Electronic Supplementary Material (ESI) for Materials Chemistry Frontiers.

Supporting Information

Aza-BODIPY encapsulated polymeric nanoparticles as effective nanodelivery system for photodynamic cancer treatment

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1. ^{1}H and ^{13}C Nuclear Magnetic resonance (NMR) spectra

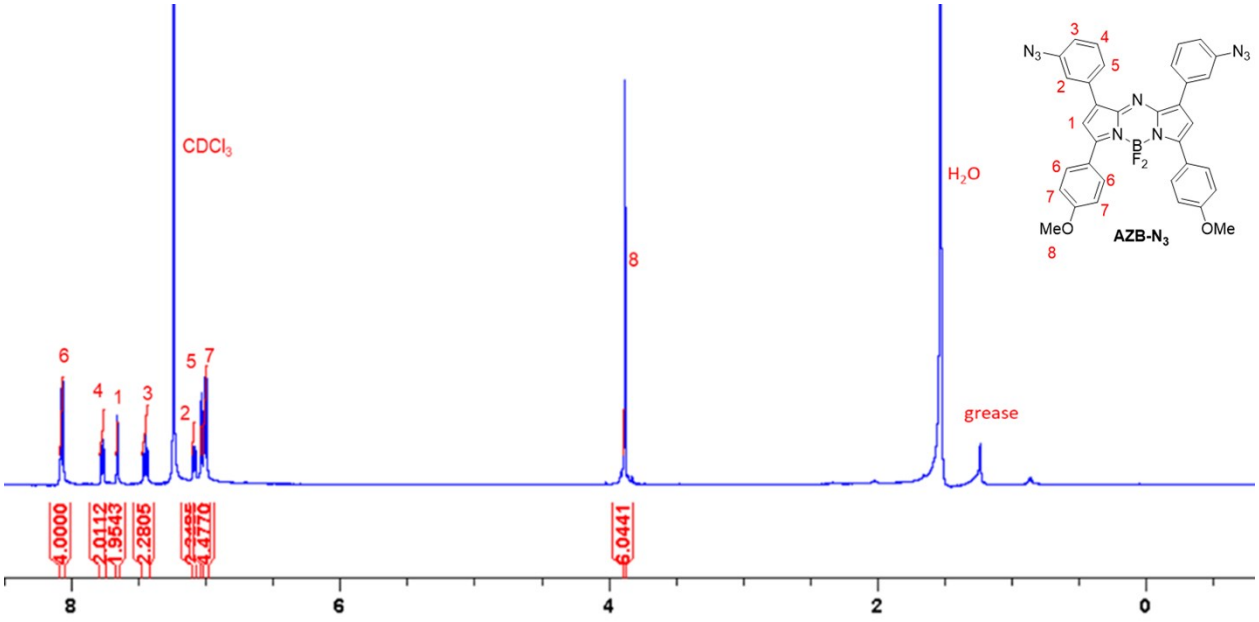


Figure S1. ^{1}H NMR spectrum of **AZB-N_3**.

