

## Supporting Information

*Madhavi Bhandari*<sup>a,†</sup>, *Héctor Soria- Carrera*<sup>b,c,d</sup>, *Jens Wohlmann*<sup>a</sup>, *Nils-Jørgen Knudsen Dal*<sup>a</sup>,  
*Jesús M. de la Fuente*<sup>b,c</sup>, *Rafael Martín-Rapún*<sup>b,c,d\*</sup>, *Gareth Griffiths*<sup>a</sup>, *Federico Fenaroli*<sup>a, e\*</sup>

<sup>a</sup> *Department of Biosciences, University of Oslo, Blindernveien 31, 0371 Oslo, Norway*

<sup>b</sup> *Instituto de Nanociencia y Materiales de Aragón (INMA), CSIC-Universidad de Zaragoza and CIBER-BBN, C/ Mariano Esquillor s/n, 50018 Zaragoza, Spain*

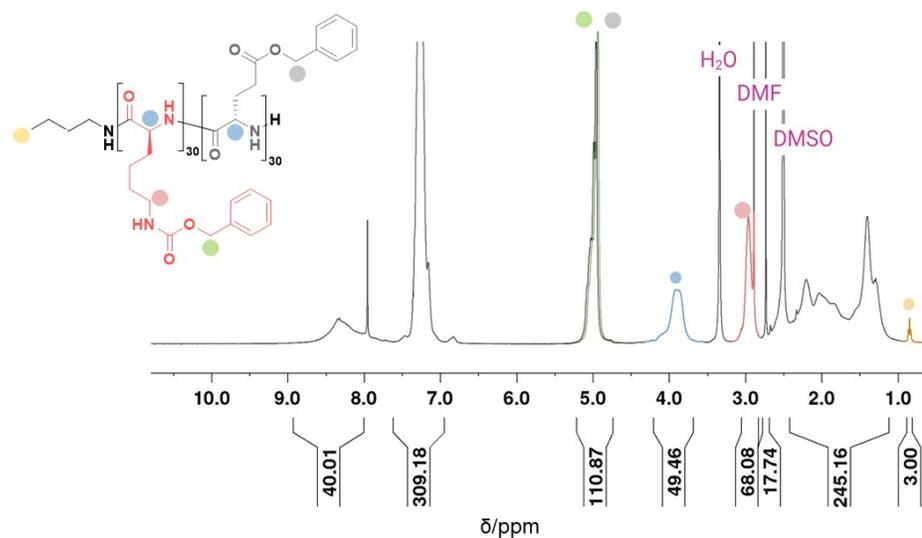
<sup>c</sup> *CIBER de Bioingeniería, Biomateriales y Nanomedicina, Instituto de Salud Carlos III, 28029 Madrid, Spain*

<sup>d</sup> *Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Zaragoza, c/Pedro Cerbuna 12, 50009 Zaragoza, Spain*

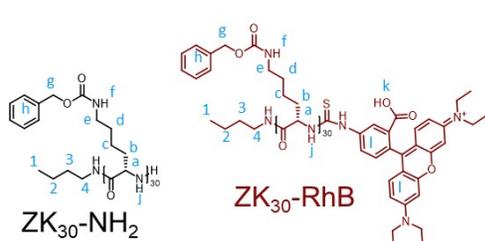
<sup>e</sup> *Department of Chemistry, Bioscience and Environmental Engineering, University of Stavanger, 4021 Stavanger, Norway*

*Present Address* † *Faculty of Health Sciences, Department of Life Sciences and Health Pharmacy, Oslo Metropolitan University, Pilestredet 50, 0167 Oslo, Norway*

