

# Combating AMR: Photoactivatable Ruthenium(II)-isoniazid Complex Exhibits Rapid Selective Antimycobacterial Activity†

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**Table S1.** Crystallographic data for *cis*-[Ru(bpy)<sub>2</sub>(INH)<sub>2</sub>][PF<sub>6</sub>]<sub>2</sub> (1.2PF<sub>6</sub>)

<i>cis</i> -[Ru(bpy) <sub>2</sub> (INH) <sub>2</sub> ][PF <sub>6</sub> ] <sub>2</sub>	
Formula	C <sub>42</sub> H <sub>48</sub> F <sub>12</sub> N <sub>10</sub> O <sub>7</sub> P <sub>2</sub> Ru
Molar mass	1195.91
Crystal system	Monoclinic
Space group	C2/c
Crystal size (mm)	0.20 x 0.08 x 0.04
Crystal character	Orange block
<i>a</i> (Å)	21.9093(7)
<i>b</i> (Å)	15.8193(3)
<i>c</i> (Å)	19.1282(12)
$\alpha$ (°)	90
$\beta$ (°)	130.884(2)
$\gamma$ (°)	90
T (K)	293(2)
Z	4
R1 [I>2 $\sigma$ (I)]	0.0798

**Table S2.** Selected bond lengths (Å) and angles (°) for *cis*-[Ru(bpy)<sub>2</sub>(INH)<sub>2</sub>][PF<sub>6</sub>]<sub>2</sub>·2.5(dioxane)

Bond length (Å) / angle (°)	<i>cis</i> -[Ru(bpy) <sub>2</sub> (INH) <sub>2</sub> ][PF <sub>6</sub> ] <sub>2</sub>
Ru1-N1	2.066(5)
Ru1-N12	2.057(4)
Ru1-N13	2.101(4)
N1-Ru-N12	78.62(18)
N12-Ru1-N13	90.26(18)
N1-Ru1-N13	91.3(2)

**Table S3.** Experimental extinction coefficients for *cis*-[Ru(bpy)<sub>2</sub>(INH)<sub>2</sub>][PF<sub>6</sub>]<sub>2</sub> in aqueous solution.

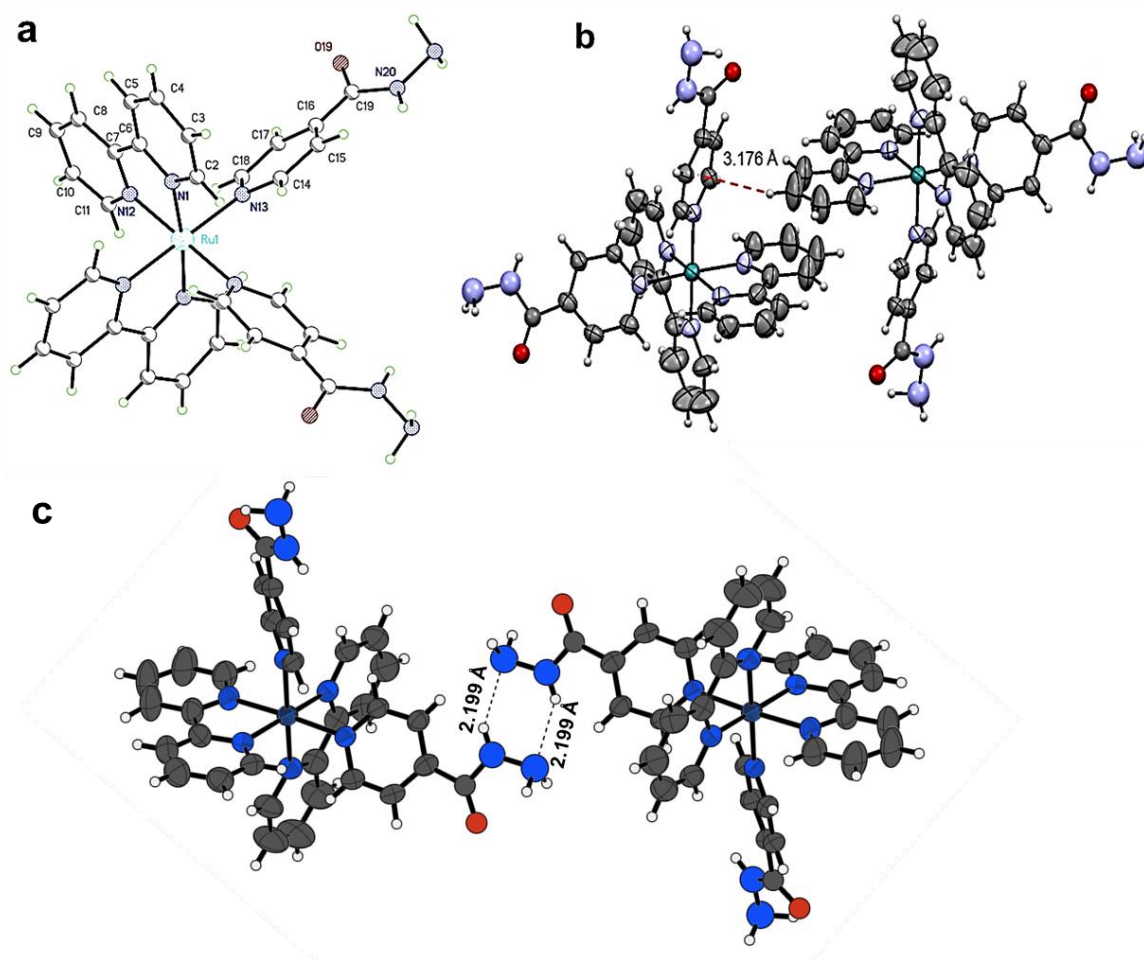
Wavelength (nm)	Extinction Coefficient (M <sup>-1</sup> cm <sup>-1</sup> )
424	15900
375	17300
288	42300

