Supporting Information for

β-cyclodextrin-poly (β-amino ester) nanoparticles are a generalizable strategy for high loading and sustained release of HDAC inhibitors

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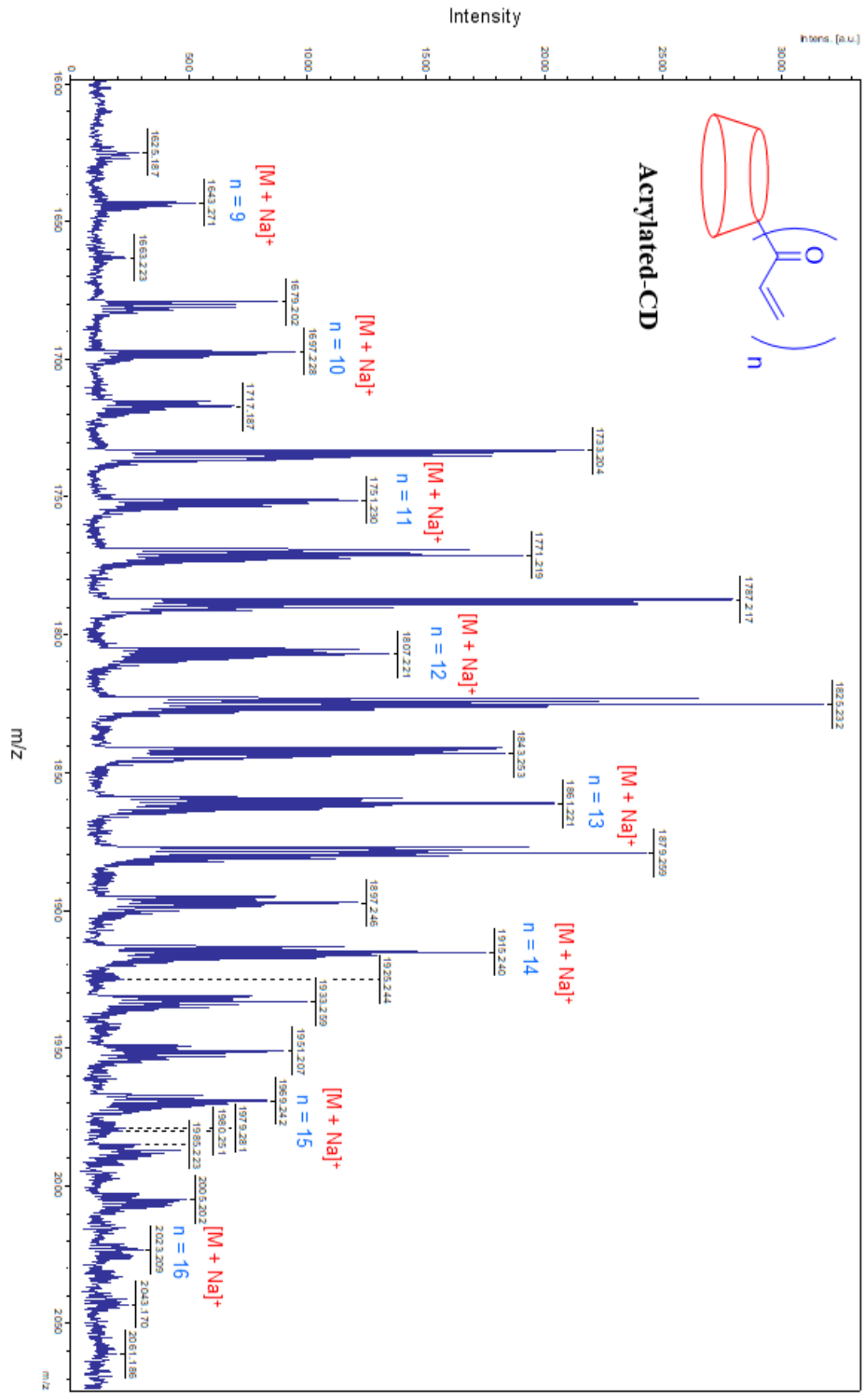

Figure S1 MALDI-Tof mass spectra of Acrylated-CD recorded in MS Bruker Autoflex MALDI-Tof mass spectrometer. Individual peaks for different degrees (n) of acrylation are identified. Spectra verified against existing reports in the literature [1].

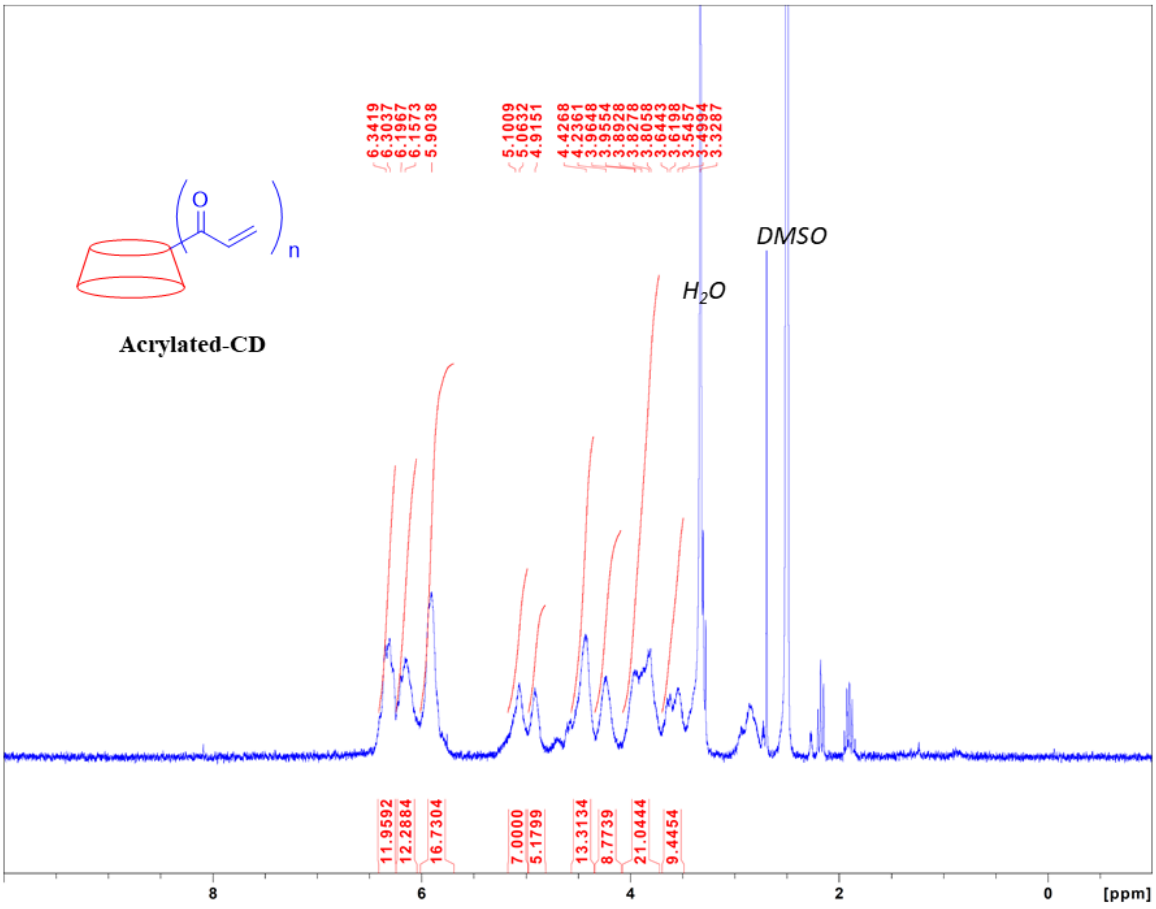

Figure S2 ^{1}H-NMR spectra of Acrylated-CD in DMSO-d_6 recorded in Bruker Avance 300 MHz NMR spectrometer. The integral labels are noted as an artifact of the software and does not affect the integrated area under the peaks. Spectra verified against existing reports in the literature [1].

