Electronic Supporting Information for

Small-molecule poly (ADP-ribose) polymerase (PARP) and PD-L1 inhibitor conjugates as dual-action anticancer agents

Samuel Ofori and Samuel G. Awuah*

Department of Chemistry, University of Kentucky, Lexington Kentucky 40506, United States

Correspondence to: awuah@uky.edu

For Table of Contents Only

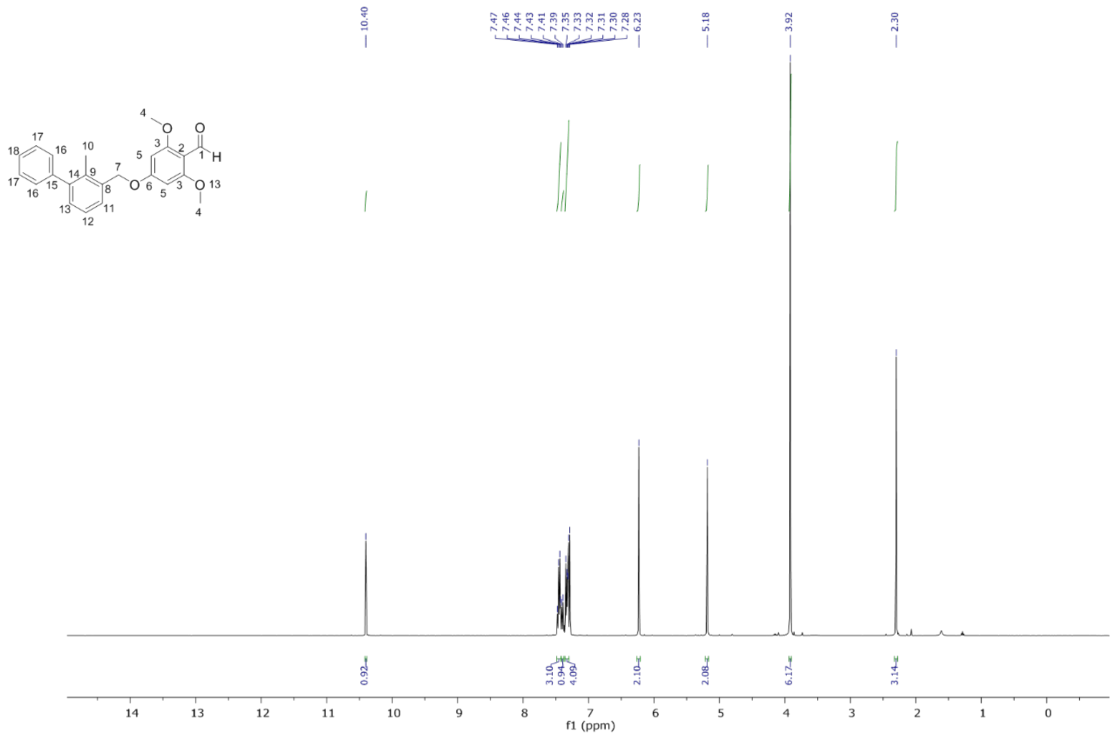

Figure S1. ^{1}H NMR spectrum of **6** (400 MHz, $CDCl_3$)

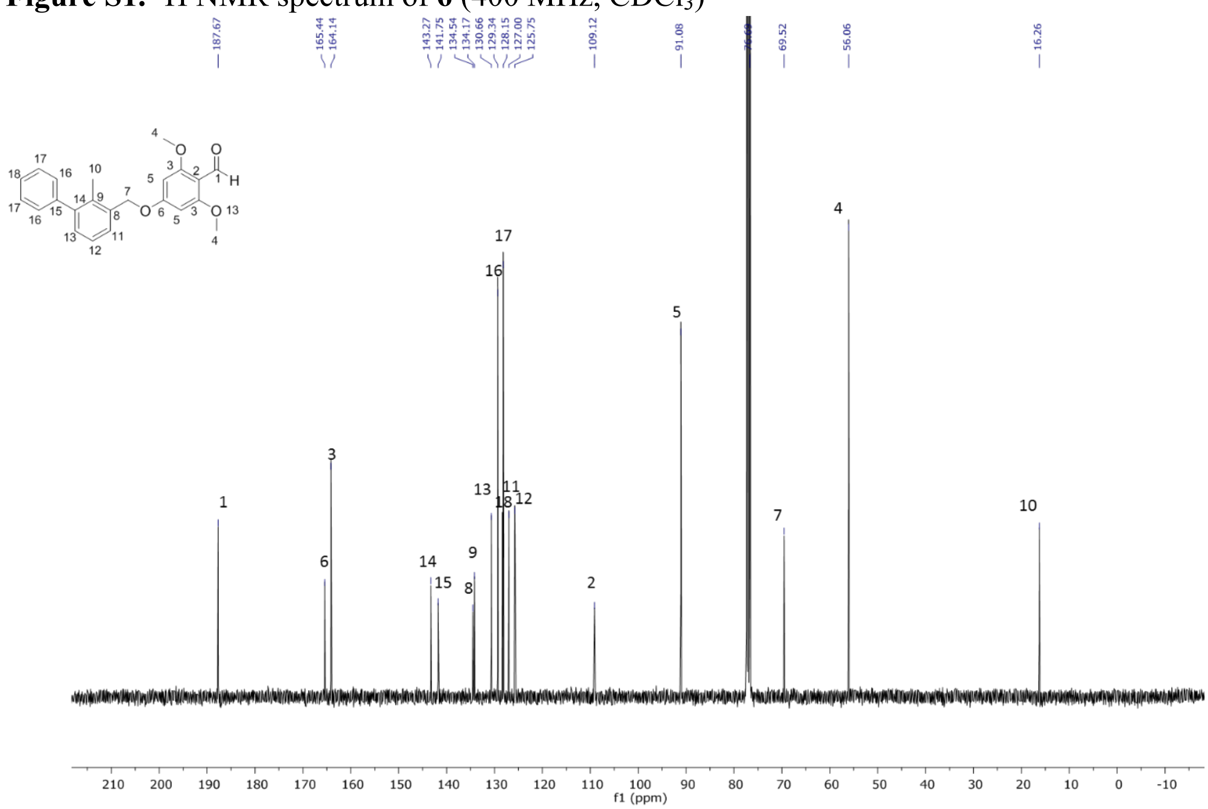

Figure S2. ^{13}C NMR spectrum of **6** (400 MHz, $CDCl_3$)

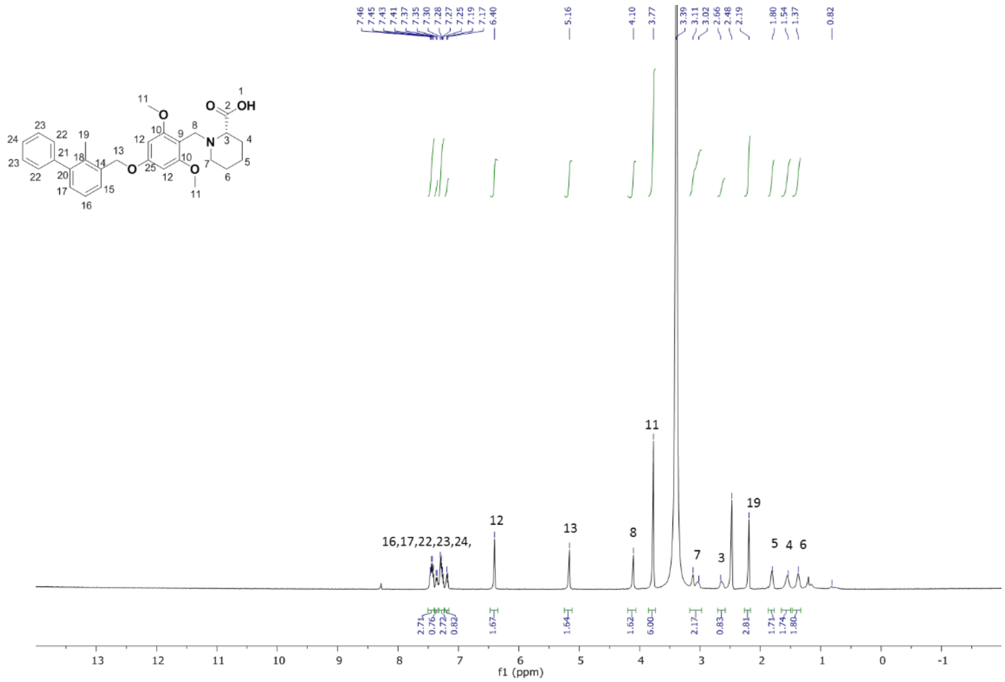

Figure S3. ^{1}H NMR spectrum of **8** (400 MHz, DMSO-d_6)

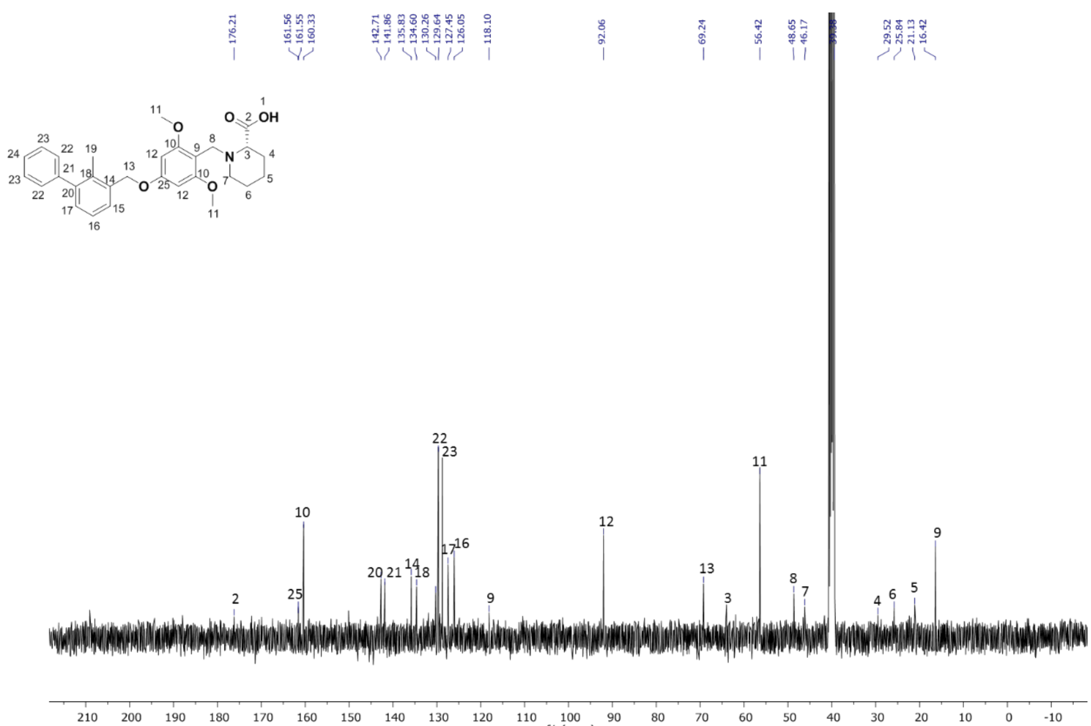

Figure S4. ^{13}C NMR spectrum of **8** (400 MHz, DMSO-d_6)

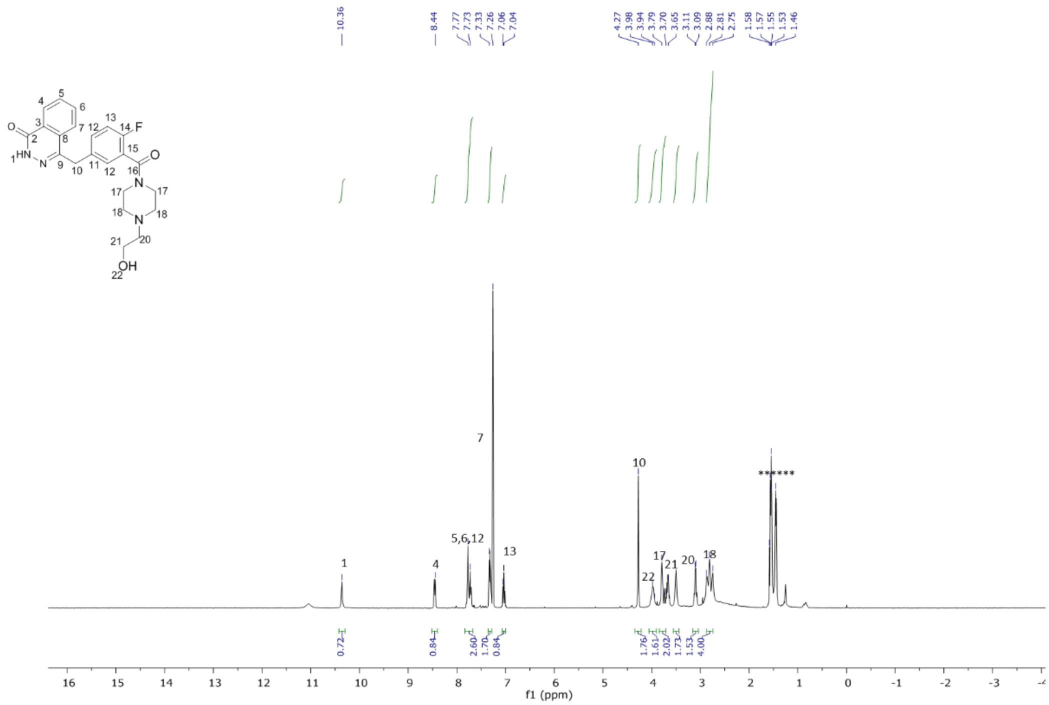

Figure S5. ^{1}H NMR spectrum of **11** (400 MHz, $CDCl_3$)