**Table S4.** TD-DFT calculated vertical singlet transitions for *cis*-[Ru(bpy)<sub>2</sub>(INH)<sub>2</sub>][PF<sub>6</sub>]<sub>2</sub>.

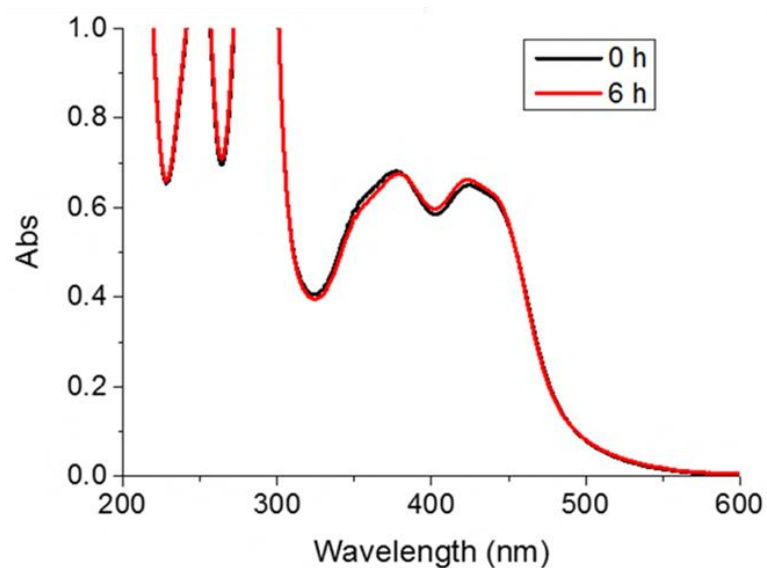
Sn	Energy (eV)	<i>f</i>	Major contribution	Character
1	2.81 (441)	0.003	HOMO→LUMO (81%)	MLCT(Ru-bpy)
3	2.91 (427)	0.004	H-1→LUMO (79%)	MLCT(Ru-bpy)
5	3.05 (407)	0.092	H-2→L+1 (76%)	MLCT(Ru-bpy)
6	3.09 (401)	0.100	H-2→LUMO (53%)	MLCT(Ru-bpy)
11	3.41 (364)	0.161	H-2→L+2 (78%)	MLLCT(Ru/bpy-INH)
12	3.50 (354)	0.013	HOMO→L+10 (55%)	MC
15	3.62 (343)	0.084	H-2→L+3 (28%)	MC/MLCT(Ru-INH)
45	4.47 (278)	0.364	HOMO→L+9 (37%)	MLCT(Ru-INH)/LC(bpy)

**Table S5.** Bond distances (Å) for the ground state (S<sub>0</sub>) geometry (in comparison to crystal structure) and the lowest-lying triplet state (T<sub>1</sub>) geometry of *cis*-[Ru(bpy)<sub>2</sub>(INH)<sub>2</sub>]<sup>2+</sup>.

