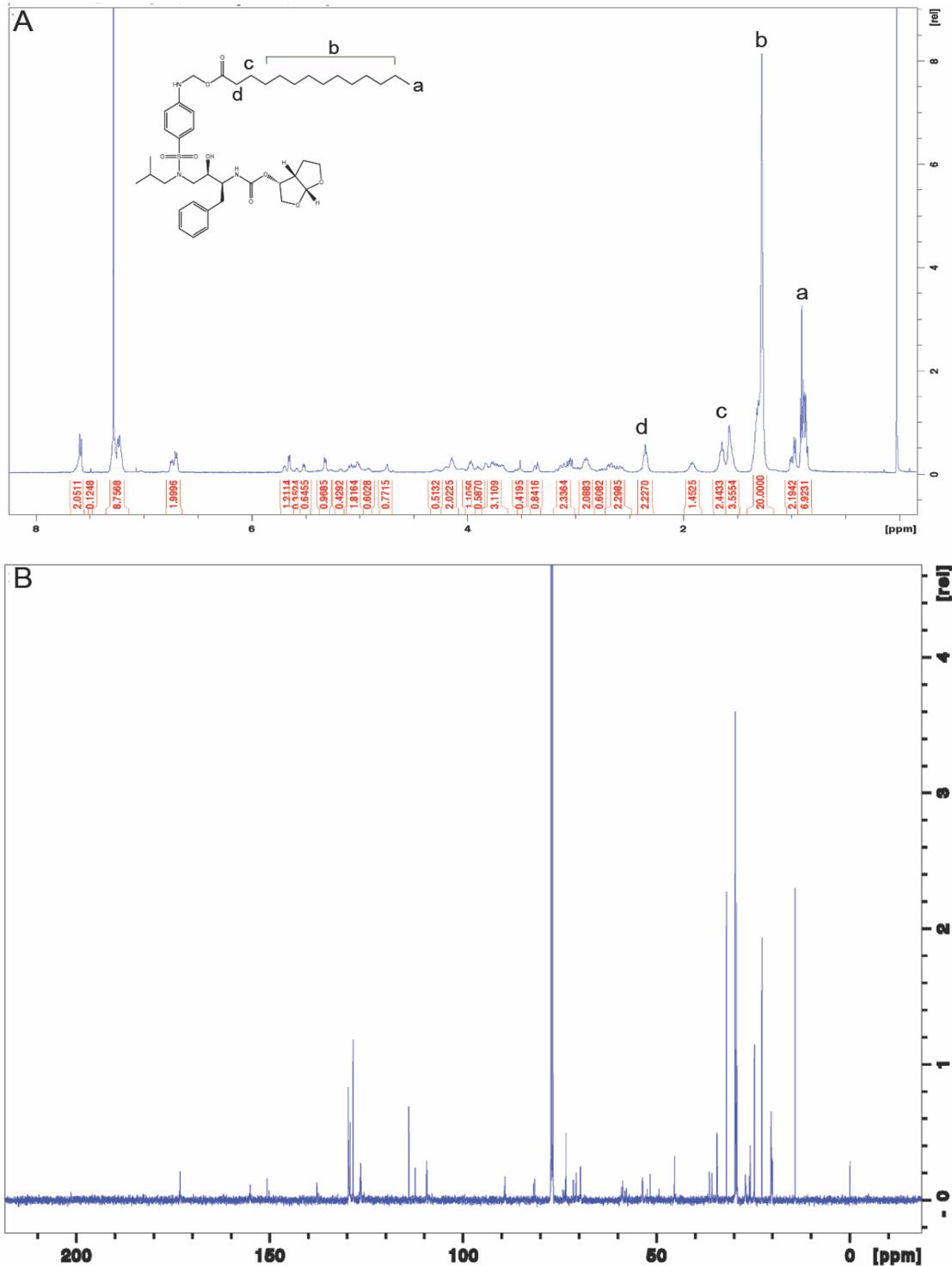


Synthesis and Characterization of Long Acting Darunavir Prodrugs

