Treatment-shortening effect of a novel regimen combining high-dose rifapentine and clofazimine in pathologically distinct mouse models of tuberculosis

Vikram Saini, Nicole C. Ammerman, Yong Seok Chang, Rokeya Tasneen, Richard E. Chaisson, Sanjay Jain, Eric Nuermberger, Jacques H. Grosset

Supplemental Materials

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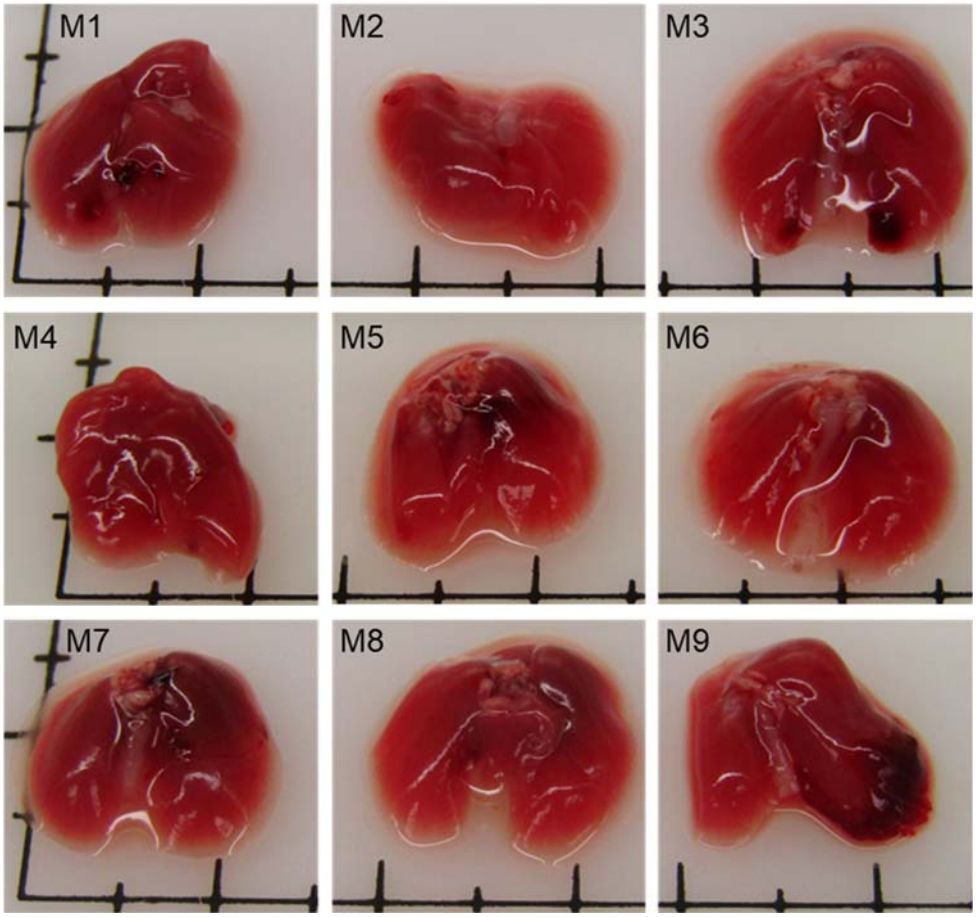

Figure S1. BALB/c mouse lungs dissected the day after infection (Week -2). CFU counts for each lung are presented in **Table S2**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

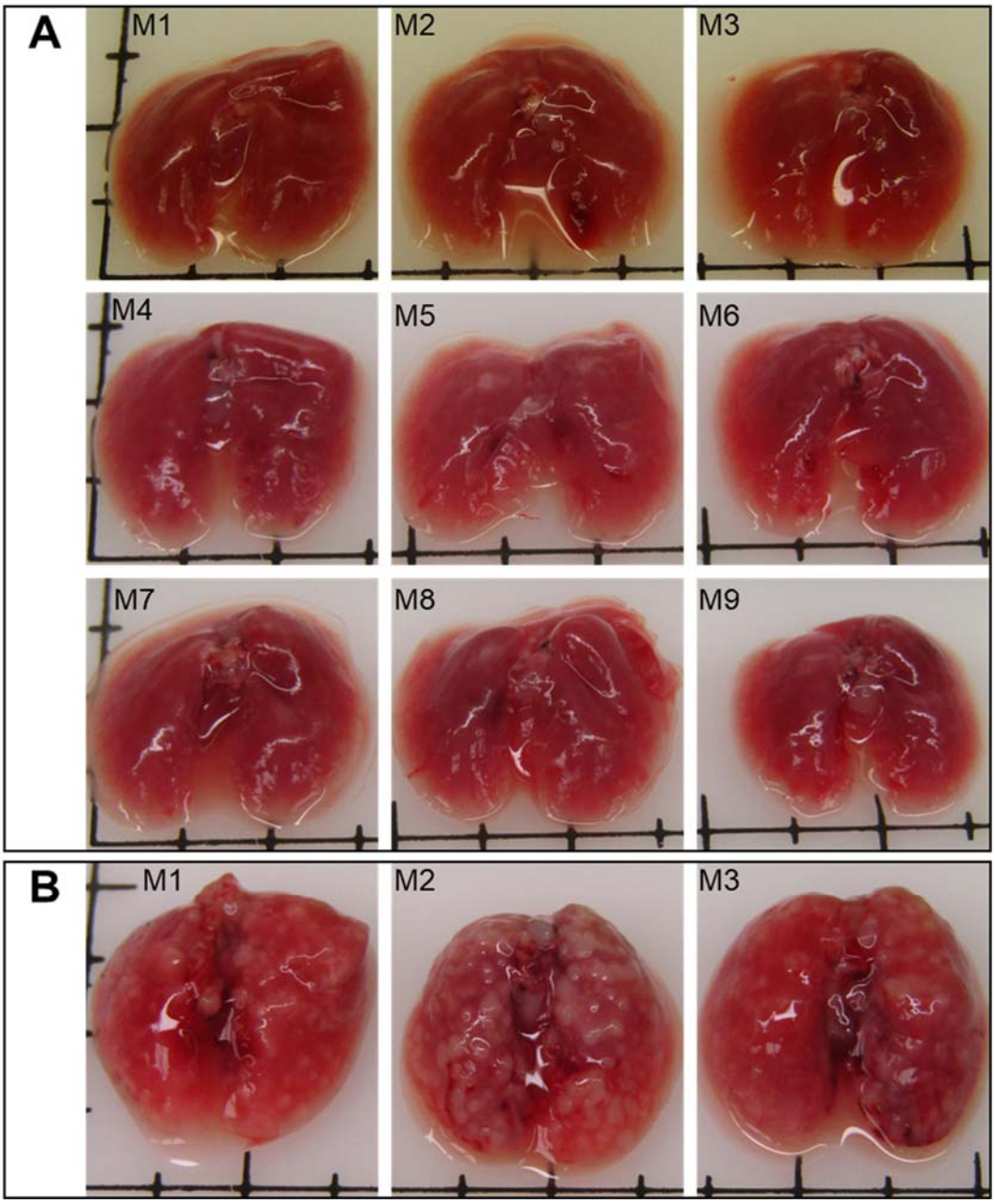

Figure S2. BALB/c mouse lungs dissected A) on the day of treatment initiation (Day 0) and B) from untreated negative control mice euthanized 3 weeks after infection (1 week after Day 0). CFU counts for each lung are presented in **Table S3**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

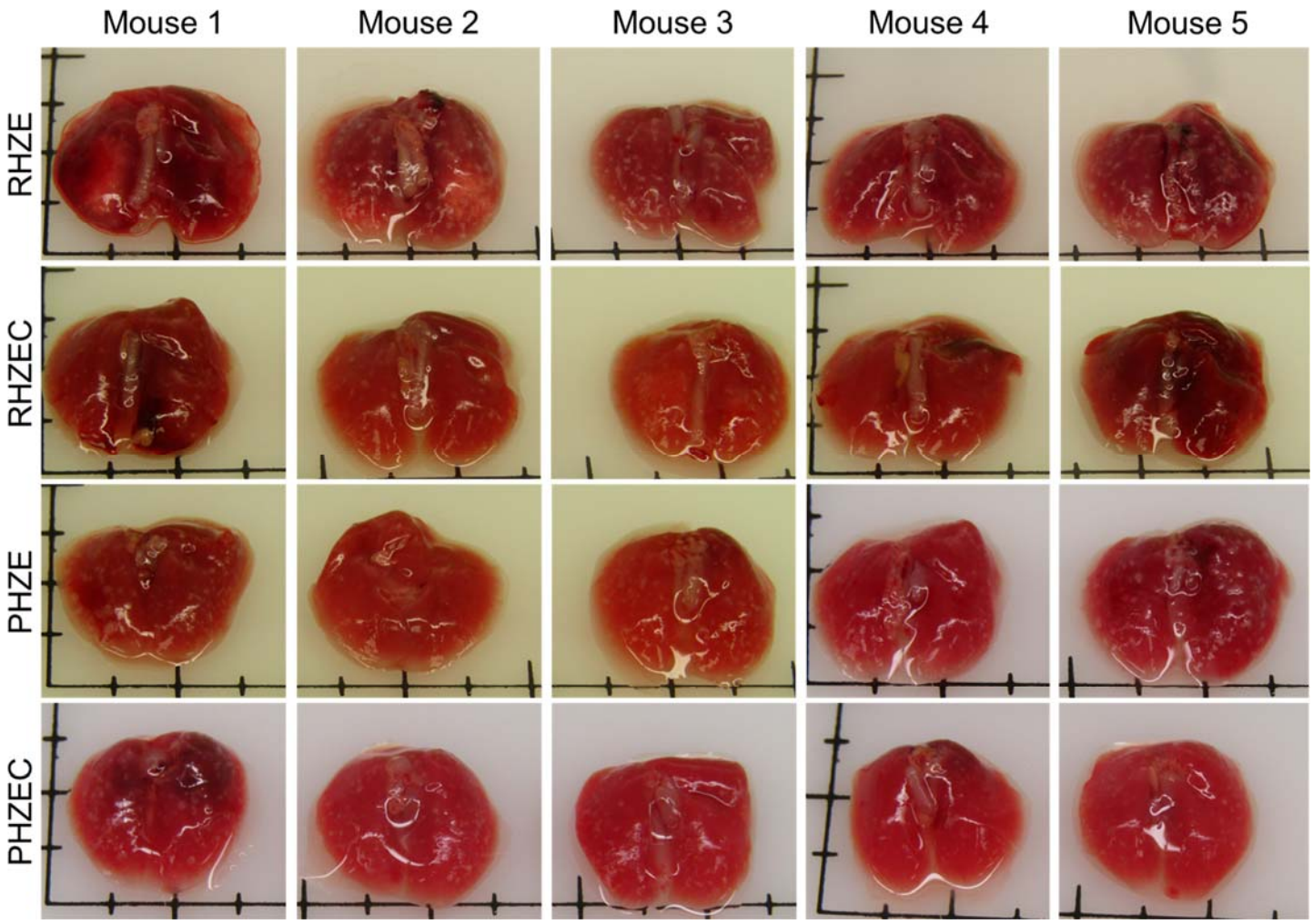

Figure S3. BALB/c mouse lungs dissected after 4 weeks of treatment. CFU counts for each lung are presented in **Table S4**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

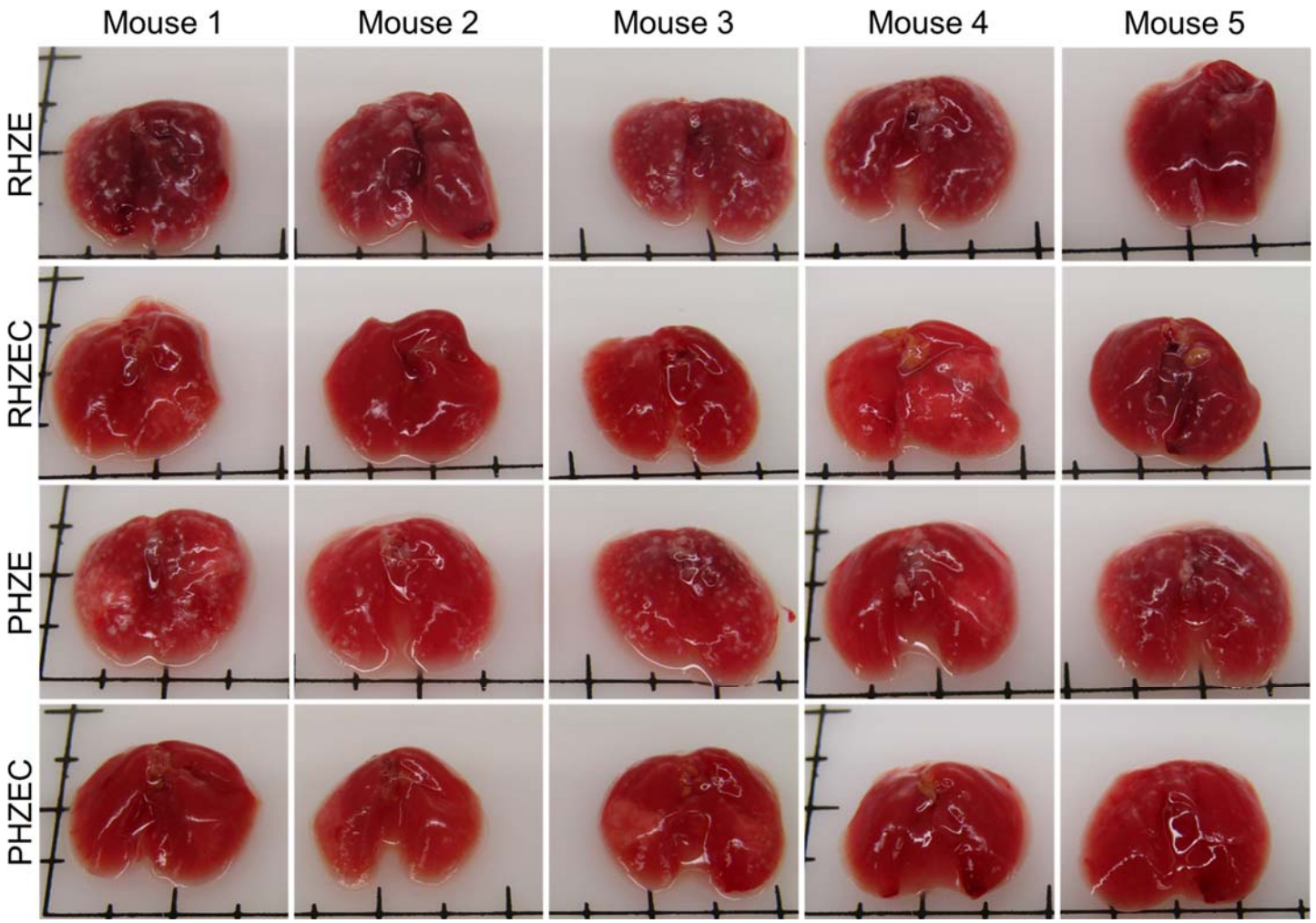

Figure S4. BALB/c mouse lungs dissected after 6 weeks of treatment. CFU counts for each lung are presented in **Table S5**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

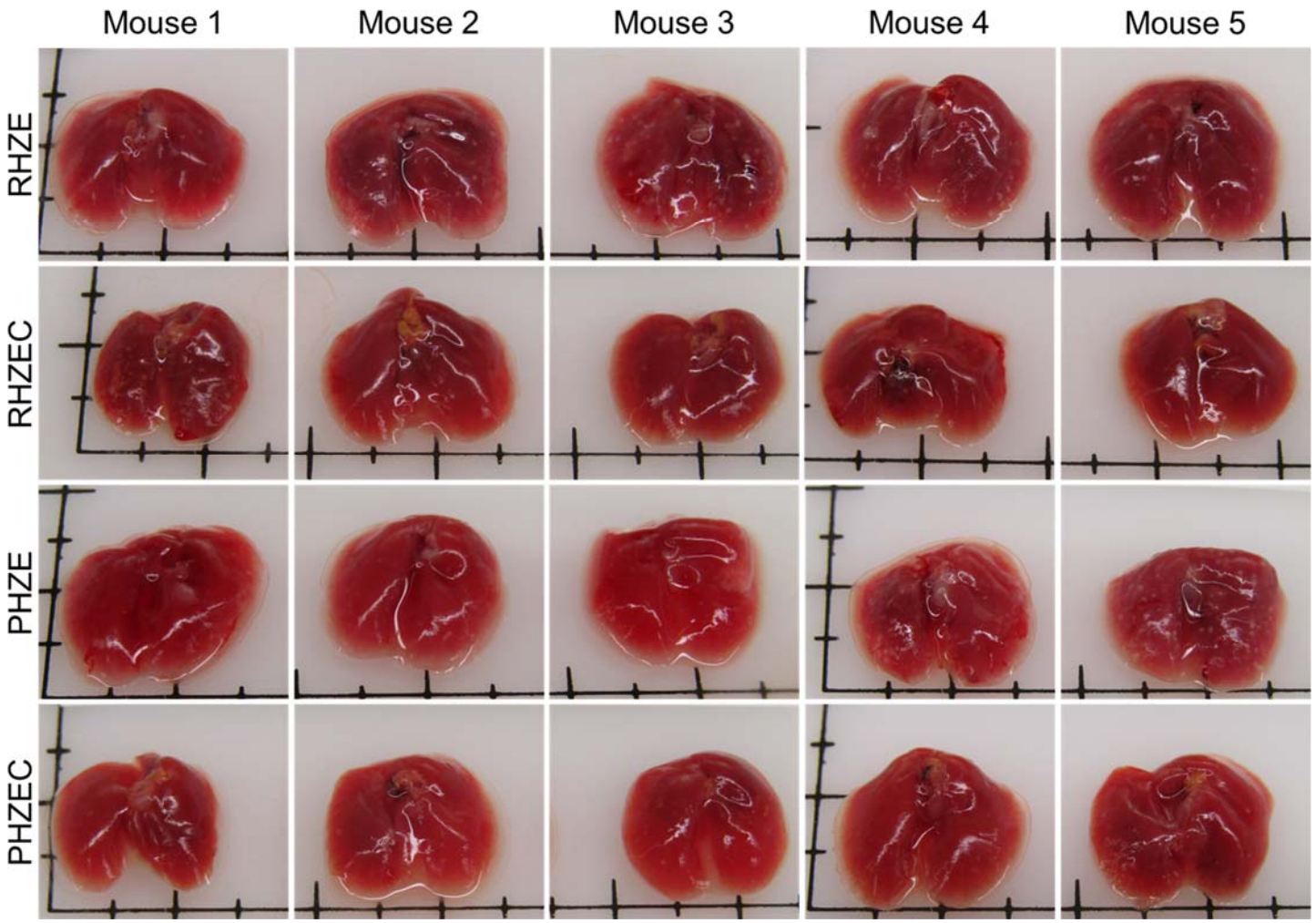

Figure S5. BALB/c mouse lungs dissected after 8 weeks of treatment. CFU counts for each lung are presented in **Table S6**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