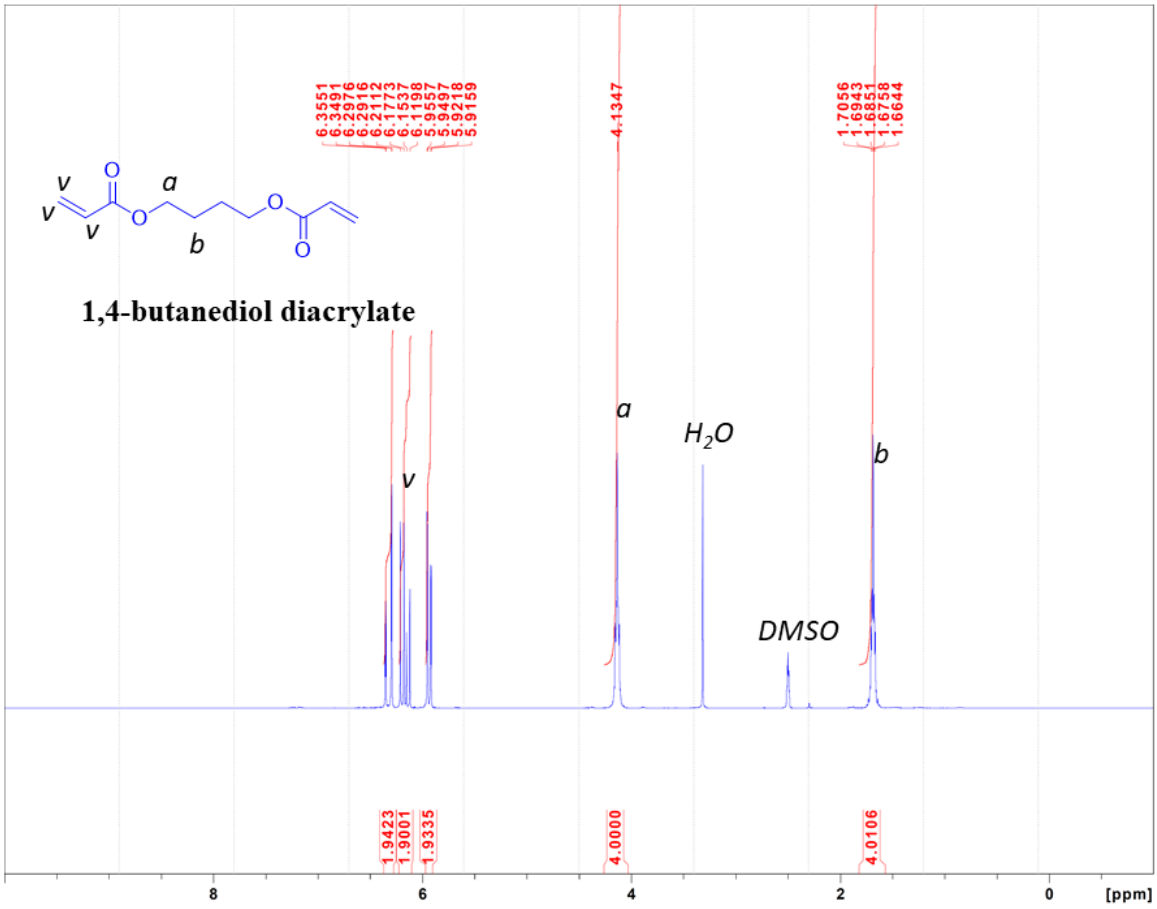

Figure S3 ^{1}H-NMR spectra of linker 1,4-butanediol diacrylate in DMSO-d_6 recorded in Bruker Avance 300 MHz NMR spectrometer. The integral labels are noted as an artifact of the software and does not affect the integrated area under the peaks.