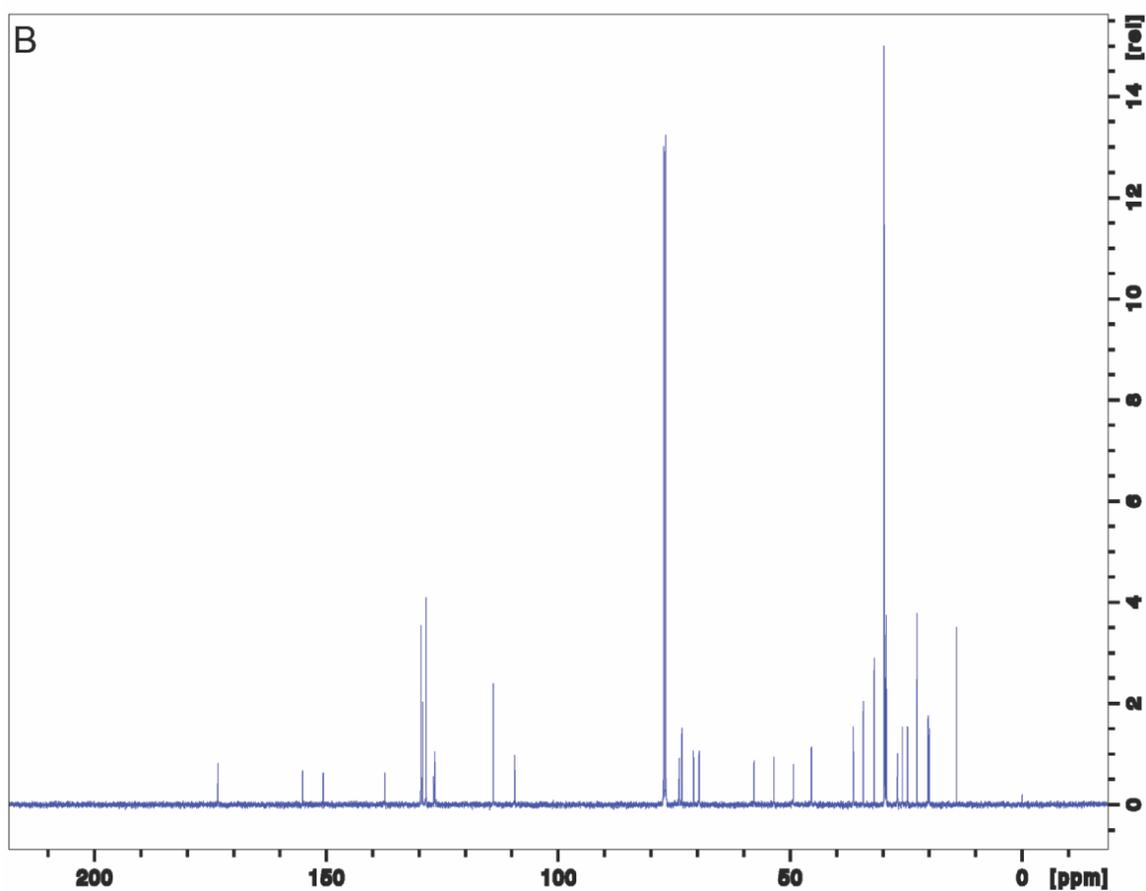
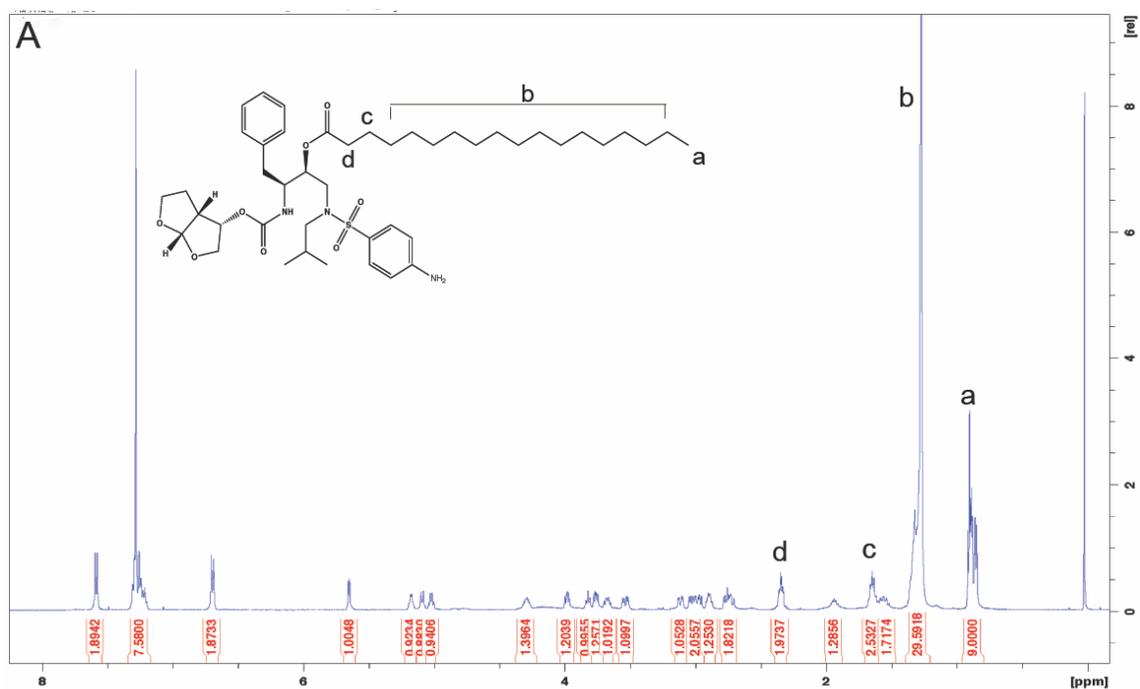
Supplemental Material