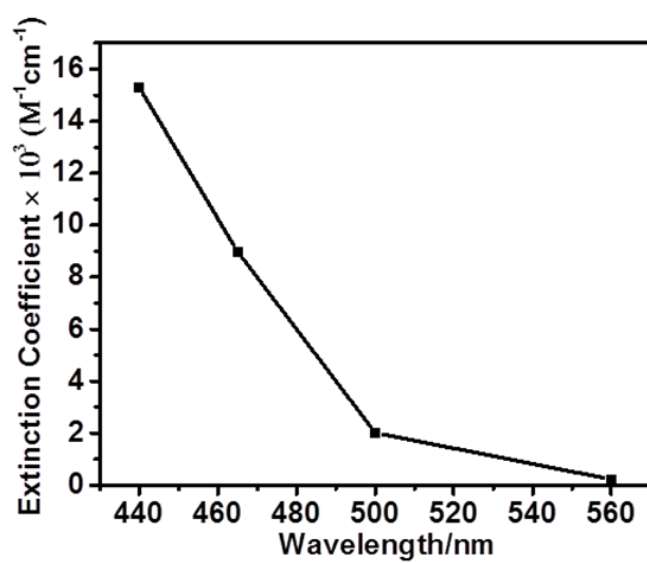
	Bond distance (Å)		T <sub>MLCT</sub>	T <sub>MC</sub>
	S <sub>0</sub>			
	DFT	X-Ray		
Ru-N <sub>1</sub>	2.124	2.066	2.081	2.179
Ru-N <sub>2</sub>	2.103	2.057	2.090	2.388
Ru-N <sub>3</sub>	2.103	2.057	2.037	2.116
Ru-N <sub>4</sub>	2.121	2.066	2.146	2.109
Ru-L <sub>5</sub>	2.167	2.101	2.208	3.790
Ru-L <sub>6</sub>	2.168	2.101	2.174	2.160



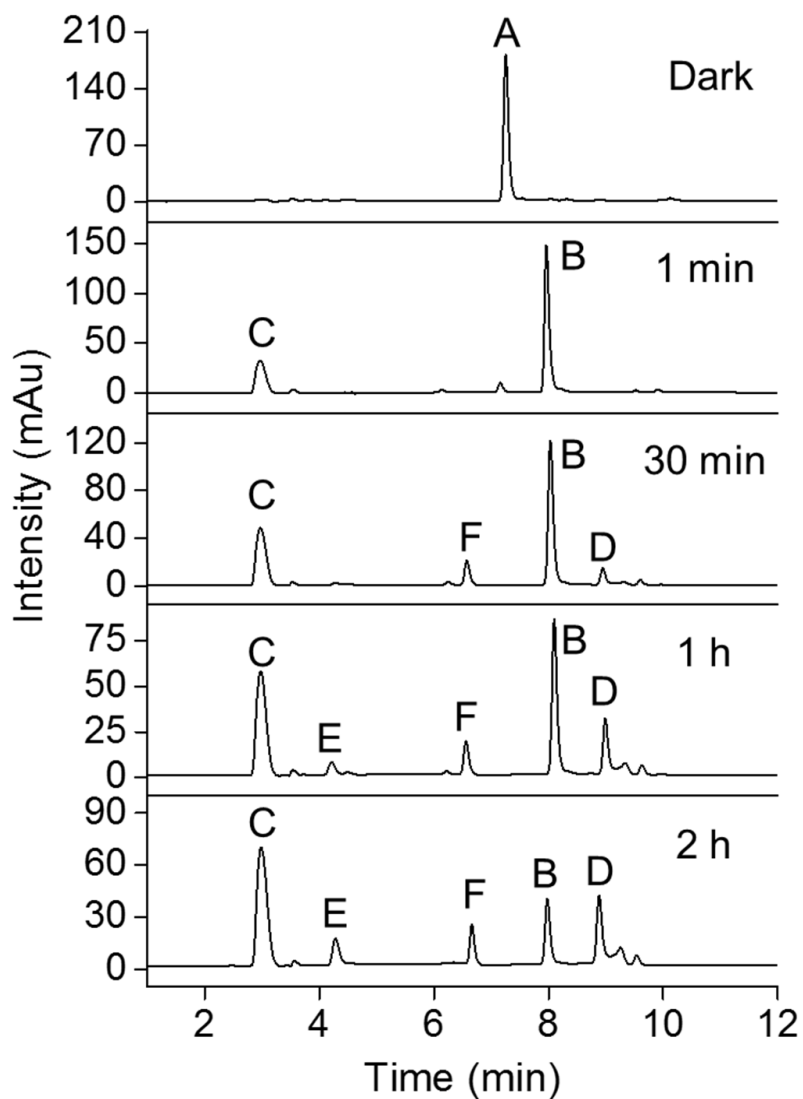
**Fig. S1** X-ray crystal structure of *cis*-[Ru(bpy)<sub>2</sub>(INH)<sub>2</sub>][PF<sub>6</sub>]<sub>2</sub>·2.5(dioxane) with counter ions, solvent and minor disordered components removed for clarity. (a) Structure of the cation *cis*-[Ru(bpy)<sub>2</sub>(INH)<sub>2</sub>]<sup>2+</sup>; (b) CH(bpy)-π(INH) interactions connecting two enantiomers in the unit cell; (c) Hydrogen bonding between the hydrazide groups of two neighbouring enantiomers from different unit cells.