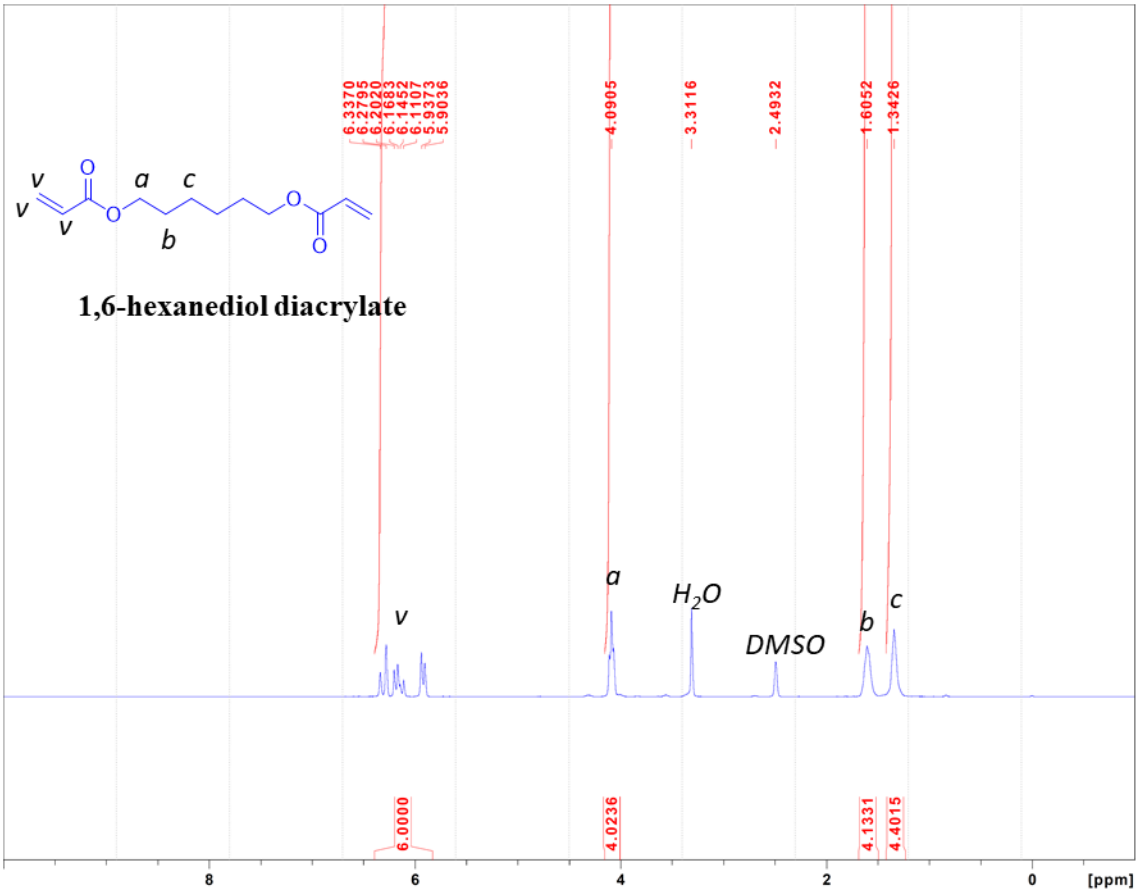

Figure S4 ^{1}H-NMR spectra of linker 1,6-hexanediol diacrylate in DMSO-d_6 recorded in Bruker Avance 300 MHz NMR spectrometer. The integral labels are noted as an artifact of the software and does not affect the integrated area under the peaks.

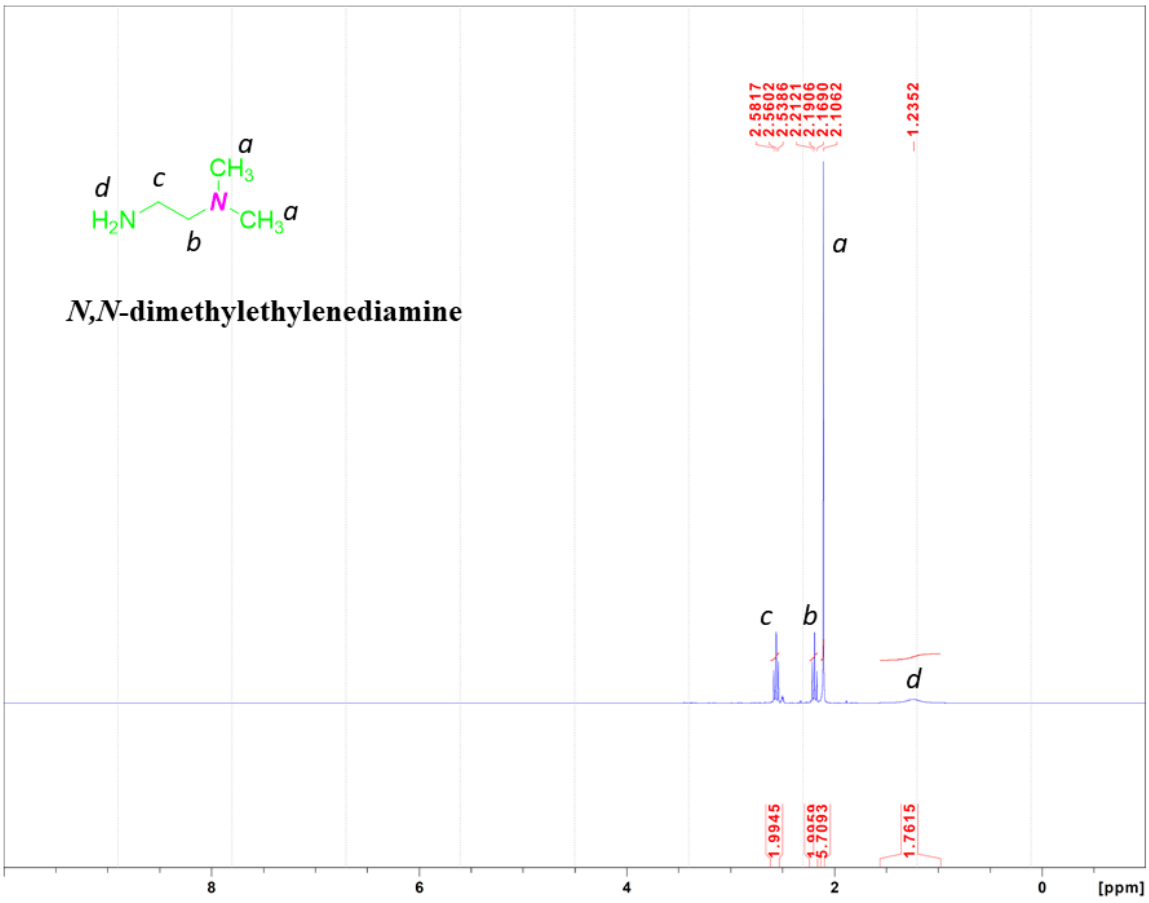

Figure S5 ^{1}H-NMR spectra of *N*,*N*-dimethylethylenediamine in DMSO-d_6 recorded in Bruker Avance 300 MHz NMR spectrometer. The integral labels are noted as an artifact of the software and does not affect the integrated area under the peaks.