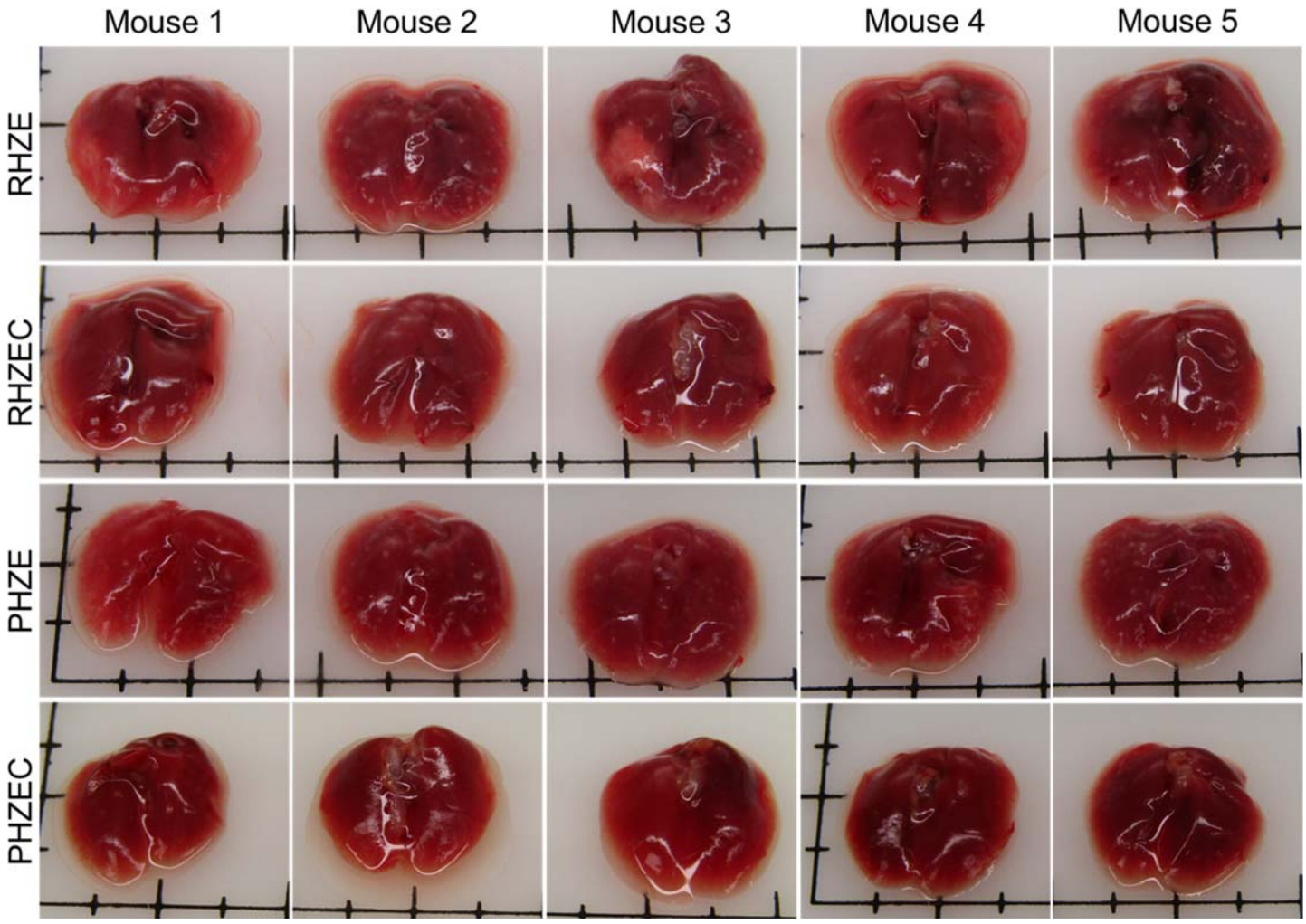

Figure S6. BALB/c mouse lungs dissected after 10 weeks of treatment. CFU counts for each lung are presented in **Table S7**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

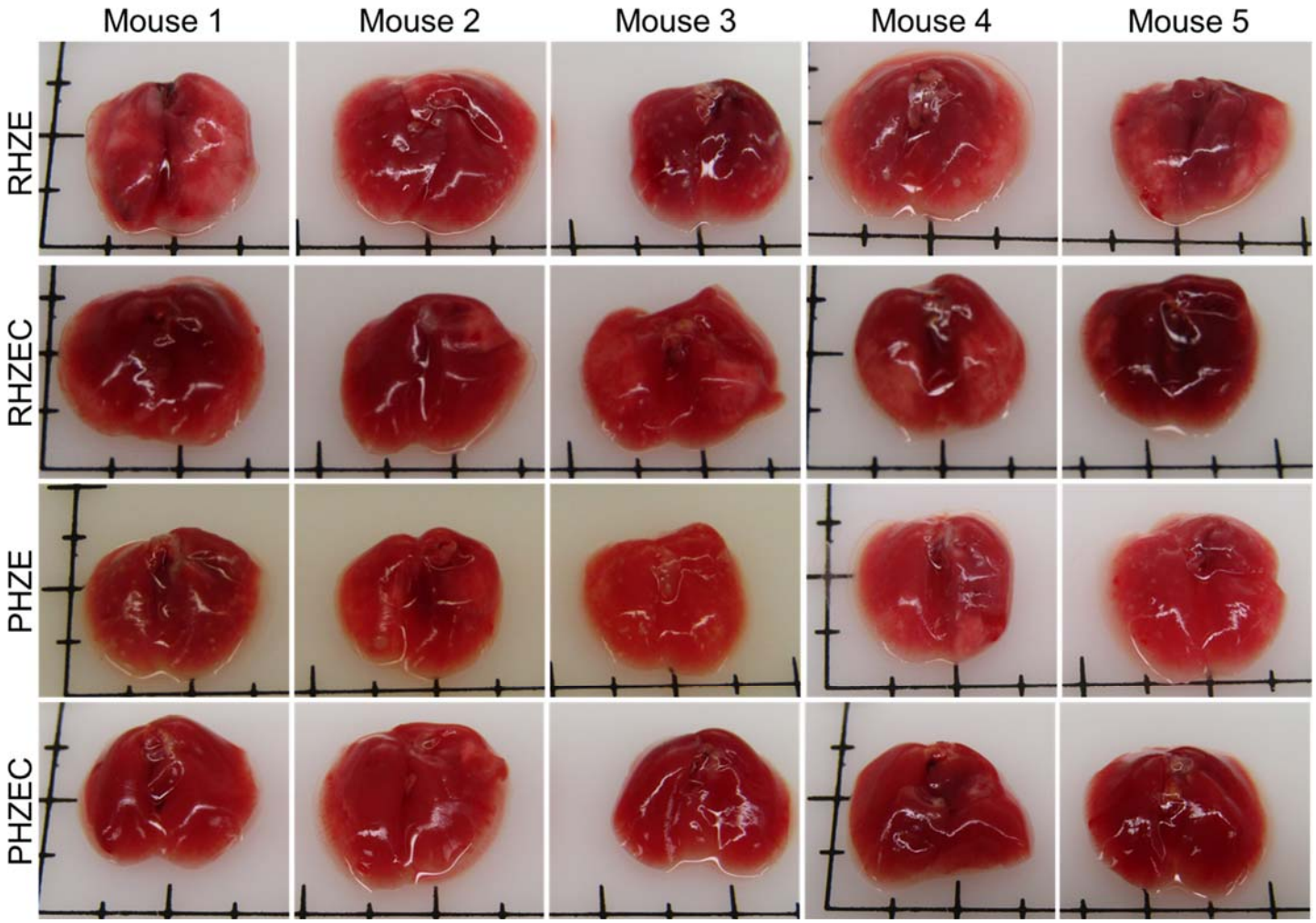

Figure S7. BALB/c mouse lungs dissected after 12 weeks of treatment. CFU counts for each lung are presented in **Table S8**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

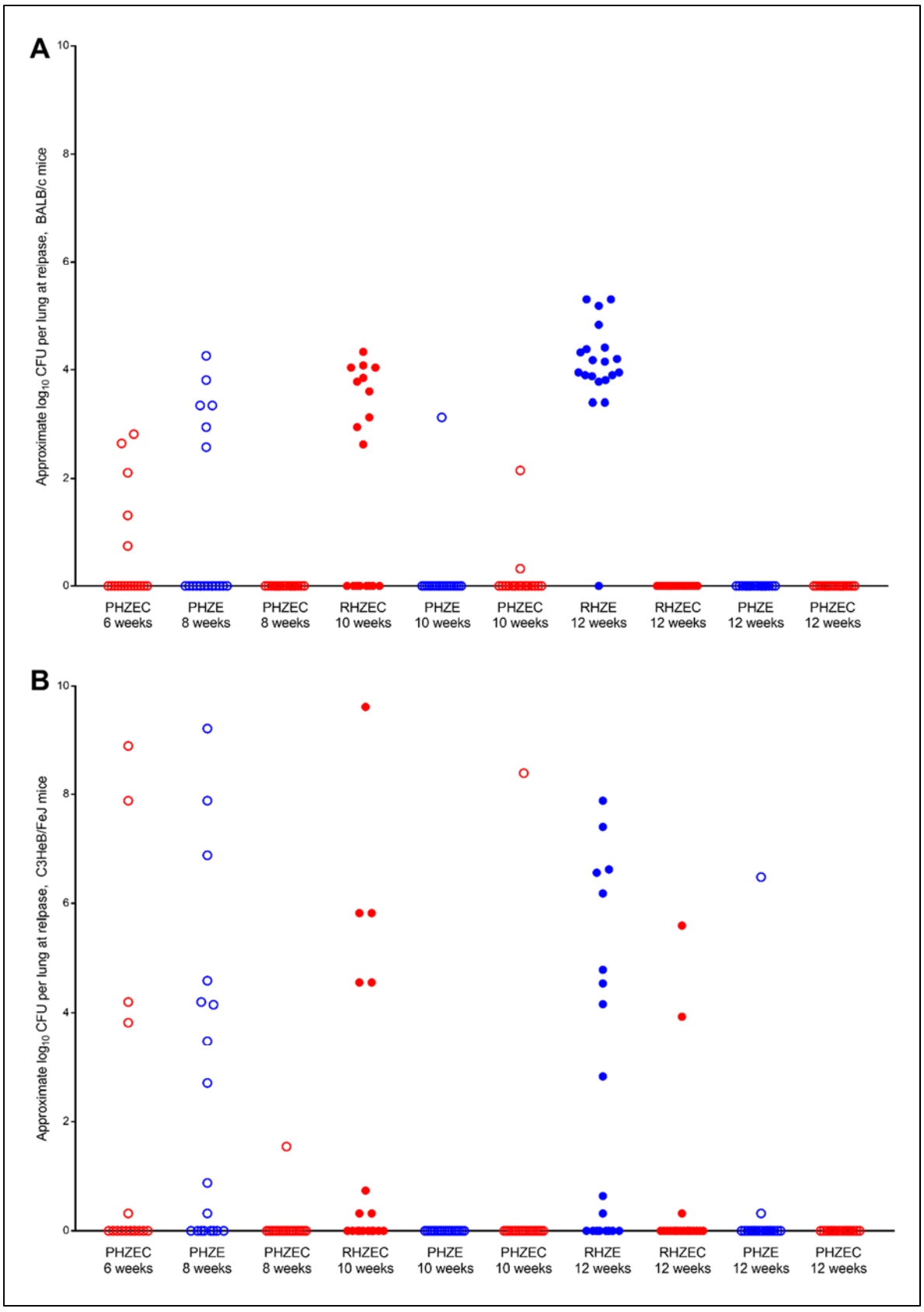

Figure S8. Approximate lung CFUs at relapse assessment for A) BALB/c and B) C3HeB/FeJ mice.

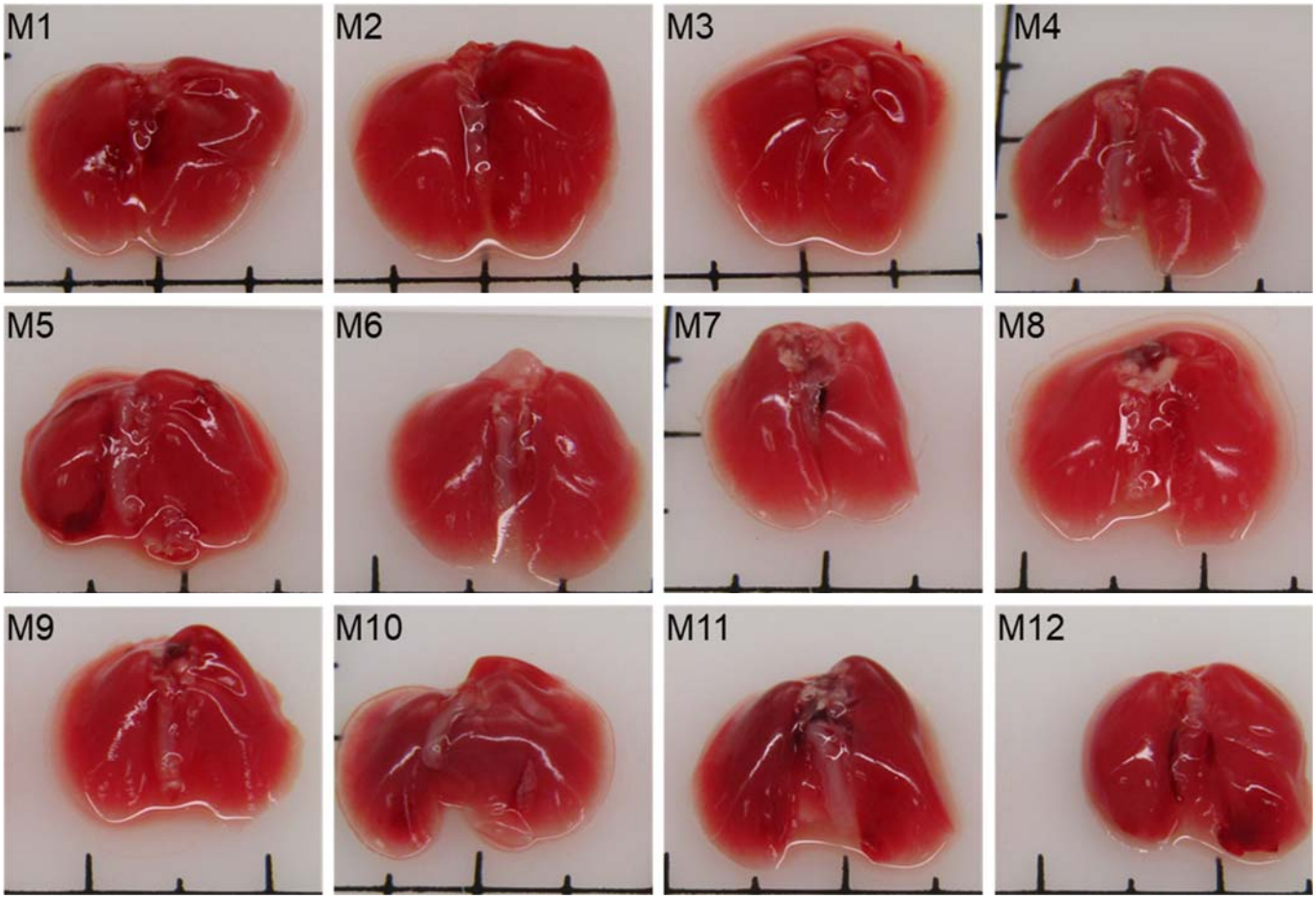

Figure S9. **C3HeB/FeJ mouse lungs dissected the day after infection (Week -6).** CFU counts for each lung are presented in **Table S2**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