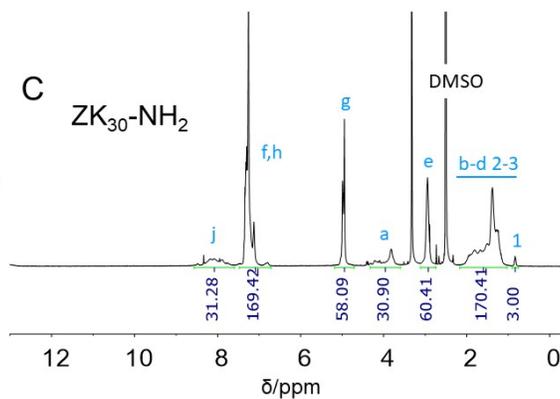
A  $ZK_{30}$ -BnE<sub>30</sub>



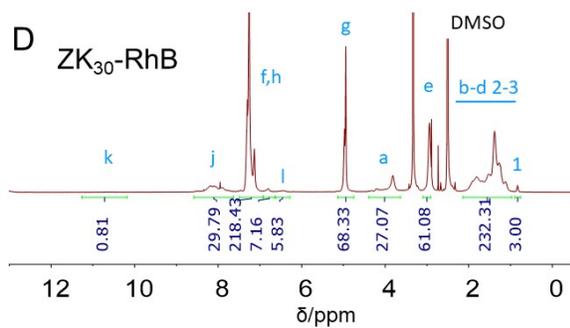
B



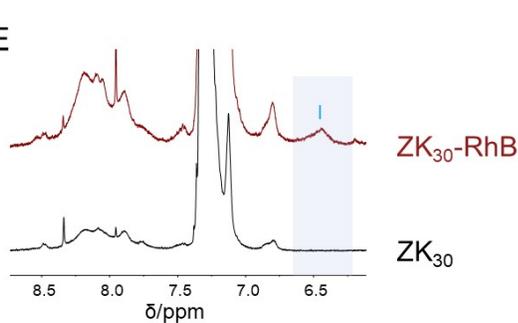
C



D

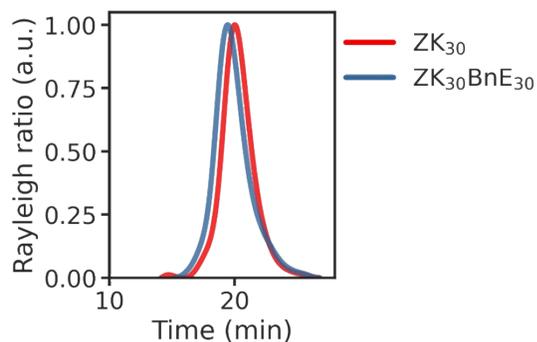


E



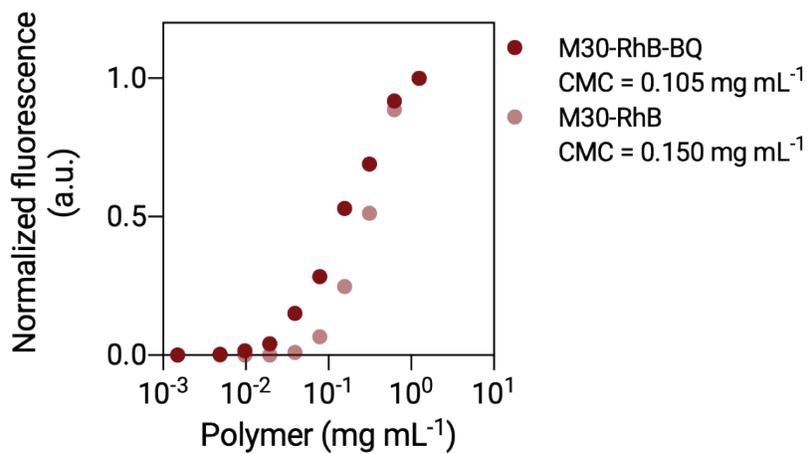
**Supporting Figure 1.** A) Structure and <sup>1</sup>H-NMR spectrum of  $ZK_{30}$ -BnE<sub>30</sub> with signal assignment. B) Structures of  $ZK_{30}$ -NH<sub>2</sub> and  $ZK_{30}$ -RhB C) <sup>1</sup>H-NMR spectrum of  $ZK_{30}$ . D) <sup>1</sup>H-NMR of  $ZK_{30}$ -RhB. E) Enlargement of the aromatic region in C and D, showing the appearance of aromatic peaks belonging to RhB in the <sup>1</sup>H-NMR spectrum of  $ZK_{30}$ -RhB (1 protons). All spectra were registered using [D<sup>6</sup>]DMSO as solvent.

A



Polymer	$M_w$ (g mol <sup>-1</sup> )	$M_n$ (g mol <sup>-1</sup> )	$\mathcal{D}$
ZK30	16670	13160	1,27
ZK30BnE30	22840	19750	1,16

B



**Supporting Figure 2.** A) GPC traces and results of ZK<sub>30</sub> and ZK<sub>30</sub>BnE<sub>30</sub>. B) Critical micellar concentration of M30-RhB micelles with and without bedaquiline.