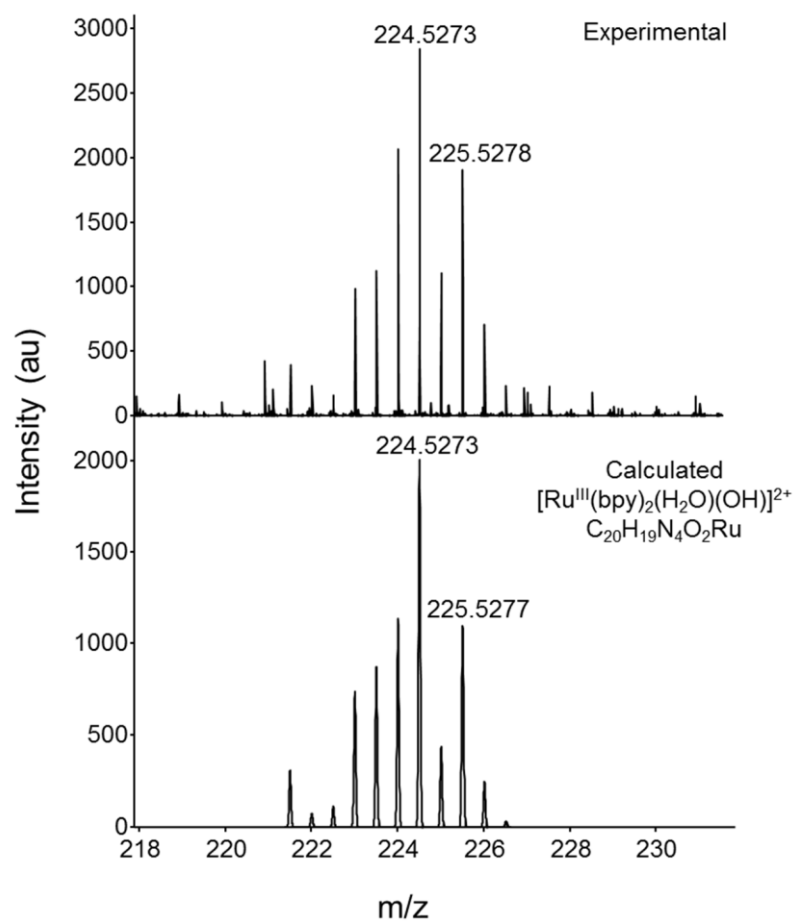
**Fig. S2** The dark stability of  $cis\text{-}[\text{Ru}(\text{bpy})_2(\text{INH})_2]^{2+}$  for 6 h in water followed by UV-visible spectroscopy.



**Fig. S3** Extinction coefficients for  $cis\text{-}[\text{Ru}(\text{bpy})_2(\text{INH})_2]^{2+}$  at the various wavelengths of photoactivation.