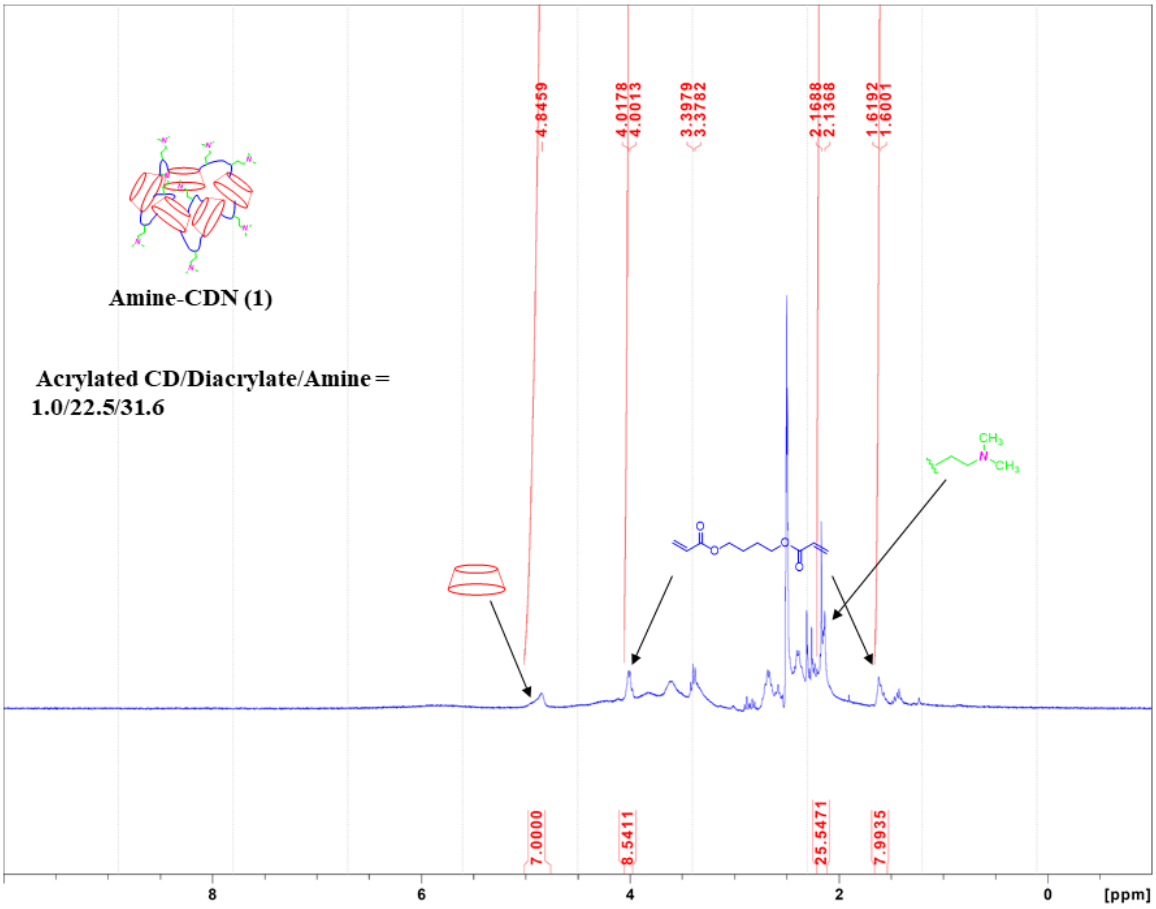

Figure S6 ^{1}H-NMR spectra of CDN-**1** in DMSO-d_6 recorded in Bruker Avance 300 MHz NMR spectrometer. Stoichiometric ratios of constituent units are recorded. Assignments of ^{1}H-NMR peaks were attributed to the protons present in the individual molecular entity, which indicates to the composition of the material (CDN-**1**). The integral labels are noted as an artifact of the software and does not affect the integrated area under the peaks.

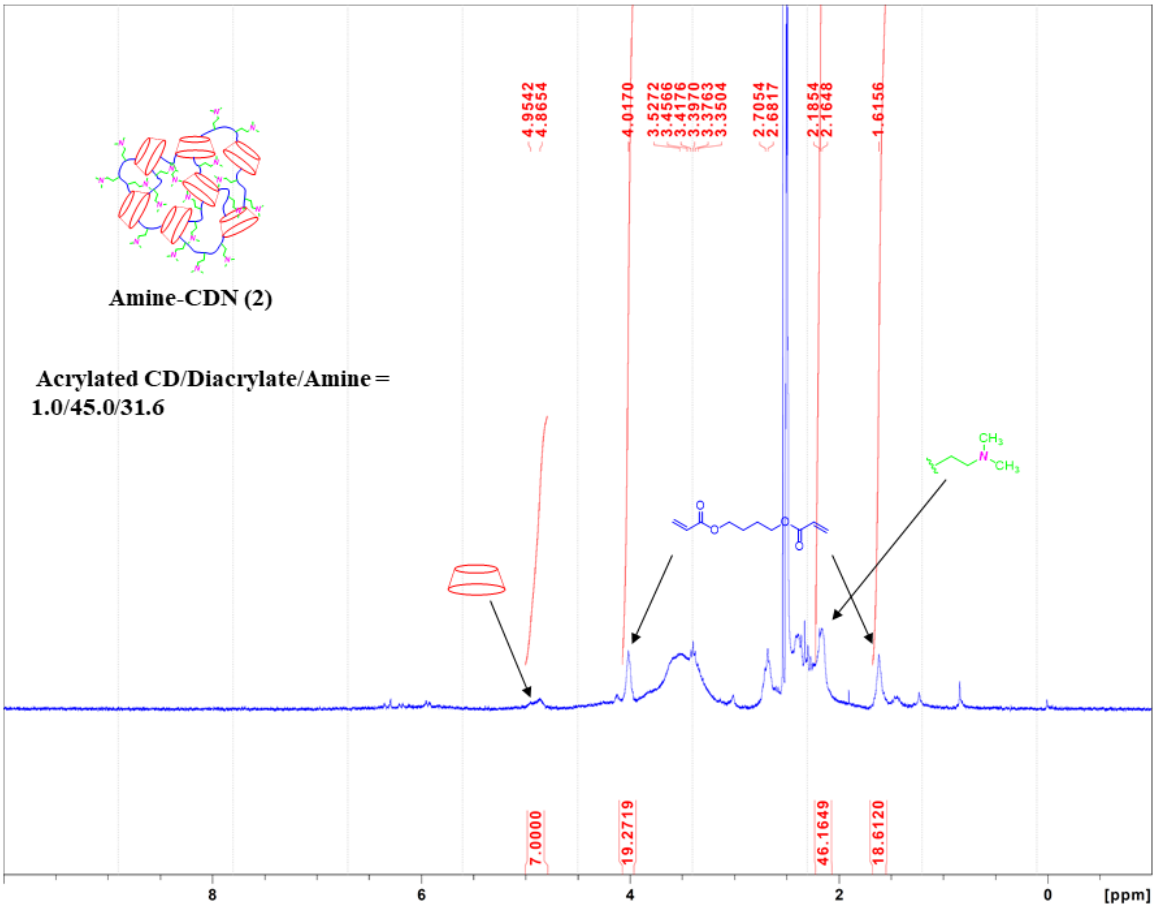

Figure S7 ^{1}H-NMR spectra of CDN-**2** in DMSO-d_6 recorded in Bruker Avance 300 MHz NMR spectrometer. Stoichiometric ratios of constituent units are recorded. Assignments of ^{1}H-NMR peaks were attributed to the protons present in the individual molecular entity, which indicates to the composition of the material (CDN-**2**). The integral labels are noted as an artifact of the software and does not affect the integrated area under the peaks.

