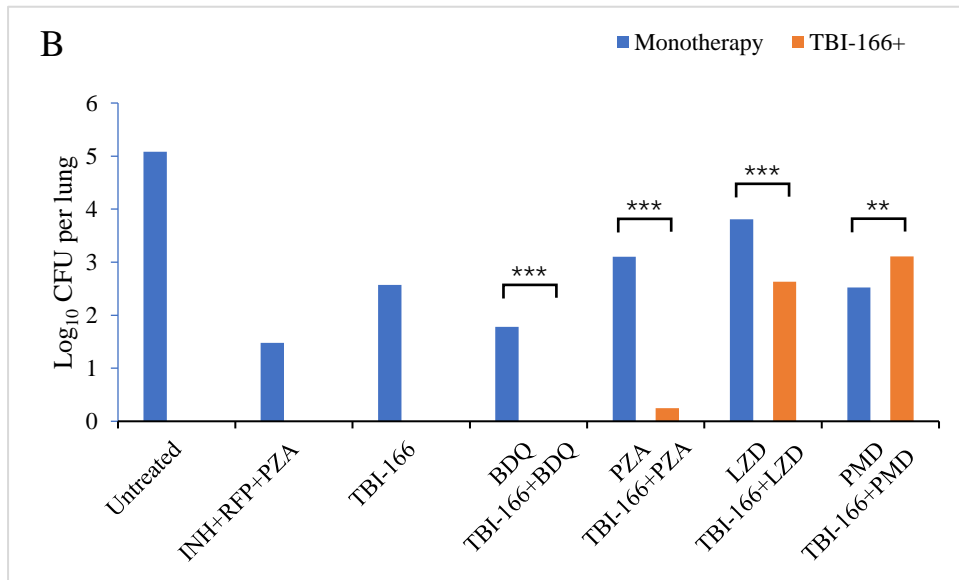


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4 **FIGS 1.** Efficacy comparison of drugs with or without TBI-166 in BALB/C mice at the  
 5 end of 4 weeks (A) or 8 weeks (B) administration. \* $P > 0.05$ , \*\* $P < 0.05$ , and \*\*\* $P <$   
 6 0.001. TBI-166+, combined with TBI-166. Isoniazid, INH; Rifampin, RFP;  
 7 Pyrazinamide, PZA; Bedaquiline, BDQ; Pretomanid, PMD; Linezolid, LZD.

8 **TABLE S1.** The exact concentrations tested for each drug in checkboard experiment

Compound	Drug concentration ( $\mu\text{g/ml}$ )
INH	0.00625 ~ 0.10
RFP	0.00625 ~ 0.10
BDQ	0.005 ~ 0.08
PMD	0.00875 ~ 0.14
LZD	0.0375 ~ 0.60
TBI-166	0.0075 ~ 0.12

9 Note: Isoniazid, INH; Rifampin, RFP; Bedaquiline, BDQ; Pretomanid, PMD; Linezolid,

10 LZD.

11 **TABLE S2.** Lung CFU counts at the indicated time points in BALB/c mice (Values are  
 12 means  $\pm$  SD, standard deviation, n=6).

Groups	Mean lung log <sub>10</sub> CFU counts $\pm$ SD at the indicated time points			
	D-18	D0	W4	W8
Untreated	2.23 $\pm$ 0.39	6.34 $\pm$ 0.04	5.60 $\pm$ 0.38	5.08 $\pm$ 0.33
INH+RFP+PZA			3.89 $\pm$ 0.23	0.50 $\pm$ 0.77
TBI-166			3.58 $\pm$ 0.26	2.57 $\pm$ 0.47
BDQ			3.83 $\pm$ 0.47	1.15 $\pm$ 0.92
PMD			4.45 $\pm$ 0.48	2.52 $\pm$ 0.43
PZA			3.70 $\pm$ 0.16	3.10 $\pm$ 0.67
LZD			5.29 $\pm$ 0.25	3.81 $\pm$ 0.40
TBI-166+BDQ			1.53 $\pm$ 0.81	Negative
TBI-166+PMD			4.44 $\pm$ 0.25	3.11 $\pm$ 0.36
TBI-166+PZA			2.36 $\pm$ 0.19	0.25 $\pm$ 0.60
TBI-166+LZD			4.01 $\pm$ 0.18	2.63 $\pm$ 0.17
TBI-166+BDQ+PMD			2.94 $\pm$ 0.26	Negative
TBI-166+BDQ+LZD			0.87 $\pm$ 0.97	Negative
TBI-166+PMD+LZD			4.45 $\pm$ 0.18	3.31 $\pm$ 0.29
TBI-166+BDQ+PMD+LZD			2.45 $\pm$ 0.23	Negative

13 Note: Isoniazid (INH), 10 mg/kg; Rifampin (RFP), 10 mg/kg; Pyrazinamide (PZA),  
 14 150 mg/kg; TBI-166 (20 mg/kg); Bedaquiline (BDQ), 25 mg/kg; Pretomanid (PMD),

15 100 mg/kg; Linezolid (LZD), 100 mg/kg. D, day; W, week. "Negative" means all mice  
16 in this group were culture-negative.