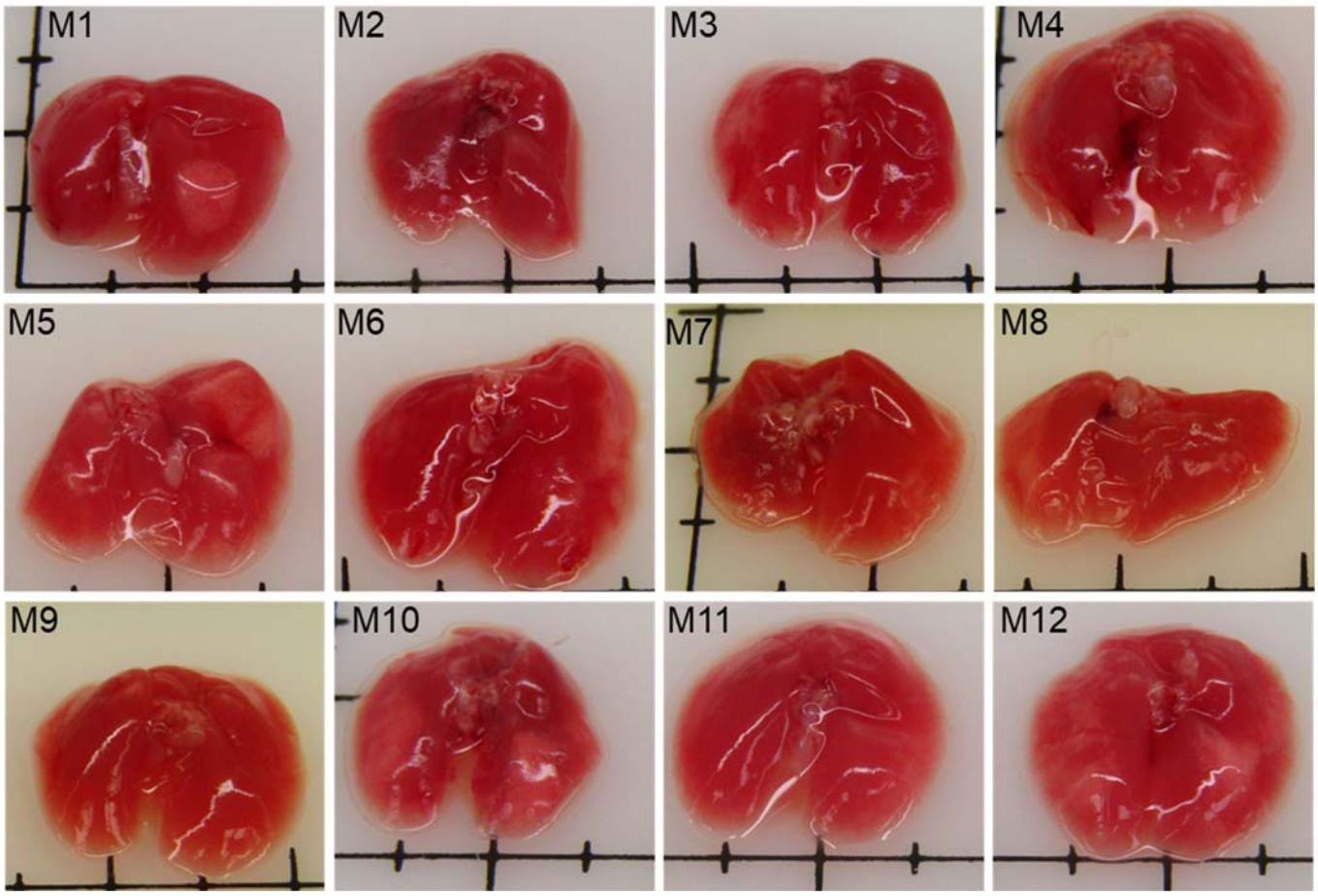

Figure S10. C3HeB/FeJ mouse lungs dissected 3 weeks after infection (Week -3). CFU counts for each lung are presented in **Table S13**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

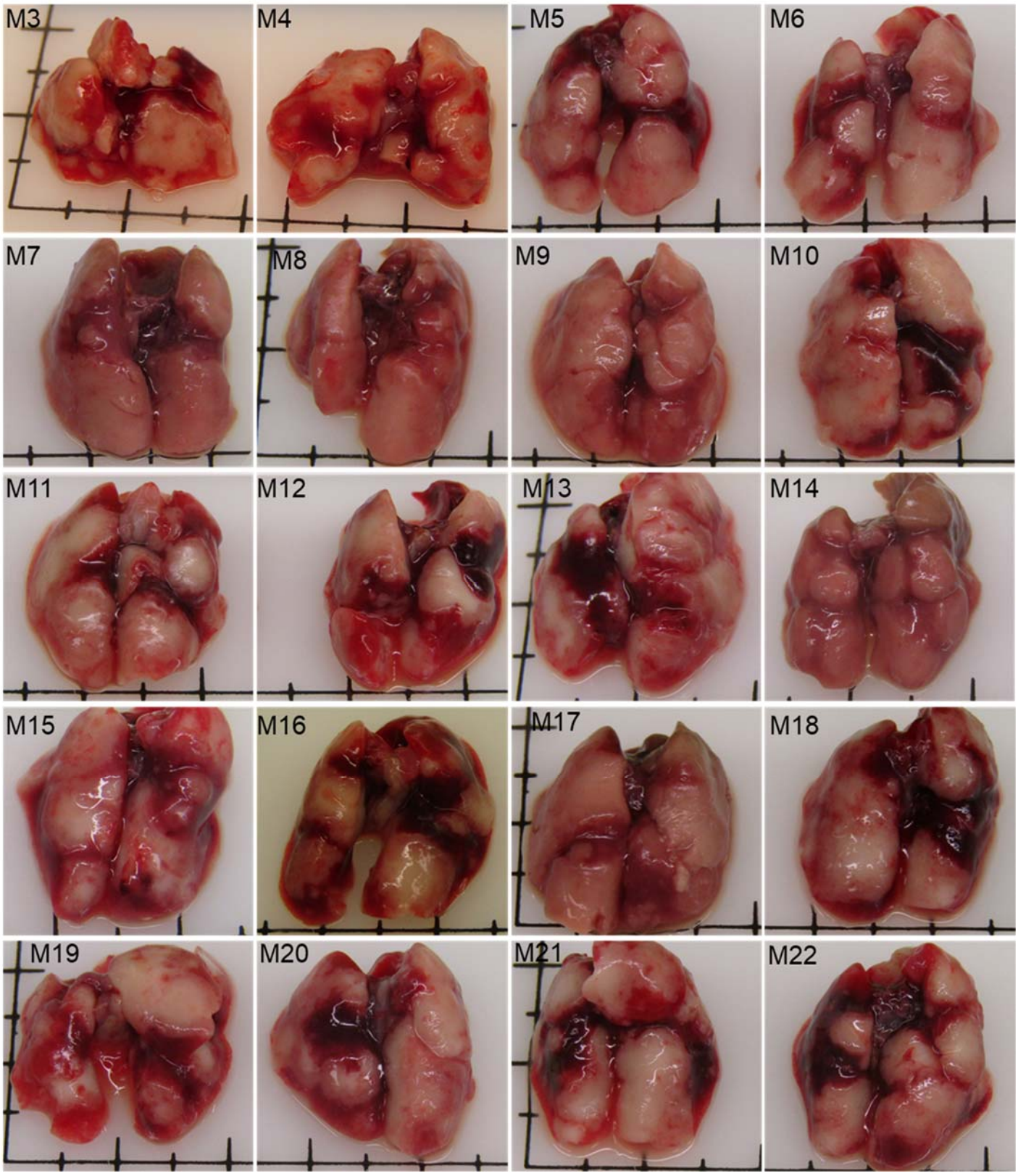

Figure S11. C3HeB/FeJ mouse lungs dissected from mice that died after Week -3 but before treatment initation on Day 0. Date of death and lung CFU counts for each mouse are presented in **Table S14**. Tick marks are every 5 mm (large tick marks are 1 cm apart). Lungs were not collected for Mouse 1 and 2.

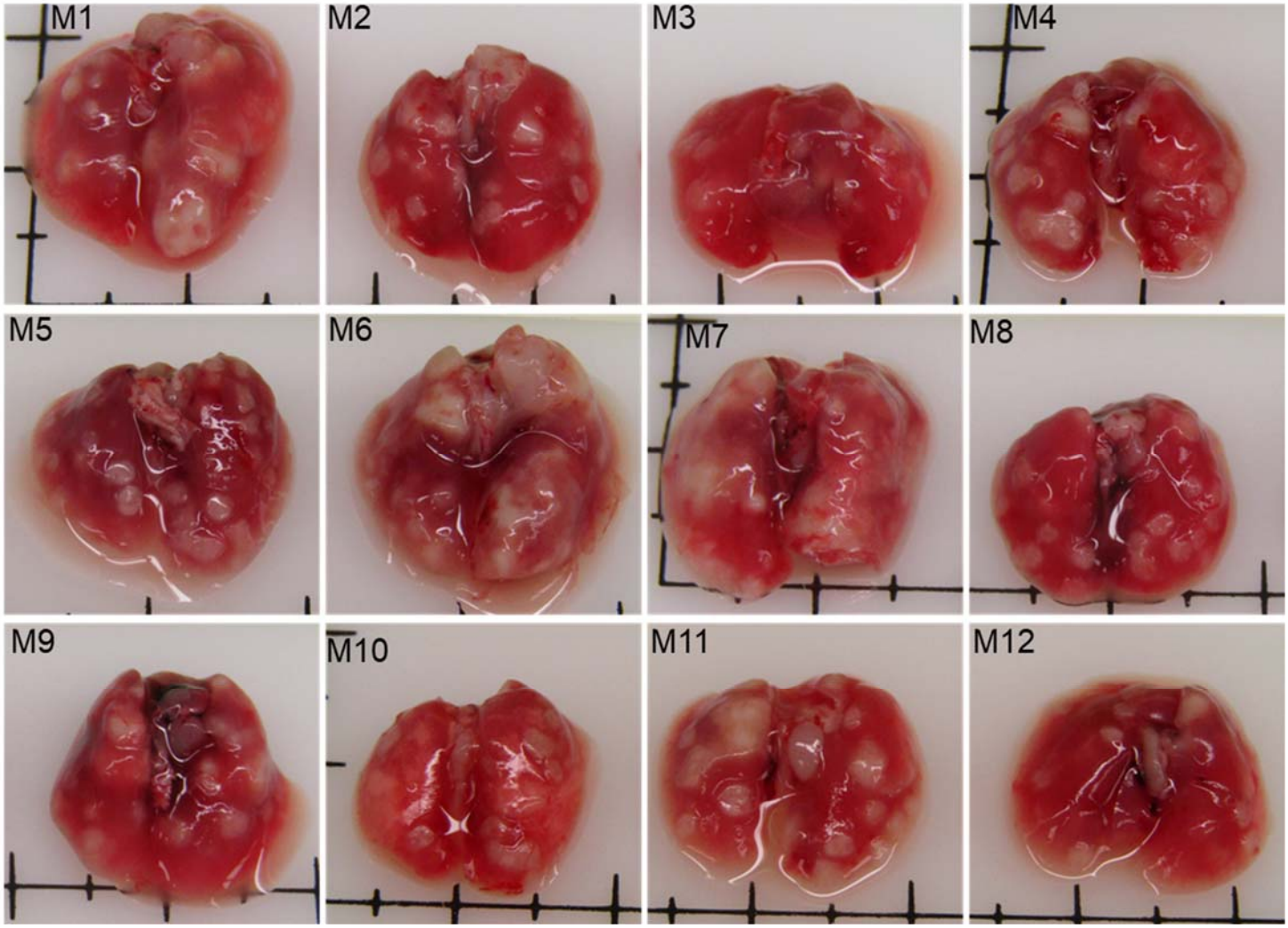

Figure S12. C3HeB/FeJ mouse lungs dissected the day of treatment initiation (Day 0). CFU counts for each lung are presented in **Table S13**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

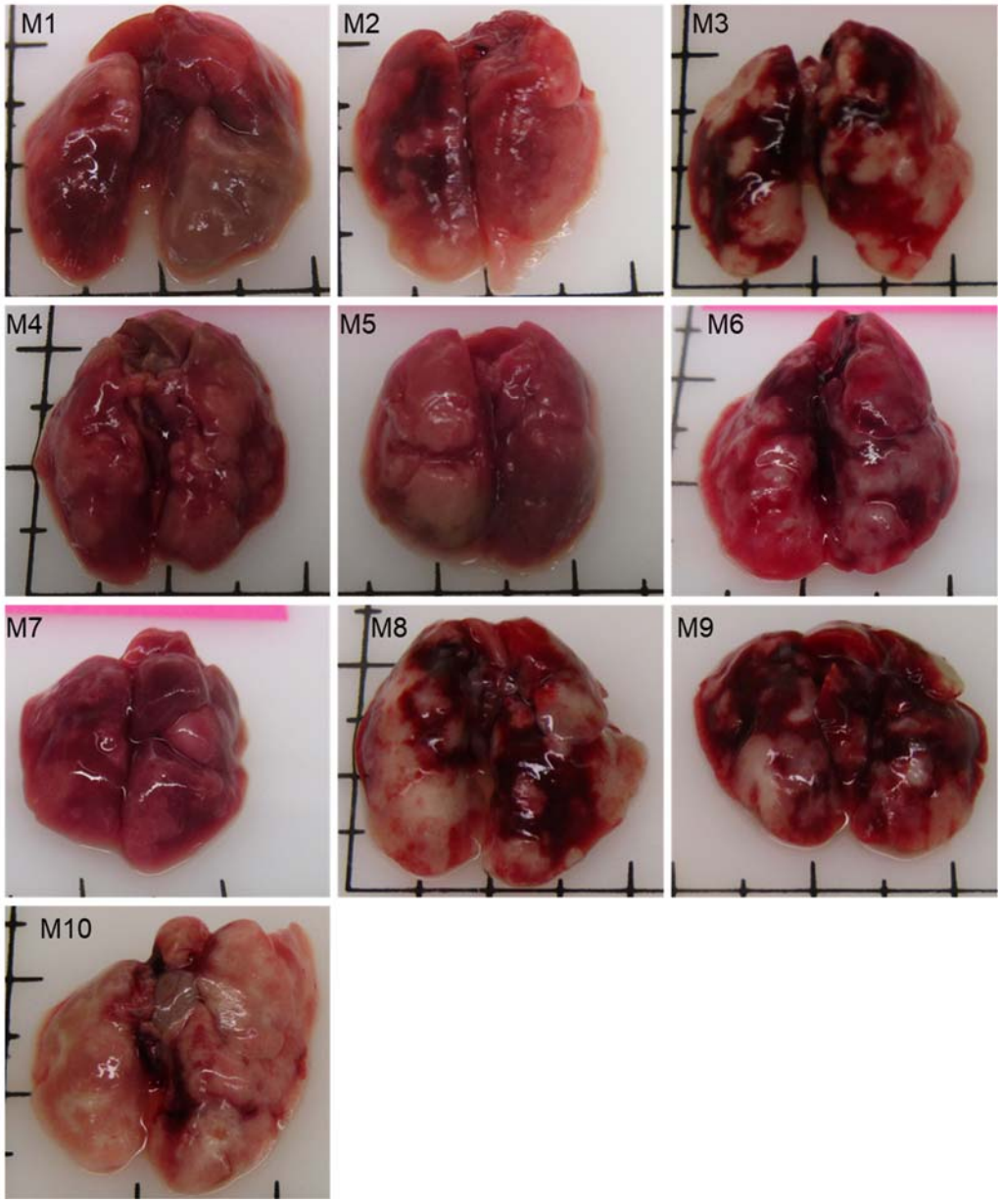

Figure S13. C3HeB/FeJ mouse lungs dissected from untreated negative control mice. Date of death and lung CFU counts for each mouse are presented in **Table S14**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

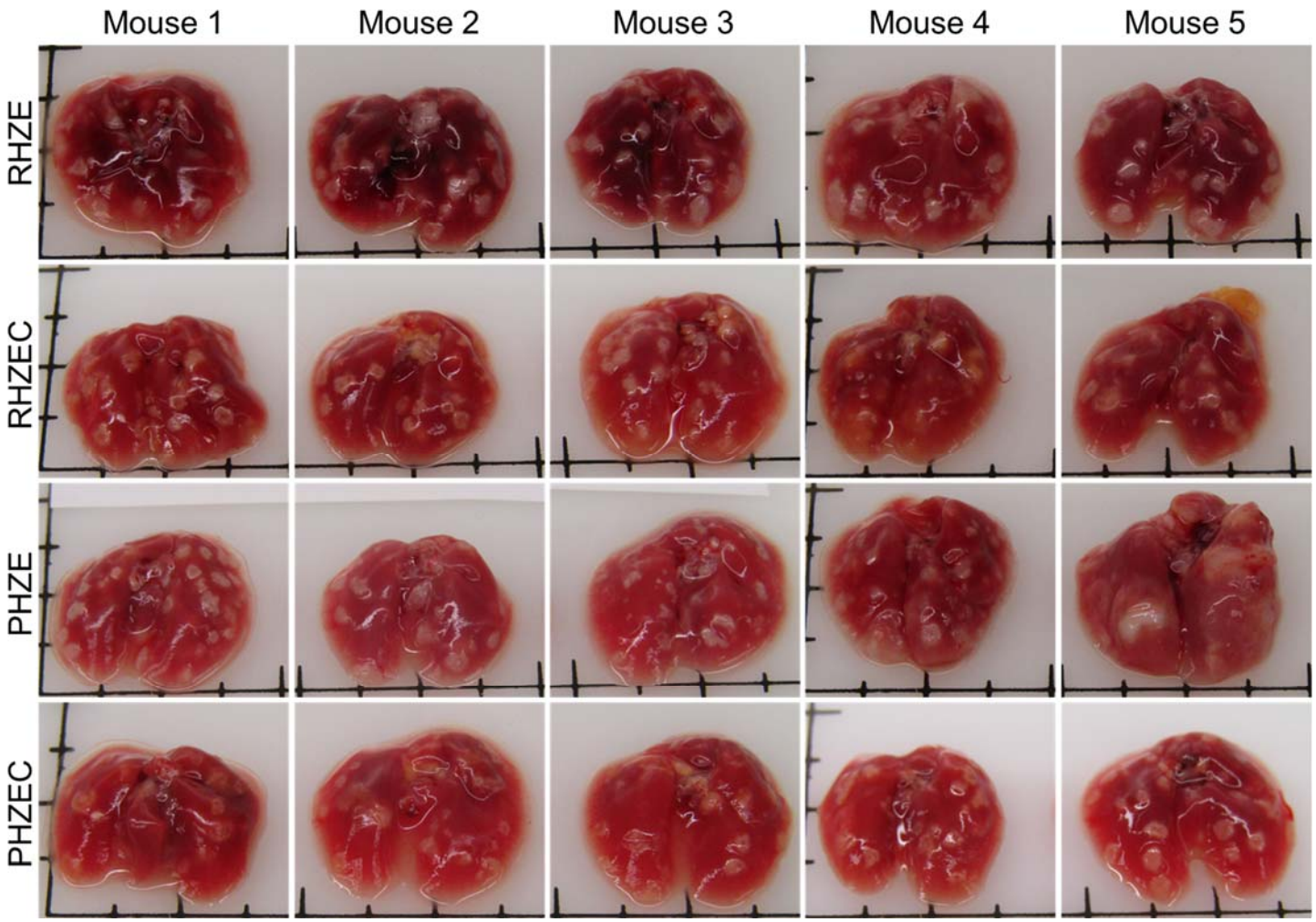

Figure S14. C3HeB/FeJ mouse lungs dissected after 4 weeks of treatment. CFU counts for each lung are presented in **Table S15**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