**Table 1.** Characterization summary for BQ and empty M30-RhB micelles.

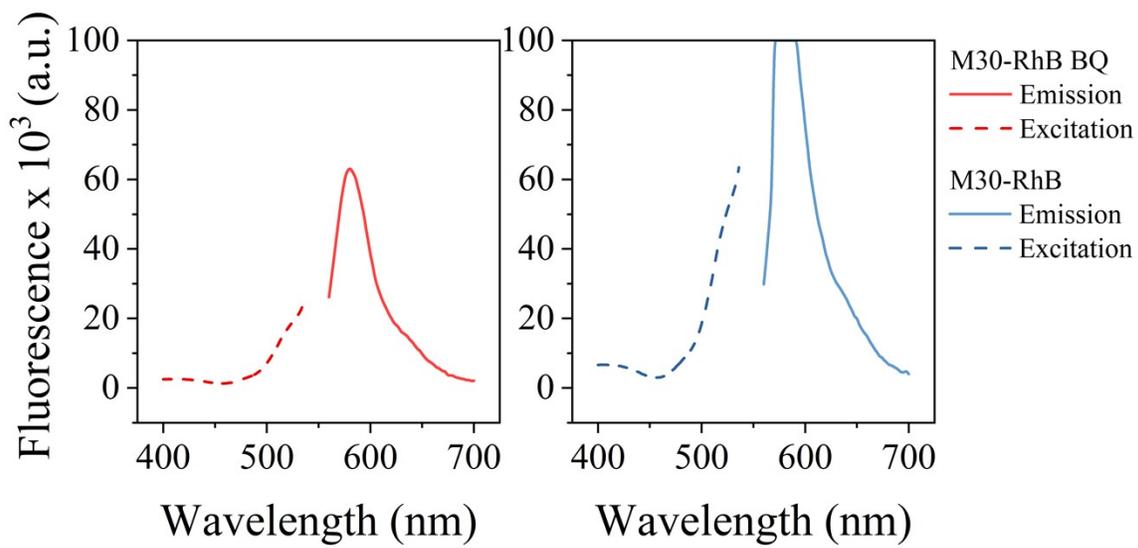
Sample	D <sub>H</sub> (nm)	PDI	ζ-potential (mV)	DL (%)	EE (%)
M30	49.7	0.118±0.007	-36.8	-	-
M30-BQ	36.1	0.119±0.009	-23.6	20	73
M30-RhB	56.7	0.186±0.02	-40.7	-	-
M30-RhB-BQ	41.3	0.135±0.01	-36.7	17	61

**D<sub>H</sub>:** Hydrodynamic diameter (nm)

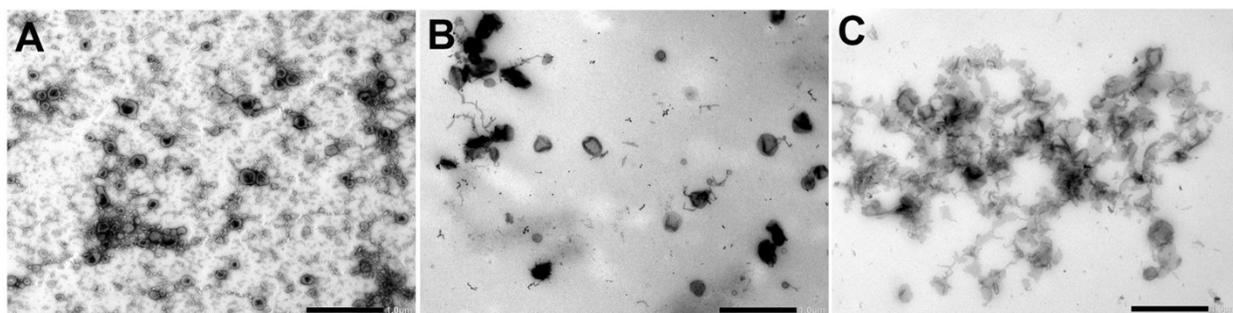
**DL:** Drug loading ( $\text{mg}_{\text{drug}}/\text{mg}_{\text{nanoparticle}}$ )

