Supporting Information

Discovery of QCA570 as an Exceptionally Potent and Efficacious Proteolysis Targeting Chimera (PROTAC) Degrader of the Bromodomain and Extra-Terminal (BET) Proteins Capable of Inducing Complete and Durable Tumor Regression

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Contents of Supporting Information:

Figure S1. Related to Figure 3. Western blotting analysis of BRD2, BRD3, and BRD4 proteins in RS4;11 cells treated with BET inhibitor **22**, compound **26** and BET degraders **27, 28, 29, 30,** and **31**. RS4;11 cells were treated for 3 h with each individual compound at indicated concentrations. BET-BRD protein degradation was determined by western blot probed with specific antibodies. Decreased levels of c-Myc were used to determine the biological activity of each compound. GAPDH was used as loading control.

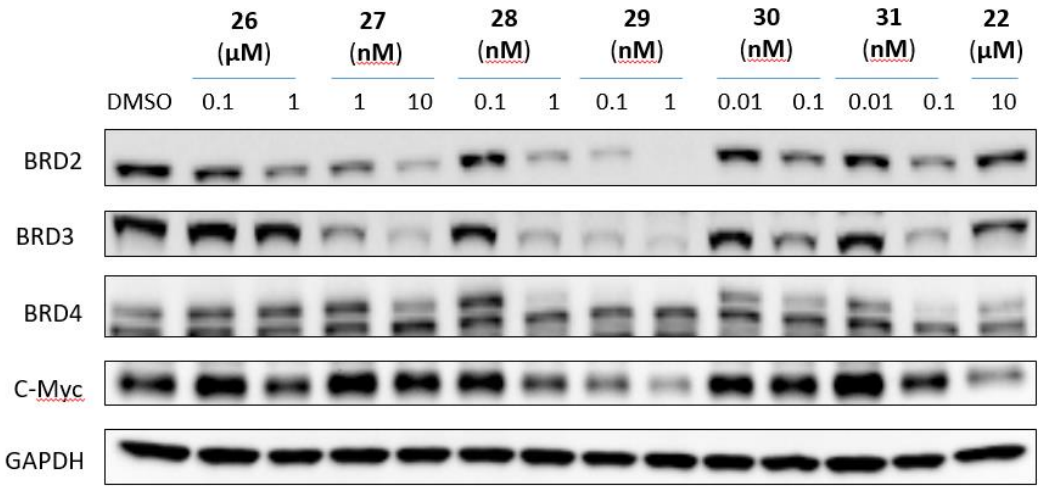


Figure S2. Western blotting analysis of GSPT1 proteins in RS4;11 cells treated with BET degrader **35**. RS4;11 and MV-4-11 cells were treated with BET degrader **35** (QCA570) and the corresponding BET inhibitor **22** (QCA276) at the indicated concentrations for 3 hours. Then cell lysates were analyzed by western blotting for protein level of GSPT1, probed with a specific GSPT1 polyclonal antibody (ab126090, Abcam). GAPDH was used as loading control.