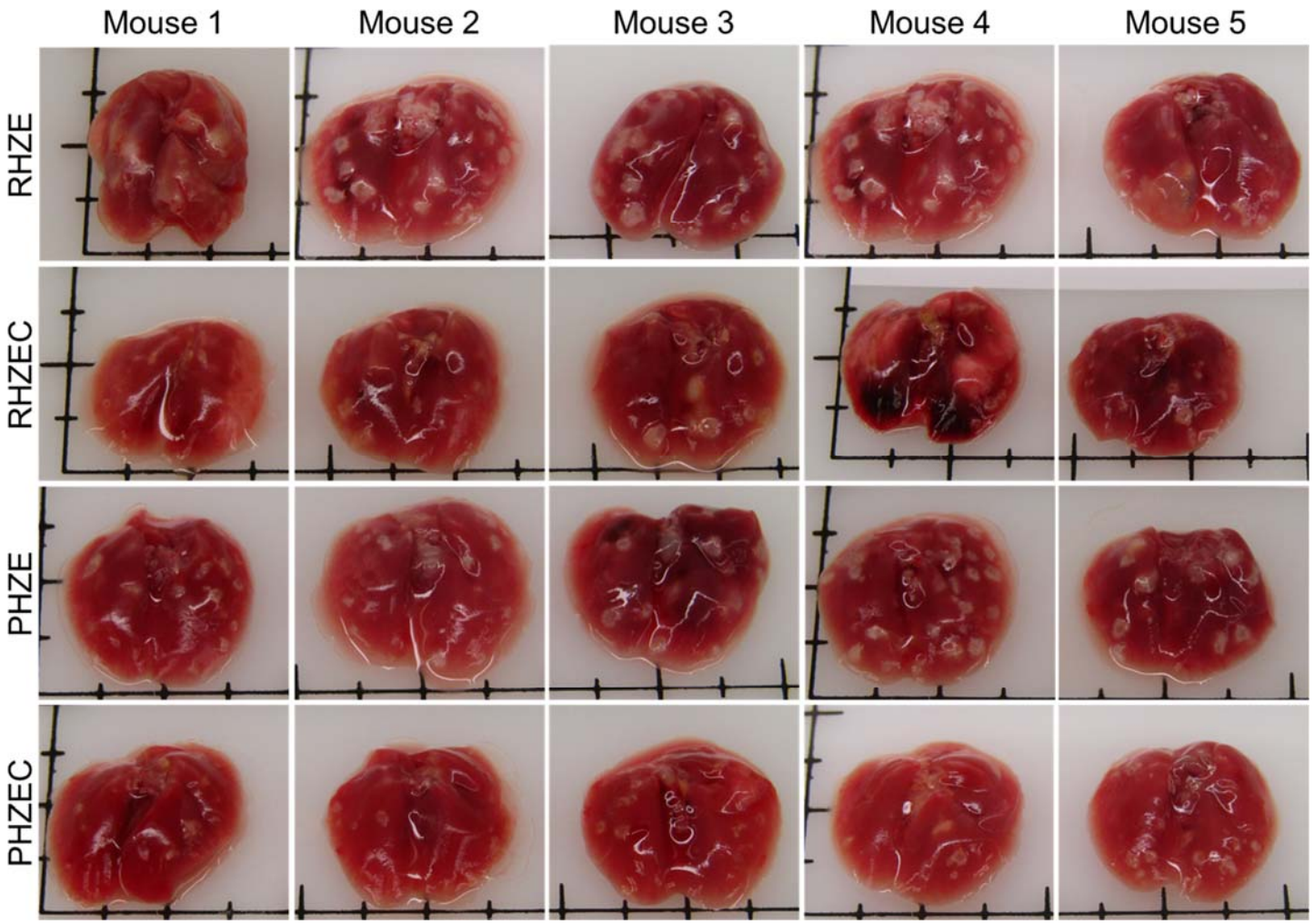

Figure S15. C3HeB/FeJ mouse lungs dissected after 6 weeks of treatment. CFU counts for each lung are presented in **Table S16**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

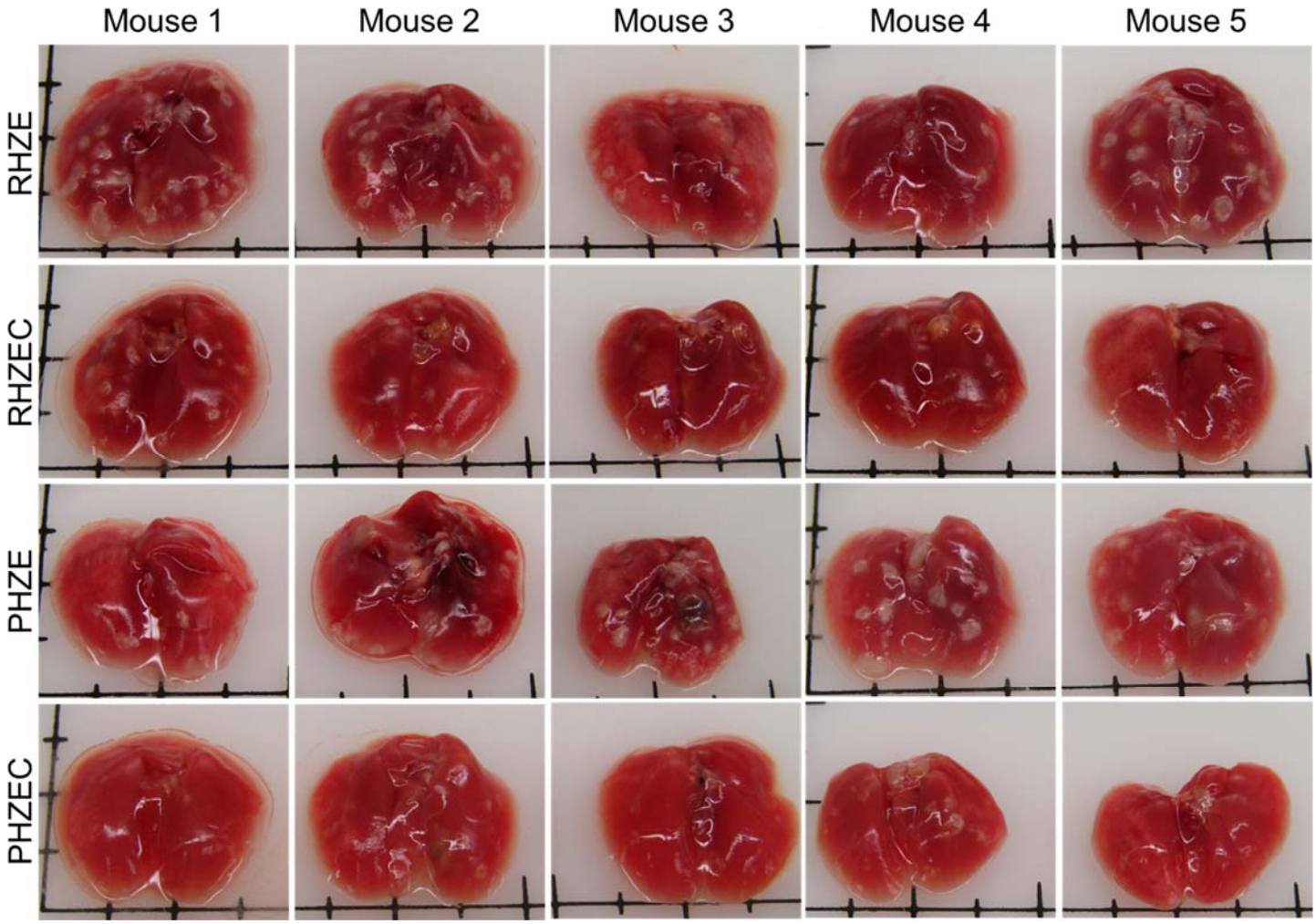

Figure S16. C3HeB/FeJ mouse lungs dissected after 8 weeks of treatment. CFU counts for each lung are presented in **Table S17**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

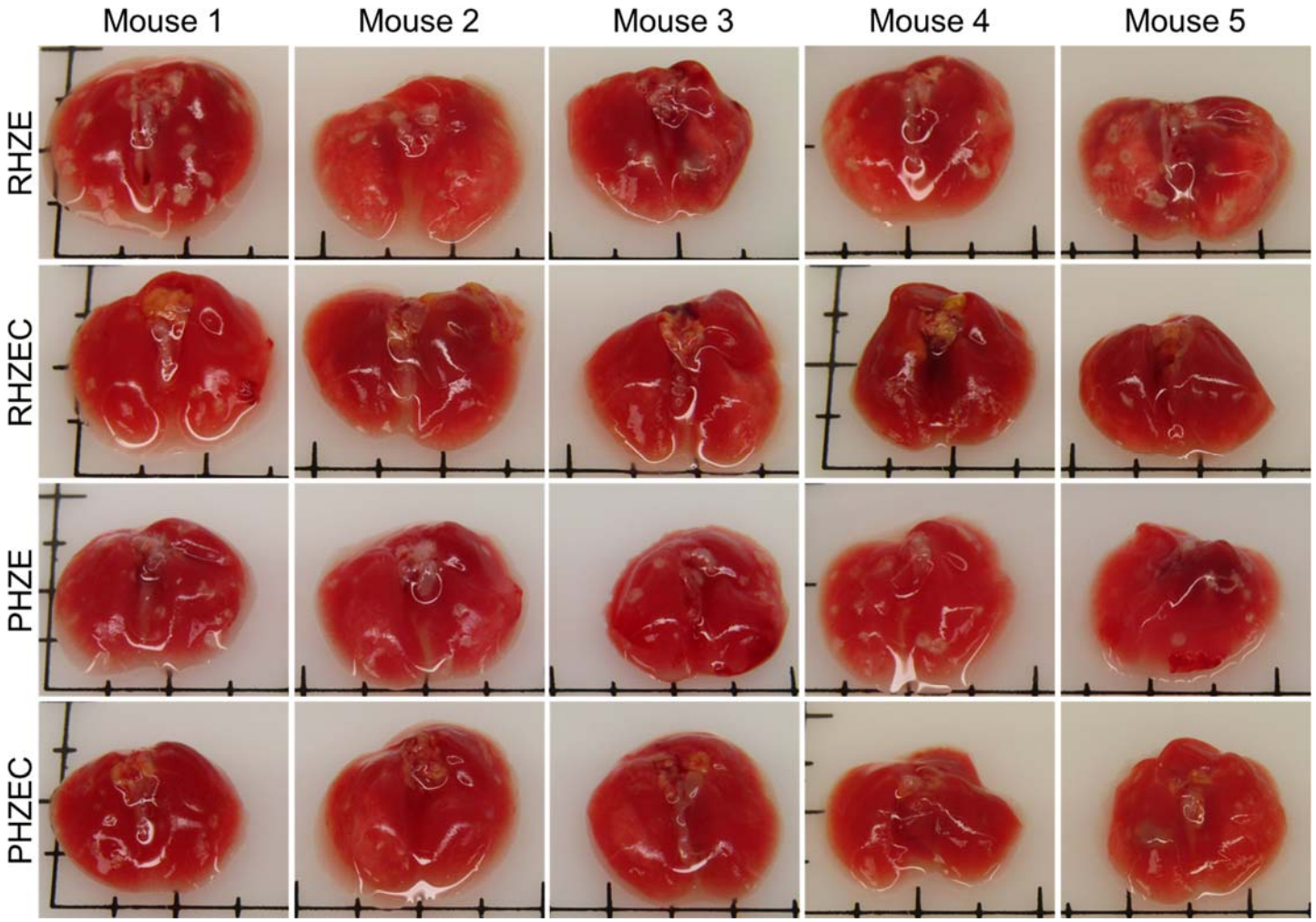

Figure S17. C3HeB/FeJ mouse lungs dissected after 10 weeks of treatment. CFU counts for each lung are presented in **Table S18**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

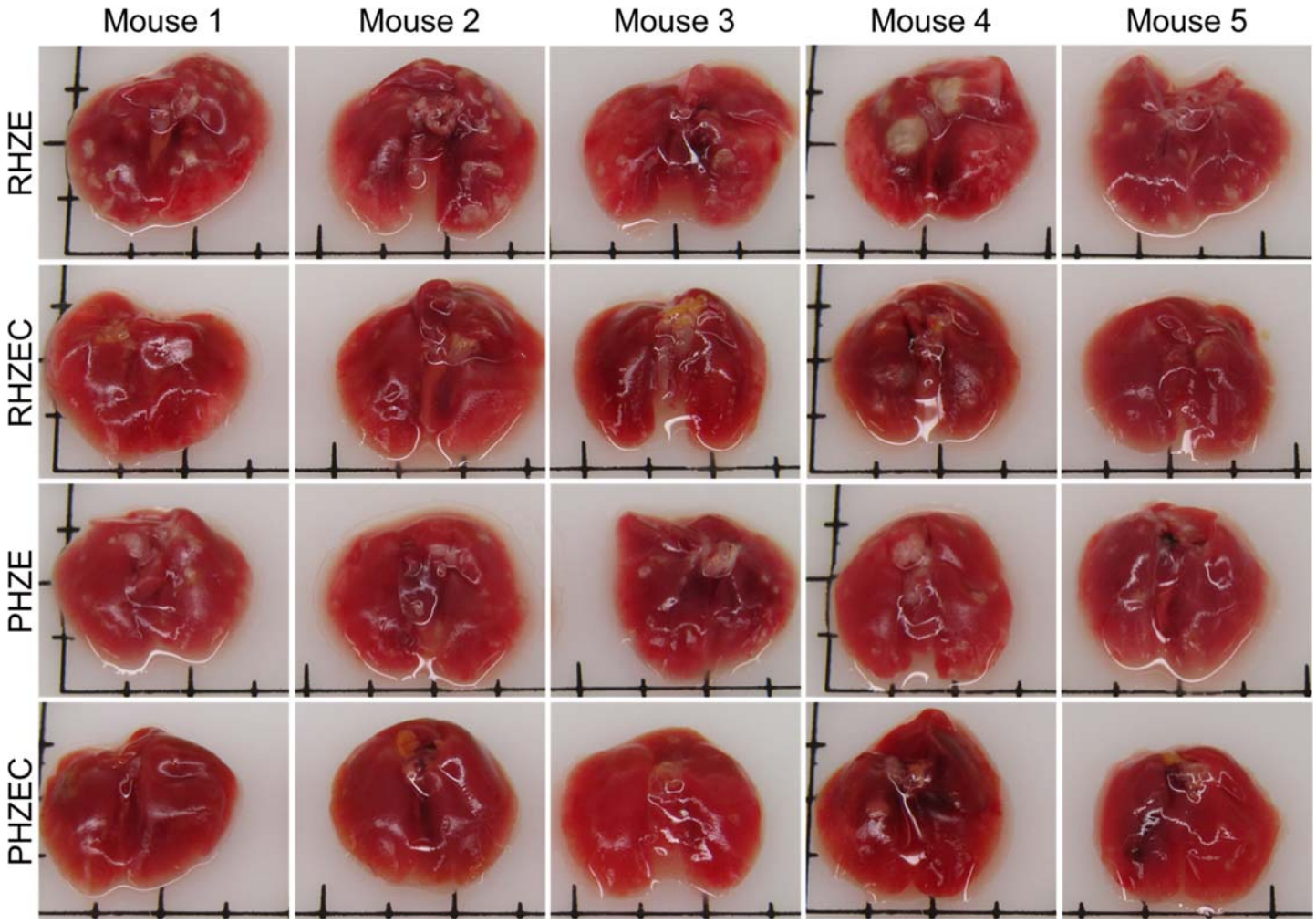

Figure S18. C3HeB/FeJ mouse lungs dissected after 12 weeks of treatment. CFU counts for each lung are presented in **Table S19**. Tick marks are every 5 mm (large tick marks are 1 cm apart).