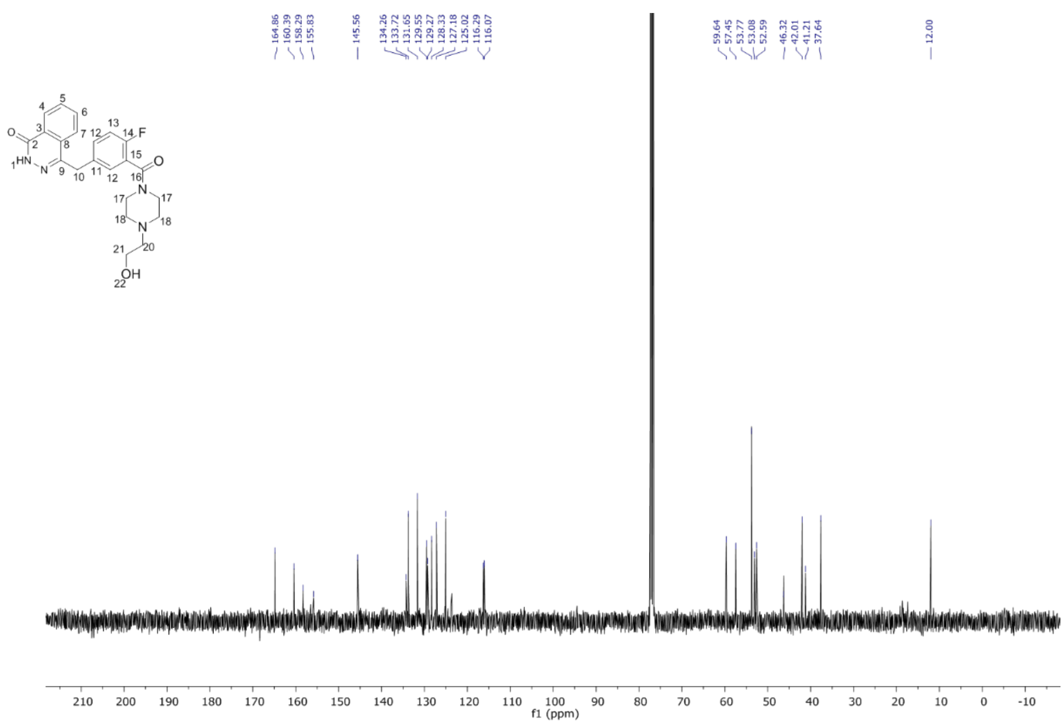

Figure S6. ^{13}C NMR spectrum of **11** (400 MHz, $CDCl_3$)

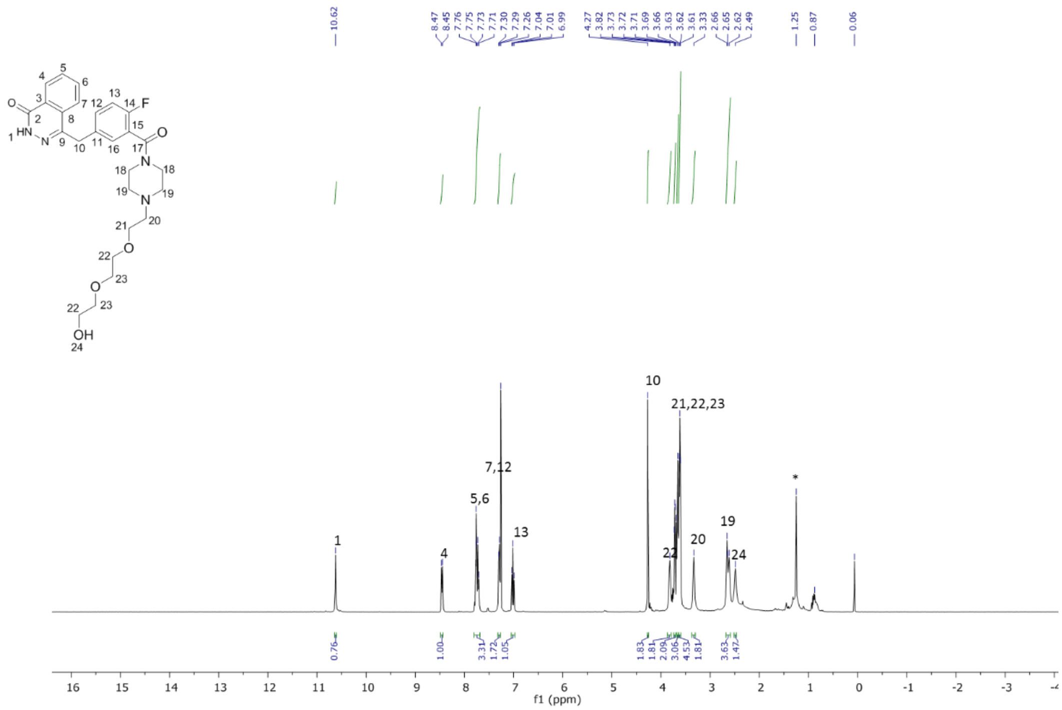

Figure S7. ^{1}H NMR spectrum of **13** (400 MHz, $CDCl_3$)

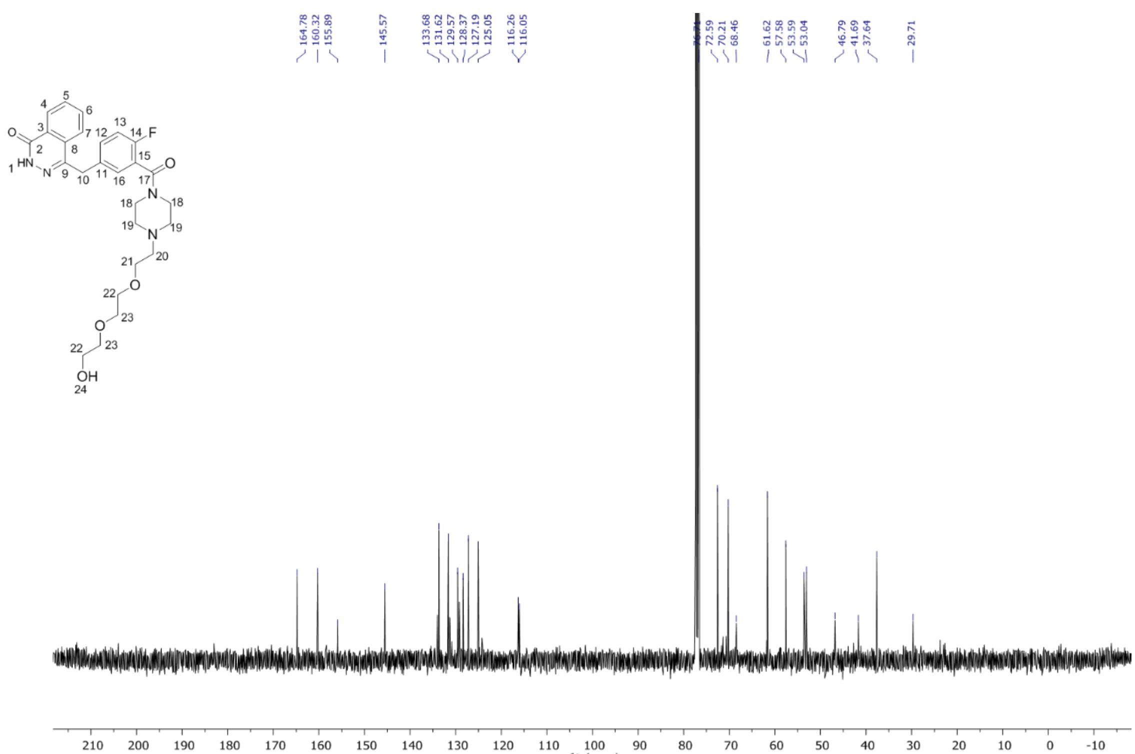

Figure S8. ^{13}C NMR spectrum of **13** (400 MHz, $CDCl_3$)

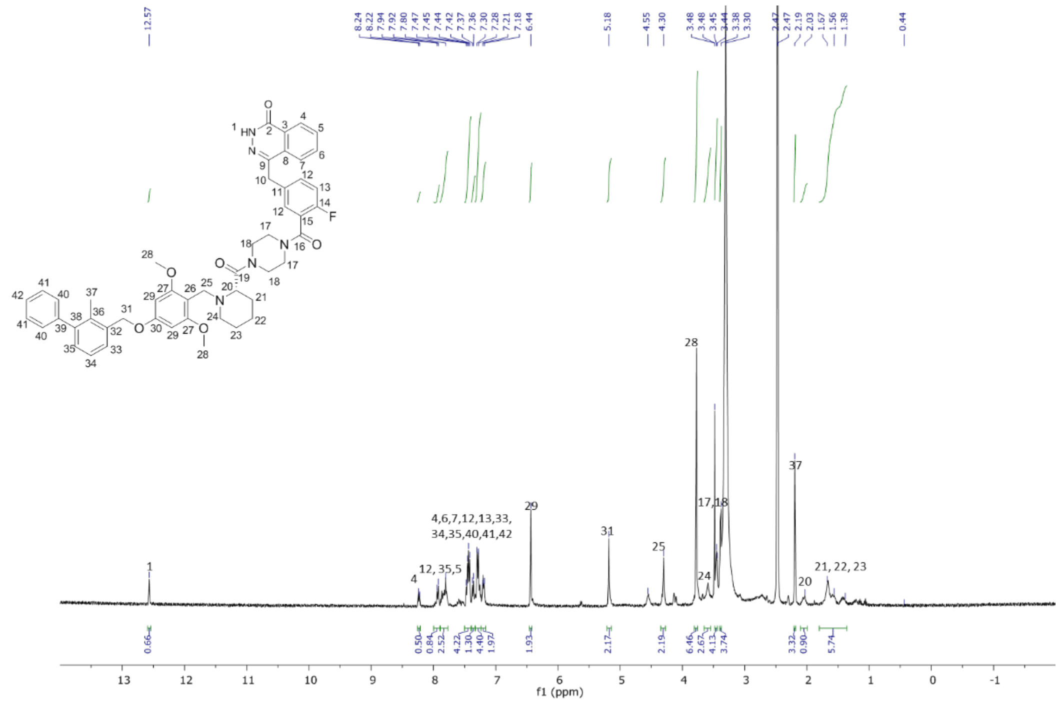

Figure S9. ^{1}H NMR spectrum of **1** (400 MHz, DMSO-d_6)

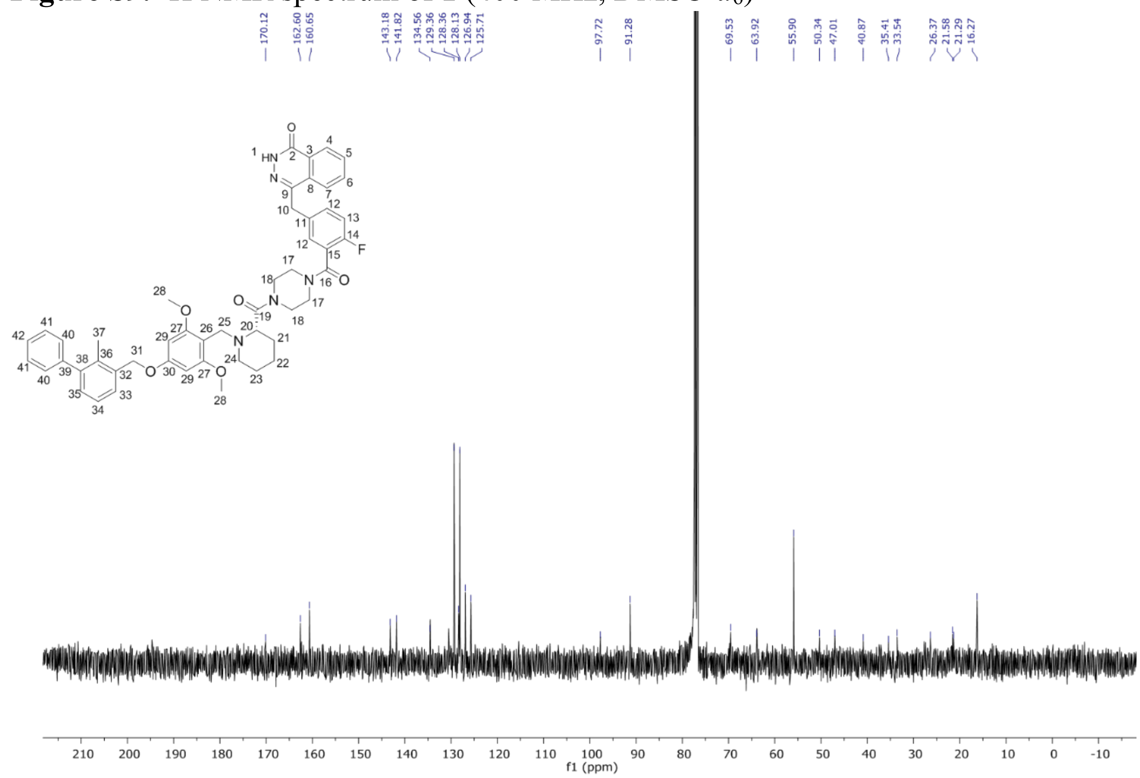

Figure S10. ^{13}C NMR spectrum of **1** (400 MHz, CDCl$_3$)