17 **TABLE S3.** Proportion of BALB/c mice with negative culture of lung at the end of  
 18 treatment.

Group	W4	W8
CMC	0/6 (0%)	0/6 (0%)
INH+RFP+PZA	0/6 (0%)	4/6 (67%)
TBI-166	0/6 (0%)	0/6 (0%)
BDQ	0/6 (0%)	2/6 (33%)
PMD	0/6 (0%)	0/6 (0%)
PZA	0/6 (0%)	0/6 (0%)
LZD	0/6 (0%)	0/6 (0%)
TBI-166+BDQ	1/6 (17%)	6/6 (100%)
TBI-166+PMD	0/6 (0%)	0/6 (0%)
TBI-166+PZA	0/6 (0%)	5/6 (83%)
TBI-166+LZD	0/6 (0%)	0/6 (0%)
TBI-166+BDQ+PMD	0/6 (0%)	6/6 (100%)
TBI-166+BDQ+LZD	3/6 (50%)	6/6 (100%)
TBI-166+PMD+LZD	0/6 (0%)	0/6 (0%)
TBI-166+BDQ+PMD+LZD	0/6 (0%)	6/6 (100%)

19 Note: Isoniazid, INH; Rifampin, RFP; Pyrazinamide, PZA; Bedaquiline, BDQ;  
 20 Pretomanid, PMD; Linezolid, LZD. D, day; W, week.

21 **TABLE S4.** Lung CFU counts at the indicated time points in C3HeB/FeJNju mice  
 22 (Values are means  $\pm$  SD, standard deviation, n=5).

Groups	Mean lung log <sub>10</sub> CFU counts $\pm$ SD at the indicated time points			
	D-32	D0	W4	W8
Untreated	1.19 $\pm$ 0.88	5.55 $\pm$ 0.32	4.94 $\pm$ 0.81	5.03 $\pm$ 0.29
TBI-166			3.18 $\pm$ 0.40	0.94 $\pm$ 0.94
INH+RFP+PZA			1.33 $\pm$ 1.19	Negative
TBI-166+BDQ+PMD			1.15 $\pm$ 0.95	Negative
TBI-166+BDQ+LZD			Negative	Negative
TBI-166+PMD+LZD			1.81 $\pm$ 1.81	Negative

23

Groups	Mean spleen log <sub>10</sub> CFU counts $\pm$ SD at the indicated time points			
	D-32	D0	W4	W8
Untreated	Negative	5.05 $\pm$ 0.09	4.70 $\pm$ 0.62	5.00 $\pm$ 0.24
TBI-166			3.44 $\pm$ 0.53	1.00 $\pm$ 1.06
INH+RFP+PZA			0.76 $\pm$ 0.97	Negative
TBI-166+BDQ+PMD			1.17 $\pm$ 0.97	Negative
TBI-166+BDQ+LZD			0.37 $\pm$ 0.65	Negative
TBI-166+PMD+LZD			1.41 $\pm$ 1.50	Negative

24 Note: Isoniazid (INH), 10 mg/kg; Rifampin (RFP), 10 mg/kg; Pyrazinamide (PZA),  
 25 150 mg/kg; TBI-166 (20 mg/kg); Bedaquiline (BDQ), 25 mg/kg; Pretomanid (PMD),  
 26 100 mg/kg; Linezolid (LZD), 100 mg/kg. D, day; W, week. "Negative" means all mice

27 in this group were culture-negative.

28 **TABLE S5.** Proportion of C3HeB/FeJNju mice with negative culture of lung or spleen  
 29 at the end of treatment.

Group	W4		W8	
	lung	spleen	lung	spleen
CMC	0/5 (0%)	0/5 (0%)	0/5 (0%)	0/5 (0%)
TBI-166	0/5 (0%)	0/5 (0%)	2/5 (40%)	2/5 (40%)
INH+RFP+PZA	2/5 (40%)	3/5 (60%)	5/5 (100%)	5/5 (100%)
TBI-166+BDQ+PMD	2/5 (40%)	2/5 (40%)	5/5 (100%)	5/5 (100%)
TBI-166+BDQ+LZD	5/5 (100%)	4/5 (80%)	5/5 (100%)	5/5 (100%)
TBI-166+PMD+LZD	2/5 (40%)	2/5 (40%)	5/5 (100%)	5/5 (100%)

30 Note: Isoniazid, INH; Rifampin, RFP; Pyrazinamide, PZA; Bedaquiline, BDQ;  
 31 Pretomanid, PMD; Linezolid, LZD. D, day; W, week.