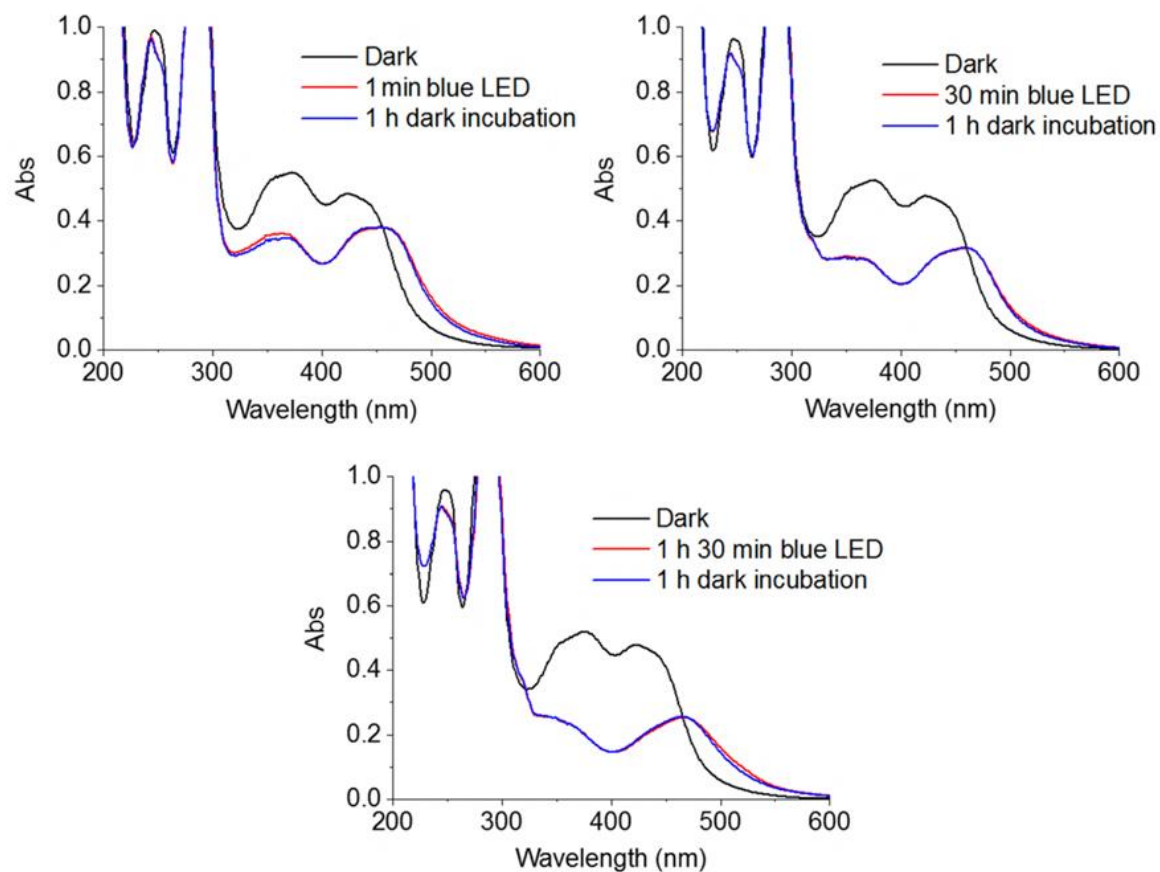


**Fig. S4** Chromatograms for *cis*-[Ru(bpy)<sub>2</sub>(INH)<sub>2</sub>]<sup>2+</sup> when photoirradiated with blue light ( $\lambda_{\text{irr}} = 465 \text{ nm}$ ,  $20 \text{ mW cm}^{-2}$ ) at 298 K for various times; Peak assignments: A: *cis*-[Ru(bpy)<sub>2</sub>(INH)<sub>2</sub>]<sup>2+</sup>; B: *cis*-[Ru(bpy)<sub>2</sub>(INH)(H<sub>2</sub>O)]<sup>2+</sup>; C: INH; D: *cis*-[Ru(bpy)<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup>; E: *trans*-[Ru(bpy)<sub>2</sub>(H<sub>2</sub>O)(OH)]<sup>2+</sup>; F: *trans*-[Ru(bpy)<sub>2</sub>(H<sub>2</sub>O)<sub>2</sub>]<sup>2+</sup>. The wavelength of detection was 254 nm.