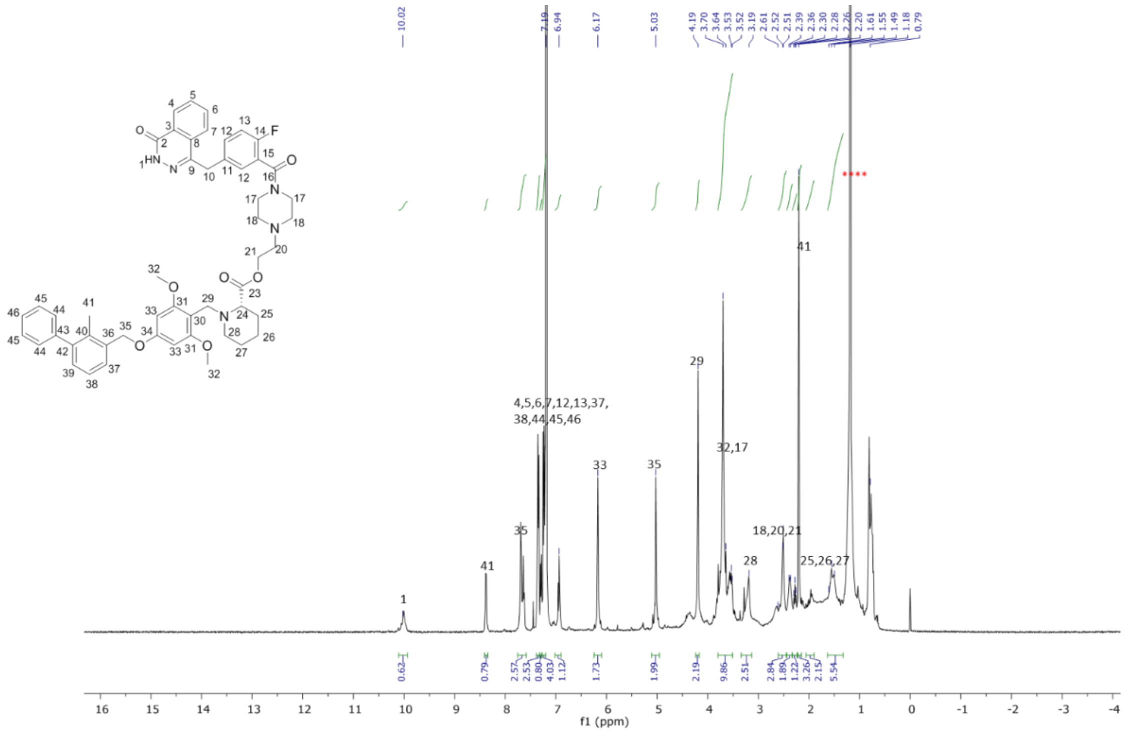

Figure S11. ^{1}H NMR spectrum of **2** (400 MHz, $CDCl_3$)

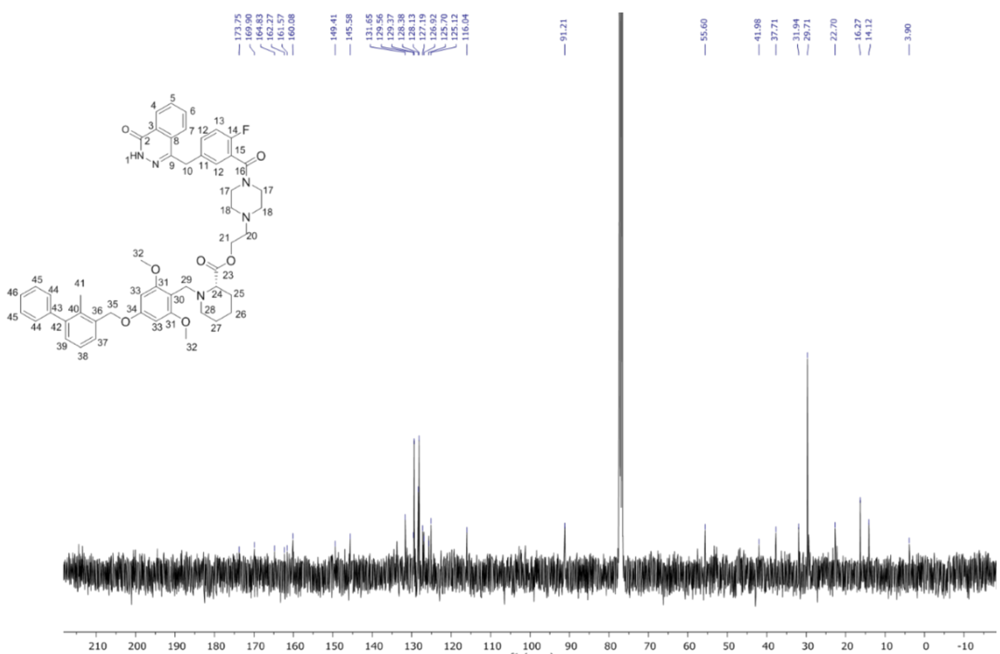

Figure S12. ^{13}C NMR spectrum of **2** (400 MHz, $CDCl_3$)

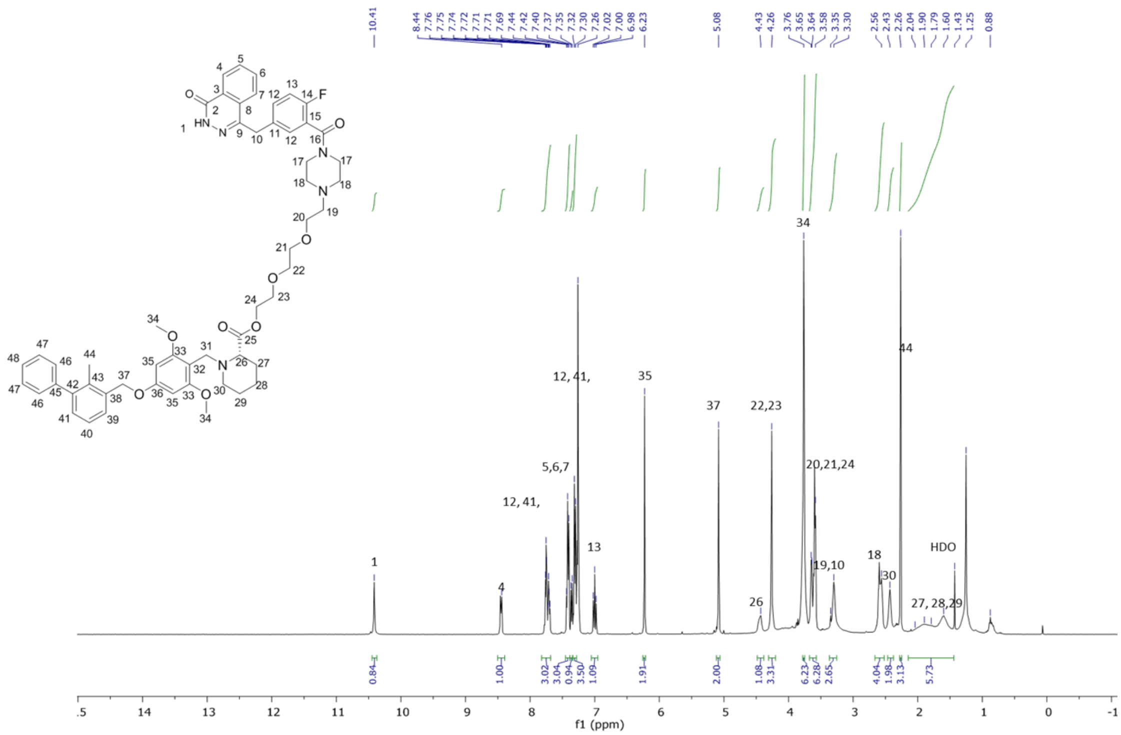

Figure S13. ^{1}H NMR spectrum of **3** (400 MHz, $CDCl_3$)

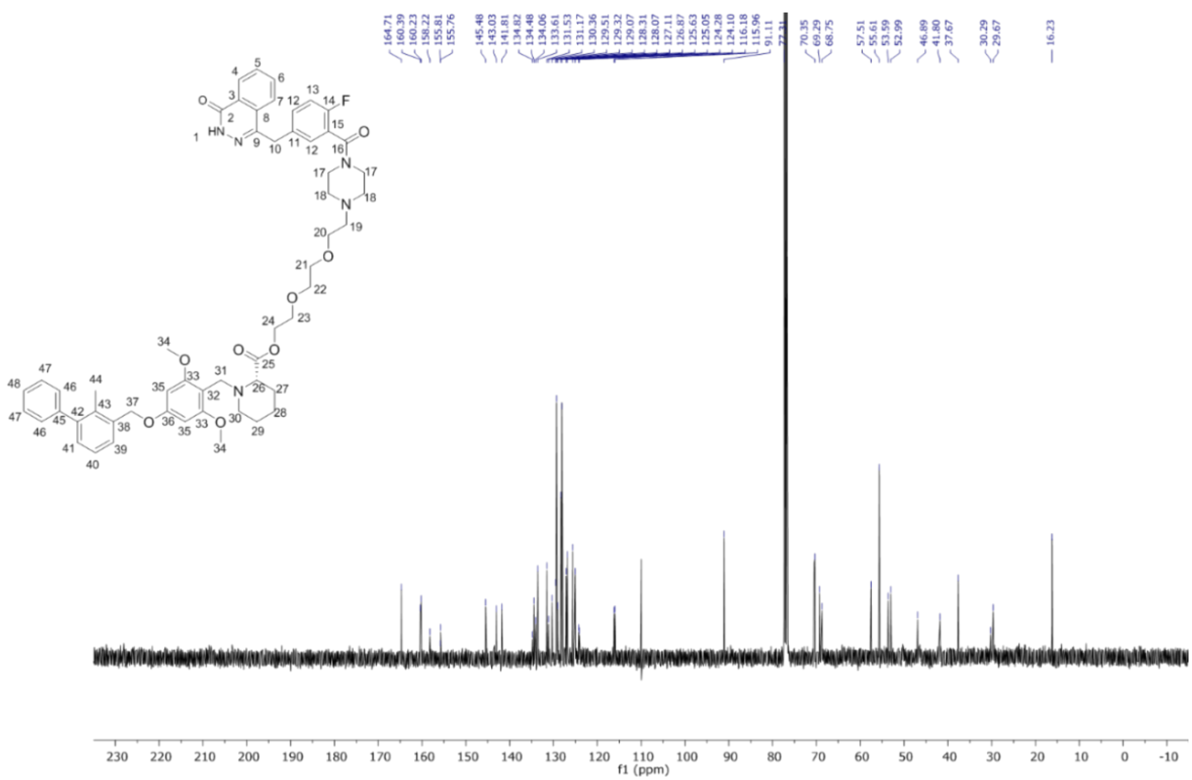

Figure S14. ^{13}C NMR spectrum of **3** (400 MHz, $CDCl_3$)