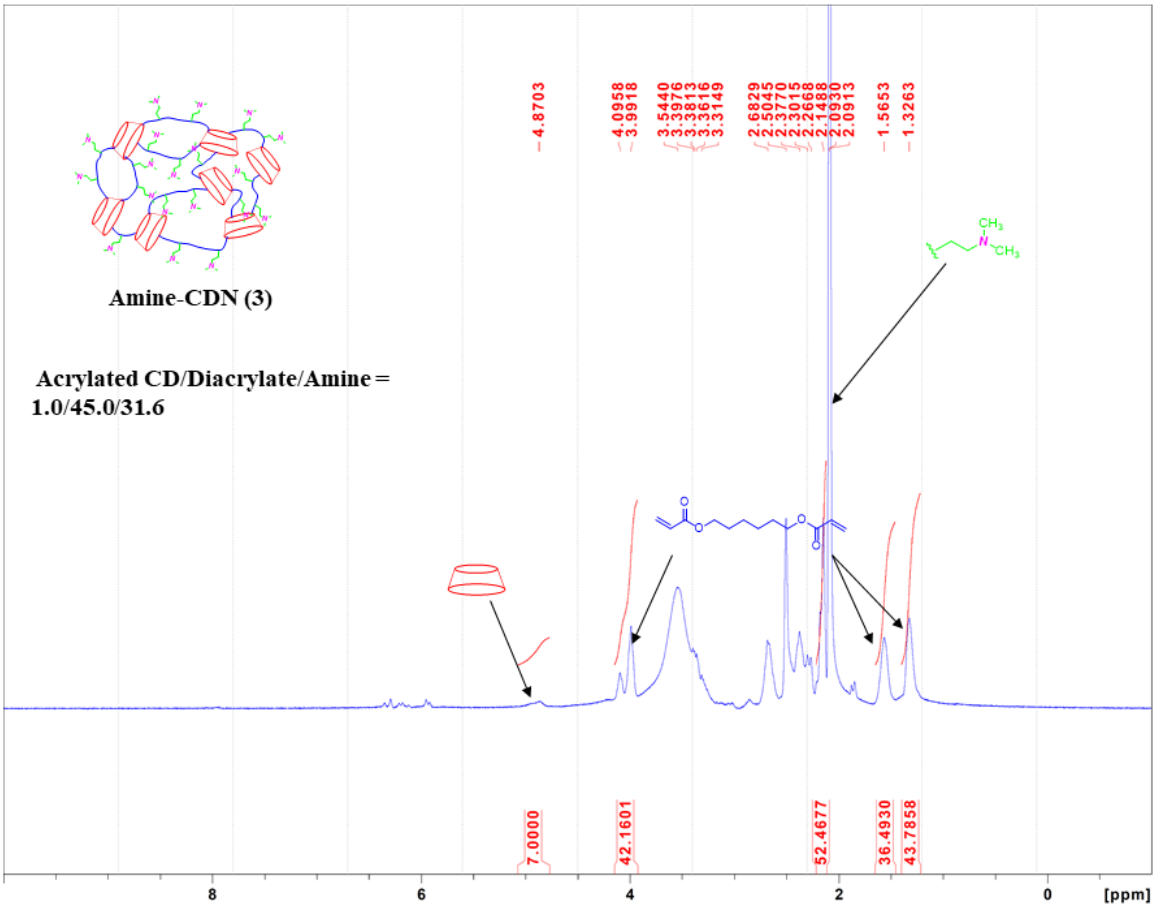

Figure S8 ^{1}H-NMR spectra of CDN-**3** in DMSO-d_6 recorded in Bruker Avance 300 MHz NMR spectrometer. Stoichiometric ratios of constituent units are recorded. Assignments of ^{1}H-NMR peaks were attributed to the protons present in the individual molecular entity, which indicates to the composition of the material (CDN-**3**). The integral labels are noted as an artifact of the software and does not affect the integrated area under the peaks.

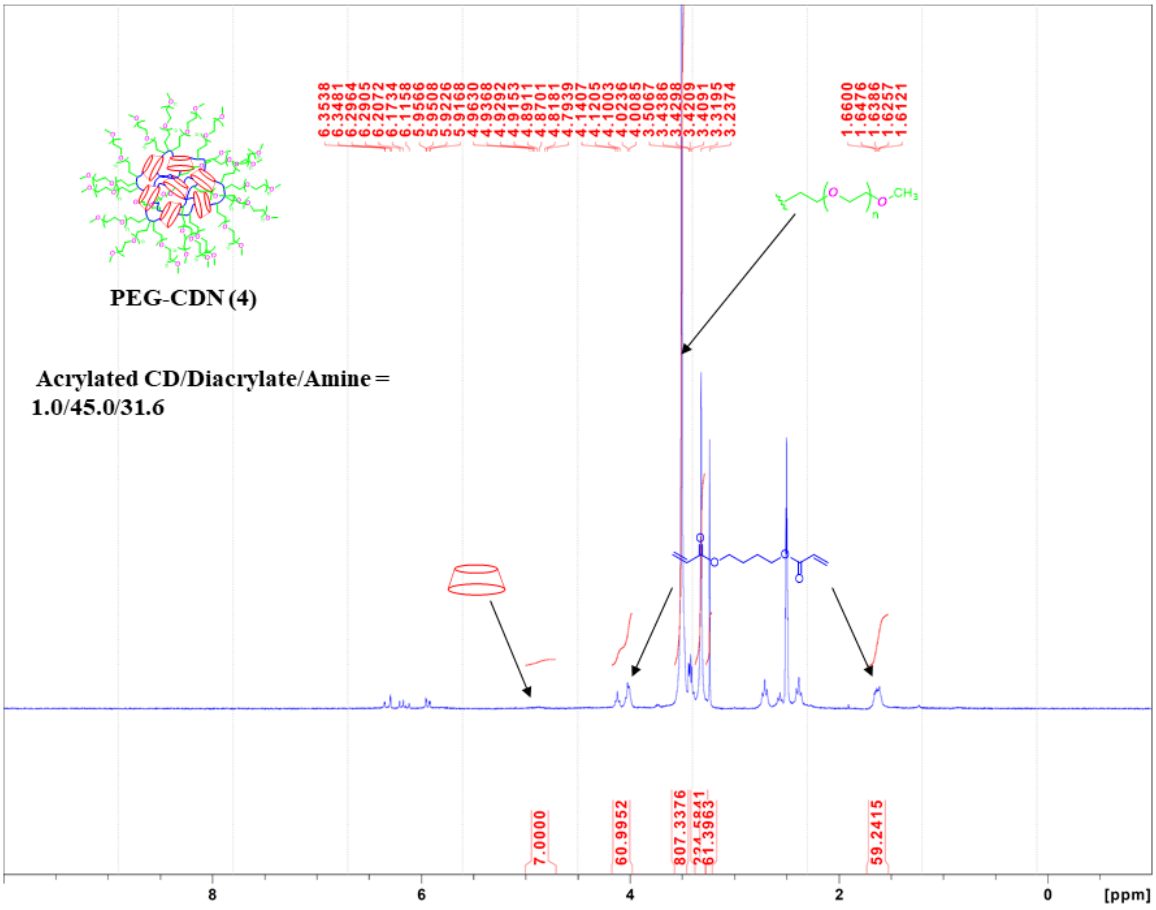

Figure S9 ^{1}H-NMR spectra of CDN-**4** in DMSO-d_6 recorded in Bruker Avance 300 MHz NMR spectrometer. Stoichiometric ratios of constituent units are recorded. Assignments of ^{1}H-NMR peaks were attributed to the protons present in the individual molecular entity, which indicates to the composition of the material (CDN-**4**). The integral labels are noted as an artifact of the software and does not affect the integrated area under the peaks.