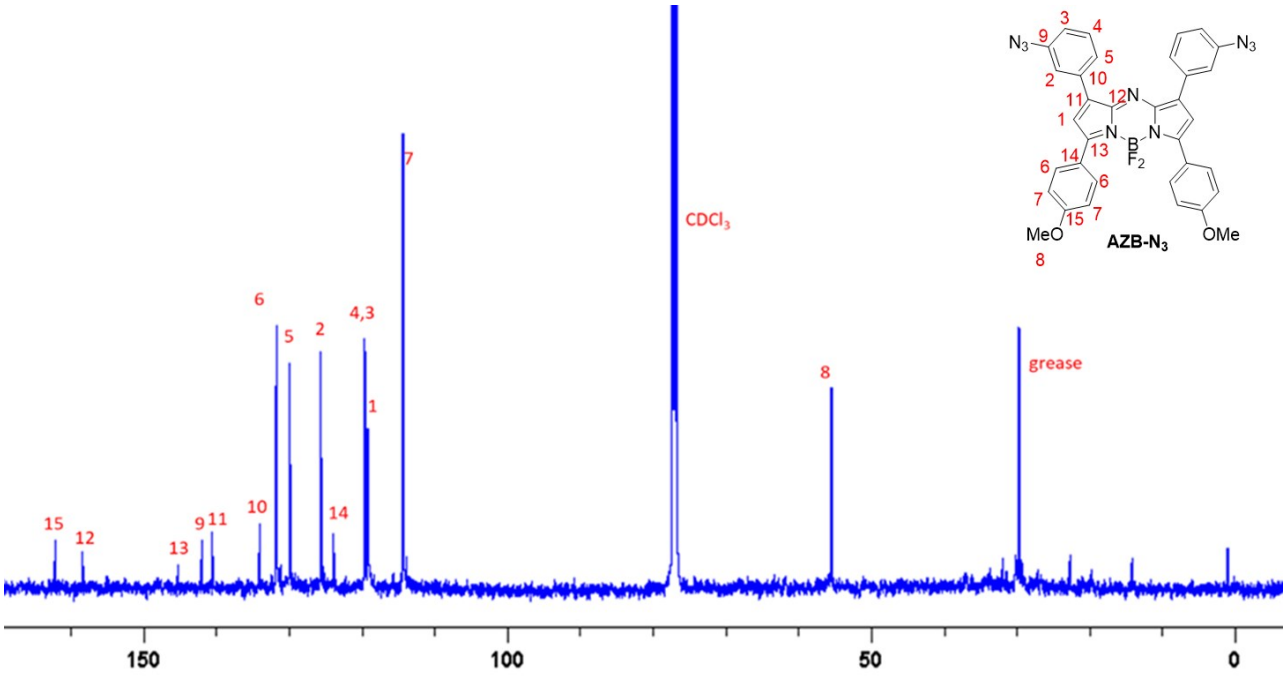


Figure S2. ^{13}C NMR spectrum of **AZB-N_3**.

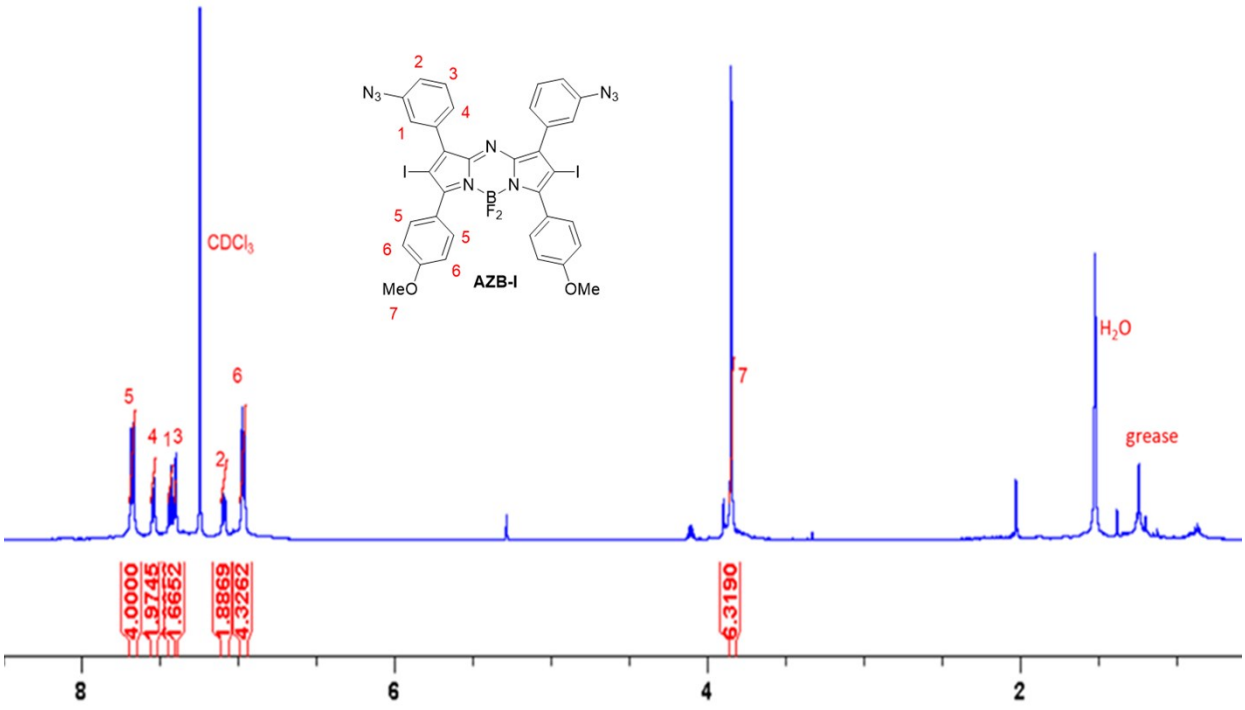


Figure S3. ^{1}H NMR spectrum of **AZB-I**.

