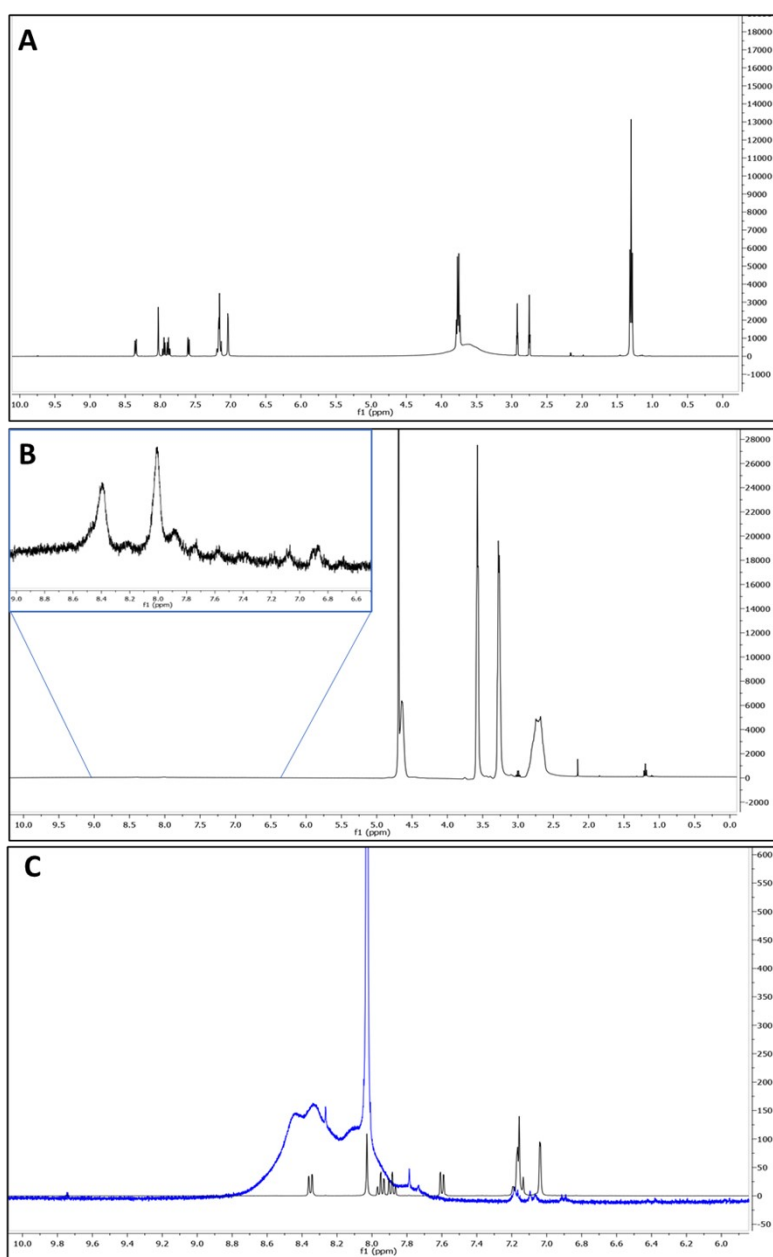


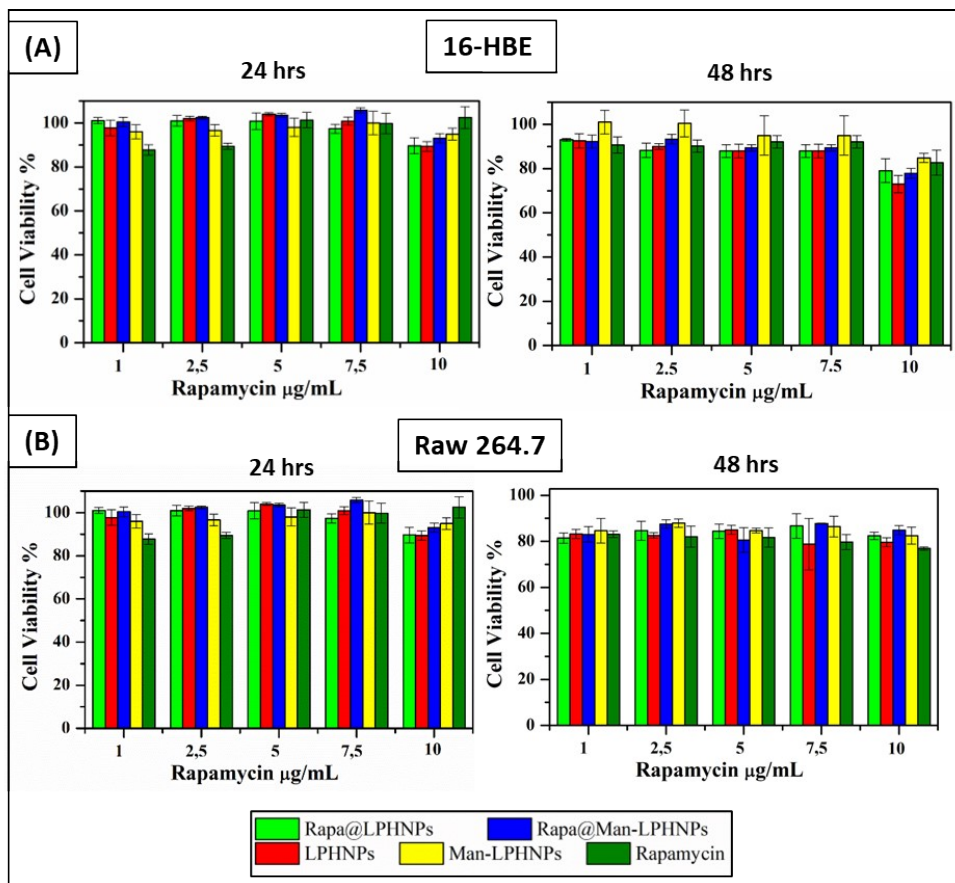
SUPPORTING INFORMATION

**Rapamycin – based inhaled therapy for potential treatment of COPD –  
related inflammation: production and characterization of aerosolizable  
Nano into Micro (NiM) particles**

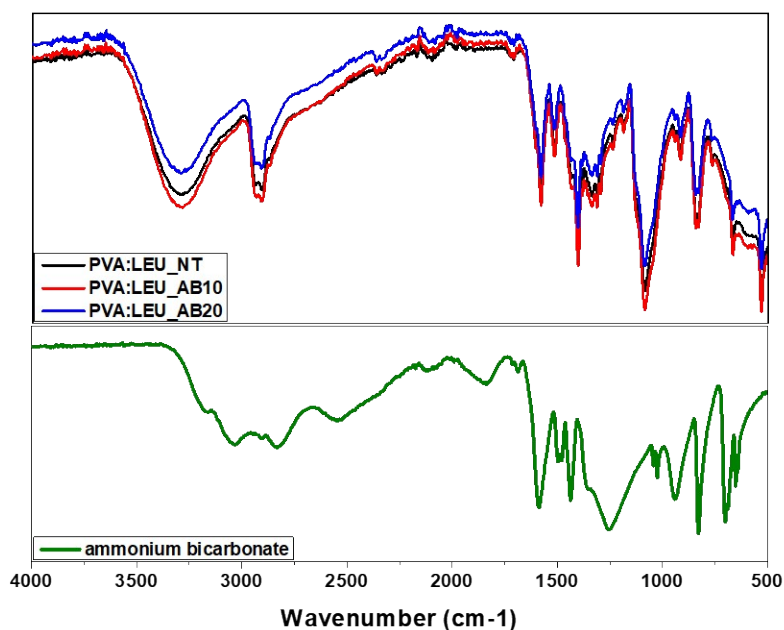
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**Fig. S1** 1H-NMR spectrum of RhB in D<sub>2</sub>O (A), PHEA-RhB copolymer in D<sub>2</sub>O (B), and 1H-NMR spectra overlap (at ppm range of 6.0-10.0) of PHEA-g-RhB (blue line) and RhB (black line) in DMF-d<sub>7</sub> (C).



**Fig. S2** Cell viability of 16-HBE (A) and Raw 264.7(B), after 24 hrs (sn) and 48 hrs (dx), after incubation in the presence of: free Rapa, empty and Rapa-loaded Man-LPHNPs at concentrations ranging between 1 - 10 µg/mL. As control samples were tested empty and Rapa-loaded LPHNPs.



**Figure S3.