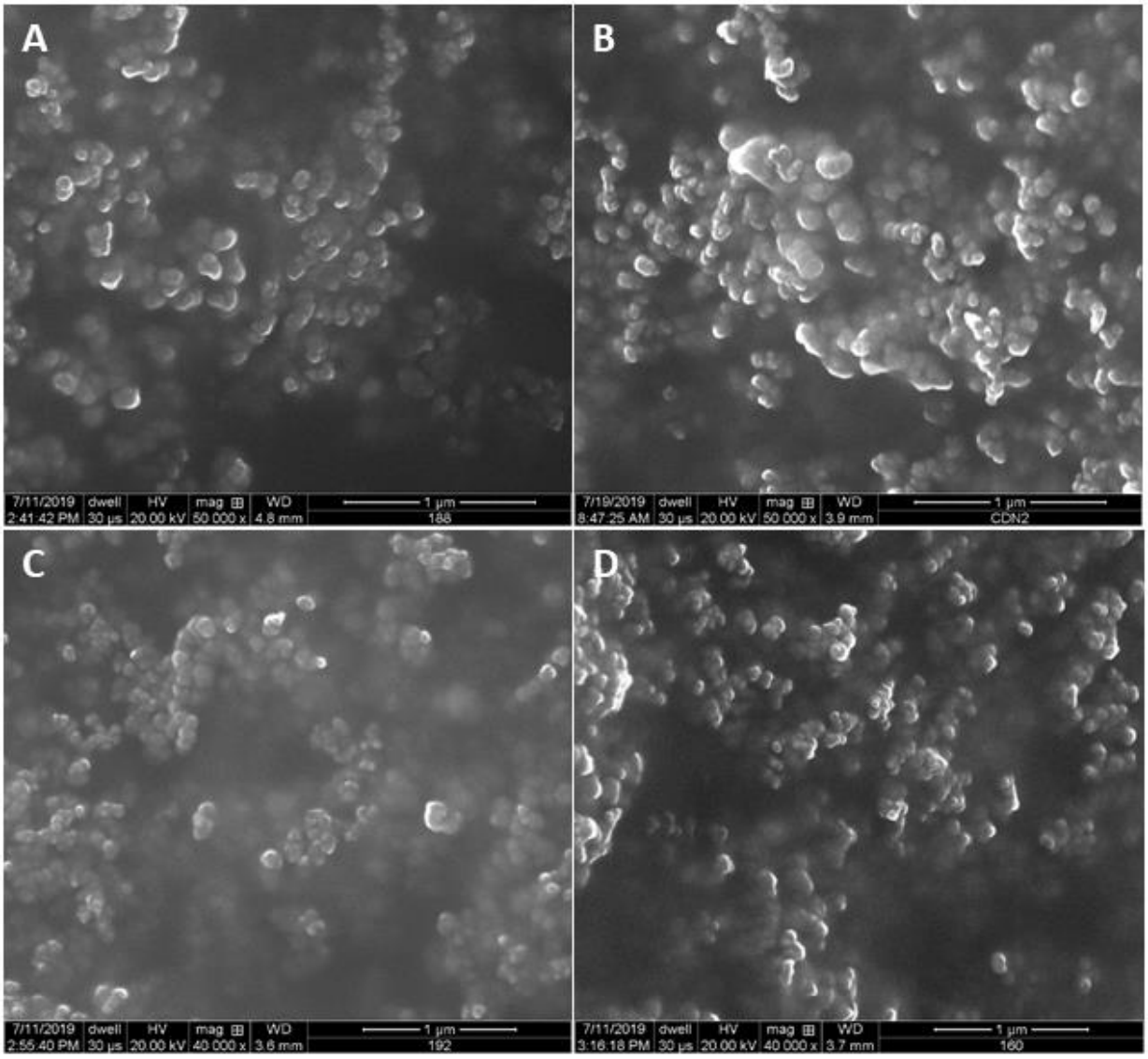

Figure S10 Scanning electron microscope images of **(A)** CDN-**1**; **(B)** CDN-**2; (C)** CDN-**3 & (D)** CDN-**4** recorded using FEI Quanta 400 environmental scanning electron microscope. Scale bar = 1µm.

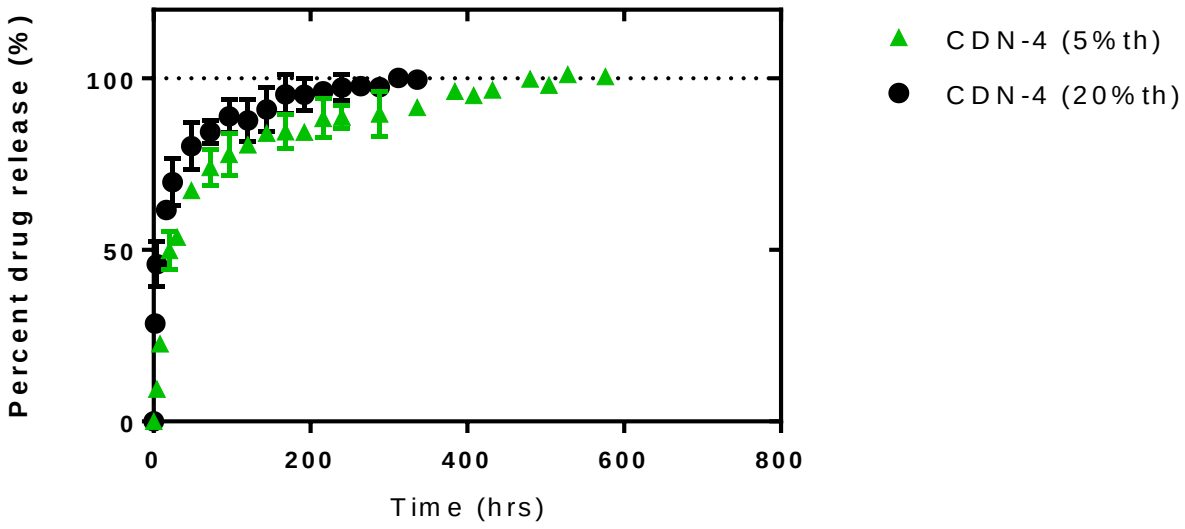

Figure S11 Controlled release of 5% (w/w) & 20% (w/w) theoretically drug-loaded CDN-**4** samples. Error bars are reported as the standard deviation of at least two separate measurements.