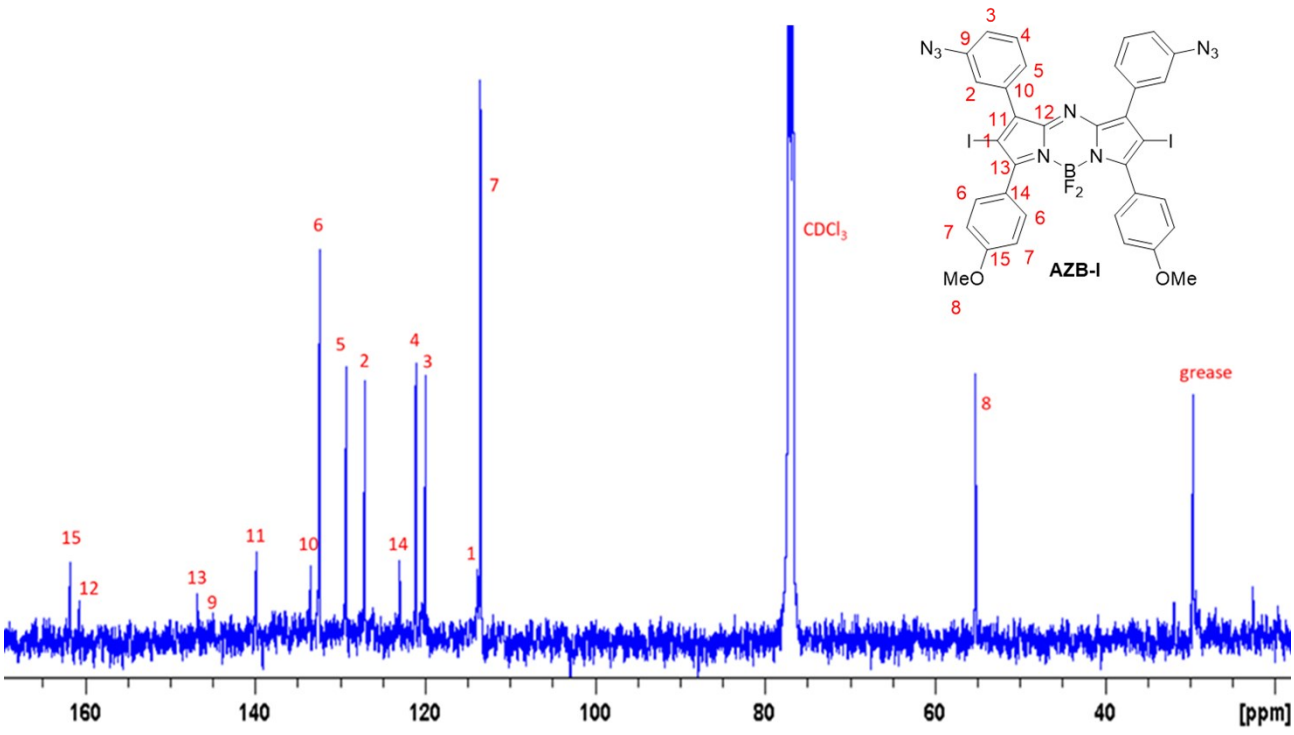


Figure S4. ^{13}C NMR spectrum of **AZB-I**.