** FT-IR spectra of PVA:LEU\_NT, PVA:LEU\_AB10 and PVA:LEU\_AB20 samples (top panel) and Ammonium bicarbonate (AB, bottom panel).

**Table S1.** Main transition temperature values of obtained samples.

Sample	T <sub>M</sub> /°C
Polymeric nanoparticles	Peak 1, 43.8
	Peak 2, 88.6
Lipid vesicles	Peak 1, 40.4
	Peak 2, 68.8
Rapa@Man-LPHNPs	Peak 1, 57.6
	Peak 2, 97.9
PVA:LEU_AB10	Peak 1, 215.0
	Peak 2, 272.3
NiM@Rapa	Peak 1, 203.8
	Peak 2, 245.0

**Table S2.** AB wt% used for the production, yield, geometric and aerodynamic diameter, density of obtained samples.

Sample	AB (wt%)	Yield (wt%)	d <sub>g</sub> ± S.D. (μm)	ρ ± S.D. (g/ml)	d <sub>aer</sub> (μm)
PVA:LEU_NT	0	38.2	6.76 ± 2.13	0.615 ± 0.071	5.29
PVA:LEU_AB10	10	37.4	7.70 ± 3.60	0.420 ± 0.060	5.00
PVA:LEU_AB20	20	38.7	7.62 ± 3.01	0.450 ± 0.008	5.09
NiM	10	37.0	6.12 ± 4.27	0.608 ± 0.035	4.76
NiM_Rapa	10	42.1	4.52 ± 3.47	0.523 ± 0.056	3.26