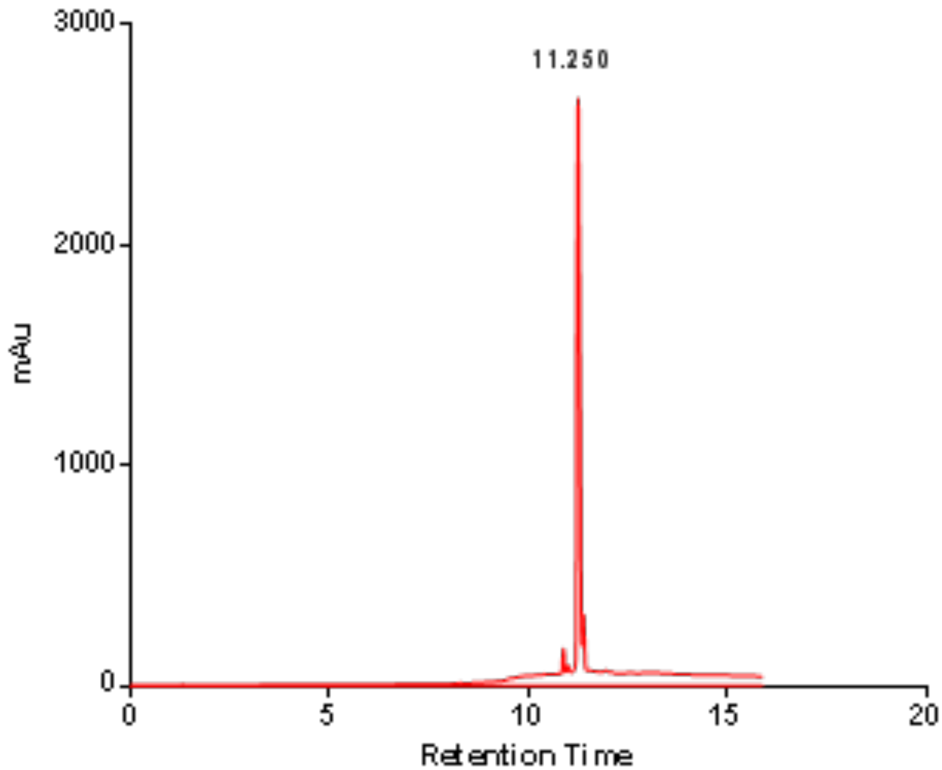

Figure S15: HPLC Chromatogram of Compound 1; RT: 11.250 min, 99.98% Purity

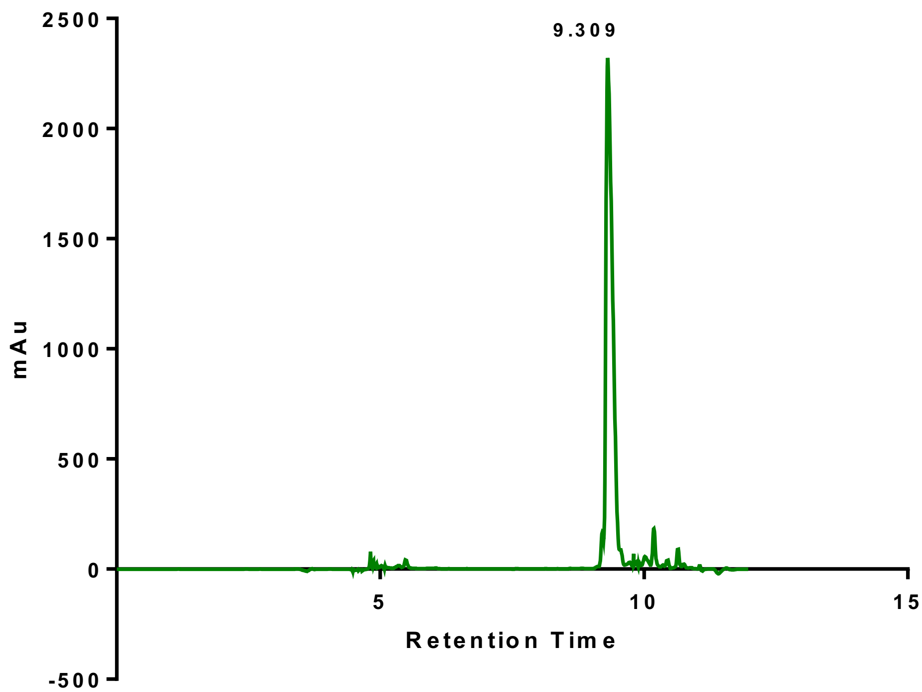

Figure S16: HPLC Chromatogram of Compound 2; RT: 9.308 min, 95.06% Purity

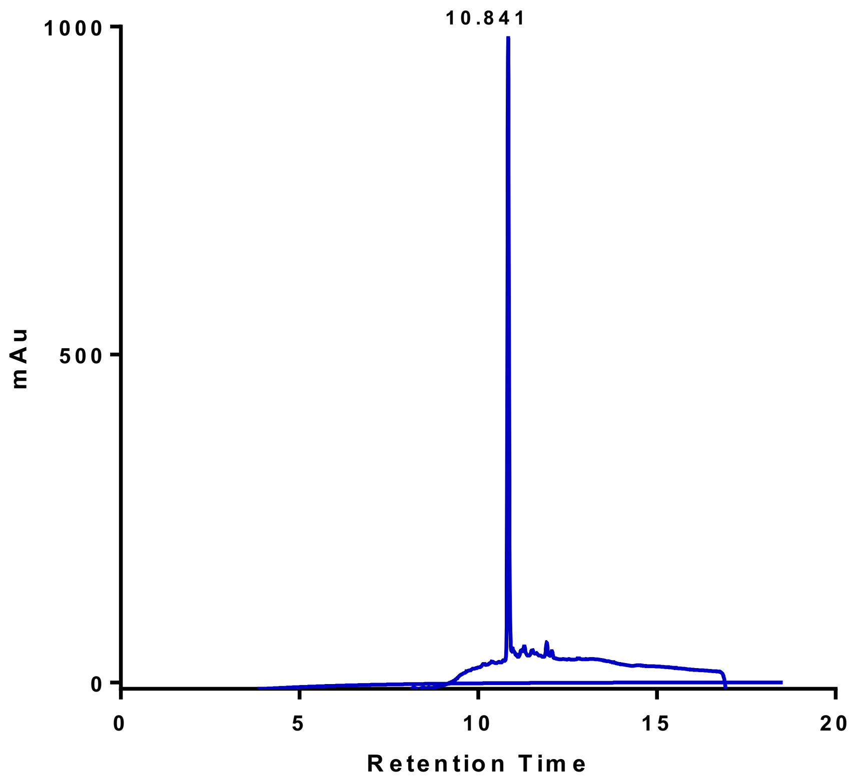

Figure S17: HPLC Chromatogram of Compound 3; RT: 10.841min, 99.10%

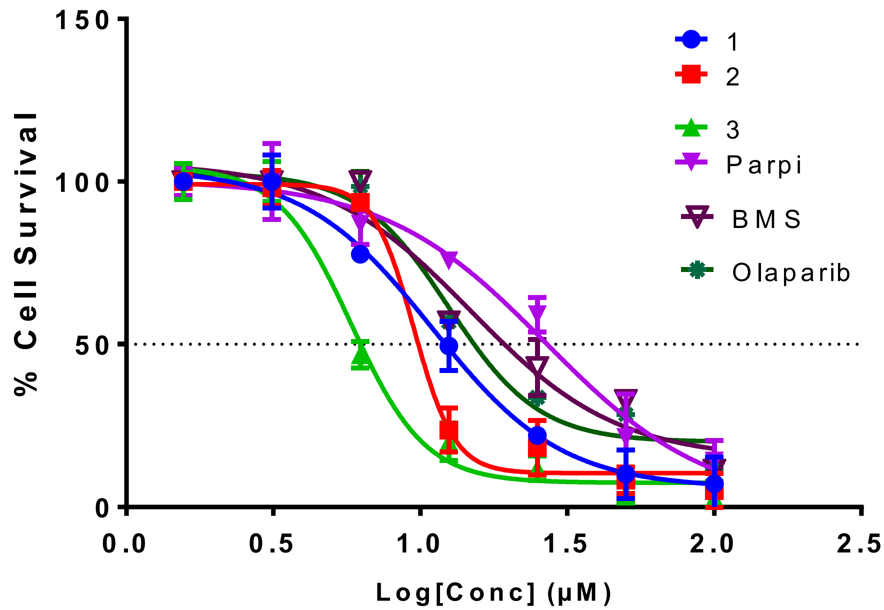

Figure S18: Dose-response curves of MDA-MB-231 cells in response to compounds

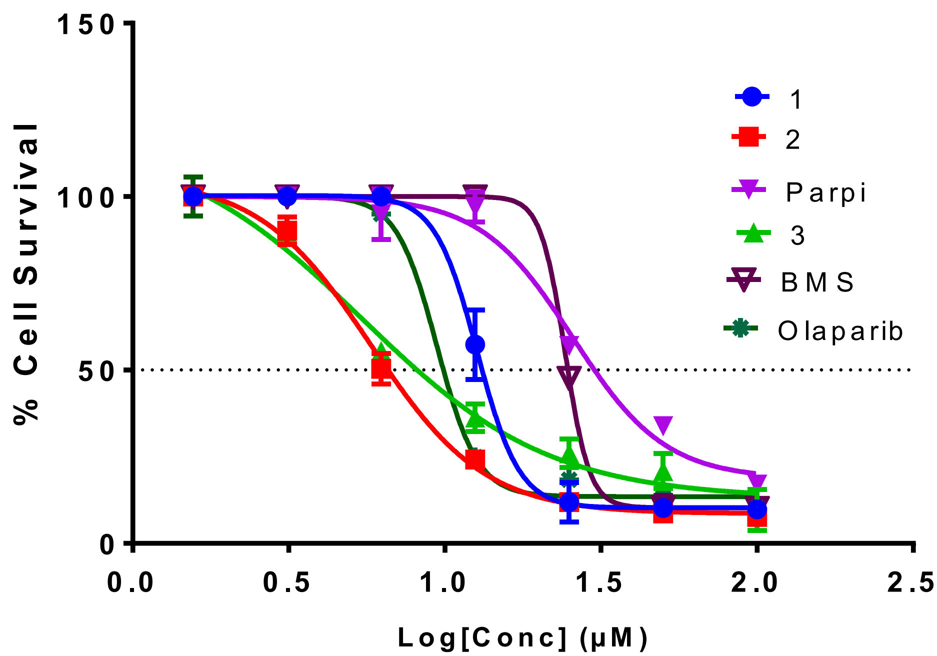

Figure S19: Dose-response curves of A2780 cells in response to compounds

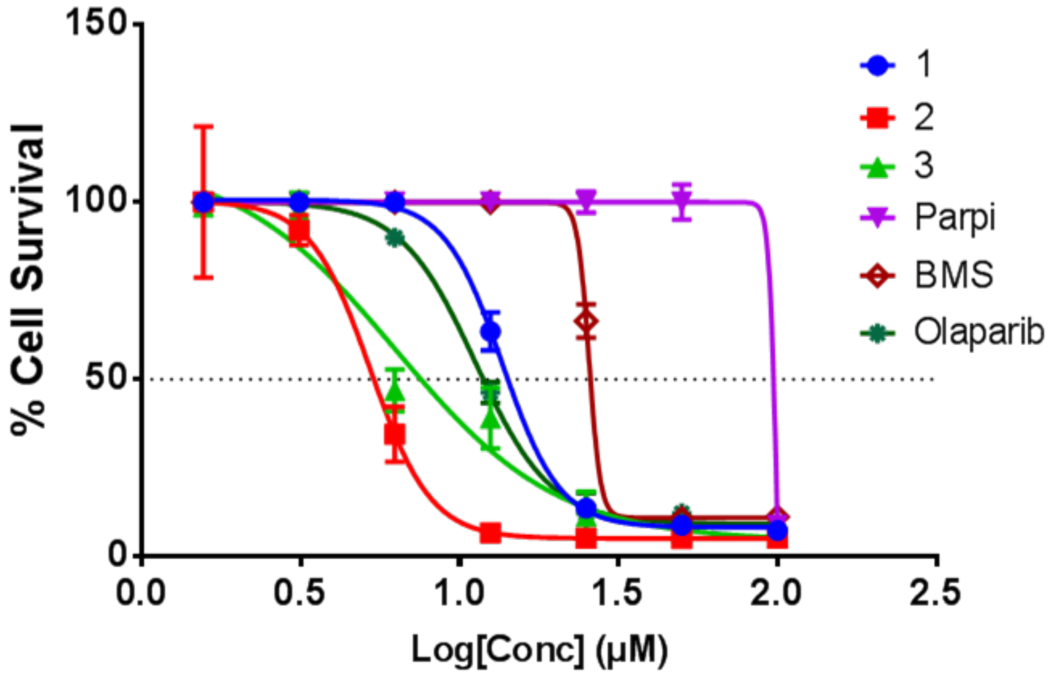

Figure S20: Dose-response curves of OVCAR8 cells in response to compounds

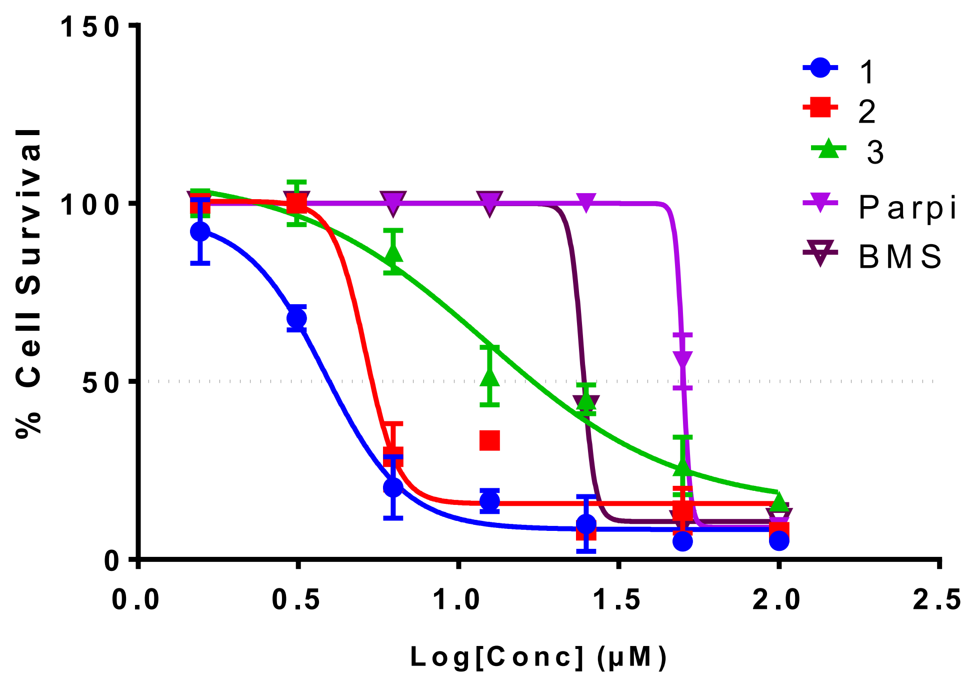

Figure S21: Dose-response curves of SKOV3 cells in response to compounds

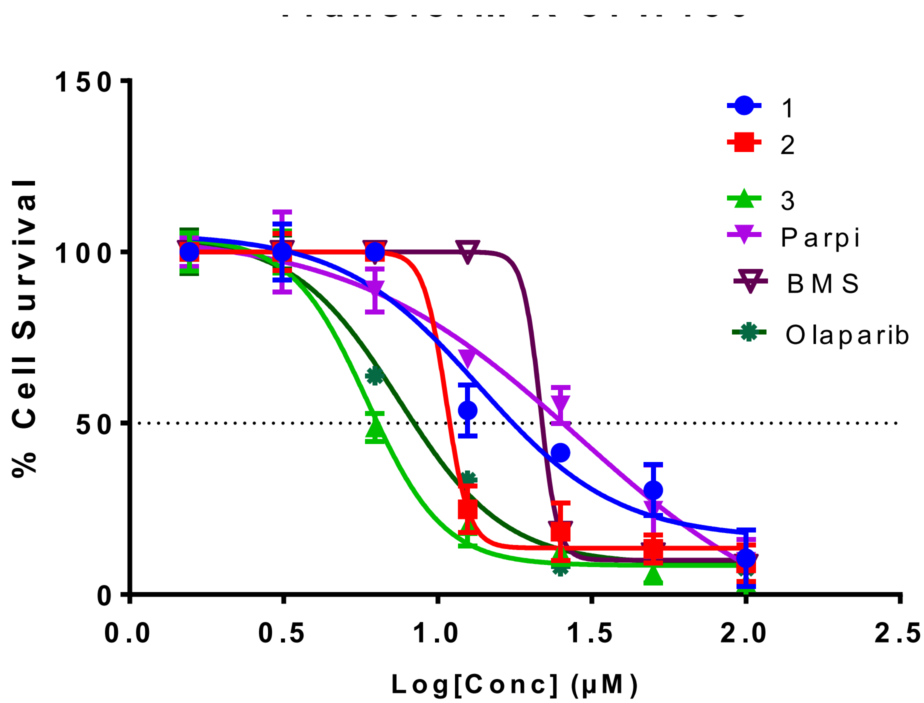

Figure S22: Dose-response curves of H460 cells in response to compounds

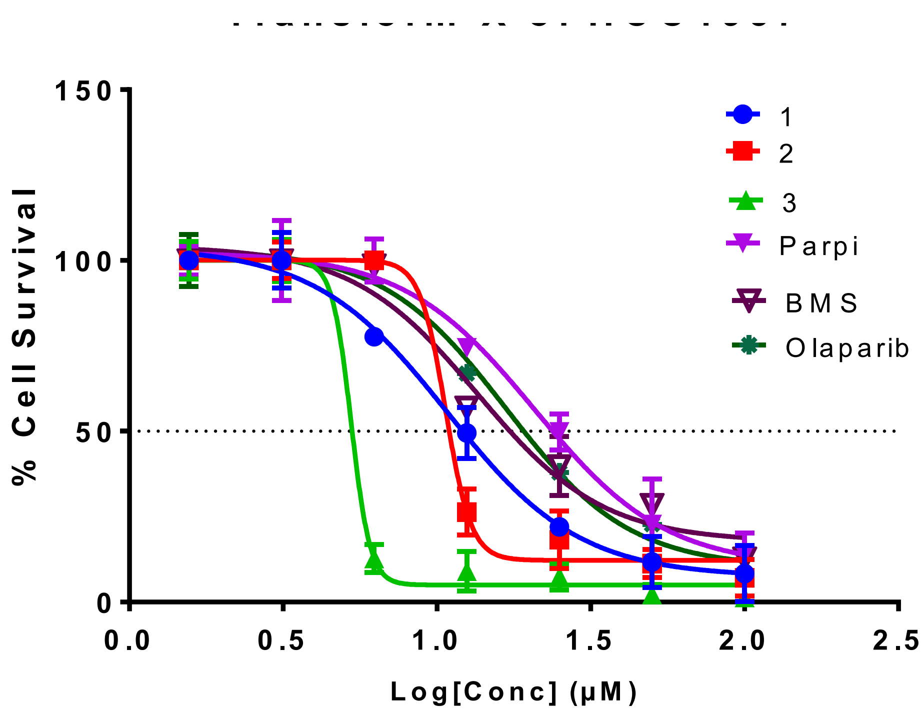

Figure S23: Dose-response curves of HCC1937 cells in response to compounds

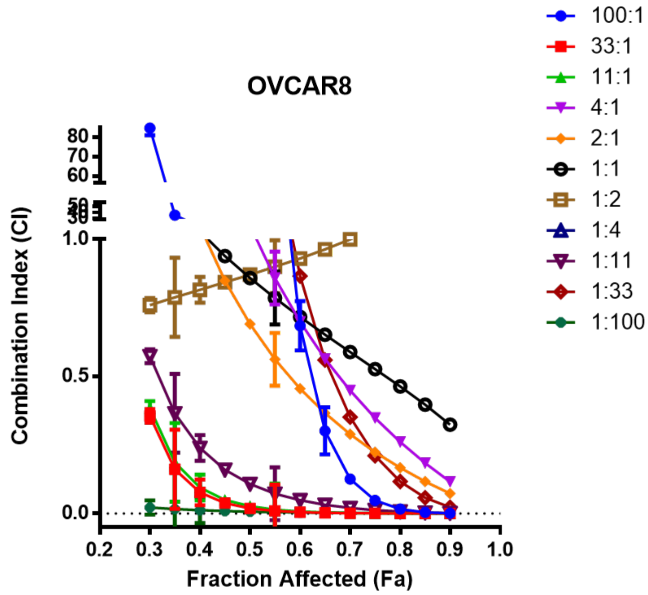

Figure S24: Combination Index values for olaparib-BMS001 combinations presented as a function of fraction affected (Fa) for OVCAR8 cells Fa= 0.9 indicates 90% cell death. Each data point is presented as mean ∓ SD obtained from three independent biological experiments. Ratios of combination of Olaparib to BMS001 are indicated (legend).

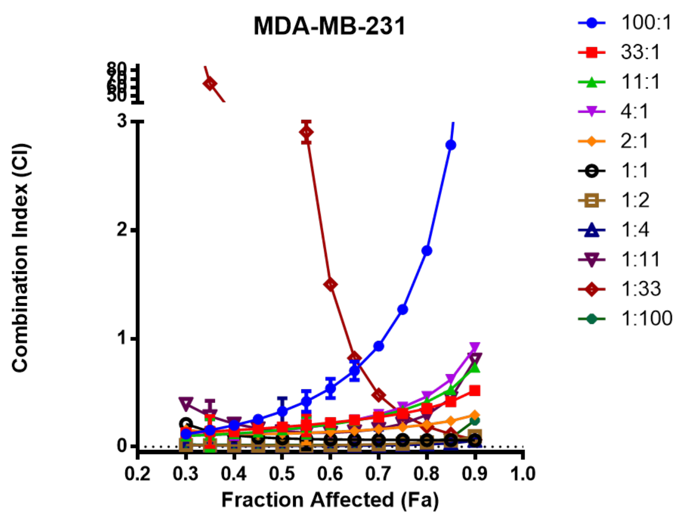