2. Mass spectrometry results

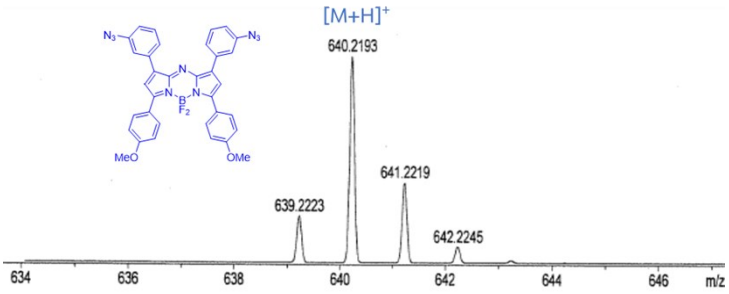


Figure S5. Mass spectrum of **AZB-N_3**.

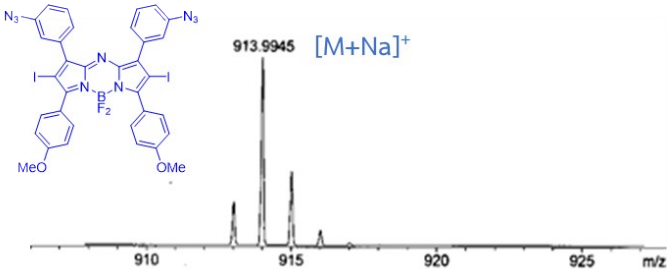


Figure S6. Mass spectrum of **AZB-I**.

3. Absorption and emission of AZB-I in water

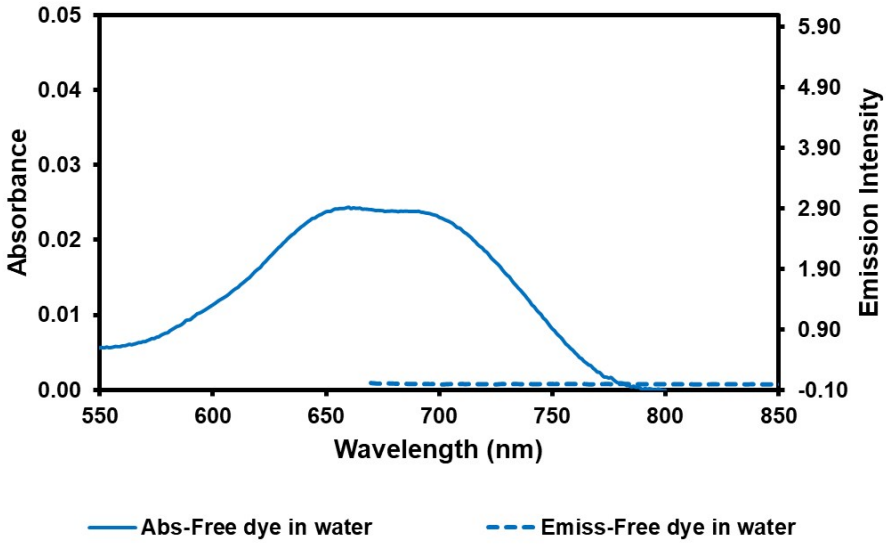


Figure S7. Absorption and emission of free dye **AZB-I** in water.

4. Intensity, number, and volume-based DLS distribution results

Table S1. Average intensity, number, and volume-based DLS sizes of **AZB-I@PEG-*b*-PCL** prepared from different amount of dye feed.

Entry[a]	Amount of dye feed (mg)	Average Intensity-based DLS size (nm) (n = 3)	Average Number-based DLS size (nm) (n = 3)	Average Volume-based DLS size (nm) (n = 3)	PDI (n = 3)
1	0.6	47.2 (± 2.0)	29.7 (± 1.7)	37.3 (± 1.5)	0.144 (± 0.014)
2	0.8	44.6 (± 4.0)	25.2 (± 0.5)	33.0 (± 0.5)	0.166 (± 0.016)
3	1.0	46.7 (± 1.3)	28.3 (± 0.6)	35.8 (± 0.6)	0.170 (± 0.010)
4	1.2	48.2 (± 1.9)	25.3 (± 1.6)	33.6 (± 1.0)	0.173 (± 0.011)

