.

5. Ren, Y.; Sun, Y.; Cheng, K.; Liu, G.; Shen, Y. *J. Label. Compd. Radiopharm.* **2009**, *52*, 139.

6. Li, Y.; Duong, H. T. T.; Jones, M. W.; Basuki, J. S.; Hu, J.; Boyer, C.; Davis, T. P. *ACS Macro Lett.* **2013**, *2*, 912-917.

7. Suzuki, K.; Bose, P.; Leong-Quong, R. Y.; Fujita, D. J.; Riabowol, K. *BMC Research Notes* **2010**, 3, 294.

8. Huang, H.; Deng, Z.; Vladimirova, O.; Wiedmer, A.; Lu, F.; Lieberman, P. M.; Patel, D. J. *Nat. Commun.* **2016**, 7, 12707.

9. Li, Y.; Duong, H. T. T.; Laurent, S.; MacMillan, A.; Whan, R. M.; Elst, L. V.; Muller, R.N.; Hu, J.; Lowe, A.; Boyer, C.; Davis, T. P. *Adv. Healthcare Mater*. **2015**, 4, 148.