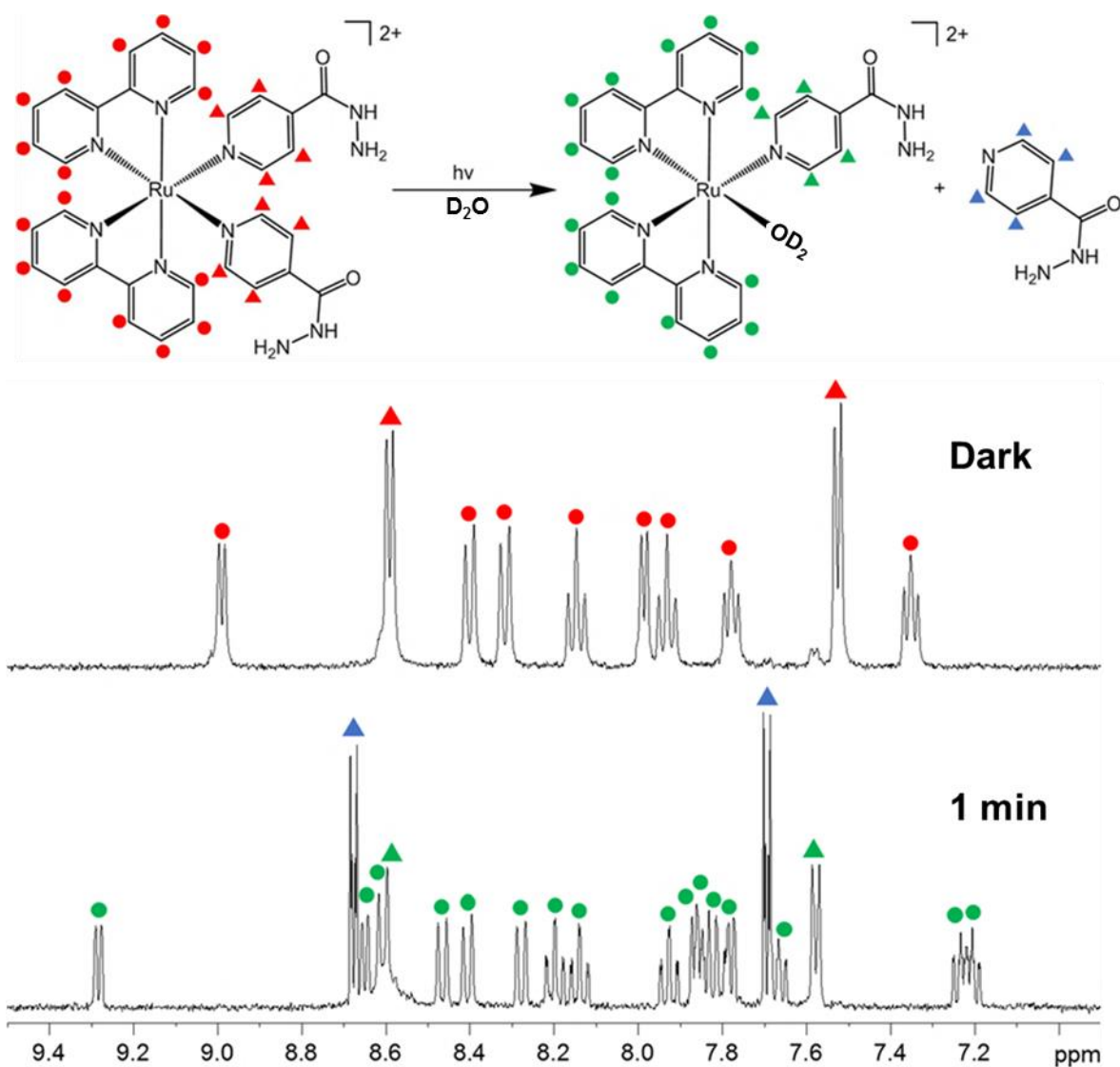


**Fig. S5** Experimental and calculated HRMS peaks for the photoproduct *cis*-[Ru(bpy)<sub>2</sub>(H<sub>2</sub>O)(OH)]<sup>2+</sup>.

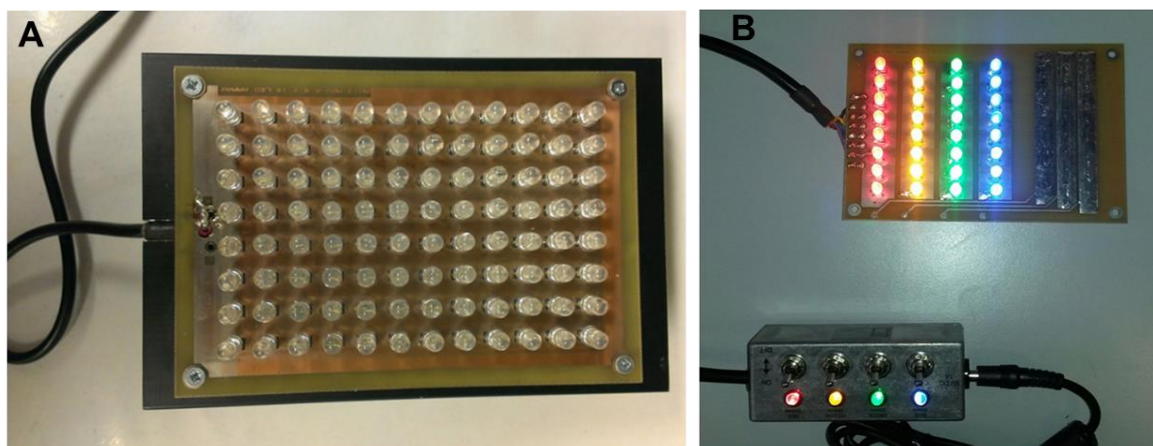




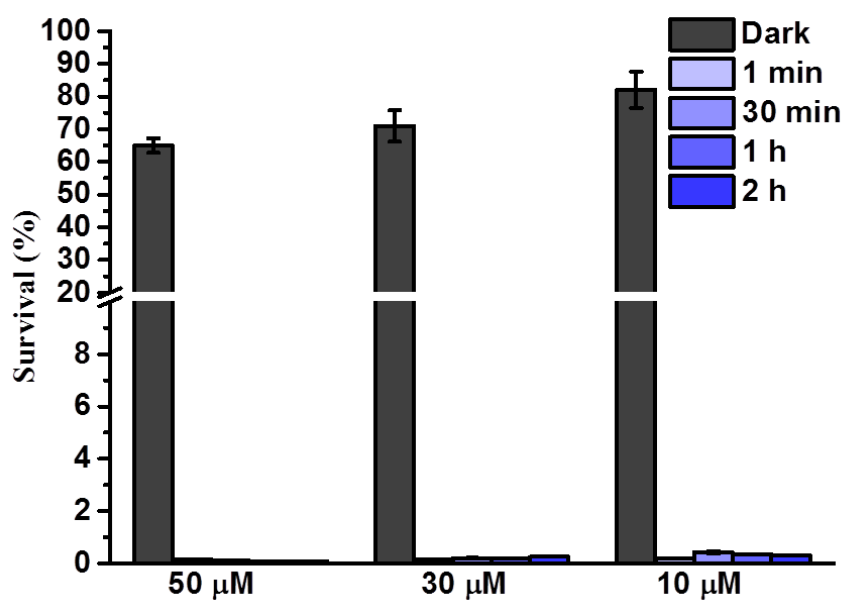
**Fig. S6** Change in UV-visible spectrum of *cis*-[Ru(bpy)<sub>2</sub>(INH)<sub>2</sub>]<sup>2+</sup> when photoirradiated with blue light ( $\lambda_{\text{irr}} = 465 \text{ nm}$ ,  $20 \text{ mW cm}^{-2}$ ) for various times at 298 K and subsequently incubated in the dark for 1 h.