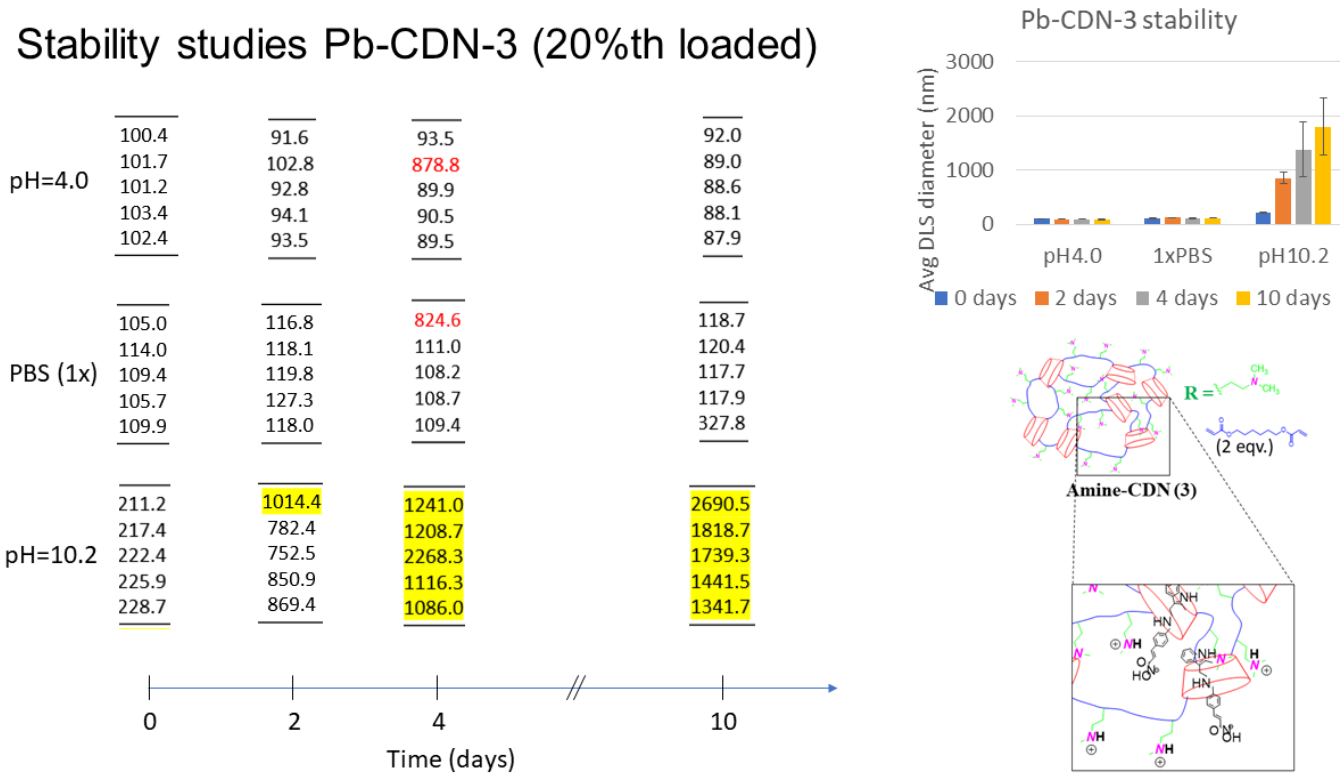

Figure S12 Stability studies of panobinostat loaded (20% theoretical) CDN-**3** nanoparticles in acidic (pH=4.0), PBS (1x, pH=7.4) and basic (pH=10.2) media. Micron aggregates are highlighted in yellow. Measurements in red are statistical outliers.

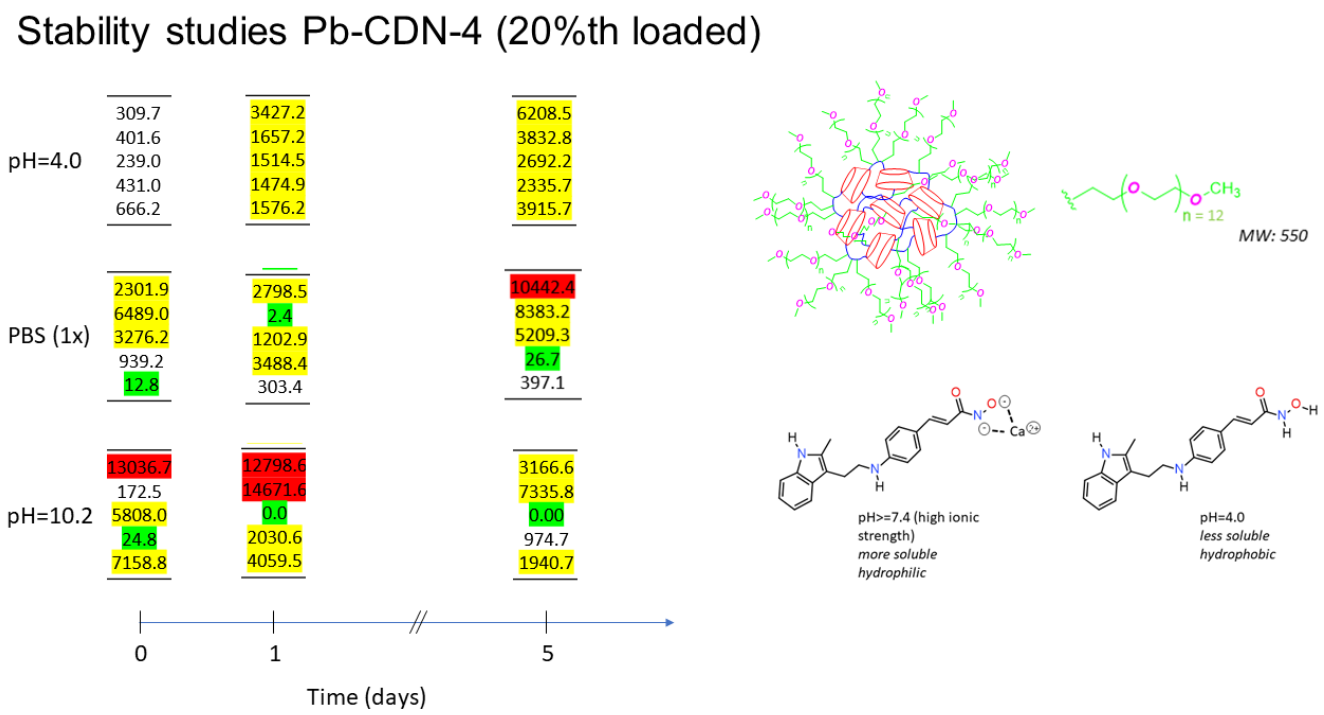

Figure S13 Stability studies of panobinostat loaded (20% theoretical) CDN-**4** nanoparticles in acidic (pH=4.0), PBS (1x, pH=7.4) and basic (pH=10.2) media. Micron aggregates are highlighted in yellow. Smaller populations (<100nm) are highlighted in green, while populations >10µm are highlighted in red.

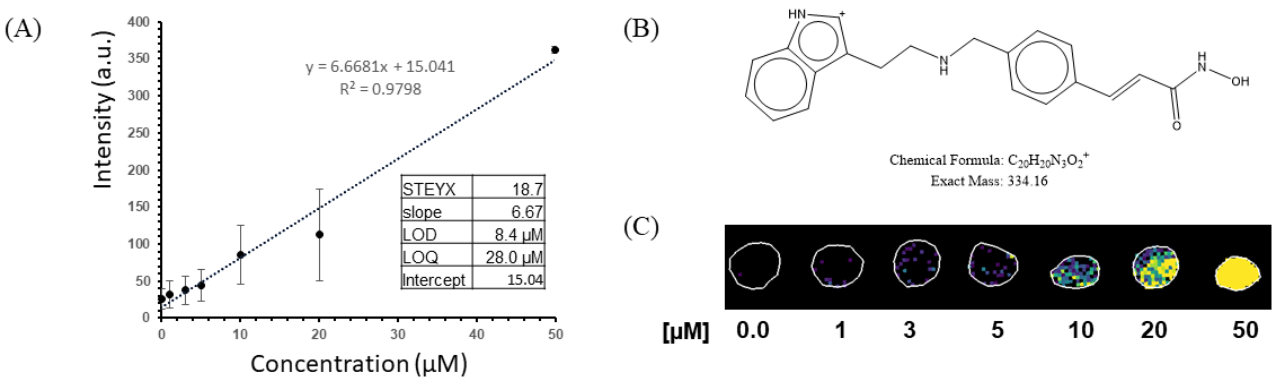

Figure S14 (A) Calibration curve for MALDI MSI quantitation of panobinostat by monitoring the intensity of the fragment ion at *m/z* 317.152; **(B)** The chemical structure of the precursor ion used for the MRM method; **(C)** ion images from the tissue mimetic model.