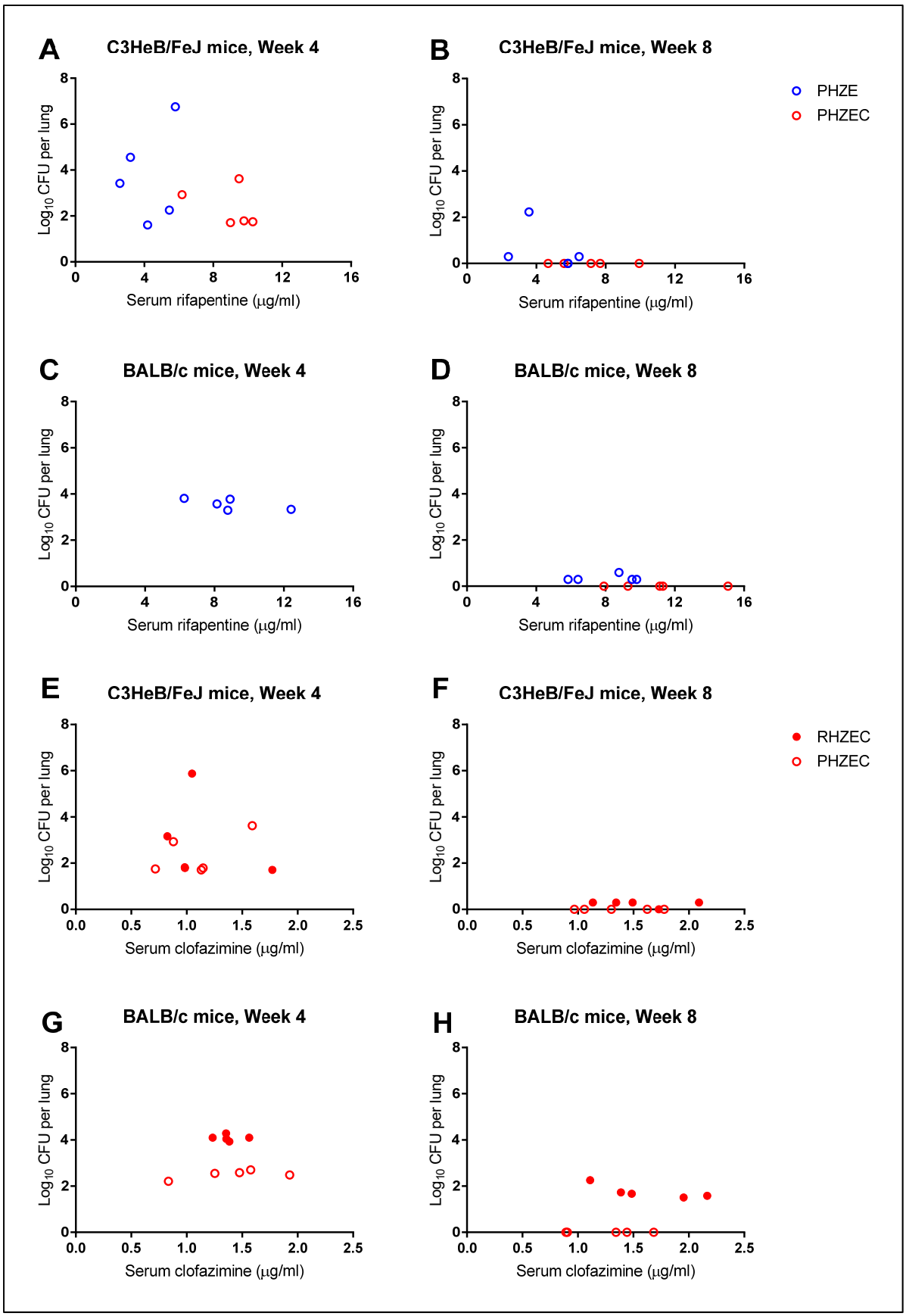

Figure S19. Trough rifapentine (A-D) and clofazimine (E-H) serum levels and lung CFU counts for individual mice after 4 (A,C,E,G) and 8 (B,D,F,H) weeks of treatment. Each data point represents one mouse.

Table S1. CFU count data used to calculate the concentration of *M. tuberculosis* suspensions used for aerosol infections. Bacterial suspensions and cognate 10-fold dilutions (0.5 mL volume) were cultured on non-selective 7H11 agar. 7H11 agar powder was manufactured by BD. All 10-fold dilutions of the bacterial suspension used for infection of C3HeB/FeJ mice were plated in duplicate, and the average CFU count was used to determine CFU/mL. The lower limit of detection for both samples was 0.48 $\log_{10}$ CFU/mL.

***M. tuberculosis* H37Rv suspension used for aerosol infection**	**Mouse strain infected**	**CFU counts for the following 10-fold dilutions: (shaded cell used to calculate CFU/mL)**								**CFU/mL**	**Log_{10} CFU/mL**
		0	**1**	**2**	**3**	**4**	**5**	**6**	**7**		
Growing culture (OD_{600} = 1.041)	BALB/c	+++	++/+++	++	+/++	+	73	3	0	14,600,000	7.16
Frozen stock (OD_{600} 1.04), diluted 15-fold in PBS	C3HeB/FeJ	++/+++	++	+/++	225	21	2	---	---	450,000	5.65
		---	++	+/++	255	24	3	---	---		

+++ indicates uniform confluent growth. ++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count.
--- indicates not determined.

Table S2. CFU count data used to calculate the number of *M. tuberculosis* implanted in mouse lungs during aerosol infection. Mice were sacrificed the day after infection. Lung homogenates and cognate 10-fold dilutions (0.5 mL volume) were cultured on selective 7H11 agar ("plain" agar) and selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by BD. The lower limit of detection was 0.78 $\log_{10}$ CFU/lung per agar type.

Mouse strain and time point	Aerosol infection run	Mouse	Agar type	CFU counts for the following 10-fold dilutions: (shaded cell used to calculate CFU/lung)				CFU/lung	Log_{10} CFU/lung
				0	1	2	3		
BALB/c, Week -2	Run 1	1	Plain	+/++	~500	40	1	20,000	4.30
			Charcoal	+/++	~500	41	2	20,500	4.31
		2	Plain	+/++	~200	26	3	13,000	4.11
			Charcoal	+/++	~300	23	1	11,500	4.06
		3	Plain	+/++	~300	39	4	19,500	4.29
			Charcoal	+/++	~300	36	4	18,000	4.26
	Run 2	4	Plain	+/++	~500	46	3	23,000	4.36
			Charcoal	+/++	~500	48	1	24,000	4.38
		5	Plain	+/++	~500	41	6	20,500	4.31
			Charcoal	+/++	~500	51	4	25,500	4.41
		6	Plain	+/++	~500	55	4	27,500	4.44
			Charcoal	+/++	~500	57	5	28,500	4.45
	Run 3	7	Plain	+/++	~300	29	2	14,500	4.16
			Charcoal	+/++	~400	23	2	11,500	4.06
		8	Plain	+/++	~400	20	1	10,000	4.00
			Charcoal	+/++	~400	25	1	12,500	4.10
		9	Plain	+/++	~300	23	2	11,500	4.06
			Charcoal	+/++	~300	18	0	9,000	3.95
C3HeB/FeJ, Week -6	Run 1	1	Plain	24	2	---	---	120	2.08
			Charcoal	18	1	---	---	90	1.96
		2	Plain	17	0	---	---	85	1.93
			Charcoal	27	0	---	---	135	2.13
		3	Plain	8	1	---	---	40	1.61
			Charcoal	17	0	---	---	85	1.93
	Run 2	4	Plain	16	4	---	---	80	1.91
			Charcoal	30	1	---	---	150	2.18
		5	Plain	8	0	---	---	40	1.61
			Charcoal	22	0	---	---	110	2.05
		6	Plain	12	0	---	---	60	1.79
			Charcoal	21	0	---	---	105	2.03
	Run 3	7	Plain	20	3	---	---	100	2.00
			Charcoal	27	4	---	---	135	2.13
		8	Plain	11	1	---	---	55	1.75
			Charcoal	24	0	---	---	120	2.08
		9	Plain	9	1	---	---	45	1.66
			Charcoal	27	1	---	---	135	2.13
	Run 4	10	Plain	12	2	---	---	60	1.79
			Charcoal	20	1	---	---	100	2.00
		11	Plain	9	0	---	---	45	1.66
			Charcoal	13	4	---	---	65	1.82
		12	Plain	3	0	---	---	15	1.20
			Charcoal	12	3	---	---	60	1.79

++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count. ~ indicates that an accurate CFU count could not be obtained due to some merged/touching colonies. --- indicates not determined.

Table S3. BALB/c lung CFU count data used to calculate CFU/lung at treatment initiation (Day 0) and for the untreated negative control mice. Lung homogenates and cognate 10-fold dilutions (0.5 mL volume) were cultured on selective 7H11 agar ("plain" agar) and selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by BD. The lower limit of detection was 0.78 and 1.71 $\log_{10}$ CFU/lung per agar type for Day 0 and Week 1 samples, respectively.

Time point	Aerosol infection run	BALB/c mouse	Agar type	CFU counts for the following 10-fold dilutions: (shaded cell used to calculate CFU/lung)								CFU/lung	Log_{10} CFU/lung
				0	1	2	3	4	5	6	7		
Day 0 (14 days post-infection)	Run 1	1	Plain	+++	++/+++	++	+	~200	12	2	---	6,000,000	6.78
			Charcoal	+++	++/+++	++	+	~200	18	1	---	9,000,000	6.95
		2	Plain	+++	+++	++/+++	+	~200	28	0	---	14,000,000	7.15
			Charcoal	+++	+++	++/+++	+	~200	23	1	---	11,500,000	7.06
		3	Plain	+++	+++	++/+++	+	~200	19	2	---	9,500,000	6.98
			Charcoal	+++	+++	++/+++	+	~200	11	2	---	5,500,000	6.74
	Run 2	4	Plain	+++	++/+++	++/+++	+/++	~300	32	2	---	16,000,000	7.20
			Charcoal	+++	++/+++	++/+++	+	~200	33	1	---	16,500,000	7.22
		5	Plain	+++	+++	++/+++	+	~200	28	1	---	14,000,000	7.15
			Charcoal	+++	+++	++/+++	+	~200	23	1	---	11,500,000	7.06
		6	Plain	+++	+++	++/+++	+/++	~200	24	3	---	12,000,000	7.08
			Charcoal	+++	++/+++	++/+++	+	~200	27	1	---	13,500,000	7.13
	Run 3	7	Plain	+++	+++	++/+++	+/++	~200	34	3	---	17,000,000	7.23
			Charcoal	+++	+++	++/+++	+	~300	33	1	---	16,500,000	7.22
		8	Plain	+++	+++	++/+++	+/++	~200	26	2	---	13,000,000	7.11
			Charcoal	+++	+++	++/+++	+/++	~300	27	4	---	13,500,000	7.13
		9	Plain	+++	+++	++/+++	+/++	~200	20	7	---	10,000,000	7.00
			Charcoal	+++	+++	++/+++	+/++	~200	38	4	---	19,000,000	7.28
Week 1 (21 days post-infection)	Run 1	1	Plain	---	+++	+++	++	+	~500	35	0	175,000,000	8.24
	Run 2	2	Plain	---	+++	+++	++/+++	++	+	74	5	370,000,000	8.57
	Run 3	3	Plain	---	+++	+++	++/+++	+/++	~500	46	7	230,000,000	8.36

+++ indicates uniform confluent growth. ++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count.
~ indicates that an accurate CFU count could not be obtained due to some merged/touching colonies. --- indicates not determined.

Table S4. BALB/c lung CFU count data used to calculate CFU/lung after 4 weeks of treatment. Lung homogenates and cognate 10-fold dilutions (0.5 mL volume) were cultured on selective 7H11 agar ("plain" agar) and selective 7H11 agar supplemented with 0.4% activated charcoal. 7H11 agar powder was manufactured by Remel Microbiology Products (all samples) and BD (one sample from each treatment group). During the study, BD 7H11 agar powder became temporarily unavailable, and therefore Remel 7H11 agar powder was used for all cultures at treatment time points. For one mouse in each treatment group, we plated homogenates in parallel on agar from both manufacturers. Only CFU counts obtained using Remel agar were used for further analyses.

Regimen	BALB/c mouse	Agar type	CFU counts for the following 10-fold dilutions: (shaded cell used to calculate CFU/lung)					CFU/lung	Log_{10} CFU/lung	LLOD
			0	1	2	3	4			
RHZE	1	Plain (BD)	---	+	171	11	0	55,000	4.74	1.71
		Charcoal (BD)	---	+	220	23	2	115,000	5.06	1.71
		Plain	+/++	+	90	9	0	45,000	4.65	0.78
		Charcoal	+/++	+	134	15	0	75,000	4.88	0.78
	2	Plain	+/++	+	67	11	1	33,500	4.53	0.78
		Charcoal	+/++	+	102	13	1	65,000	4.81	0.78
	3	Plain	+/++	+	91	16	0	80,000	4.90	0.78
		Charcoal	+/++	+	115	15	0	75,000	4.88	0.78
	4	Plain	+/++	+	77	3	0	38,500	4.59	0.78
		Charcoal	+/++	+	134	13	2	65,000	4.81	0.78
	5	Plain	+/++	+	70	10	0	35,000	4.54	0.78
		Charcoal	+/++	+	104	13	2	65,000	4.81	0.78
RHZEC	1	Plain (BD)	---	+	33	4	0	16,500	4.22	1.71
		Charcoal (BD)	---	+	48	3	0	24,000	4.38	1.71
		Plain	+	~200	17	0	0	8,500	3.93	0.78
		Charcoal	+/++	~250	22	1	0	11,000	4.04	0.78
	2	Plain	+	~200	13	2	0	6,500	3.81	0.78
		Charcoal	+/++	~250	25	1	0	12,500	4.10	0.78
	3	Plain	~100	~150	17	0	0	8,500	3.93	0.78
		Charcoal	+/++	~150	14	1	0	7,000	3.85	0.78
	4	Plain	+	~200	15	0	0	7,500	3.88	0.78
		Charcoal	+/++	~200	25	0	0	12,500	4.10	0.78
	5	Plain	~100	~250	38	3	0	19,000	4.28	0.78
		Charcoal	+/++	~250	25	1	0	12,500	4.10	0.78
PHZE	1	Plain (BD)	---	19	2	0	0	950	2.98	1.71
		Charcoal (BD)	---	62	11	0	0	3,100	3.49	1.71
		Plain	0	11	0	0	0	550	2.74	0.78
		Charcoal	+	44	6	0	0	2,200	3.34	0.78
	2	Plain	3	38	9	1	0	1,900	3.28	0.78
		Charcoal	+	75	11	0	0	3,750	3.57	0.78
	3	Plain	3	47	11	0	0	2,350	3.37	0.78
		Charcoal	+/++	105	12	0	0	6,000	3.78	0.78
	4	Plain	8	48	10	0	0	2,400	3.38	0.78
		Charcoal	+/++	106	13	1	0	6,500	3.81	0.78
	5	Plain	0	15	7	0	0	750	2.88	0.78
		Charcoal	+	40	9	1	0	2,000	3.30	0.78
PHZEC	1	Plain (BD)	---	7	0	1	0	350	2.55	1.71
		Charcoal (BD)	---	17	0	0	0	850	2.93	1.71
		Plain	0	5	1	0	0	250	2.40	0.78
		Charcoal	118	6	0	0	0	300	2.48	0.78
	2	Plain	0	0	0	0	0	0	0	0.78
		Charcoal	55	7	2	0	0	350	2.55	0.78
	3	Plain	0	0	1	1	0	500	2.70	0.78
		Charcoal	112	6	1	0	1	300	2.48	0.78
	4	Plain	0	1	0	0	0	50	1.71	0.78
		Charcoal	32	1	0	0	0	160	2.21	0.78
	5	Plain	0	2	1	0	0	100	2.00	0.78
		Charcoal	76	8	0	0	0	380	2.58	0.78

LLOD, lower limit of detection in log_{10} CFU/lung. ++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count. ~ indicates that an accurate CFU count could not be obtained due to some merged/ touching colonies. --- indicates not determined.

Table S5. BALB/c lung CFU count data used to calculate CFU/lung after 6 weeks of treatment. Lung homogenates and cognate 10-fold dilutions (0.5 mL volume) were cultured on selective 7H11 agar ("plain" agar) and selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by Remel Microbiology Products. The lower limit of detection was 0.78 $\log_{10}$ CFU/lung per agar type.

Regimen	BALB/c mouse	Agar type	CFU counts for the following 10-fold dilutions: (shaded cell used to calculate CFU/lung)				CFU/lung	Log_{10} CFU/lung
			0	1	2	3		
RHZE	1	Plain	+	79	8	1	3,950	3.60
		Charcoal	+	57	2	0	2,850	3.45
	2	Plain	+	~220	23	3	11,500	4.06
		Charcoal	+	~250	23	1	11,500	4.06
	3	Plain	+/++	~250	37	5	18,500	4.27
		Charcoal	+	~230	27	5	13,500	4.13
	4	Plain	+	~135	17	0	8,500	3.93
		Charcoal	+	~140	12	0	6,000	3.78
	5	Plain	+	~155	17	3	8,500	3.93
		Charcoal	+	~115	11	2	5,500	3.74
RHZEC	1	Plain	0	21	2	0	1,050	3.02
		Charcoal	+	27	1	0	1,350	3.13
	2	Plain	5	51	6	1	2,550	3.41
		Charcoal	+	47	4	0	2,350	3.37
	3	Plain	0	12	2	0	600	2.78
		Charcoal	+	19	2	0	950	2.98
	4	Plain	55	21	3	1	1,050	3.02
		Charcoal	+/++	23	2	0	1,150	3.06
	5	Plain	12	40	4	0	2,000	3.30
		Charcoal	+	36	3	0	1,800	3.26
PHZE	1	Plain	2	1	0	0	10	1.04
		Charcoal	17	2	0	0	85	1.93
	2	Plain	0	0	0	0	0	0
		Charcoal	6	0	0	0	30	1.49
	3	Plain	1	3	0	0	150	2.18
		Charcoal	30	2	1	0	150	2.18
	4	Plain	0	0	0	0	0	0
		Charcoal	20	2	0	0	100	2.00
	5	Plain	1	0	0	0	5	0.78
		Charcoal	4 (Contam.)	0 (Contam.)	0	0	20	1.32
PHZEC	1	Plain	0	0	0	0	0	0
		Charcoal	0	0	0	0	0	0
	2	Plain	0	0	0	0	0	0
		Charcoal	0	0	0	0	0	0
	3	Plain	0	0	0	0	0	0
		Charcoal	4	0	0	0	20	1.32
	4	Plain	0	0	0	0	0	0
		Charcoal	1	0	0	0	5	0.78
	5	Plain	0	0	0	0	0	0
		Charcoal	3	1	0	0	15	1.20

++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count. ~ indicates that an accurate CFU count could not be obtained due to some merged/touching colonies. Contam. indicates fungal or bacterial contamination was observed on the agar.