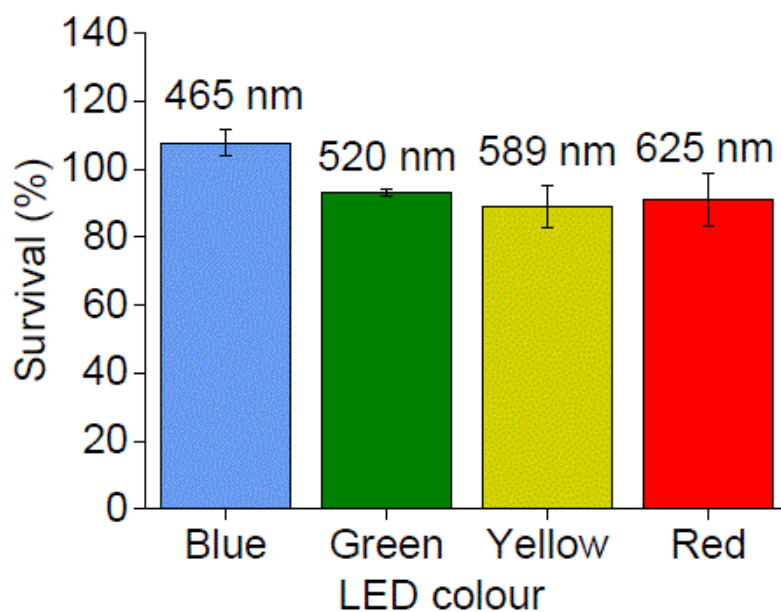
**Fig. S7**  $^1\text{H}$  NMR spectrum (400 MHz) of  $\text{cis-}[\text{Ru}(\text{bpy})_2(\text{INH})_2]^{2+}$  in  $\text{D}_2\text{O}$  before (top spectrum) and after 1 min photoirradiation (bottom spectrum) using the blue LED ( $\lambda_{\text{irr}} = 465$  nm,  $20 \text{ mW cm}^{-2}$ ) at 298 K, with schematic of the photoreaction;  $\text{cis-}[\text{Ru}(\text{bpy})_2(\text{INH})_2]^{2+} = \bullet$  (with bound INH  $\blacktriangle$ ),  $\text{cis-}[\text{Ru}(\text{bpy})_2(\text{INH})(\text{D}_2\text{O})]^{2+} = \bullet$  (with bound INH  $\blacktriangle$ ), free INH =  $\blacktriangle$ .



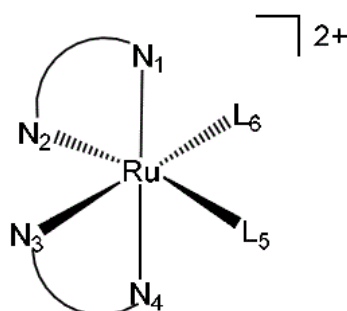
**Fig. S8** Images of (A) 96-array of blue LEDs (465 nm, 20 mW cm<sup>-2</sup>) and (B) 32-array multi-colored LEDs (625 nm, 589 nm, 520 nm and 465 nm, 5 mW cm<sup>-2</sup>).