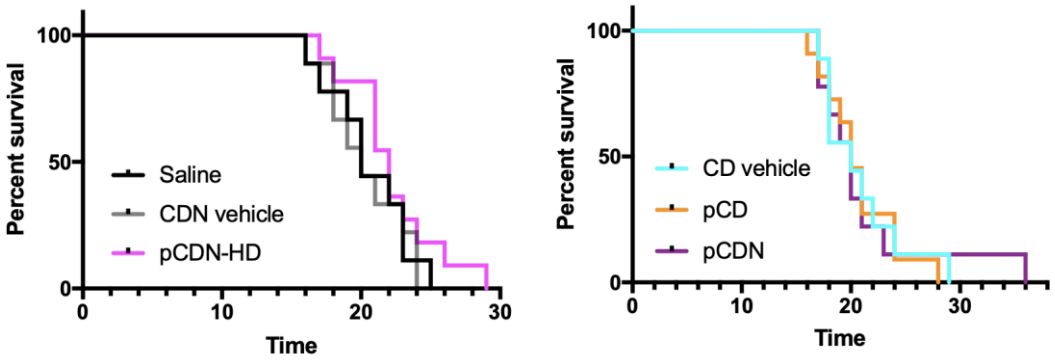

Figure S15 Kaplan-Meier curve showing survival of mice bearing orthotopic GL261 tumors following CED administration of various treatments.

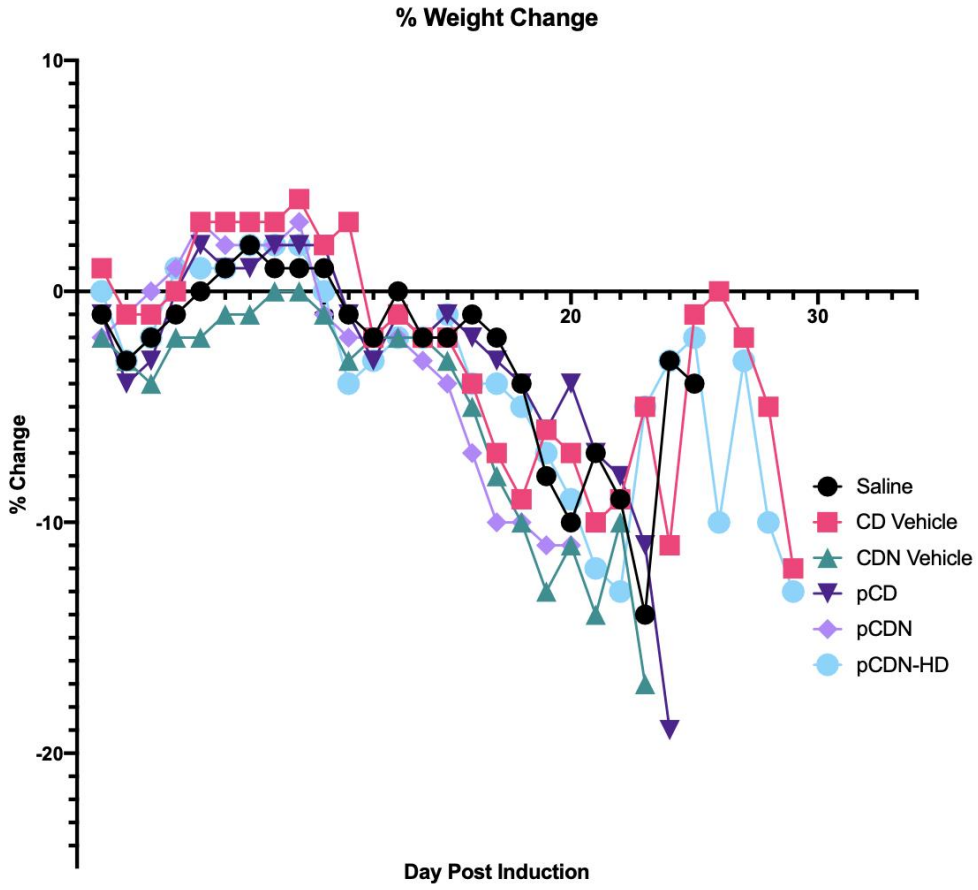

Figure S16 Plots of post treatment weight changes for mice bearing orthotopic GL261 tumors following CED administration of various treatments.

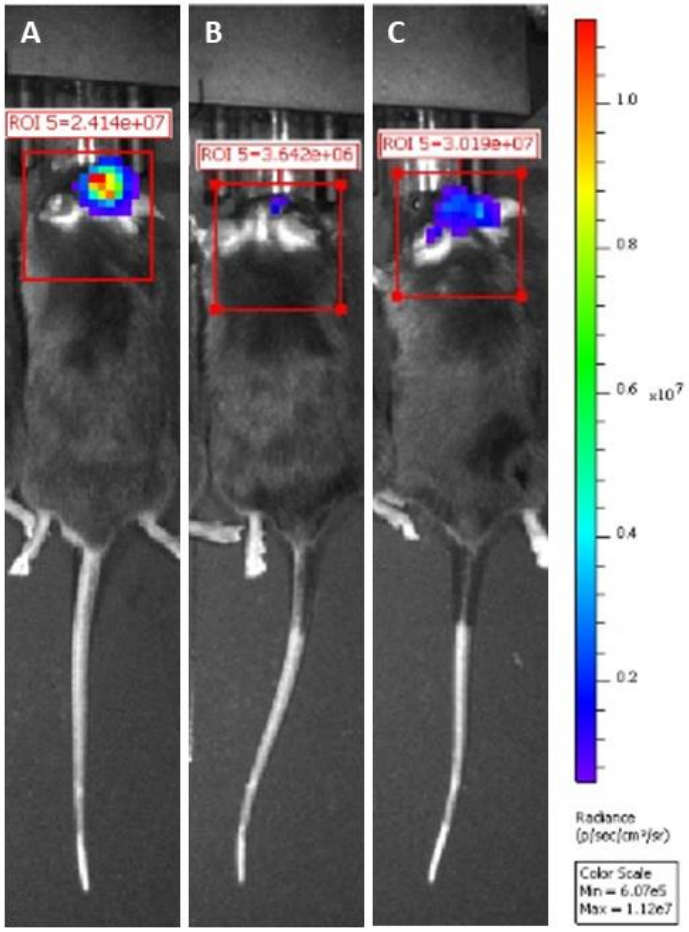

Figure S17 Tumor IVIS imaging of a representative mouse from pCDN-HD cohort **(A)** pre-treatment (1 day before); **(B)** post-treatment (after 4 days); **(C)** post-treatment (after 8 days).

References

[1] Gil, E.S.; Wu, L.; Xu, L.; Lowe, T.L. β-Cyclodextrin-poly (β-Amino Ester) Nanoparticles for Sustained Drug Delivery across the Blood−Brain Barrier. *Biomacromolecules* **2012**, *13*, 3533-3541. https://doi.org/10.1021/bm3008633