Table S6. BALB/c lung CFU count data used to calculate CFU/lung after 8 weeks of treatment. Undiluted lung homogenates were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal (five agar plates per sample, 0.5 mL homogenate per plate). All 7H11 agar powder was manufactured by Remel Microbiology Products. The lower limit of detection was 0.30 $\log_{10}$ CFU/lung per sample.

Regimen	BALB/c mouse	Agar type	CFU counts from undiluted lung homogenate (total on five plates used to calcluate CFU/lung):					CFU/lung	Log_{10} CFU/lung
			Plate 1	Plate 2	Plate 3	Plate 4	Plate 5		
RHZE	1	Charcoal	111	107	131	94	73	516	2.71
	2	Charcoal	60	55	77	60	27	279	2.45
	3	Charcoal	140	142	135	121	71	609	2.79
	4	Charcoal	92	93	79	83	44	391	2.59
	5	Charcoal	93	78	68	78	61	378	2.58
RHZEC	1	Charcoal	46	32	43	28	33	182	2.26
	2	Charcoal	6	1	7	7	10	31	1.51
	3	Charcoal	14	7	13	6	13	53	1.73
	4	Charcoal	7	9	5	10	15	46	1.67
	5	Charcoal	10	9	3	9	6	37	1.58
PHZE	1	Charcoal	0	3	0	0	0	3	0.60
	2	Charcoal	1	0	0	0	0	1	0.30
	3	Charcoal	1	0	0	0	0	1	0.30
	4	Charcoal	0	0	1	0	0	1	0.30
	5	Charcoal	1	0	0	0	0	1	0.30
PHZEC	1	Charcoal	0	0	0	0	0	0	0
	2	Charcoal	0	0	0	0	0	0	0
	3	Charcoal	0	0	0	0	0	0	0
	4	Charcoal	0	0	0	0	0	0	0
	5	Charcoal	0	0	0	0	0	0	0

Table S7. BALB/c lung CFU count data used to calculate CFU/lung after 10 weeks of treatment. Undiluted lung homogenates were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal (five agar plates per sample, 0.5 mL homogenate per plate). All 7H11 agar powder was manufactured by Remel Microbiology Products. The lower limit of detection was 0.30 $\log_{10}$ CFU/lung per sample.

Regimen	BALB/c mouse	CFU counts from undiluted lung homogenate (total on five plates used to calcluate CFU/lung):					CFU/lung	Log_{10} CFU/lung
		Plate 1	Plate 2	Plate 3	Plate 4	Plate 5		
RHZE	1	10	6	6	4	2	28	1.46
	2	20	17	17	21	7	82	1.92
	3	12	14	19	18	2	65	1.82
	4	14	18	5	12	10	59	1.78
	5	9	4	5	4	2	24	1.40
RHZEC	1	0	0	0	2	0	2	0.48
	2	0	0	0	0	0	0	0
	3	0	0	0	0	0	0	0
	4	1	0	0	1	0	2	0.48
	5	1	0	0	0	1	2	0.48
PHZE	1	0	0	0	0	0	0	0
	2	0	0	1	0	0	1	0.30
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0
PHZEC	1	0	0	0	0	0	0	0
	2	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0	0
	3	0	0	0	0	0	0	0
	4	0	0	0	0	0	0	0
	5	0	0	0	0	0	0	0

Contam. indicates fungal or bacterial contamination was observed on the agar. In this case, the contamination was in the form of a few discreet colonies that did not preclude reading the sample.

Table S8. BALB/c lung CFU count data used to calculate CFU/lung after 12 weeks of treatment. Undiluted lung homogenates were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal (five agar plates per sample, 0.5 mL homogenate per plate). All 7H11 agar powder was manufactured by Remel Microbiology Products. The lower limit of detection was 0.30 $\log_{10}$ CFU/lung per sample.

Regimen	BALB/c mouse	Agar type	CFU counts from undiluted lung homogenate (total on five plates used to calcluate CFU/lung):					CFU/lung	Log_{10} CFU/lung
			Plate 1	Plate 2	Plate 3	Plate 4	Plate 5		
RHZE	1	Charcoal	0	2	3	1	0	6	0.85
	2	Charcoal	0	0	1	2	2	5	0.78
	3	Charcoal	1	2	0	1	1	5	0.78
	4	Charcoal	1	1	0	2	1	5	0.78
	5	Charcoal	0	0	0	1	0	1	0.30
RHZEC	1	Charcoal	0	0	0	0	0	0	0
	2	Charcoal	0	0	0	0	0	0	0
	3	Charcoal	0	0	0	0	0	0	0
	4	Charcoal	0	0	0	0	0	0	0
	5	Charcoal	0	0	0	0	0	0	0
PHZE	1	Charcoal	0	0	0	0	0	0	0
	2	Charcoal	0	0	0	0	0	0	0
	3	Charcoal	Contam.	Contam.	Contam.	Contam.	Contam.	---	---
	4	Charcoal	0	0	0	0	0	0	0
	5	Charcoal	0	0	0	0	0	0	0
PHZEC	1	Charcoal	0	0	0	0	0	0	0
	2	Charcoal	0	0	0	0	0	0	0
	3	Charcoal	0	0	0	0	0	0	0
	4	Charcoal	0	0	0	0	0	0	0
	5	Charcoal	0	0	0	0	0	0	0

Contam. indicates fungal or bacterial contamination was observed on the agar. In this case, the contamination covered the agar surface, preventing reading of the sample.

Table S9. Lung CFU data from BALB/c mice assessed for relapse after 6 weeks of treatment. Mice were sacrificed 6 months after stopping treatment. Undiluted lung homogenates (2.25 mL homogenate over 4 agar plates) and cognate 10^{-2} and 10^{-4} dilutions (1 agar plate each, 0.5 mL per plate) were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by BD. The lower limit of detection was 0.32 $\log_{10}$ CFU/lung per sample.

BALB/c mouse	CFU counts for the following dilutions: (shaded cells used to approximate CFU/lung)						CFU/lung (approximate)	Log_{10} CFU/lung (approximate)
	Undiluted				10^{-2} dilution	10^{-4} dilution		
	Plate 1	Plate 2	Plate 3	Plate 4				
1	0	0	0	0	0	0	0	0
2	0	0	0	0	0	0	0	0
3	24	33	30	27	0	0	127	2.11
4	0	0	0	0	0	0	0	0
5	0	0	0	0	0	0	0	0
6	0	0	0	0	0	0	0	0
7	0	0	0	0	0	0	0	0
8	0	0	0	0	0	0	0	0
9	0	0	0	0	0	0	0	0
10	0	0	0	0	0	0	0	0
11	0	0	0	0	0	0	0	0
12	~100	~100	~100	~100	3	0	444	2.65
13	0	1	2	1	0	0	4	0.74
14	7	2	4	5	1	0	20	1.32
15	0	0	0	0	0	0	0	0
16	0	0	0	0	0	0	0	0
17	0	0	0	0	0	0	0	0
18	~150	~150	~150	~150	1	0	667	2.82

~ indicates that an accurate CFU count could not be obtained due to some merged/touching colonies.

Table S10. Lung CFU data from BALB/c mice assessed for relapse after 8 weeks of treatment. Mice were sacrificed 6 months after stopping treatment. Undiluted lung homogenates (2.25 mL homogenate over 4 agar plates) and cognate 10^{-2} and 10^{-4} dilutions (1 agar plate each, 0.5 mL per plate) were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by BD. The lower limit of detection was 0.32 $\log_{10}$ CFU/lung per sample.

Regimen	BALB/c mouse	CFU counts for the following dilutions: (shaded cells used to approximate CFU/lung)						CFU/lung (approximate)	Log_{10} CFU/lung (approximate)
		Undiluted				10^{-2} dilution	10^{-4} dilution		
		Plate 1	Plate 2	Plate 3	Plate 4				
PHZE (NOTE)	1	0	0	0	0	0	0	0	0
	2	~500	~500	~500	~500	1	0	2,222	3.35
	3	0	0	0	0	0	0	0	0
	4	~500	~500	~500	~500	2	0	2,222	3.35
	5	0	0	0	0	0	0	0	0
	6	0	0	0	0	0	0	0	0
	7	0	0	0	0	0	0	0	0
	8	83	65	89	101	0	0	376	2.58
	9	0	0	0	0	0	0	0	0
	10	+	+	+	+	13	0	6,500	3.81
	11	0	0	0	0	0	0	0	0
	12	0	0	0	0	0	0	0	0
	13	0	0	0	0	0	0	0	0
	14	0	0	0	0	0	0	0	0
	15	0	0	0	0	0	0	0	0
	16	0	0	0	0	0	0	0	0.00
	17	~200	~200	~200	~200	2	0	889	2.95
	18	0	0	0	0	0	0	0	0
	19	+	+	+	+	36	1	18,000	4.26
	20	0	0	0	0	0	0	0	0
PHZEC	1-6	0	0	0	0	0	0	0	0
	7	0	0	0	0	0/Contam.	0	0	0
	8-18	0	0	0	0	0	0	0	0

+ indicates individual colonies too numerous to accurately count. ~ indicates that an accurate CFU count could not be obtained due to some merged/ touching colonies. Contam. indicates fungal or bacterial contamination was observed on the agar. In this case, the contamination was in the form of a few discreet colonies that did not preclude reading the sample. **NOTE:** According to the original experiment design (Table 1 in the main text), this group should have included 18 mice; however, an additional two mice were accidentally included in the group of mice withdrawn from treatment at Week 8.

Table S11. Lung CFU data from BALB/c mice assessed for relapse after 10 weeks of treatment. Mice were sacrificed 6 months after stopping treatment. Undiluted lung homogenates (2.25 mL homogenate over 4 agar plates) and cognate 10^{-2} and 10^{-4} dilutions (1 agar plate each, 0.5 mL per plate) were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by BD. The lower limit of detection was 0.32 $\log_{10}$ CFU/lung per sample.

Regimen	BALB/c mouse	CFU counts for the following dilutions: (shaded cells used to approximate CFU/lung)						CFU/lung (approximate)	Log_{10} CFU/lung (approximate)
		Undiluted				10^{-2} dilution	10^{-4} dilution		
		Plate 1	Plate 2	Plate 3	Plate 4				
RHZEC	1	+	+	+	+	24	0	12,000	4.08
	2	0	0	0	0	0	0	0	0
	3	108	97	79	97	0	0	423	2.63
	4	+	+	+	+	14	0	7,000	3.85
	5	+	+	+	+	8	0	4,000	3.60
	6	0	0	0	0	0	0	0	0
	7	~300	~300	~300	~300	1	0	1,333	3.13
	8	+	+	+	+	22	0	11,000	4.04
	9	0	0	0	0	0	0	0	0
	10	0	0	0	0	0	0	0	0
	11	+	+	+	+	12	0	6,000	3.78
	12	+	+	+	+	22	0	11,000	4.04
	13	+/++	+/++	+/++	+/++	43	0	21,500	4.33
	14	0	0	0	0	0	0	0	0.00
	15	0/Contam.	0	0	0	0	0	0	0.00
	16	0	0	0	0	0	0	0	0.00
	17	5	8	6	2	0	0	23	1.39
	18	0	0	0	0	0	0	0	0.00
PHZE	1-12	0	0	0	0	0	0	0	0
	13	~300	~300	~300	~300	1	0	1,333	3.13
	14-18	0	0	0	0	0	0	0	0
PHZEC	1-5	0	0	0	0	0	0	0	0
	6	36	23	32	36	0	0	141	2.15
	7	0	0	0	1	0	0	1	0.32
	8-18	0	0	0	0	0	0	0	0

++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count. ~ indicates that an accurate CFU count could not be obtained due to some merged/touching colonies. Contam. indicates fungal or bacterial contamination was observed on the agar. In this case, the contamination was in the form of a few discreet colonies that did not preclude reading the sample.

Table S12. Lung CFU data from BALB/c mice assessed for relapse after 12 weeks of treatment. Mice were sacrificed 6 months after stopping treatment. Undiluted lung homogenates (2.25 mL homogenate over 4 agar plates) and cognate 10^{-2} and 10^{-4} dilutions (1 agar plate each, 0.5 mL per plate) were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by BD. The lower limit of detection was 0.32 $\log_{10}$ CFU/lung per sample.

Regimen	BALB/c mouse	CFU counts for the following dilutions: (shaded cells used to approximate CFU/lung)						CFU/lung (approximate)	Log_{10} CFU/lung (approximate)
		Undiluted				10^{-2} dilution	10^{-4} dilution		
		Plate 1	Plate 2	Plate 3	Plate 4				
RHZE	1*	~500	~500	~500	~500	---	---	2,500	3.40
	2	+	+	+	+	18	1	9,000	3.95
	3	+	+	+	+	42	0	21,000	4.32
	4	+	+	+	+	18	0	9,000	3.95
	5	+	+	+	+	13	0	6,500	3.81
	6	+	+	+	+	12	0	6,000	3.78
	7	0	0	0	0	0	0	0	0
	8	+	+	+	+	15	0	7,500	3.88
	9	++	++	++	++	~300	1	150,000	5.18
	10	++/+++	++/+++	++/+++	++/+++	~500	4	200,000	5.30
	11	+	+	+	+	28	0	14,000	4.15
	12	+	+	+	+	30	0	15,000	4.18
	13	+	+	+	+	16	0	8,000	3.90
	14	+/++	+/++	+/++	+/++	48	0	24,000	4.38
	15	+	+	+	+	16	0	8,000	3.90
	16	++	++	++	++	135	0	67,500	4.83
	17	~500	~500	~500	~500	5	0	2,500	3.40
	18	+	+	+	+	32	0	16,000	4.20
	19	+/++	+/++	+/++	+/++	52	2	26,000	4.41
	20	++	++	++	++	~200	4	200,000	5.30
RHZEC	1-20	0	0	0	0	0	0	0	0
PHZE (NOTE)	1-18	0	0	0	0	0	0	0	0
PHZEC	1-20	0	0	0	0	0	0	0	0

+++ indicates uniform confluent growth. ++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count. ~ indicates that an accurate CFU count could not be obtained due to some merged/touching colonies. --- indicates not determined. *One month after stopping treatment, this mouse was euthanized due to illness. **NOTE:** According to the original experiment design (Table 1 in the main text), this group should have included 20 mice; however, an additional two mice were accidentally included in the group of mice withdrawn from treatment at Week 8. Therefore, only 18 mice were remaining in this relapse group.

Table S13. C3HeB/FeJ lung CFU count data used to calculate CFU/lung 3 weeks after infection (Week -3) and on the day of treatment initiation (Day 0). Lung homogenates and cognate 10-fold dilutions (0.5 mL volume) were cultured on selective 7H11 agar ("plain" agar) and selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by BD. The lower limit of detection was 0.78 $\log_{10}$ CFU/lung per agar type.

Time point	Aerosol infection run	C3HeB/FeJ mouse	Agar type	CFU counts for the following 10-fold dilutions: (shaded cell used to calculate CFU/lung)								CFU/lung	$\log_{10}$ CFU/lung
				0	1	2	3	4	5	6	7		
Week -3	Run 1	1	Plain	+++	+++	++/+++	~300	58	5	---	---	2,900,000	6.46
			Charcoal	+++	+++	++/+++	~300	49	2	---	---	2,450,000	6.39
		2	Plain	+++	+++	++/+++	~400	22	4	---	---	1,100,000	6.04
			Charcoal	++/+++	+++	++/+++	~400	31	0	---	---	1,550,000	6.19
		3	Plain	++/+++	++	+	~150	8	0	---	---	400,000	5.60
			Charcoal	+++	++	+	~150	15	1	---	---	750,000	5.88
	Run 2	4	Plain	+++	++/+++	++	~700	77	7	---	---	3,850,000	6.59
			Charcoal	+++	++/+++	++	~700	53	8	---	---	2,650,000	6.42
		5	Plain	+++	++/+++	+/++	~400	41	6	---	---	2,050,000	6.31
			Charcoal	+++	++/+++	+/++	~400	36	2	---	---	1,800,000	6.26
		6	Plain	+++	++/+++	+/++	~600	70	10	---	---	3,500,000	6.54
			Charcoal	+++	++/+++	+/++	~600	79	11	---	---	3,950,000	6.60
	Run 3	7	Plain	+++	+++	+/++	~800	92	7	---	---	4,600,000	6.66
			Charcoal	+++	+++	+/++	~800	97	3	---	---	4,850,000	6.69
		8	Plain	+++	++/+++	+/++	~800	100	1	---	---	5,000,000	6.70
			Charcoal	+++	++/+++	+/++	~800	96	6	---	---	4,800,000	6.68
		9	Plain	+++	++/+++	+/++	~500	33	5	---	---	1,650,000	6.22
			Charcoal	+++	++/+++	+/++	~500	37	2	---	---	1,850,000	6.27
	Run 4	10	Plain	+++	++/+++	++	~500	61	4	---	---	3,050,000	6.48
			Charcoal	+++	++/+++	+/++	~500	64	12	---	---	3,200,000	6.51
		11	Plain	+++	++/+++	+/++	~300	20	1	---	---	1,000,000	6.00
			Charcoal	+++	++/+++	+/++	~300	25	3	---	---	1,250,000	6.10
		12	Plain	+++	+++	++	~350	55	11	---	---	2,750,000	6.44
			Charcoal	+++	+++	+/++	~350	45	4	---	---	2,250,000	6.35
Day 0	Run 1	1	Plain	+++	+++	++/+++	++	+	~250	43	2	215,000,000	8.33
			Charcoal	+++	+++	++/+++	++	+	~300	38	2	190,000,000	8.28
		2	Plain	+++	++/+++	++	+	~180	17	2	0	8,500,000	6.93
			Charcoal	+++	++/+++	++	+	---	17	1	0	8,500,000	6.93
		3	Plain	+++	+++	++/+++	+/++	~200	39	9	0	19,500,000	7.29
			Charcoal	+++	+++	++/+++	+/++	---	42	6	0	21,000,000	7.32
	Run 2	4	Plain	+++	+++	++/+++	+/++	~250	44	5	0	22,000,000	7.34
			Charcoal	+++	+++	++/+++	+/++	~250	57	3	0	28,500,000	7.45
		5	Plain	+++	+++	++/+++	+	~150	19	3	0	9,500,000	6.98
			Charcoal	+++	+++	++/+++	+	~145	10	0	0	5,000,000	6.70
		6	Plain	+++	+++	+++	++	+/++	+	34	9	170,000,000	8.23
			Charcoal	+++	+++	+++	++	+/++	+	65	6	325,000,000	8.51
	Run 3	7	Plain	+++	+++	+++	++/+++	+/++	+	128	12	600,000,000	8.78
			Charcoal	+++	+++	+++	++/+++	+/++	+	67	7	335,000,000	8.53
		8	Plain	+++	+++	++/+++	+/++	~200	24	3	0	12,000,000	7.08
			Charcoal	+++	+++	++/+++	+/++	~200	13	3	0	6,500,000	6.81
		9	Plain	+++	+++	+++	++	+	210	15	2	75,000,000	7.88
			Charcoal	+++	+++	+++	++	+	~250	17	1	85,000,000	7.93
	Run 4	10	Plain	+++	+++	++	+	119	2	0	0	1,000,000	6.00
			Charcoal	+++	+++	++	+	~125	9	0	0	4,500,000	6.65
		11	Plain	+++	+++	++/+++	+/++	~200	16	2	0	8,000,000	6.90
			Charcoal	+++	+++	++/+++	+/++	---	17	0	0	8,500,000	6.93
		12	Plain	+++	+++	++	+	99	8	0	0	4,000,000	6.60
			Charcoal	+++	+++	++	+	85	10	0	0	4,250,000	6.63

+++ indicates uniform confluent growth. ++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count.
~ indicates that an accurate CFU count could not be obtained due to some merged/touching colonies. --- indicates not determined.