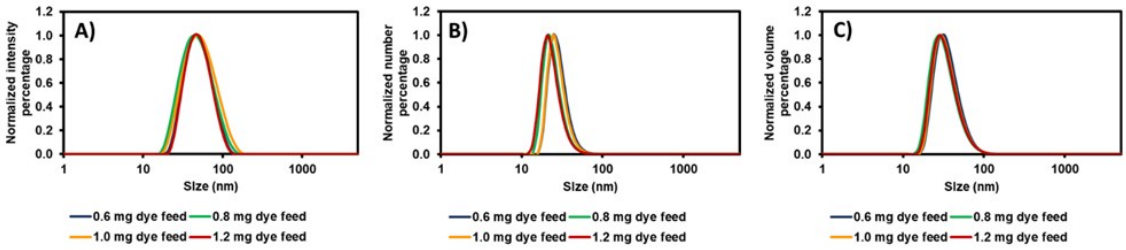


Figure S8. Dynamic Light Scattering (DLS) intensity-based (A), number-based (B), and volume-based size distributions.

5. Stability test and *In vitro* dye-releasing profile of AZB-I@PEG-*b*-PCL NPs

Stability test

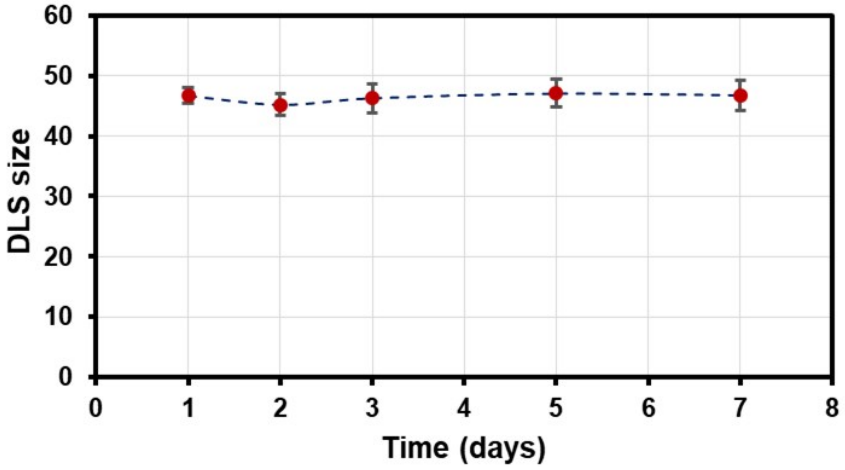


Figure S9. The DLS size evolution of **AZB-I@PEG-*b*-PCL** NPs (1 mg dye feed) incubated in physiological conditions (phosphate buffer solution 0.1M, pH 7.4, 37 ^{o}C) for 7 days.

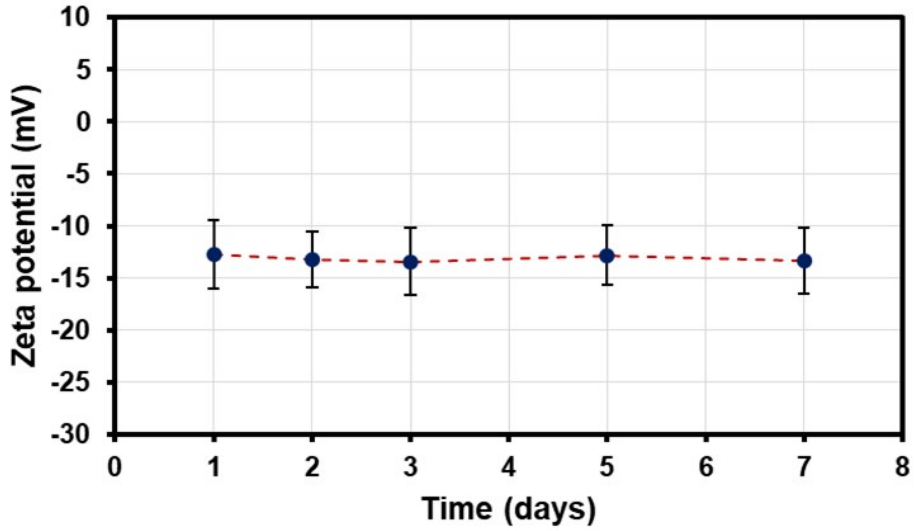


Figure S10. The zeta potential evolution of **AZB-I@PEG-*b*-PCL** NPs (1 mg dye feed) incubated in physiological conditions (phosphate buffer solution 0.1M, pH 7.4, 37 ^{o}C) for 7 days.

