

S8 Table. *In vivo* treatment efficacy of the 14 top 4-drug experimental regimens identified from studies in *M. tuberculosis* infected THP-1 macrophages using the PRS platform.

Group	Treatment ^a Drug combination (mg/kg)	Lung burden in mouse (log ₁₀ CFU)					Mean ± SE
		1	2	3	4	5	
A	Sham	7.59	7.33	7.61	7.63	7.65	7.56 ± 0.06
B	Standard Regimen ^b INH,RIF,EMB,PZA (25,10,100,150)	4.69	4.78	4.78	4.79	4.36	4.68 ± 0.08
C	PRS Regimen II CFZ,BDQ,PZA,EMB (25,30,450,100)	0.78	0.78	0.00	0.95	0.60	0.62 ± 0.17
D	Experimental Regimen ^c RPT,AC,DLM,SQ109 (10,200-50,2.5,25)	3.78	3.61	3.77	3.83	3.79	3.76 ± 0.04
E	Experimental Regimen RPT,AC,DLM,PA824 (10,200-50,2.5,100)	≥5.00	≥5.00	≥5.00	≥5.00	≥5.00	
F	Experimental Regimen RPT,AC,PA824,SQ109 (10,200-50,100,25)	≥5.00	≥5.00	≥5.00	≥5.00	≥5.00	
G	Experimental Regimen RPT,AC,BDQ,SQ109 (10,200-50,30,25)	3.06	3.01	2.60	2.76	2.89	2.86 ± 0.08
H	Experimental Regimen RPT,AC,CFZ,DLM (10,200-50,25,2.5)	2.65	3.33	3.31	2.99	3.28	3.11 ± 0.13
I	Experimental Regimen RPT,AC,BDQ,DLM (10,200-50,30,2.5)	2.95	3.17	2.77	2.64	3.20	2.95 ± 0.11
J	Experimental Regimen RPT,AC,BDQ,CFZ (10,200-50,30,25)	1.56	2.10	2.27	1.87	1.74	1.91 ± 0.13
K	Experimental Regimen RPT,DLM,PA824,SQ109 (10,2.5,100,25)	≥5.00	≥5.00	≥5.00	≥5.00	≥5.00	
L	Experimental Regimen CFZ,AC,BDQ,DLM (25,200-50,30,2.5)	1.40	1.72	1.20	1.78	1.91	1.60 ± 0.13
M	Experimental Regimen CFZ,AC,BDQ,PZA (25,200-50,30,450)	0.48	1.08	0.60	0.85	0.30	0.66 ± 0.14
N	Experimental Regimen CFZ,AC,DLM,PA824 (25,200-50,2.5,100)	≥5.00	≥5.00	≥5.00	≥5.00	≥5.00	
O	Experimental Regimen CFZ,BDQ,PA824,SQ109 (25,30,100,25)	3.24	3.15	3.40	3.28	3.24	3.26 ± 0.04
P	Experimental Regimen CFZ,BDQ,DLM,PZA (25,30,2.5,450)	0.74	1.26	1.23	0.70	0.90	0.97 ± 0.12
Q	Experimental Regimen CFZ,BDQ,DLM,PA824 (25,30,2.5,100)	3.34	3.12	3.23	3.19	3.48	3.27 ± 0.06

^aBALB/c mice (17 groups, 5 mice/group) were infected with 2.5 log₁₀ CFU of *M. tuberculosis* Erdman by aerosol. Two weeks later, the number of bacteria in the lung increased to 6.01 logs at which time the treatment were initiated. The mice received sham treatment or treatment with the Standard Regimen, PRS Regimen II, or one of the fourteen top 4-drug experimental regimens by oral gavage 5 days per week (Monday-Friday) for 3 weeks. Three days after the last treatment, mice were euthanized to determine the lung burden of *M. tuberculosis*.

^bRIF in the Standard Regimen represents rifampicin.

^cRPT in all experimental regimens represents rifapentine.