Table S14. C3HeB/FeJ lung CFU count data used to calculate CFU/lung of mice that died after Week -3 but before Day 0 and of the untreated negative control mice. Lung homogenates and cognate 10-fold dilutions (0.5 mL volume) were cultured on selective 7H11 agar. 7H11 agar powder was manufactured by BD (pretreatment samples) or Remel Microbiology Products (untreated control samples). The lower limit of detection was 5.70 $\log_{10}$ CFU/lung.

Pretreatment or untreated control	C3HeB/FeJ mouse	Assigned group*	Death date (days post-infection)	CFU counts for the following 10-fold dilutions: (shaded cell used to calculate CFU/lung)				CFU/lung	Log_{10} CFU/lung
				5	6	7	8		
Pretreatment deaths	1	Pre-assignment	29	Lungs not recovered				---	---
	2	Pre-assignment	30	Lungs not recovered				---	---
	3	Pre-assignment	38	+	~250	23	3	1,150,000,000	9.06
	4	Untreated (Run 4)	38	+	~300	38	1	1,900,000,000	9.28
	5	Pre-assignment	42	+	~300	26	4	1,300,000,000	9.11
	6	Pre-assignment	42	+	~150	20	4	1,000,000,000	9.00
	7	Pre-assignment	42	+	~500	78	7	3,900,000,000	9.59
	8	Pre-assignment	42	+	~300	31	3	1,550,000,000	9.19
	9	Pre-assignment	42	+	~150	11	2	550,000,000	8.74
	10	Pre-assignment	42	+	~200	24	2	1,200,000,000	9.08
	11	Pre-assignment	42	+	~400	60	7	3,000,000,000	9.48
	12	Pre-assignment	42	+	~200	19	0	950,000,000	8.98
	13	Pre-assignment	43	+	~250	33	2	1,650,000,000	9.22
	14	Pre-assignment	43	+	~200	30	2	1,500,000,000	9.18
	15	Pre-assignment	43	+	~250	27	2	1,350,000,000	9.13
	16	Untreated (Run 3)	44	+	~150	21	2	1,050,000,000	9.02
	17	Pre-assignment	45	+	~300	41	0	2,050,000,000	9.31
	18	Pre-assignment	45	+	~200	25	1	1,250,000,000	9.10
	19	PHZEC Week 12 Relapse	47	+	~250	24	0	1,200,000,000	9.08
	20	PHZEC Week 6 Relapse	47	+	~200	14	2	700,000,000	8.85
	21	PHZE Week 10 Relapse	47	+	~250	17	1	850,000,000	8.93
	22	RHZEC Week 12 Relapse	47	+	~300	50	5	2,500,000,000	9.40
Untreated negative controls**	1	Run 3	96	+/++	108	20	0	1,000,000,000	9.00
	2	Run 2	110	+	~120	15	0	750,000,000	8.88
	3	Run 4	121	+	~200	28	0	1,400,000,000	9.15
	4	Run 1	134	+	~150	15	3	750,000,000	8.88
	5	Run 2	134	+	~150	18	1	900,000,000	8.95
	6	Run 3	134	+	~150	16	1	800,000,000	8.90
	7	Run 1	141	+	62	8	0	310,000,000	8.49
	8	Run 2	169	+/++	~300	39	4	1,950,000,000	9.29
	9	Run 4	172	~500	68	6	0	340,000,000	8.53
	10	Run 1	183	~80	11	1	0	55,000,000	7.74

++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count. ~ indicates that an accurate CFU count could not be obtained due to some merged/touching colonies. --- indicates not determined. *After infection, mice from each aerosol infection run were kept separately to determine lung CFU counts at Week -6, Week -3, Day 0; and to keep for virulence/mortality controls. All other mice were randomized and were assigned to treatment regimen groups 2 days before starting treatment. "Pre-assignment" indicates that mice died/were euthanized prior to treatment group assignment. For the 4 mice that died after assignment, the regimens and time points of their assignment are given. **One mouse each from aerosol infection run 3 and run 4 died/was euthanized before Day 0 and are included as pretreatment deaths in this table.

Table S15. C3HeB/FeJ lung CFU count data used to calculate CFU/lung after 4 weeks of treatment. Lung homogenates and cognate 10-fold dilutions (0.5 mL volume) were cultured on selective 7H11 agar ("plain" agar) and selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by Remel Microbiology Products. The lower limit of detection was 0.78 $\log_{10}$ CFU/lung per agar type.

Regimen	C3HeB/FeJ mouse (body mass)	Agar type	CFU counts for the following 10-fold dilutions (shaded cell used to calculate CFU/lung):					CFU/lung	$\log_{10}$ CFU/lung
			0	1	2	3	4		
RHZE	1 (25.6 g)	Plain	Sample lost (homogenizer broke)					---	---
		Charcoal						---	---
	2 (29.7 g)	Plain	140	46	1	1	0	2,300	3.36
		Charcoal	+	65	9	0	0	3,250	3.51
	3 (26.3 g)	Plain	+	98	6	1	0	4,900	3.69
		Charcoal	+	124	14	0	0	7,000	3.85
	4 (29.8 g)	Plain	+	~150	21	3	0	10,500	4.02
		Charcoal	+	~150	29	5	0	14,500	4.16
	5 (32.5 g)	Plain	+	102	5	0	0	2,500	3.40
		Charcoal	+	79	9	0	0	3,950	3.60
RHZEC	1 (26.2 g)	Plain	0	0	0	0	0	0	0
		Charcoal	12	1	1	0	0	60	1.79
	2 (22.1 g)	Plain	3	0	0	0	0	15	1.20
		Charcoal	10	0	0	1	0	50	1.71
	3 (27.9 g)	Plain	79	29	3	0	0	1,450	3.16
		Charcoal	+	28	4	1	0	1,400	3.15
	4 (26.5 g)	Plain	++	++	+	~155	12	600,000	5.78
		Charcoal	+++	++/+++	+	~121	15	750,000	5.88
	5 (29.0 g)	Plain	3	0	0	0	0	15	1.20
		Charcoal	13	0	0	0	0	65	1.82
PHZE	1 (25.8 g)	Plain	0	1	0	0	0	50	1.71
		Charcoal	36	6	2	0	0	180	2.26
	2 (25.6 g)	Plain	0	0	0	0	0	0	0
		Charcoal	8	3	1	0	0	40	1.61
	3 (33.0 g)	Plain	55	41	7	0	0	2,050	3.31
		Charcoal	+	53	10	0	0	2,650	3.42
	4 (30.2 g)	Plain	~400	~300	73	8	0	36,500	4.56
		Charcoal	+/++	+	55	7	2	27,500	4.44
	5 (21.4 g)	Plain	+++	++	+/++	+	114	5,700,000	6.76
		Charcoal	+++	++	+/++	+	75	3,750,000	6.57
PHZEC	1 (23.8 g)	Plain	0	1	0	0	0	50	1.71
		Charcoal	11	5	0	0	0	55	1.75
	2 (25.4 g)	Plain	7	4	2	0	0	200	2.30
		Charcoal	133	17	1	0	0	850	2.93
	3 (22.6 g)	Plain	2	12	4	1	0	600	2.78
		Charcoal	+	83	6	1	0	4,150	3.62
	4 (26.8 g)	Plain	0	0	0	0	0	0	0
		Charcoal	12	2	0	0	0	60	1.79
	5 (28.1 g)	Plain	0	1	0	0	0	50	1.71
		Charcoal	9	1	1	0	0	45	1.66

+++ indicates uniform confluent growth. ++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count. ~ indicates that an accurate CFU count could not be obtained due to some merged/touching colonies. --- indicates not determined.

Table S16. C3HeB/FeJ lung CFU count data used to calculate CFU/lung after 6 weeks of treatment. Lung homogenates and cognate 10-fold dilutions (0.5 mL volume) were cultured on selective 7H11 agar ("plain" agar) and selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by Remel Microbiology Products. The lower limit of detection was 0.78 $\log_{10}$ CFU/lung per agar type.

Regimen	C3HeB/FeJ mouse (body mass)	Agar type	CFU counts for the following 10-fold dilutions (shaded cell used to calculate CFU/lung):				CFU/lung	Log_{10} CFU/lung
			0	1	2	3		
RHZE	1 (24.01 g)	Plain	++/+++	++	+	121	605,000	5.78
		Charcoal	++/+++	++	+	129	645,000	5.81
	2 (37.65 g)	Plain	~200	57	6	1	2,850	3.45
		Charcoal	+	69	5	1	3,450	3.54
	3 (33.10 g)	Plain	+	~200	24	6	12,000	4.08
		Charcoal	+/++	~300	28	5	14,000	4.15
	4 (29.61 g)	Plain	13	10	1	0	500	2.70
		Charcoal	100	7	3	0	350	2.55
	5 (28.51 g)	Plain	+/++	+	112	10	50,000	4.70
		Charcoal	++	+	112	10	50,000	4.70
RHZEC	1 (26.95 g)	Plain	0	0	0	0	0	0
		Charcoal	0	1	0	0	50	1.71
	2 (30.17 g)	Plain	85	14	0	0	700	2.85
		Charcoal	~200	28	3	0	1,400	3.15
	3 (32.26 g)	Plain	71	15	1	0	750	2.88
		Charcoal	~300	25	3	0	1,250	3.10
	4 (31.18 g)	Plain	0	0	0	0	0	0
		Charcoal	0	1	0	0	50	1.71
	5 (28.37 g)	Plain	3	1	0	0	50	1.71
		Charcoal	10	1	0	0	50	1.71
PHZE	1 (27.43 g)	Plain	0	0	0	0	0	0
		Charcoal	2	0	0	0	10	1.04
	2 (36.11 g)	Plain	0	0	0	0	0	0
		Charcoal	0	1	0	0	50	1.71
	3 (31.23 g)	Plain	0	0	0	0	0	0
		Charcoal	8	1	1	0	40	1.61
	4 (28.64 g)	Plain	0	0	0	0	0	0
		Charcoal	0	0	0	0	0	0
	5 (26.83 g)	Plain	0	0	0	0	0	0
		Charcoal	18	1	0	0	90	1.96
PHZEC	1 (33.18 g)	Plain	0	0	0	0	0	0
		Charcoal	0	0	0	0	0	0
	2 (29.29 g)	Plain	0	0	0	0	0	0
		Charcoal	2	0	0	0	10	1.04
	3 (27.64 g)	Plain	0	0	0	0	0	0
		Charcoal	2	0	0	0	10	1.04
	4 (27.84 g)	Plain	0	0	0	0	0	0
		Charcoal	4	0	0	0	20	1.32
	5 (33.54 g)	Plain	0	0	0	0	0	0
		Charcoal	1	0	0	0	5	0.78

+++ indicates uniform confluent growth. ++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count.
~ indicates that an accurate CFU count could not be obtained due to some merged/touching colonies.

Table S17. C3HeB/FeJ lung CFU count data used to calculate CFU/lung after 8 weeks of treatment. Undiluted lung homogenates were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal (five agar plates per sample, 0.5 mL homogenate per plate). All 7H11 agar powder was manufactured by Remel Microbiology Products. The lower limit of detection was 0.30 $\log_{10}$ CFU/lung per sample.

Regimen	C3HeB/FeJ mouse	Body mass (g)	Agar type	CFU counts from undiluted lung homogenate (total on five plates used to calcluate CFU/lung):					CFU/lung	$\log_{10}$ CFU/lung
				Plate 1	Plate 2	Plate 3	Plate 4	Plate 5		
RHZE	1	29.7	Charcoal	1	3	0	3	5	12	1.11
	2	34.3	Charcoal	6	4	3	7	4	24	1.40
	3	26.2	Charcoal	1	3	2	2	0	8	0.95
	4	35.1	Charcoal	8	6	7	6	10	37	1.58
	5	34.5	Charcoal	325	325	325	325	325	1,625	3.21
RHZEC	1	33.4	Charcoal	0	0	0	0	0	0	0
	2	30.9	Charcoal	1	0	0	0	0	1	0.30
	3	29.9	Charcoal	0	1	0	0	0	1	0.30
	4	27.2	Charcoal	0	0	0	0	1	1	0.30
	5	32.1	Charcoal	0	0	0	1	0	1	0.30
PHZE	1	31.3	Charcoal	0	0	1	0	0	1	0.30
	2	28.6	Charcoal	0	0	0	0	0	0	0
	3	38.5	Charcoal	46	43	42	32	4	167	2.23
	4	28.0	Charcoal	0	0	1	0	0	1	0.30
	5	32.7	Charcoal	0	0	0	0	0	0	0
PHZEC	1	25.8	Charcoal	0	0	0	0	0	0	0
	2	37.1	Charcoal	0	0	0	0	0	0	0
	3	27.7	Charcoal	0	0	0	0	0	0	0
	4	33.1	Charcoal	0	0	0	0	0	0	0
	5	28.8	Charcoal	0	0	0	0	0	0	0

Table S18. C3HeB/FeJ lung CFU count data used to calculate CFU/lung after 10 weeks of treatment. Undiluted lung homogenates were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal (five agar plates per sample, 0.5 mL homogenate per plate). All 7H11 agar powder was manufactured by Remel Microbiology Products. The lower limit of detection was 0.30 $\log_{10}$ CFU/lung per sample.

Regimen	C3HeB/FeJ mouse	Body mass (g)	Agar type	CFU counts from undiluted lung homogenate (total on five plates used to calcluate CFU/lung):					CFU/lung	Log_{10} CFU/lung
				Plate 1	Plate 2	Plate 3	Plate 4	Plate 5		
RHZE	1	34.8	Charcoal	2	0	2	2	4	10	1.04
	2	33.5	Charcoal	3	1	4	1	0	9	1.00
	3	31.7	Charcoal	18	7	11	12	9	57	1.76
	4	34.8	Charcoal	0	1	1	1	1	4	0.70
	5	36.7	Charcoal	2	0	0	0	0	2	0.48
RHZEC	1	39.7	Charcoal	1	1	0	0	0	2	0.48
	2	28.9	Charcoal	26	22	32	20	4	104	2.02
	3	28.4	Charcoal	0	0	0	0	0	0	0
	4	31.7	Charcoal	43	34	29	32	7	145	2.16
	5	31.6	Charcoal	0	0	0	0	0	0	0
PHZE	1	36.2	Charcoal	0	0	0	0	0	0	0
	2	24.7	Charcoal	0	0	0	0	0	0	0
	3	31.1	Charcoal	0	0	0	0	0	0	0
	4	34.4	Charcoal	0	0	0	0	0	0	0
	5	35.5	Charcoal	0	0	0	0	0	0	0
PHZEC	1	38.8	Charcoal	0	0	0	0	0	0	0
	2	30.9	Charcoal	0	0	0	0	0	0	0
	3	37.8	Charcoal	0	0	0	0	0	0	0
	4	35.6	Charcoal	0	0	0	0	0	0	0
	5	34.0	Charcoal	0	0	0	0	0	0	0

Table S19. C3HeB/FeJ lung CFU count data used to calculate CFU/lung after 12 weeks of treatment. Undiluted lung homogenates were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal (five agar plates per sample, 0.5 mL homogenate per plate). All 7H11 agar powder was manufactured by Remel Microbiology Products. The lower limit of detection was 0.30 $\log_{10}$ CFU/lung per sample.