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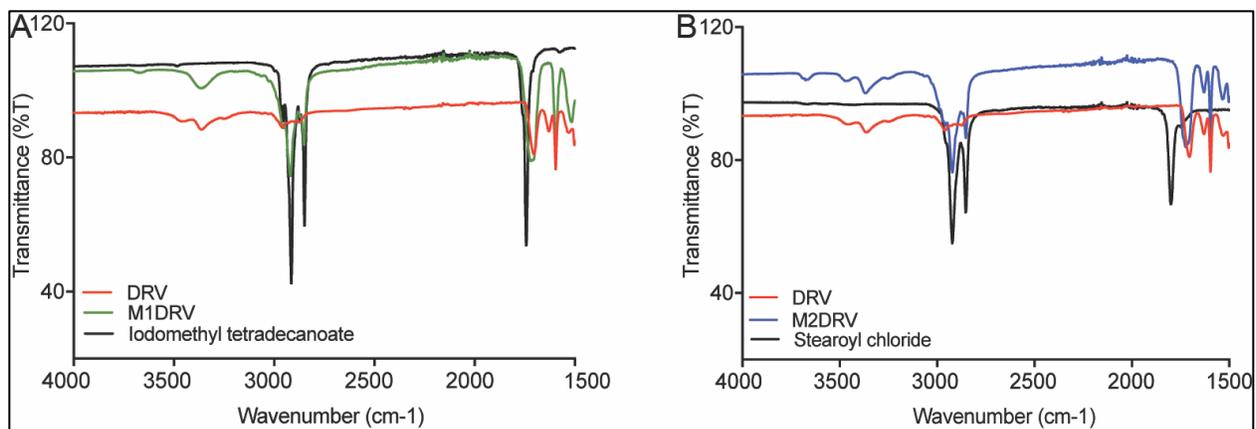
Supplementary Figures



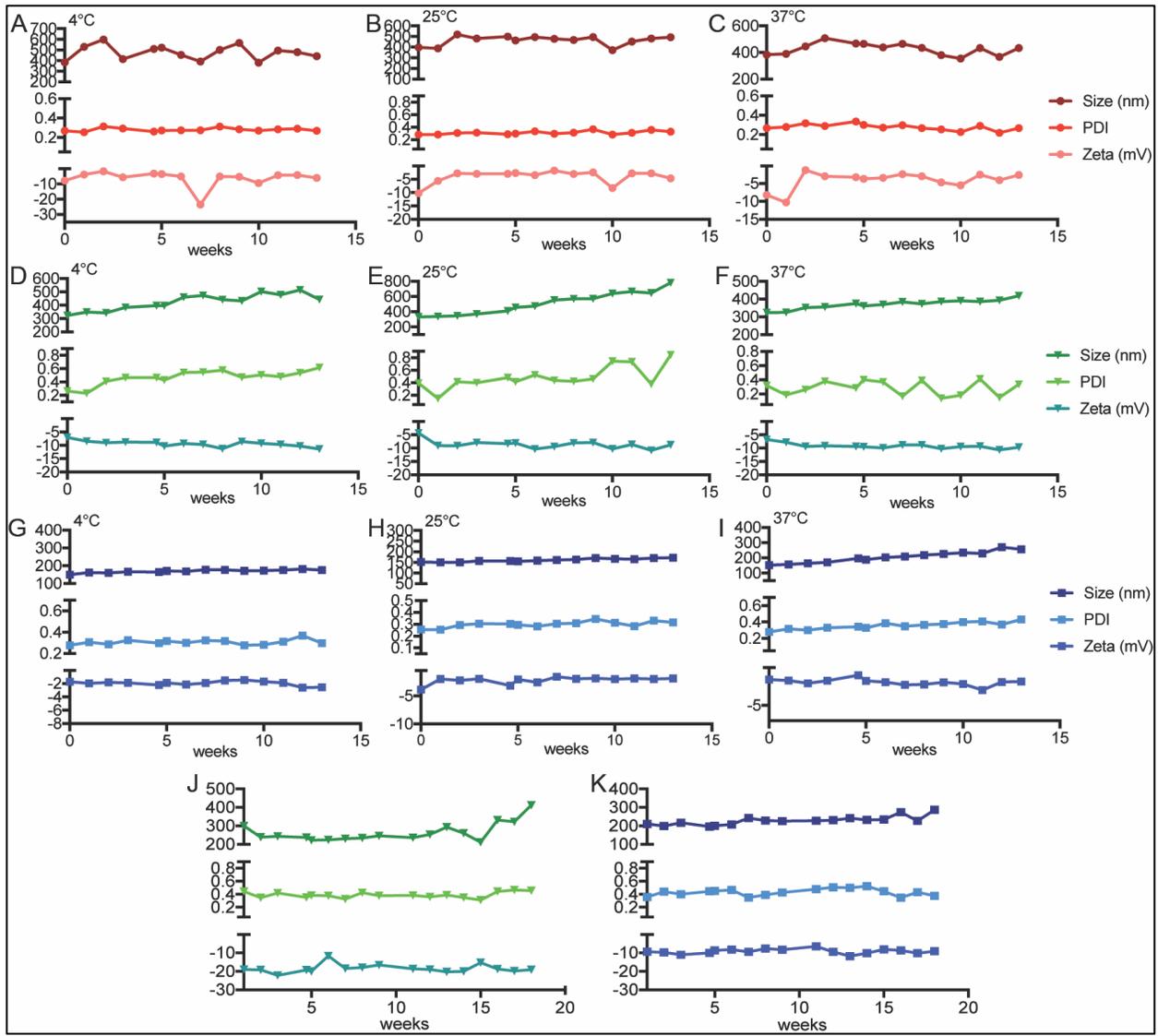
Supplemental Figure 1: NMR Characterization of M1DRV (A) ¹H NMR spectrum reflecting the additional terminal methyl and methylene protons of the fatty esters. **(B)** ¹³C NMR spectrum showing the addition of carbon peaks corresponding to the carbonyl groups at 173 ppm and aliphatic carbon atoms from the fatty acids