6. *In vitro* dye-releasing profile

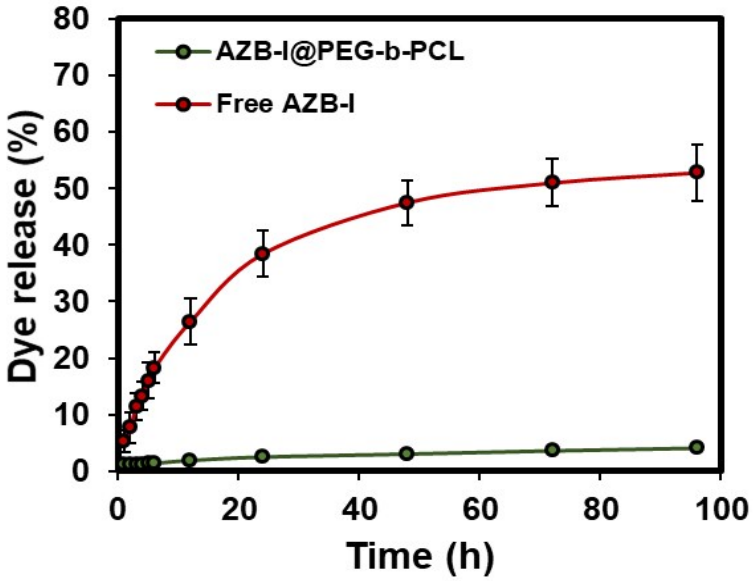


Figure S11. *In vitro* **AZB-I** release profile from **AZB-I@PEG-*b*-PCL** NPs. Free **AZB-I** release was used as control. Error bars represents mean ± standard deviation (n= 3).

7. Singlet oxygen generation of AZB-I@PEG-*b*-PCL NPs

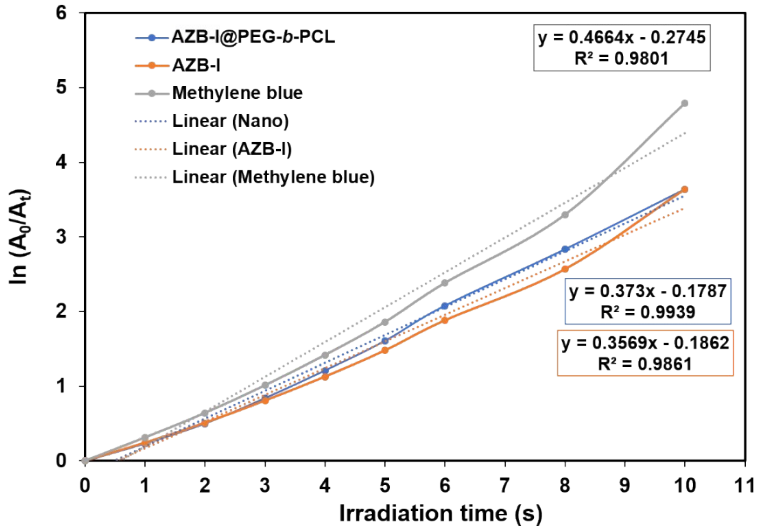


Figure S12. The first order kinetic plot of DPBF vs irradiation times.