Figure S25: The combination Index values for olaparib-BMS001 combinations presented as a function of fraction affected (Fa) for MDA-MB-231 cells. Fa= 0.9 indicates 90% cell death. Each data point is presented as mean ± SD obtained from three independent biological experiments. Ratios of combination of Olaparib to BMS001 are indicated (legend).

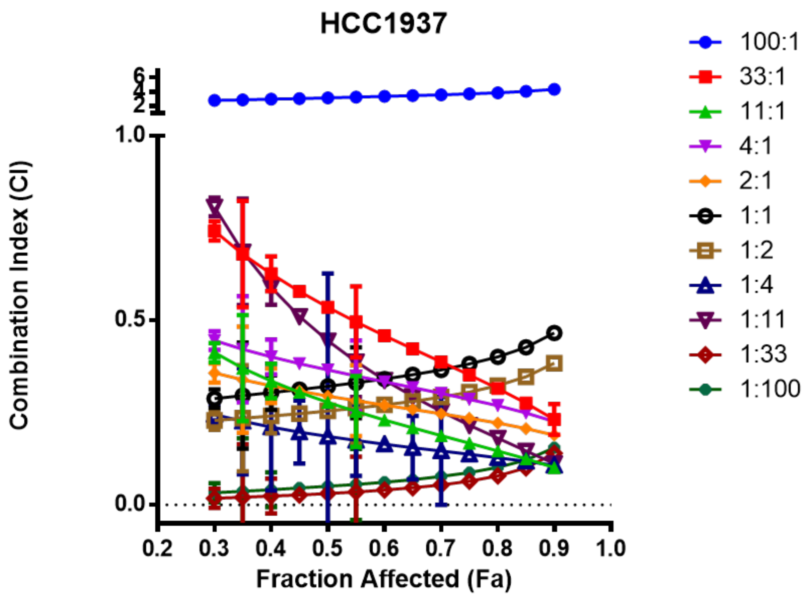

Figure S26: The combination Index values for olaparib-BMS001 combinations presented as a function of fraction affected (Fa) for HCC1937 cells. Fa= 0.9 indicates 90% cell death. Each data point is presented as mean ± SD obtained from three independent biological experiments. Ratios of combination of Olaparib to BMS001 are indicated (legend).

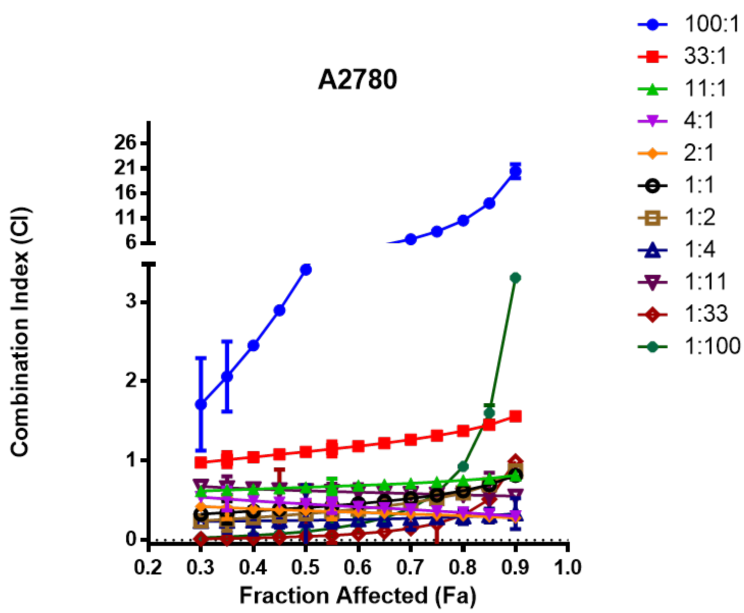

Figure S27: The combination Index values for olaparib-BMS001 combinations presented as a function of fraction affected (Fa) for A2780 cells. Fa= 0.9 indicates 90% cell death. Each data point is presented as mean ± SD obtained from three independent biological experiments. Ratios of combination of Olaparib to BMS001 are indicated (legend).

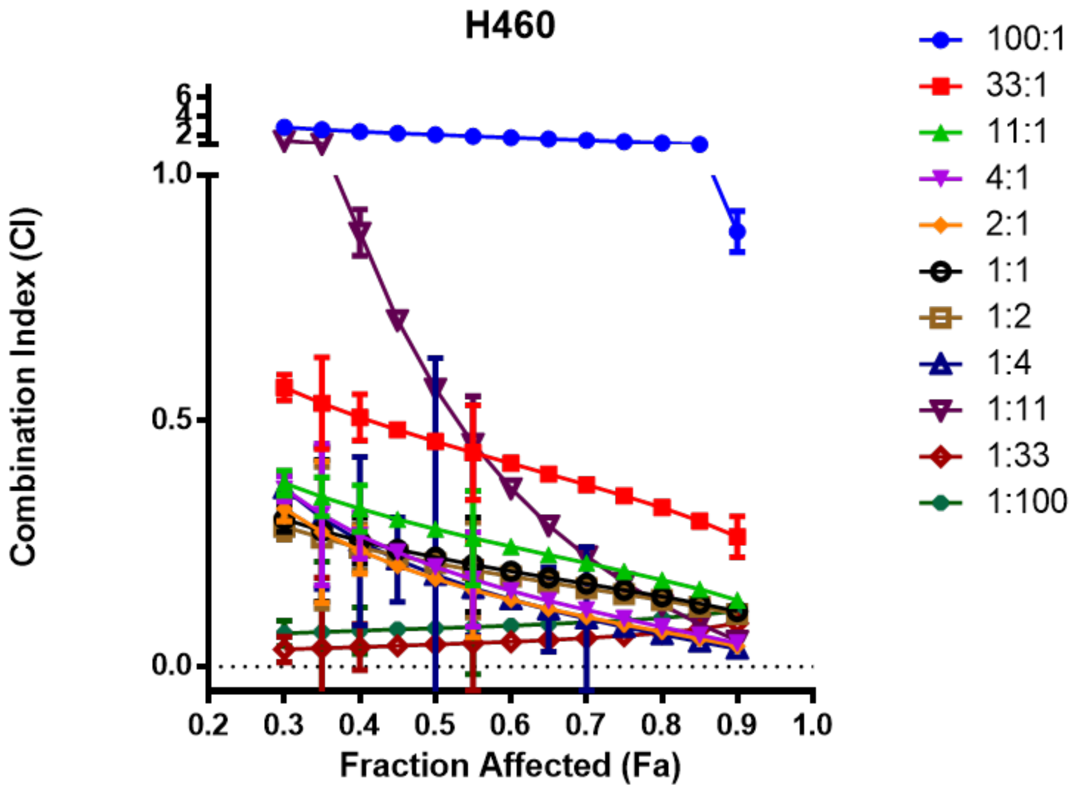

Figure S28: The combination Index values for olaparib-BMS001 combinations presented as a function of fraction affected (Fa) for H460cells. Fa= 0.9 indicates 90% cell death. Each data point is presented as mean ± SD obtained from three independent biological experiments. Ratios of combination of Olaparib to BMS001 are indicated (legend).