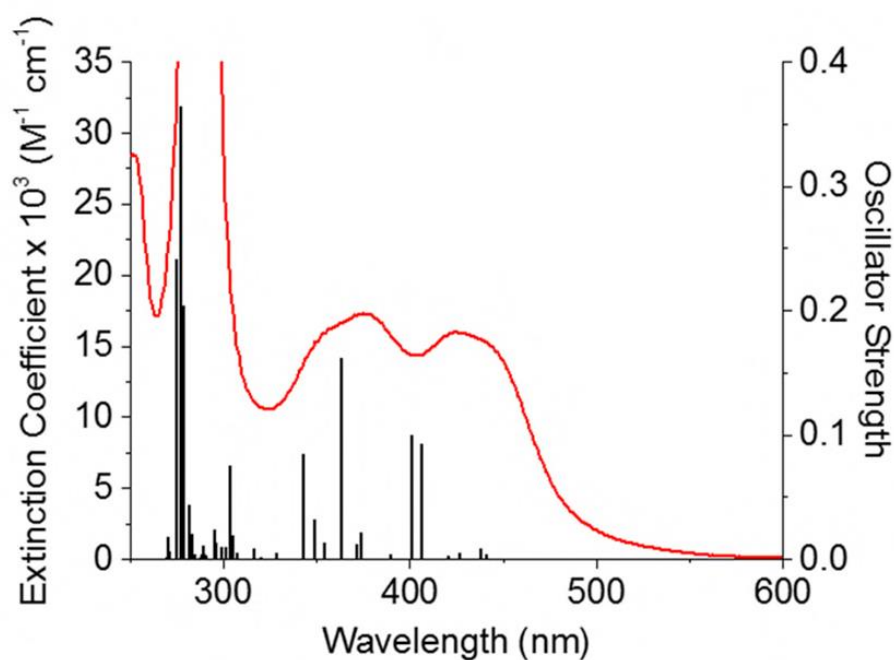
**Fig. S9** *M. smegmatis* when incubated with **1** in the dark or photoirradiated using the 96-array blue LED ( $\lambda_{irr} = 465$  nm, 20 mW cm<sup>-2</sup>) for various times at 298 K, The survival at each photoirradiation time point was compared to the light control in the absence of the complex, while the survival for the complex in the dark was compared to the dark control in the absence of complex.



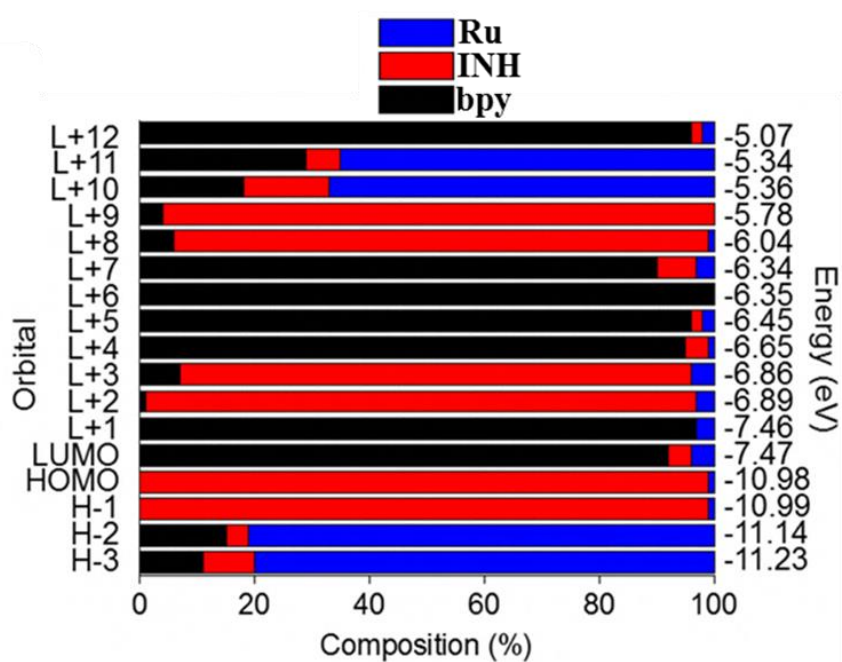
**Fig. S10** Photo survival of *M. smegmatis* using the 32-array of multi-colored LEDs ( $\lambda_{\text{irr}} = 465 \text{ nm}$ ,  $520 \text{ nm}$ ,  $589 \text{ nm}$  and  $625 \text{ nm}$ ,  $5 \text{ mW cm}^{-2}$ ) at  $298 \text{ K}$  for  $30 \text{ min}$ .  $p$  values were calculated by comparing the light samples to the dark control and are labelled as follows,  $p \leq 0.05 = *$ ,  $p \leq 0.01 = **$ .



**Fig. S11** Atom labels for  $\text{cis-}[\text{Ru}(\text{bpy})_2(\text{INH})_2]^{2+}$ , where  $\text{N}_1$ ,  $\text{N}_2$ ,  $\text{N}_3$  and  $\text{N}_4$  belong to the chelating ligand ( $N-N'$ ), and  $\text{L}_5$  and  $\text{L}_6$  belong to the monodentate ligand ( $\text{L}$ ).



**Fig. S12** Experimental absorption spectra (red line, left axis) and TD-DFT calculated vertical singlet transitions (black bars, right axis) for *cis*-[Ru(bpy)<sub>2</sub>(INH)<sub>2</sub>]<sup>2+</sup> with water as the solvent.



**Fig. S13** Composition of selected molecular orbitals for the ground state ( $S_0$ ) geometry of *cis*- [Ru(bpy)<sub>2</sub>(INH)<sub>2</sub>]<sup>2+</sup>.