8. Colocalization study of AZB-I@PEG-*b*-PCL NPs with Lyso- and MitoTrackers

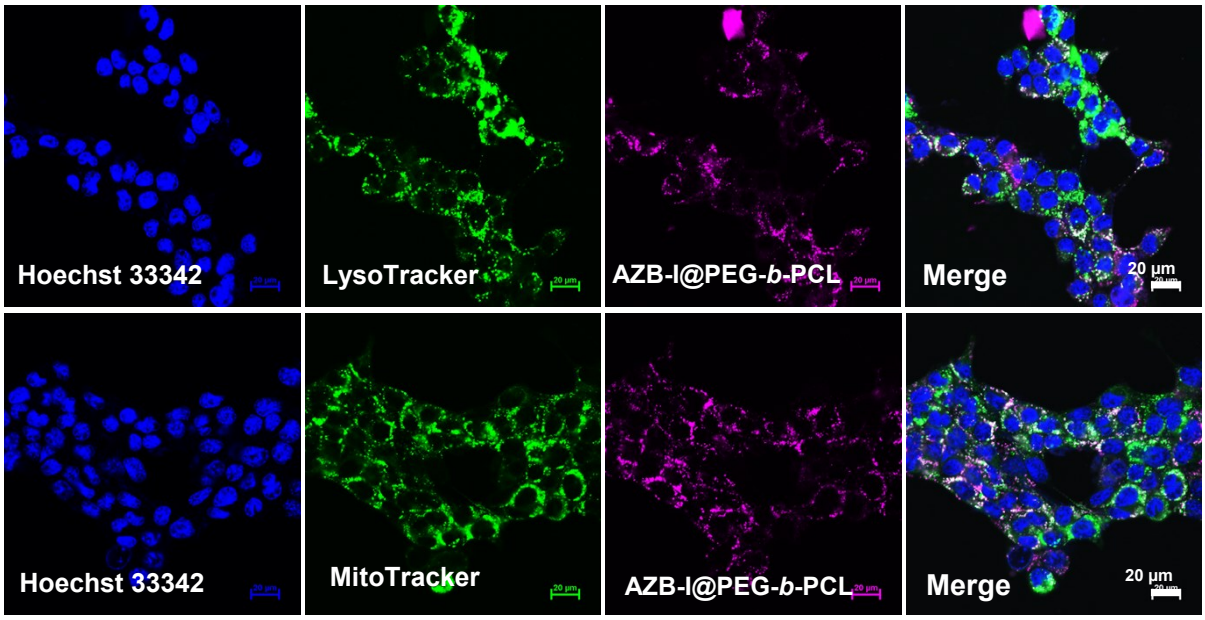


Figure S13. Colocalization study of AZB-I@PEG-b-PCL with LysoTracker (Top row) and MitoTracker (Bottom row).

9. Biocompatibility of **AZB-I@PEG-*b*-PCL** with normal cells

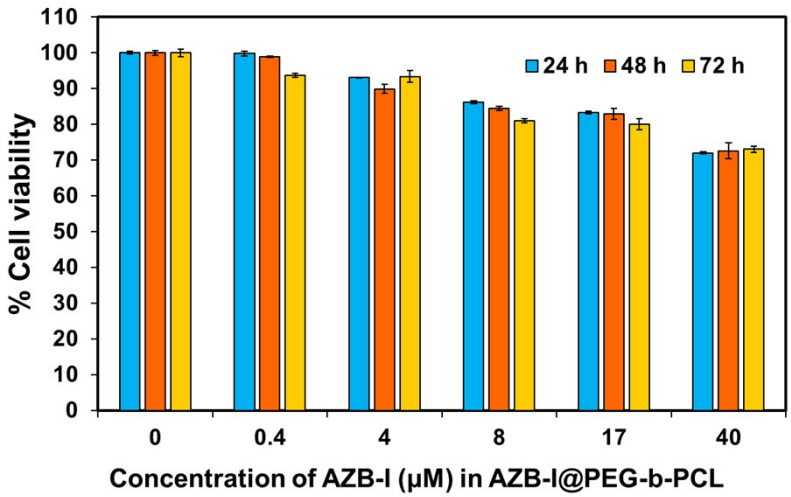


Figure S14. Relative cell viability of HEK-293 cells after treated various concentration of **AZB-I** within **AZB-I@PEG-b-PCL** NPs and the cells were kept in the dark for 24, 48 and 72 h (data are presented as means ± SD (n = 3).

