Extended-Release of Opioids using Fentanyl-based Polymeric Nanoparticles for Enhanced Pain Management

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$^1$H NMR spectra of fentanyl initiators

$^1$H NMR (500 MHz, CDCl$_3$)

Figure S1. $^1$H NMR spectrum of Fen-OH.

Figure S2. $^1$H NMR spectrum of Fen-Br.
Figure S3. $^1$H NMR spectrum of Fen-Acry-EtOH.
HPLC spectra of fentanyl initiators

Figure S4 Chromatographic profile of Fen-OH.

Figure S5 Chromatographic profile of Fen-Br.

Figure S6 Chromatographic profile of Fen-Acry-EtOH.
$^1$H NMR spectra of fentanyl polymers

Figure S7 $^1$H NMR spectrum of Fen-PLGA.

Figure S8 $^1$H NMR spectrum of Fen-Acry-PLGA.
GPC traces

**Figure S9** GPC trace of Fen-PLGA.

**Figure S10** GPC trace of Fen-Acry-PLGA.
DLS traces

**Figure S11** Size distribution of Fen-PLA NPs measured by DLS.

**Figure S12** Size distribution of Fen-PLGA NPs measured by DLS.

**Figure S13** Size distribution of Fen-Acry-PLGA NPs measured by DLS.
Figure S14 Size distribution of Fen-OH-PLGA NPs measured by DLS.
Zeta potential

Figure S15 Intensity distribution of the zeta potential of Fen-PLA NPs.

Figure S16 Intensity distribution of the zeta potential of Fen-PGLA nanoparticles.

Figure S17 Intensity distribution of the zeta potential of Fen-Acry-PGLA nanoparticles.
Figure S18  ESEM images: (a) Fen-PLA, Fen-PLGA, Fen-Acry-PLGA.
In vivo activity

Figure S19 Hot plat test: each point shows the % of MPE induced by fentanyl at different concentrations.

Figure S20 The change in mouse weight throughout the testing period.
Dissolvable microneedle arrays (MNA)

Figure S21 Tip-loaded dissolvable MNAs created using the micromilling/elastomer molding/spin-casting technique for patient-friendly delivery of opioid biohybrids in skin: (a) Optical microscope images of the elastomer mold after tip loading with the NPs; and (b) bright field microscope images of the tip-loaded dissolvable MNAs along with merged bright field and fluorescence microscope image of the tip portion of the individual microneedle.