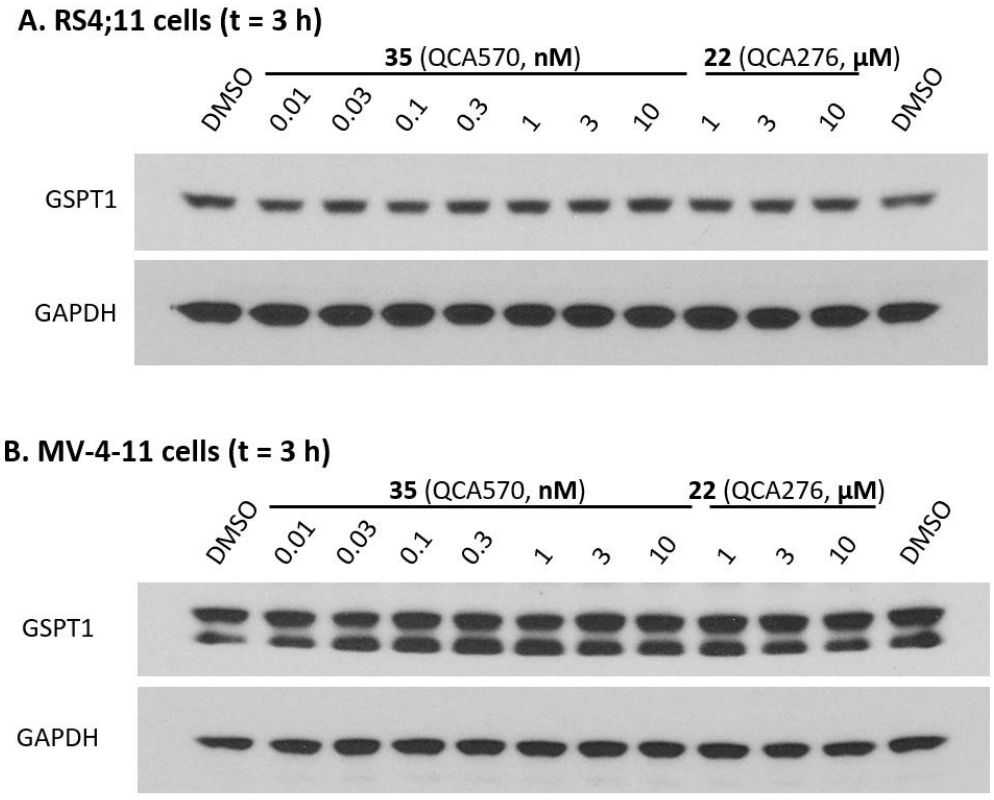
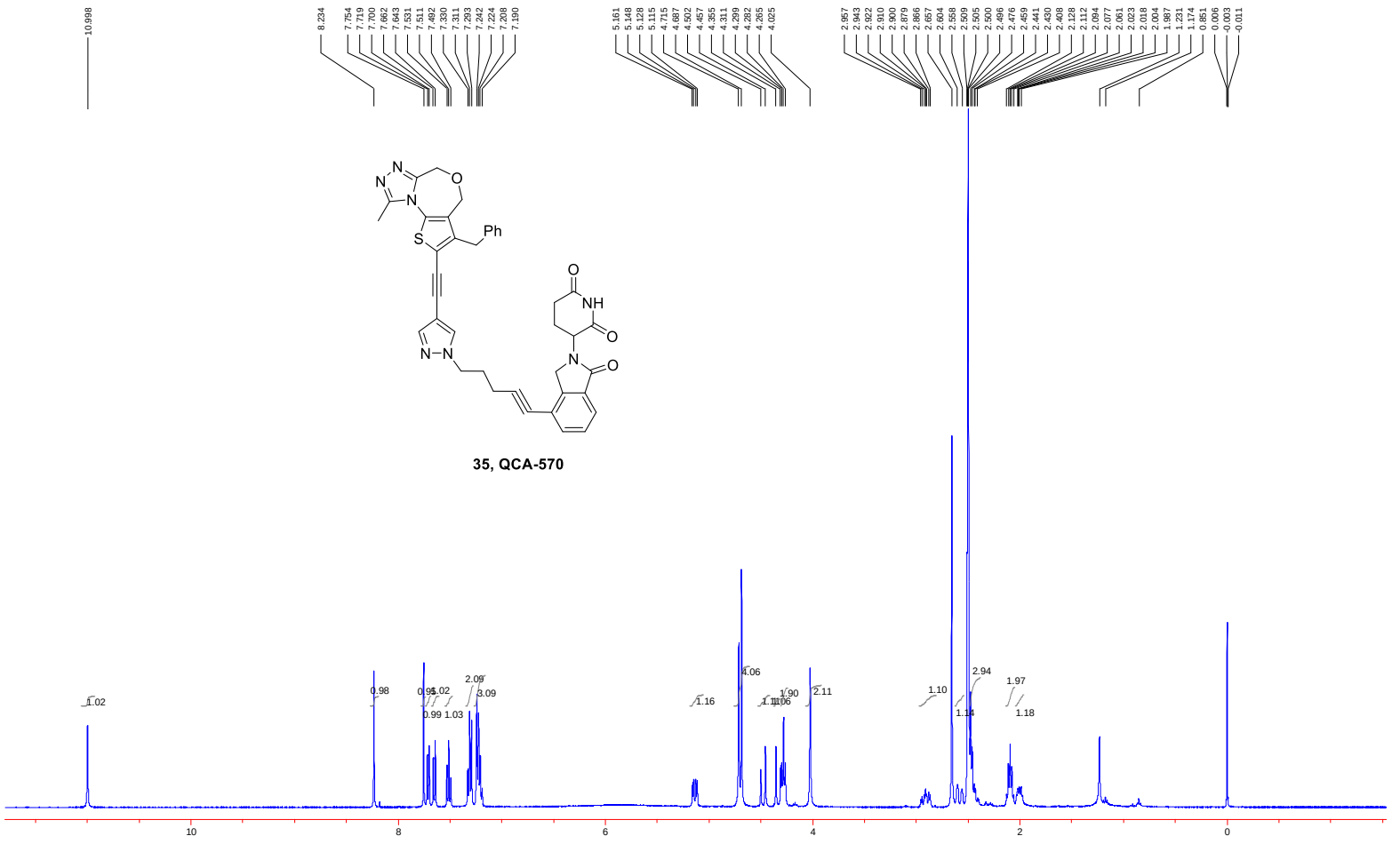


Figure S3. ^{1}H NMR of **35**.