10. Mice body weight changes of **AZB-I@PEG-*b*-PCL** at 160 mg/kg

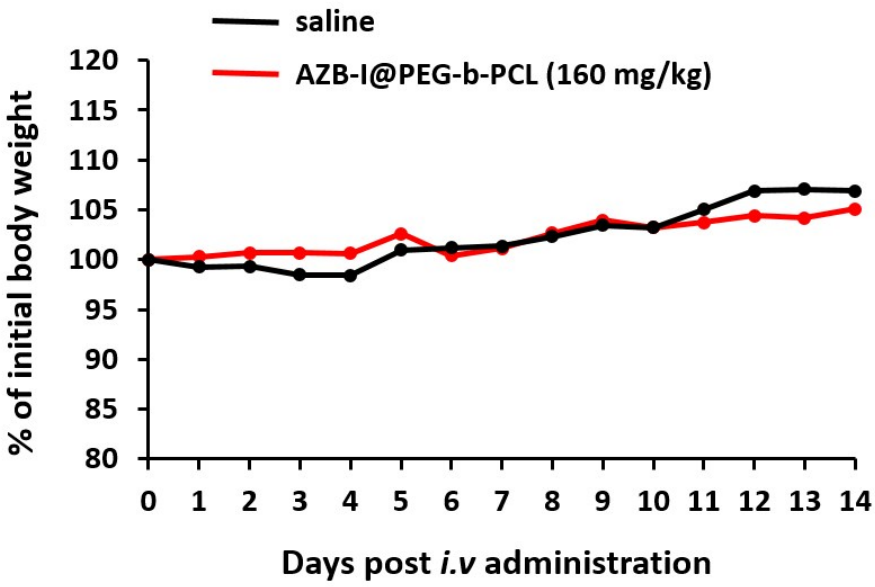
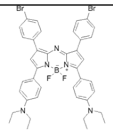
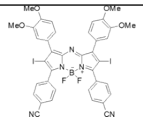
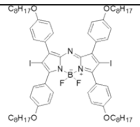
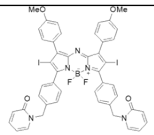
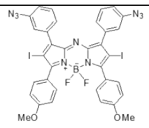


Figure S15. Mice body weight changes of **AZB-I@PEG-*b*-PCL** at 160 mg/kg (red) and control saline (black) post single i.v administration.

Table S2. The formulations and the obtained DLS sizes of **AZB-I@PEG-*b*-PCL** compared with those of other aza-BODIPY-based nanoparticles

Entry	Structure	Polymer used	λ_{Abs} / λ_{Emiss} (nm)	Homogenization	Average DLS size (nm)	Reference
1		PEG-*b*-PLA	860 /925	Sonication (180 W)	138.4±17.3	[1]
2		PEG	652 / 730	Sonication (200 W)	81.7 ± 7.5	[2]
3		PEG	690 / 775	Sonication (180 W)	68.1 ± 9.7	[3]
4		DSPE-mPEG 5000	678 / 712	Sonication (220 W)	142	[4]
5		DSPE-mPEG 5000	580 / 720	Sonication (175 W)	66.3 ± 6.6	[5]
6		PEG-*b*-PCL	693/ 730	Stirring	44.6 (± 4.0) – 48.2 (± 1.9)	This work

* PEG-co-PLA = polyethylene glycol-*b*- polylactic acid, PEG = polyethylene glycol, DSPE-mPEG5000 = 1,2-distearoyl-sn-glycero-3-phospho ethanolamine-N-[methoxy(polyethylene glycol)-5000]

References

[1] Tian J, Zhou J, Shen Z, Ding L, Yu J-S, Ju H. A pH-activatable and aniline-substituted photosensitizer for near-infrared cancer theranostics. Chemical Science. 2015;6(10):5969-77.

[2] Chen D, Tang Q, Zou J, Yang X, Huang W, Zhang Q, et al. pH-Responsive PEG–Doxorubicin-Encapsulated Aza-BODIPY Nanotheranostic Agent for Imaging-Guided Synergistic Cancer Therapy. Advanced Healthcare Materials. 2018;7(7):1701272.

[3] Chen D, Zhang J, Tang Y, Huang X, Shao J, Si W, et al. A tumor-mitochondria dual targeted aza-BODIPY-based nanotheranostic agent for multimodal imaging-guided phototherapy. Journal of Materials Chemistry B. 2018;6(27):4522-30.

[4] Zhao M, Xu Y, Xie M, Zou L, Wang Z, Liu S, et al. Halogenated Aza-BODIPY for Imaging-Guided Synergistic Photodynamic and Photothermal Tumor Therapy. Advanced Healthcare Materials. 2018;7(18):1800606.

[5] Xiao W, Wang P, Ou C, Huang X, Tang Y, Wu M, et al. 2-Pyridone-functionalized Aza-BODIPY photosensitizer for imaging-guided sustainable phototherapy. Biomaterials. 2018;183:1-9.