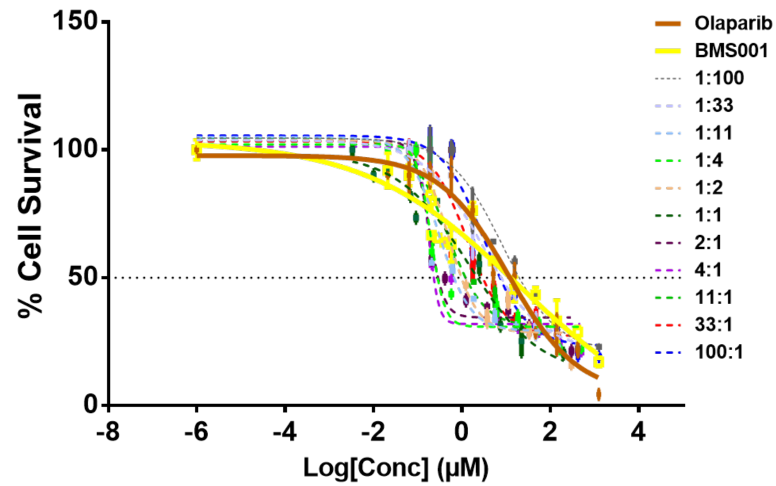

Figure S29: Dose-Response curve of OVCAR8 cell lines for Olaparib or BMS given as a monotherapy, or in combination. For both monotherapy and combination, cells were treated with three-fold serial dilution of Olaparib/BMS (maximum concentration was 1.25mM, minimum concentration = 12.5µM, same multiples were used for 100:1, 33:1, 11:1 and the reverse, eg. , 100:1 = 1.25mM Ola + 12.5µM BMS001). For 1:1 - the Olaparib: BMS001 concentration were set at 100µM: 100µM, the same multiples were used for 1:2, 2:1, 1:4, 4:1). Each data point is presented as mean ±SD obtained from three independent biological experiments.

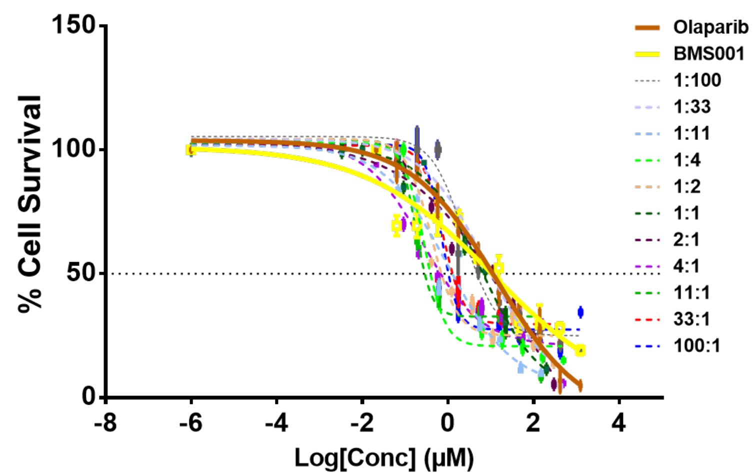

Figure S30: Dose-Response curve of MDA-MB-231cell lines for Olaparib or BMS given as a monotherapy, or in combination. For both monotherapy and combination, cells were treated with three-fold serial dilution of Olaparib/BMS (maximum concentration was 1.25mM, minimum concentration = 12.5µM, same multiples were used for 100:1, 33:1, 11:1 and the reverse, e.g. 100:1 = 1.25mM Ola + 12.5µM BMS001).For 1:1 - the Olaparib: BMS001 concentration were set at 100µM: 100µM, the same multiples were used for 1:2, 2:1, 1:4, 4:1). Each data point is presented as mean ±SD obtained from three independent biological experiments.

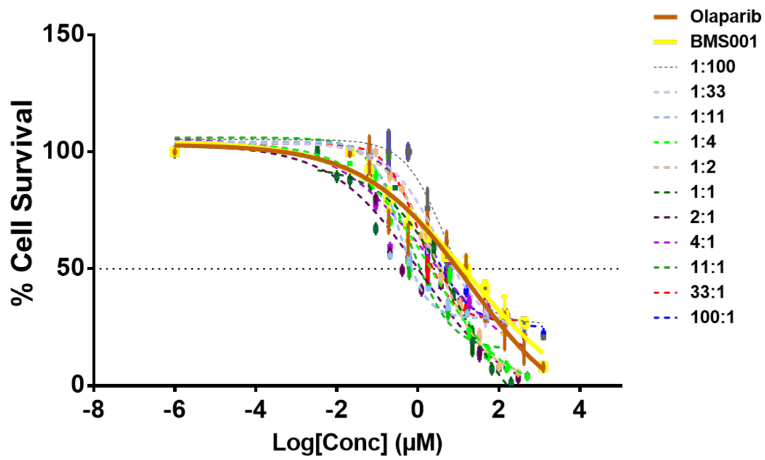

Figure S31: Dose-Response curve of HCC1937 cell lines for Olaparib or BMS given as a monotherapy, or in combination. For both monotherapy and combination, cells were treated with three-fold serial dilution of Olaparib/BMS (maximum concentration was 1.25mM, minimum concentration = 12.5µM, same multiples were used for 100:1, 33:1, 11:1 and the reverse, eg. , 100:1 = 1.25mM Ola + 12.5µM BMS001 stock).. For 1:1 - the Olaparib: BMS001 concentration were set at 100µM: 100µM, the same multiples were used for 1:2, 2:1, 1:4, 4:1). Each data point is presented as mean ±SD obtained from three independent biological experiments.

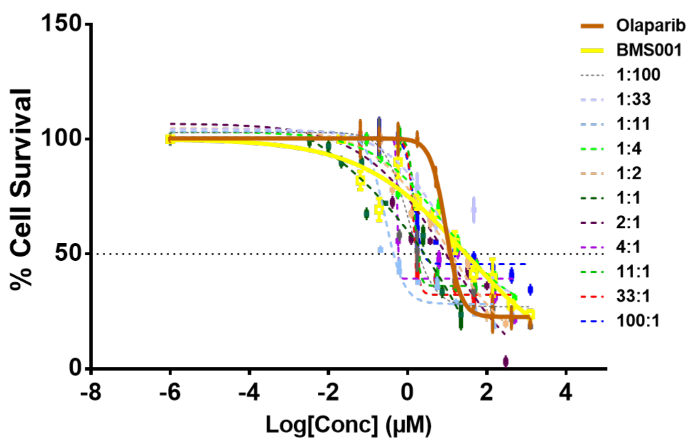

Figure S32: Dose-Response curve of HCC1937 cell lines for Olaparib or BMS given as a monotherapy, or in combination. For both monotherapy and combination, cells were treated with three-fold serial dilution of Olaparib/BMS (maximum concentration was 1.25mM, minimum concentration = 12.5µM, same multiples were used for 100:1, 33:1, 11:1 and the reverse, eg. , 100:1 = 1.25mM Ola + 12.5µM BMS001).For 1:1 - the Olaparib: BMS001 concentration were set at 100µM: 100µM, the same multiples were used for 1:2, 2:1, 1:4, 4:1). Each data point is presented as mean ±SD obtained from three independent biological experiments.

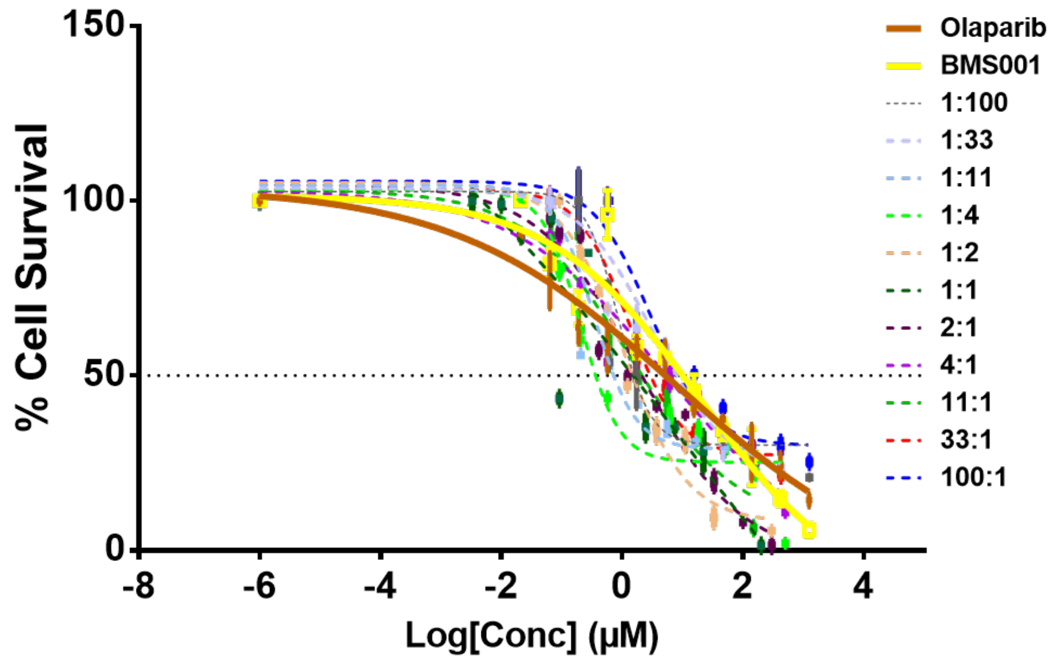

Figure S33: Dose-Response curve of H460 cell lines for Olaparib or BMS given as a monotherapy, or in combination. For both monotherapy and combination, cells were treated with three-fold serial dilution of Olaparib/BMS (maximum concentration was 1.25mM, minimum concentration = 12.5µM, same multiples were used for 100:1, 33:1, 11:1 and the reverse, eg. , 100:1 = 1.25mM Ola + 12.5µM BMS001).For 1:1 - the Olaparib: BMS001 concentration were set at 100µM: 100µM, the same multiples were used for 1:2, 2:1, 1:4, 4:1). Each data point is presented as mean ±SD obtained from three independent biological experiments.

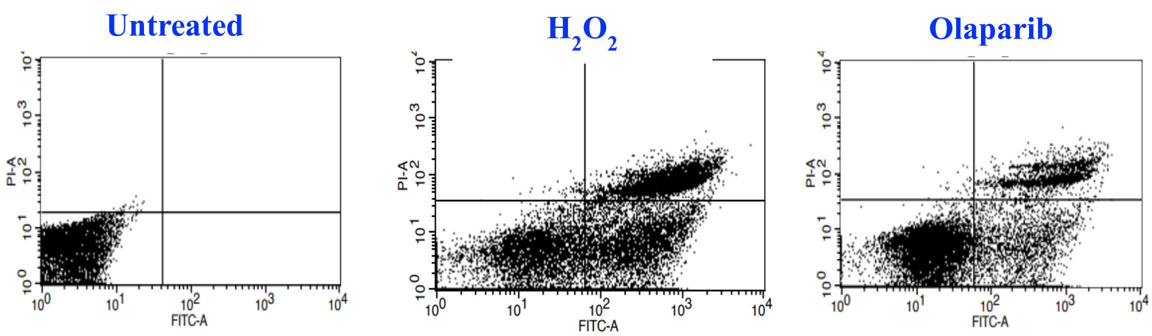

Figure S34: Apoptosis induced by olaparib in MDA-MB-231 cells with respective controls.