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7.700
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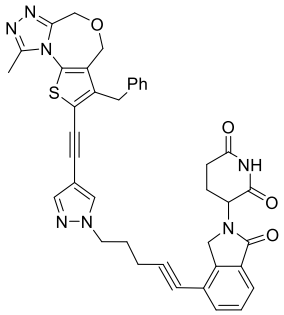
7.242
7.224
7.208
7.190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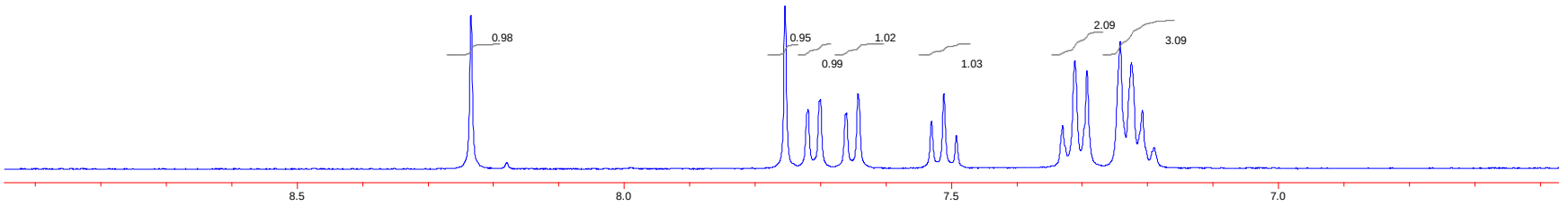
N
N
O
S
Ph
O
NH
O
N
O
N–N

35, QCA-570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8.0
7.5
7.0

Figure S4. ^{13}C NMR spectrum of compound **35**.

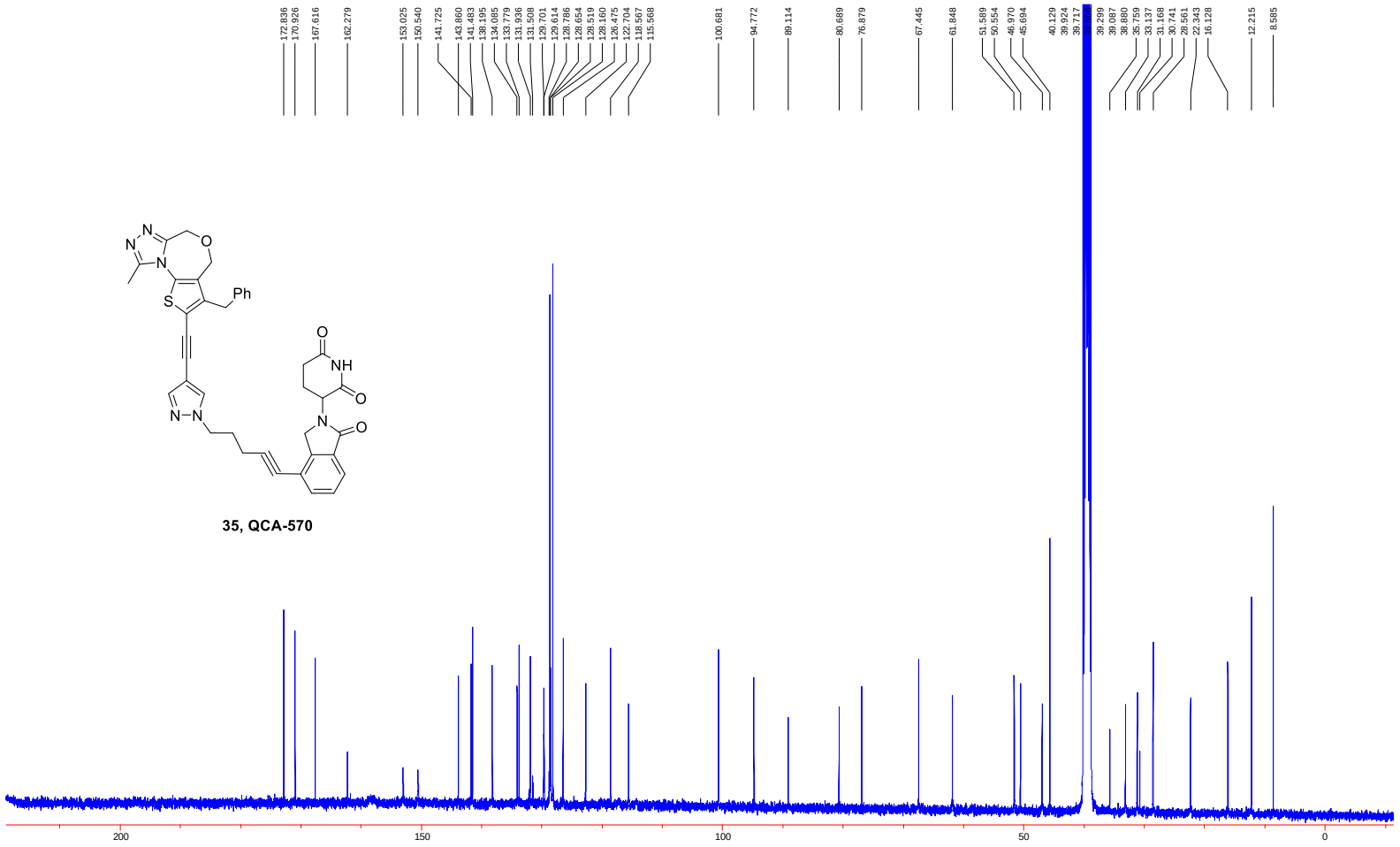

Figure S5. UPLC-MS results for compound **35**.