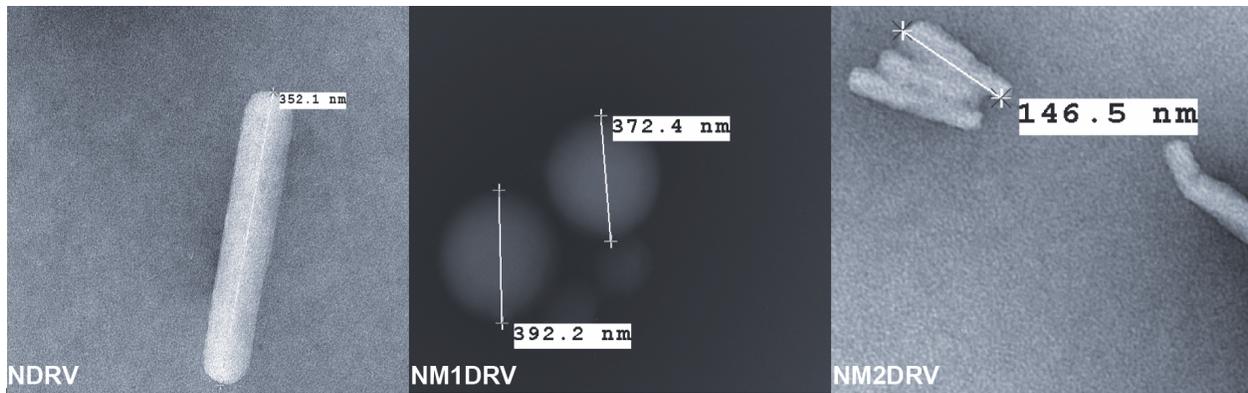
Supplemental Figure 2: NMR Characterization of M2DRV (A) ^1H NMR spectrum reflecting the additional terminal methyl and methylene protons of the stearoyl esters. **(B)** ^{13}C NMR spectrum showing the addition of carbon peaks corresponding to the carbonyl groups at 173 ppm and aliphatic carbon atoms from the fatty acids.



Supplemental Figure 3: Characterization of prodrugs. FTIR spectra for **M1DRV (A)** and **M2DRV (B)**. Absorption bands at 2917, 2915 and 2848 cm⁻¹ represent asymmetric and symmetric C-H stretches in the long chain fatty acids.



Supplemental Figure 4: Characterization and stability of DRV, M1DRV and M2DRV nanoformulations. (A-C) stability of NDRV over 13 weeks at different temperatures; 4°C, 25°C, and 37°C. **(D-F)** stability of NM1DRV over 13 weeks. **(G-I)** stability of NM2DRV over 13 weeks. **(J)** and **(K)** stability measurements of concentrated NM1DRV and NM2DRV over 18 weeks at 4°C. The concentrated formulations reflect PK dosing suspensions.



Supplemental Figure 5: Formulation morphologies by transmission electron microscopy. NDRV and NM2DRV were rod-shaped while **NM1DRV** exhibited spherical nanoparticle morphologies. The three formulations have diameters in the nanometer range.