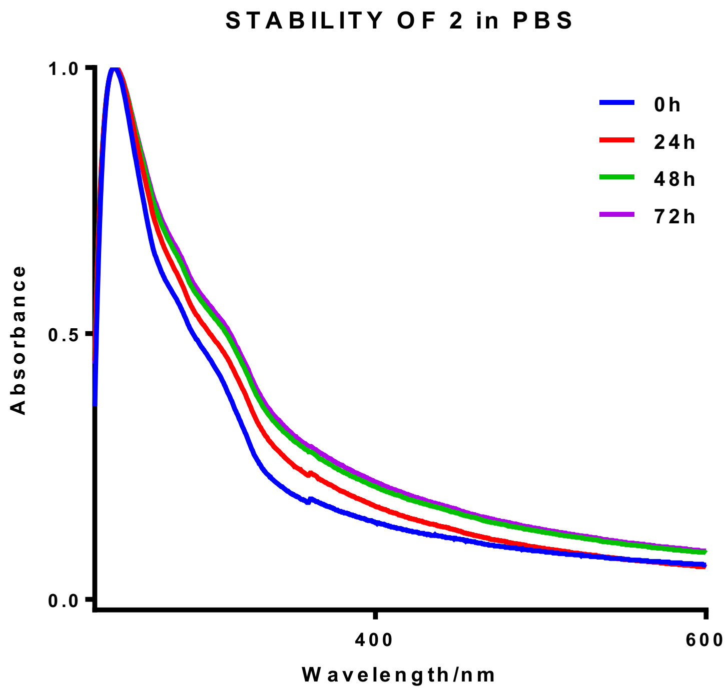

Figure S35: UV absorption profile of conjugate **2** in PBS

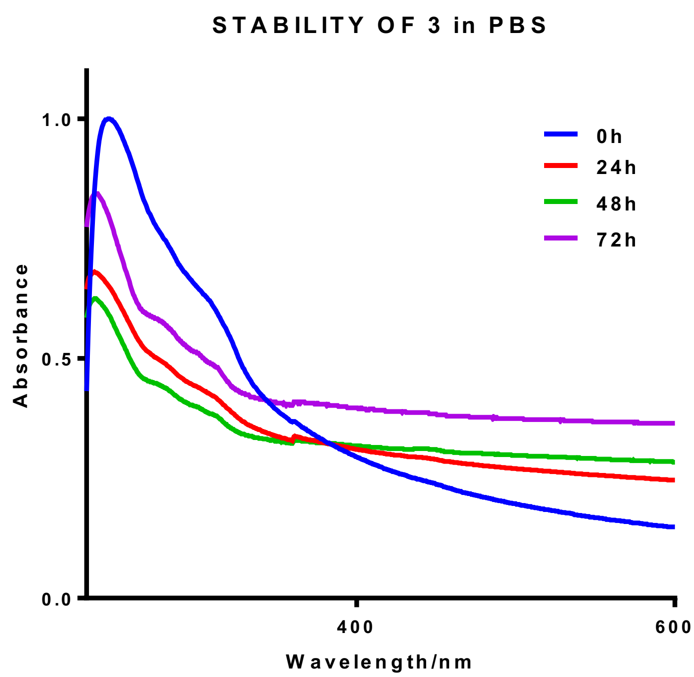

Figure S36: UV absorption profile of conjugate **3** in PBS

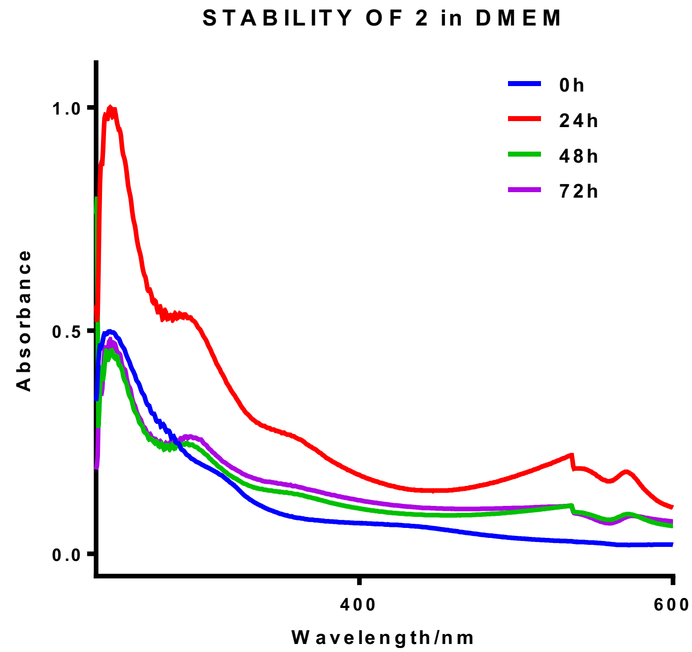

Figure S37: UV absorption profile of conjugate **2** in DMEM

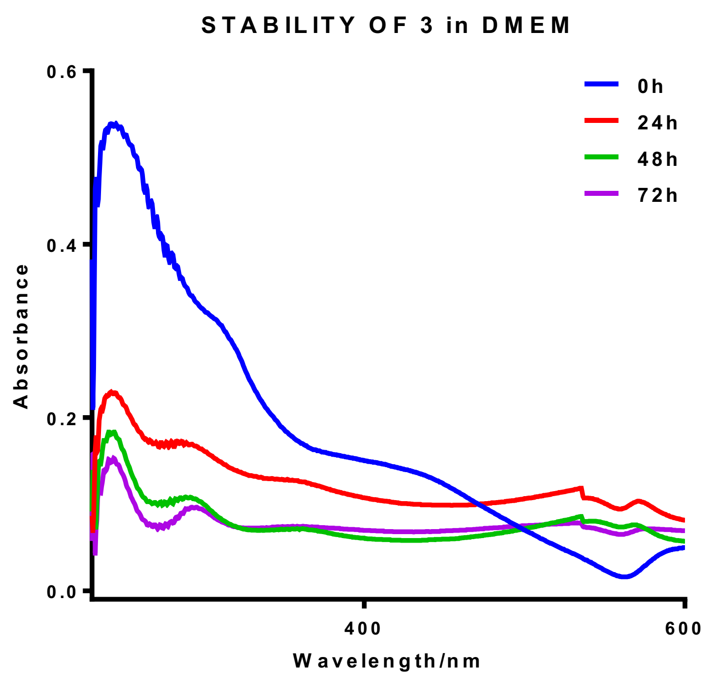

Figure S38: UV absorption profile of conjugate **3** in DMEM

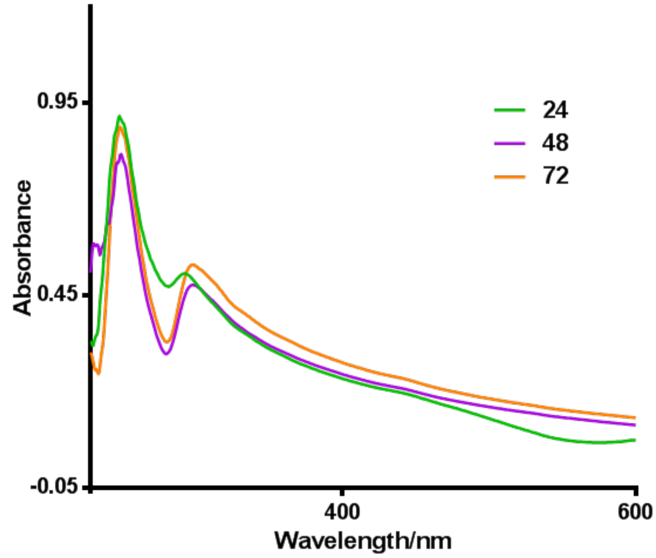

Figure S39: UV absorption profile of conjugate **1** in BSA after time points (in hours)

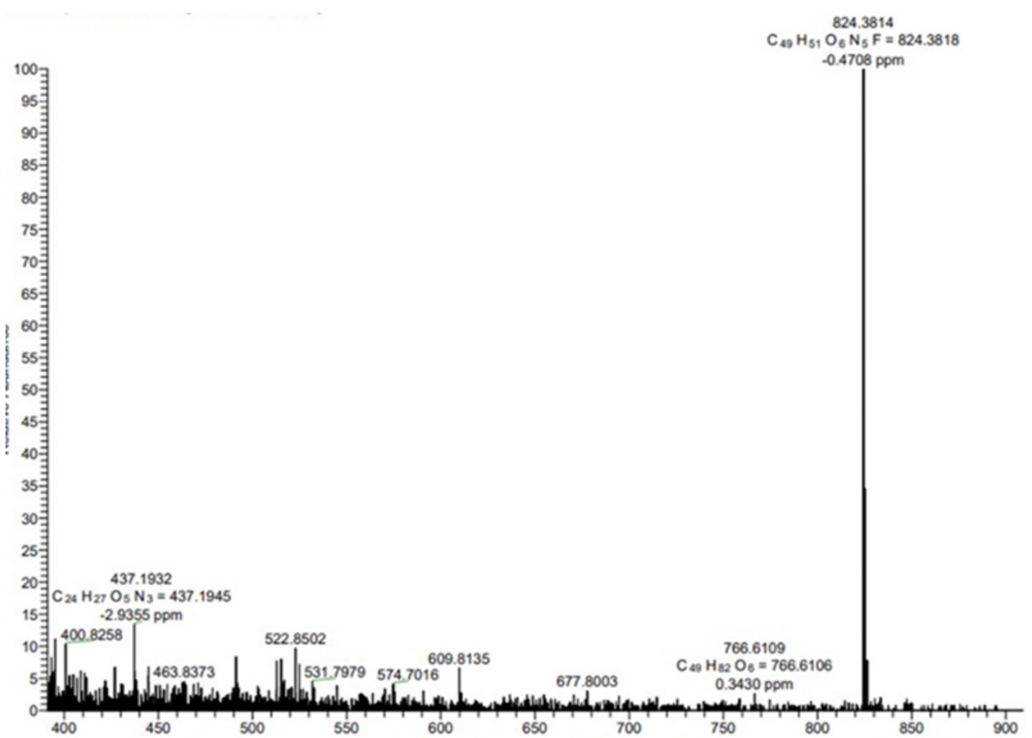

Figure S40: Mass spectra of an extract of Conjugate **1**-BSA mix after 72 h

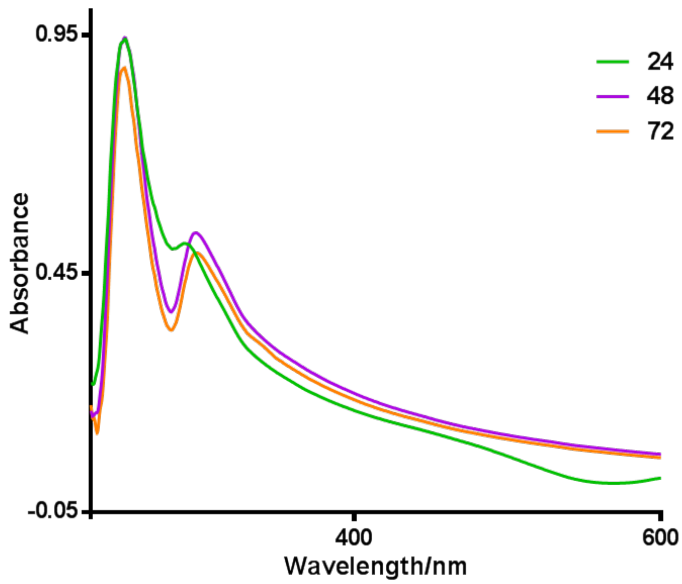

Figure S41: UV absorption profile of conjugate **2** in BSA after time points (in hours)