**PDI:** polydispersity index

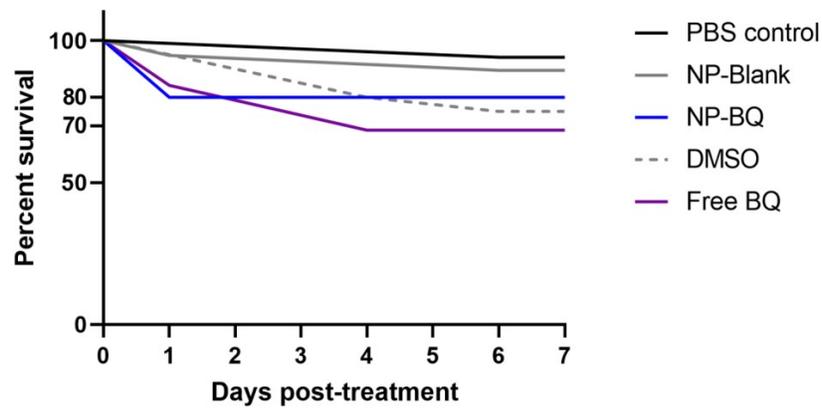
**Encapsulation efficiency:** Hydrodynamic diameter ( $\text{mg}_{\text{drug encapsulated}}/\text{mg}_{\text{drug in the feed}}$ )



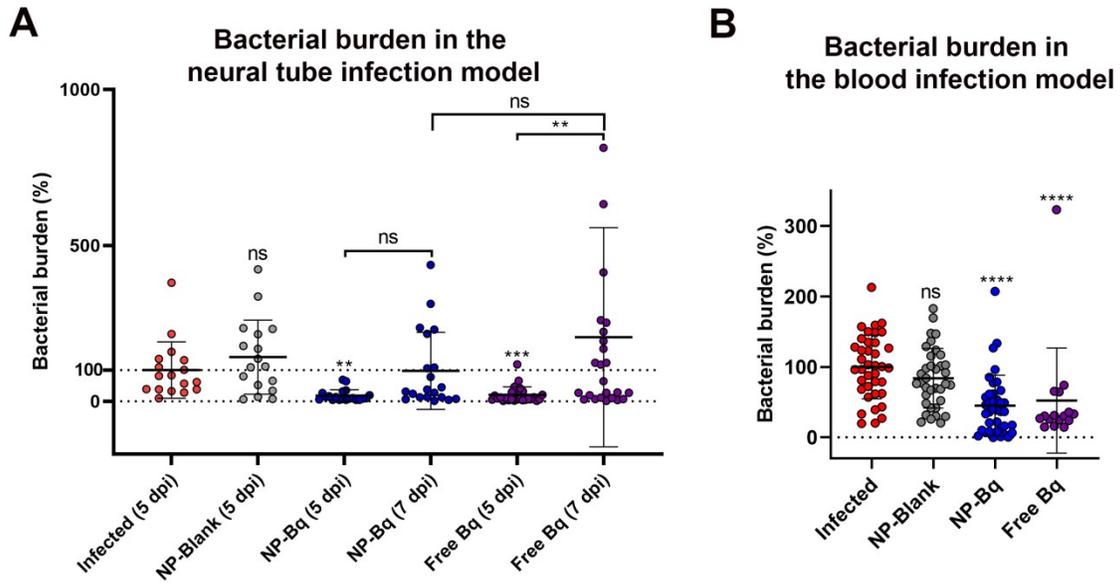
**Supporting Figure 3.** Fluorescence spectra for BQ loaded and empty fluorescent micelles (M30-RhB-BQ and M30-RhB).



**Supporting Figure 4.** Transmission electron micrograph of M30-BQ NP (A), M30-RhB NP (B) and M30 NP (C). Scale bars indicates 1  $\mu\text{m}$ .



**Supporting Figure 5.** *In vivo* toxicity assay, survival graph. BQ drug, either NP-encapsulated or in free form, was injected into the PCV of wild type zebrafish embryos at 2 dpf. 20 nL of encapsulated BQ (NP-BQ, M30-BQ), empty NPs (NP-Blank, M30) and PBS control were injected. The doses of NP-BQ, NP-Blank and free drug dissolved in DMSO injected were 8.3 ng per embryo. Data was analyzed by Log-rank (Mantel-Cox) test and show the cumulative mortality of one experiment, N (embryos per group)  $\geq 17$ .



**Supporting Figure 6.** Bacterial burden analysis via fluorescence pixel count comparing therapeutic efficacy of free (dissolved in DMSO) versus encapsulated BQ (NP-BQ, M30-BQ). NP-blank (M30) was used as a control. The graph in A shows the results on the neural tube model of infection while the one in B represents our assessment in the blood infection model. In A analysis has been performed at 5 and 7 days after infection while in B we carried out only one analysis at day 7. Statistical analysis was performed using a Kruskal-Wallis test, followed by Dunn's multiple comparisons test. N (embryos per group on the day of infection) in A  $\geq 17$ , while in B  $\geq 16$ . Bars indicate mean  $\pm$  SD.