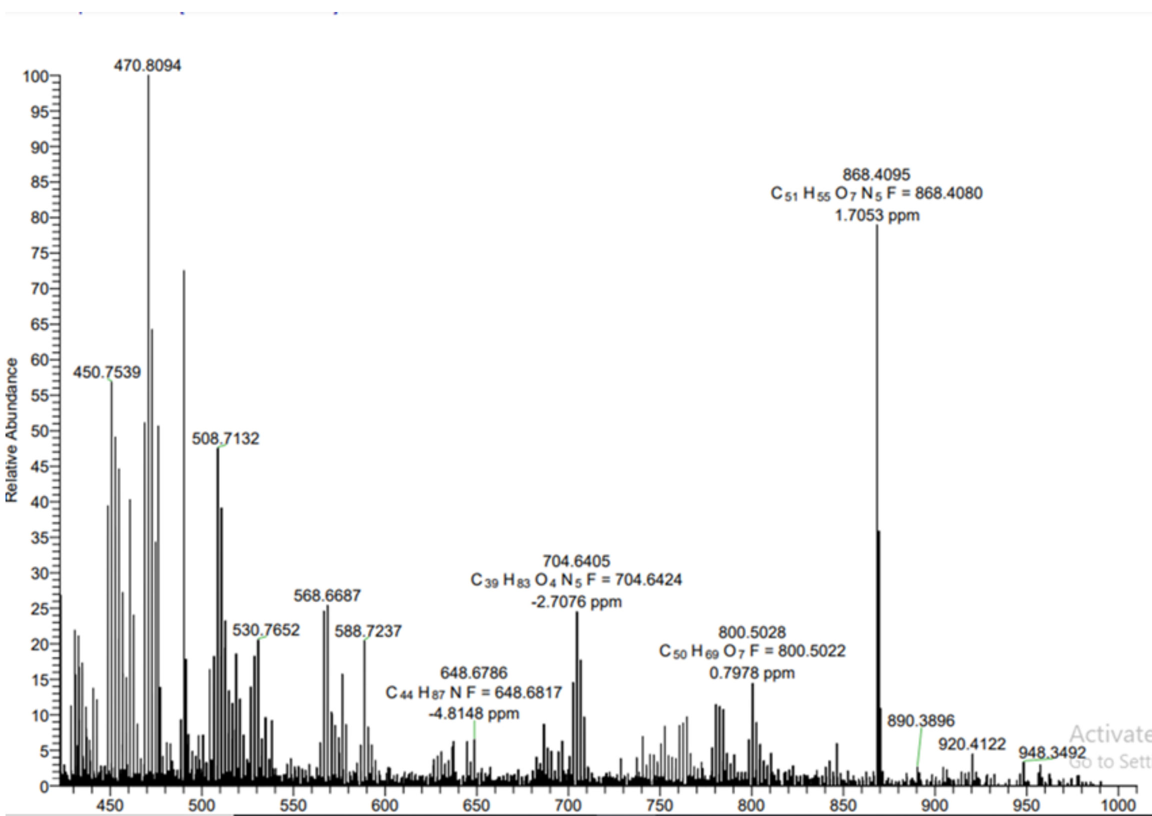

Figure S42: Mass spectra of an extract of Conjugate **2**-BSA mix after 72 h

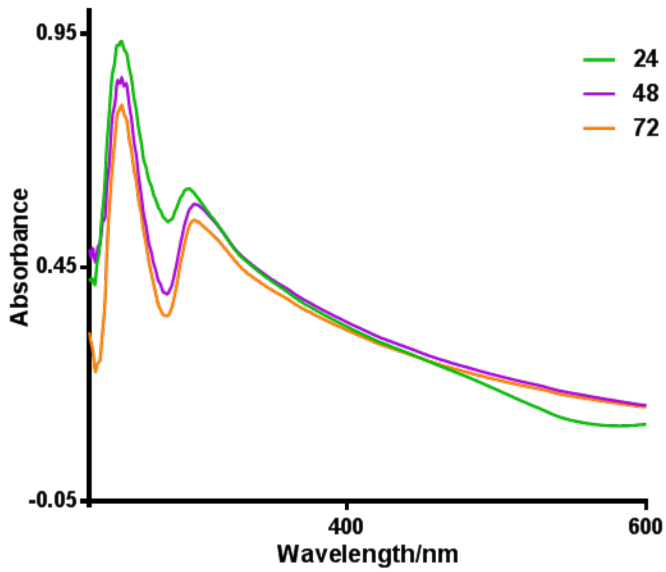

Figure S43: UV absorption profile of conjugate **3** in BSA after time points (in hours)

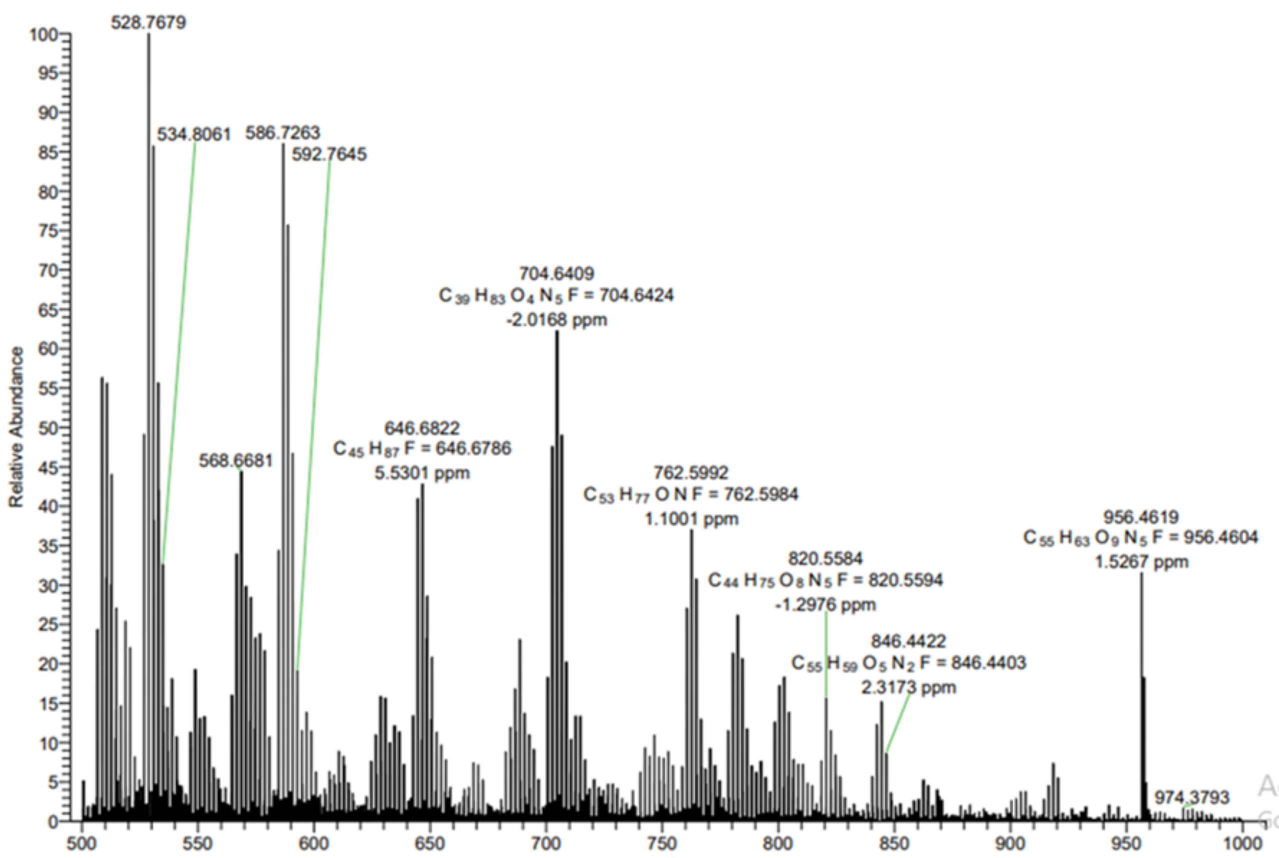

Figure S44: Mass spectra of an extract of Conjugate **3**-BSA mix after 72 h

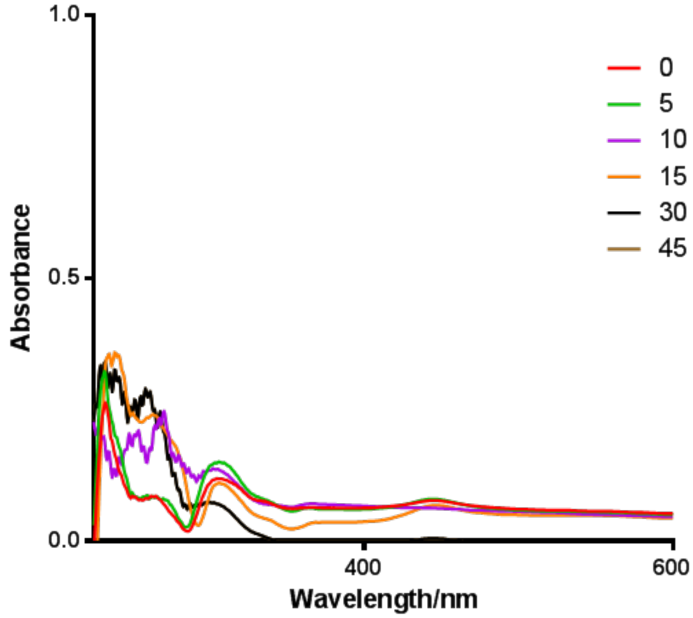

Figure S45: UV absorption profile of conjugate **1** incubated with liver microsomes at time points: 0, 5, 10 ,15, 30, 45 minutes.

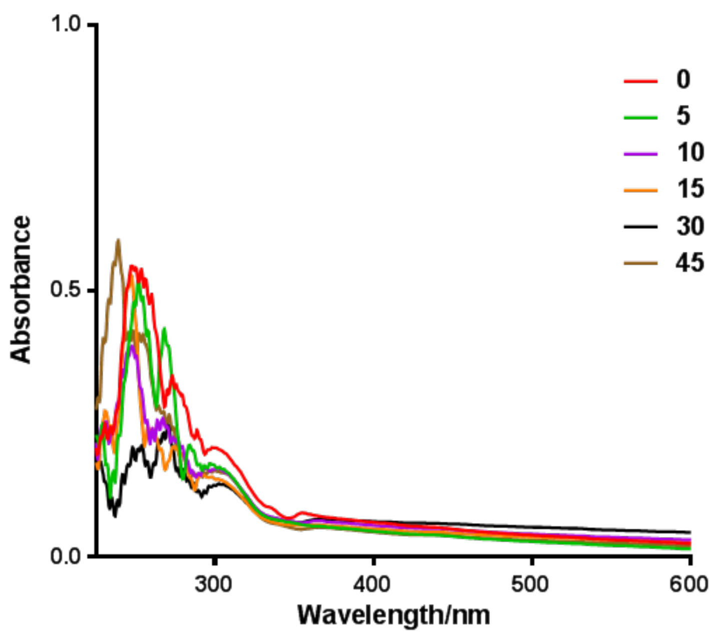

Figure S46: UV absorption profile of conjugate **2** incubated with liver microsomes at time points: 0, 5, 10, 15, 30 45minutes.

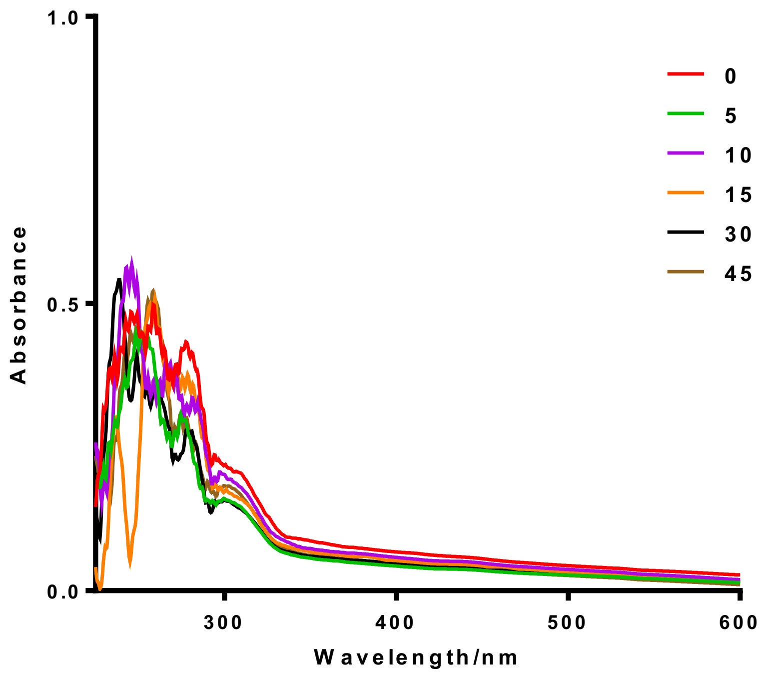

Figure S47: UV absorption profile of conjugate **3** incubated with liver microsomes at time points: 0, 5, 10, 15, 30 45minutes.

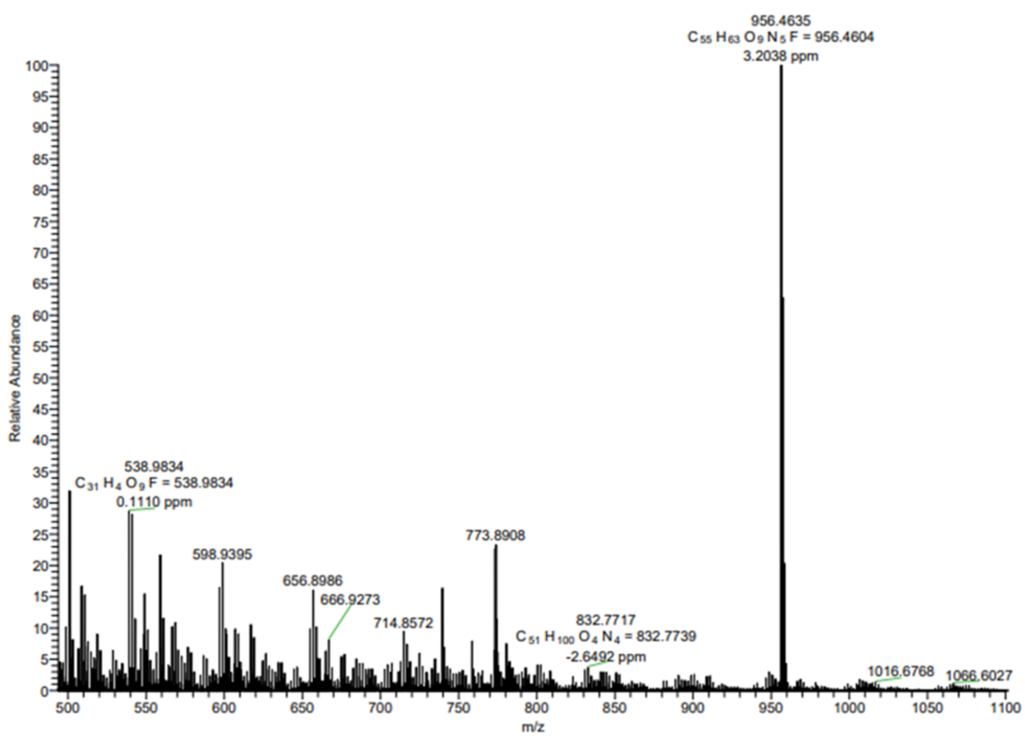

Figure S48: Mass spectra of an extract of Conjugate **3**-microsome mix after 45minute incubation.