Regimen	C3HeB/FeJ mouse	Body mass (g)	Agar type	CFU counts from undiluted lung homogenate (total on five plates used to calcluate CFU/lung):					CFU/lung	Log_{10} CFU/lung
				Plate 1	Plate 2	Plate 3	Plate 4	Plate 5		
RHZE	1	34.75	Charcoal	0	1	0	0	0	1	0.30
	2	36.35	Charcoal	0	0	0	0	0	0	0
	3	38.04	Charcoal	0	0	0	0	0	0	0
	4	36.38	Charcoal	13	16	15	10	6	60	1.79
	5	35.95	Charcoal	0	0	0	0	0	0	0
RHZEC	1	34.78	Charcoal	0	0	0	0	0	0	0
	2	40.57	Charcoal	0	0	0	0	0	0	0
	3	32.26	Charcoal	0	0	0	0	0	0	0
	4	30.49	Charcoal	0	0	0	0	0	0	0
	5	36.15	Charcoal	0	0	0	0	0	0	0
PHZE	1	33.29	Charcoal	0	0	0	0	0	0	0
	2	33.71	Charcoal	0	0	0	0	0	0	0
	3	35.79	Charcoal	0	0	0	0	0	0	0
	4	27.92	Charcoal	0	0	0	0	0	0	0
	5	33.34	Charcoal	0	0	0	0	0	0	0
PHZEC	1	31.70	Charcoal	0	0	0	0	0	0	0
	2	27.94	Charcoal	0	0	0	0	0	0	0
	3	40.81	Charcoal	0	0	0	0	0	0	0
	4	27.54	Charcoal	0	0	0	0	0	0	0
	5	33.59	Charcoal	0	0	0	0	0	0	0

Table S20. Lung CFU data from C3HeB/FeJ mice assessed for relapse after 6 weeks of treatment. Mice were sacrificed 6 months after stopping treatment. Unless otherwise stated, undiluted lung homogenates (2.25 mL homogenate over 4 agar plates) and cognate 10^{-2} and 10^{-4} dilutions (1 agar plate each, 0.5 mL per plate) were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by BD. The lower limit of detection was 0.32 $\log_{10}$ CFU/lung per sample, except for mouse 1 (see NOTE 1).

C3HeB/FeJ mouse	Body mass (g)	CFU counts for the following dilutions: (shaded cells used to approximate CFU/lung)						CFU/lung (approximate)	$\log_{10}$ CFU/lung (approximate)
		Undiluted				10^{-2} dilution	10^{-4} dilution		
		Plate 1	Plate 2	Plate 3	Plate 4				
1 (NOTE 1)	---	---	---	---	---	---	---	800,000,000	8.90
2 (NOTE 2)	---	+/Contam.	+/Contam.	+/Contam.	+/Contam.	Contam.	Contam.	6,667	3.82
3	48.2	0	0	0	0	0	0	0	0
4	49.1	0	0	0	0	0	0	0	0
5	43.8	0	0	0	0	0	0	0	0
6	41.7	0	0	0	0	0	0	0	0
7	45.1	0	0	0	0	0	0	0	0
8	48.3	+	+	+	+	32	0	16,000	4.20
9	37.7	0	0	0	0	0	0	0	0
10	50.5	0	0	0	0	0	0	0	0
11	50.4	0	0	0	0	0	0	0	0
12	25.5	+++	+++	+++	+++	+/++	+	75,000,000	7.88
13	35.3	1	0	0	0	0	0	1	0.32
14	46.7	0	0	0	0	0	0	0	0
15	46.8	0	0	0	0	0	0	0	0
16	42.5	0	0	0	0	0	0	0	0
17	38.1	0	0	0	0	0	0	0	0
18	---	Mouse died on Day 0, before treatment was administered (NOTE 3)						---	---

+++ indicates uniform confluent growth. ++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count, approximated at 1,500 CFU. --- indicates not determined. Contam. indicates fungal or bacterial contamination was observed on the agar. For the undiluted homogenate samples, the contamination did not preclude reading the sample. **NOTE 1:** Mouse 1 died 32 days prior to the relapse time point. Because a high bacterial burden was expected, the 10^{-5} to 10^{-8} dilutions of lung homogenate were plated, with the following CFU counts: 10^{-5} dilution, "+" CFU; 10^{-6} dilution, ~150 CFU; 10^{-7} dilution, 16 CFU (used to calculate CFU/lung); 10^{-8} dilution, 1 CFU (lower limit of detection was 5.70 $\log_{10}$ CFU/lung). **NOTE 2:** Mouse 2 died 3 days prior to the relapse time point. **NOTE 3:** This mouse is included in the "Pretreatment deaths" CFU table (**Table S14**) as C3HeB/FeJ mouse 20.

Table S21. Lung CFU data from C3HeB/FeJ mice assessed for relapse after 8 weeks of treatment. Mice were sacrificed 6 months after stopping treatment. Unless otherwise stated, undiluted lung homogenates (2.25 mL homogenate over 4 agar plates) and cognate 10^{-2} and 10^{-4} dilutions (1 agar plate each, 0.5 mL per plate) were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by BD. The lower limit of detection was 0.32 $\log_{10}$ CFU/lung per sample, except for PHZE mouse 1 (see NOTE).

Regimen	C3HeB/FeJ mouse	Body mass (g)	CFU counts for the following dilutions: (shaded cells used to approximate CFU/lung)						CFU/lung (approximate)	Log_{10} CFU/lung (approximate)
			Undiluted				10^{-2} dilution	10^{-4} dilution		
			Plate 1	Plate 2	Plate 3	Plate 4				
PHZE	1 (NOTE)	---	---	---	---	---	---	---	1,650,000,000	9.22
	2	---	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0	0
	3	---	Contam.	Contam.	Contam.	Contam.	+	0	7,500,000	6.88
	4	32.38	+++	+++	+++	+++	++/+++	+	75,000,000	7.88
	5	51.50	+	+	+	+	28	0	14,000	4.15
	6	48.33	+	+	+	+	1	0	500	2.70
	7	43.42	2	0	1	3	0	0	7	0.88
	8	53.64	+/Contam.	+/Contam.	+/Contam.	+/Contam.	6	0	3,000	3.48
	9	45.70	1	0	0	0	0	0	1	0.32
	10	46.02	0	0	0	0	0	0	0	0
	11	51.64	+	+	+	+	32	0	16,000	4.20
	12-16	45.69-53.34	0	0	0	0	0	0	0	0
	17	43.86	+/++	+/++	+/++	+/++	78	0	39,000	4.59
	18	41.95	0	0	0	0	0	0	0	0
PHZEC	1	50.69	9	8	9	4	0	0	33	1.54
	2-18	36.25-50.46	0	0	0	0	0	0	0	0

+++ indicates uniform confluent growth. ++ indicates non-uniform confluent growth. + indicates individual colonies too numerous to accurately count, approximated at 1,500 CFU. --- indicates not determined. Contam. indicates fungal or bacterial contamination was observed on the agar. Except for the PHZE Mouse 3 undiluted lung homogenate samples, the contamination did not preclude reading the samples. **NOTE:** PHZE mouse 1 died 32 days prior to the relapse time point. Because a high bacterial burden was expected, the 10^{-5} to 10^{-8} dilutions of lung homogenate were plated, with the following CFU counts: 10^{-5} dilution, "+/++" CFU; 10^{-6} dilution, "+" CFU; 10^{-7} dilution, 33 CFU (used to calculate CFU/lung); 10^{-8} dilution, 2 CFU (lower limit of detection was 5.70 $\log_{10}$ CFU/lung).

Table S22. Lung CFU data from C3HeB/FeJ mice assessed for relapse after 10 weeks of treatment. Mice were sacrificed 6 months after stopping treatment. Unless otherwise indicated, undiluted lung homogenates (2.25 mL homogenate over 4 agar plates) and cognate 10^{-2} and 10^{-4} dilutions (1 agar plate each, 0.5 mL per plate) were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by BD. The lower limit of detection was 0.32 $\log_{10}$ CFU/lung per sample, except for RHZEC mouse 2 (see NOTE 2).

Regimen	C3HeB/FeJ mouse	Body mass (g)	CFU counts for the following dilutions: (shaded cells used to approximate CFU/lung)						CFU/lung (approximate)	$\log_{10}$ CFU/lung (approximate)
			Undiluted				10^{-2} dilution	10^{-4} dilution		
			Plate 1	Plate 2	Plate 3	Plate 4				
RHZEC	1 (NOTE 1)	16.8	.+++	+++	+++	+++	---	---	665,000	5.82
	2 (NOTE 2)	33.40	+++	Contam.	Contam.	Contam.	+++	++/+++	4,125,000,000	9.62
	3	43.95	+/++	+/++	+/++	+/++	0	0	36,667	4.56
	4	47.05	+/++	+/++	+/++	+/++	0	0	36,667	4.56
	5	48.85	1	1	1	1	0	0	4	0.74
	6	43.95	+++	+++	+++	+++	++/+++	133	665,000	5.82
	7	49.26	0	1	0	0	0	0	1	0.32
	8-17	36.77-50.54	0	0	0	0	0	0	0	0
	18	48.03	0	0	0	1	0	0	1	0.32
PHZE	1	---	Mouse died on Day 0, before treatment was administered (NOTE 3)						---	---
	2-18	29.84-54.22	0	0	0	0	0	0	0	0
PHZEC	1 (NOTE 4)	---	0	0	0	0	0	0	0	0
	2-13	41.18-51.72	0	0	0	0	0	0	0	0
	14	43.73	+++	+++	+++	+++	+++	+/++	250,000,000	8.40
	15-18	34.79-49.52	0	0	0	0	0	0	0	0

+++ indicates uniform confluent growth, approximated at 150,000 CFU. ++ indicates non-uniform confluent growth, approximated at 15,000 CFU. + indicates individual colonies too numerous to accurately count, approximated at 1,500 CFU. --- indicates not determined. Contam. indicates fungal or bacterial contamination was observed on the agar which precluded reading the sample. **NOTE 1:** RHZEC Mouse 1 died 31 days prior to the relapse time point. Only undiluted lung homogenate was plated. CFU/lung was approximated using data from RHZEC Mouse 6. **NOTE 2:** Due to contamination that required discarding plates before reading, the lower limit of detection of this sample was 0.78 $\log_{10}$ CFU/mL. **NOTE 3:** This mouse is included in the "Pretreatment deaths" CFU table (**Table S14**) as C3HeB/FeJ mouse 21. **NOTE 4:** PHZEC mouse 1 died 2 days prior to the relapse time point.

Table S23. Lung CFU data from C3HeB/FeJ mice assessed for relapse after 12 weeks of treatment. Mice were sacrificed 6 months after stopping treatment. Undiluted lung homogenates (2.25 mL homogenate over 4 agar plates) and cognate 10^{-2} and 10^{-4} dilutions (1 agar plate each, 0.5 mL per plate) were cultured on selective 7H11 agar supplemented with 0.4% activated charcoal. All 7H11 agar powder was manufactured by BD. The lower limit of detection was 0.32 $\log_{10}$ CFU/lung per sample.

Regimen	C3HeB/FeJ mouse	Body mass (g)	CFU counts for the following dilutions: (shaded cells used to approximate CFU/lung)						CFU/lung (approximate)	Log_{10} CFU/lung (approximate)
			Undiluted				10^{-2} dilution	10^{-4} dilution		
			Plate 1	Plate 2	Plate 3	Plate 4				
RHZE	1-3	47.69-53.34	0	0	0	0	0	0	0	0
	4	53.53	++	++	++	++	+	72	3,600,000	6.56
	5	41.43	0	0	1	2	0	0	3	0.64
	6	48.39	0	0	0	0	0	0	0	0
	7	49.68	0	0	1	0	0	0	1	0.32
	8	44.47	++/+++	++/+++	++/+++	++/+++	0	0	4,125,000	6.62
	9	52.17	+++	+++	+++	+++	++/+++	+	75,000,000	7.88
	10	54.03	~150	~150	~150	~150	1	0	667	2.82
	11	41.62	+	+	+	+	29	0	14,500	4.16
	12	50.42	0	0	0	0	0	0	0	0
	13	50.04	+++	+++	+++	+++	++/+++	~500	25,000,000	7.40
	14	49.13	++/+++	++/+++	++/+++	++/+++	+	30	1,500,000	6.18
	15	43.29	+/++	+/++	+/++	+/++	124	1	62,000	4.79
	16	52.08	+/++	+/++	+/++	+/++	70	0	35,000	4.54
	17-19	36-23-50.11	0	0	0	0	0	0	0	0
	20	---	Mouse died 29 days before relapse time point; lungs were not recovered.						---	---
RHZEC	1-6	45.77-51.88	0	0	0	0	0	0	0	0
	7	38.09	+	+	+	+	17	1	8,500	3.93
	8-14	39.20-50.80	0	0	0	0	0	0	0	0
	15	44.18	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0	0	0	0
	16	51.02	1	0	0	0	0	0	1	0.32
	17	45.29	0	0	0	0	0	0	0	0.00
	18 (NOTE 1)	14.97	++	++	++	++	+	8	400,000	5.60
	19	---	Mouse died 38 days into treatment due to gavage accident.						---	---
	20	---	Mouse died on Day 0, before treatment was administered (NOTE 2)						---	---
PHZE	1 (NOTE 3)	---	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0	0
	2	---	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0	0	0	0
	3	---	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0	0	0	0
	4	---	0	0	0	0	0	0	0	0
	5	---	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0/Contam.	0	0
	6-14	40.67-53.83	0	0	0	0	0	0	0	0
	15	43.33	0	0	1	0	0	0	1	0.32
	16	39.12	+++	+++	+++	+++	+/++	60	3,000,000	6.48
	17-20	42.54-52.63	0	0	0	0	0	0	0	0
PHZEC	1-18	37.50-52.74	0	0	0	0	0	0	0	0.00
	19	---	Mouse died 6 days before relapse time point (cage flood); lungs were not recovered.						---	---
	20	---	Mouse died on Day 0, before treatment was administered (NOTE 4)						---	---

+++ indicates uniform confluent growth, approximated at 150,000 CFU. ++ indicates non-uniform confluent growth, approximated at 15,000 CFU. + indicates individual colonies too numerous to accurately count, approximated at 1,500 CFU. --- indicates not determined. Contam. indicates fungal or bacterial contamination was observed on the agar. The contamination did not preclude reading the samples. NOTE 1: RHZEC Mouse 18 died 55 days after stopping treatment. **NOTE 2:** This mouse is included in the "Pretreatment deaths" CFU table (**Table S14**) as C3HeB/FeJ mouse 22. **NOTE 3**: PHZE mice 1-5 died 45 days before the relapse time point due to a cage flood. **NOTE 4:** This mouse is included in the "Pretreatment deaths" CFU table as C3HeB/FeJ mouse 19.

Table S24. Trough clofazimine and rifapentine serum concentrations for individual mice after 4, 8, and 12 weeks of treatment with clofazimine- and rifapentine-containing regimens, respectively. Serum samples were obtained at sacrifice, about 72 hours after dosing. For each time point and treatment group, the mouse number corresponds to the mouse number in the corresponding CFU count data tables.

Mouse strain	Regimen	Mouse	Serum clofazimine (μg/mL)			Serum rifapentine (μg/mL)		
			Week 4	Week 8	Week 12	Week 4	Week 8	Week 12
BALB/c	RHZEC	1	1.36	1.11	1.55	---	---	---
		2	1.56	1.95	1.92	---	---	---
		3	1.38	1.39	1.12	---	---	---
		4	1.23	1.49	1.37	---	---	---
		5	1.35	2.17	2.13	---	---	---
	PHZE	1	---	---	---	12.42	8.77	8.05
		2	---	---	---	8.15	5.84	7.83
		3	---	---	---	8.90	9.80	10.40
		4	---	---	---	6.25	9.54	10.07
		5	---	---	---	8.77	6.41	9.20
	PHZEC	1	1.93	1.68	1.81	samples lost	11.14	10.94
		2	1.25	1.34	2.00		15.07	15.65
		3	1.58	1.44	1.39		11.31	4.91
		4	0.83	0.89	1.87		7.91	16.01
		5	1.48	0.90	1.97		9.30	13.03
C3HeB/FeJ	RHZEC	1	0.98	1.73	1.98	---	---	---
		2	1.77	1.13	1.65	---	---	---
		3	0.83	1.34	1.68	---	---	---
		4	1.05	2.09	2.52	---	---	---
		5	0.98	1.49	1.21	---	---	---
	PHZE	1	---	---	---	5.46	6.46	3.02
		2	---	---	---	4.19	5.83	6.67
		3	---	---	---	2.58	3.58	6.15
		4	---	---	---	3.20	2.38	4.36
		5	---	---	---	5.80	5.82	5.22
	PHZEC	1	0.72	1.78	1.44	10.29	7.15	8.31
		2	0.88	1.06	2.06	6.19	7.68	12.86
		3	1.59	1.30	1.68	9.50	9.93	6.83
		4	1.15	0.97	2.94	9.78	4.68	10.23
		5	1.13	1.62	1.54	9.00	5.61	12.97

--- indicates not applicable.

Table S25. Relapse data of mice receiving the standard first-line regimen from six previous studies evaluating clofazimine and high-dose rifapentine in BALB/c mice. For drug regimens, the number before each regimen or regimen phase indicates the duration of administration in months, where 1 month equals 4 weeks. Drug abbreviations and doses are as follows: R, rifampin 10 mg/kg; H, isoniazid 10 mg/kg; Z, pyrazinamide 150 mg/kg; E, ethambutol 100 mg/kg.

Reference	Mean (SD) log_{10} CFU/lung on Day 0	Regimen	Proportion of mice with culture-positive relapse by treatment duration			
			12 weeks	16 weeks	20 weeks	24 weeks
Rosenthal *et al.* 2008	7.21 (0.07)	2RHZ/1RH	15/15	---	---	---
Rosenthal *et al.* 2012	7.48 (0.10)	2RHZ/1RH	15/15	---	---	---
Tyagi *et al.* 2015	9.02 (0.37)	2RHZE/4RH	---	5/15	3/15	1/10
Ammerman *et al.* 2018, Study 1	6.67 (0.34)	2RHZE/2RH	---	7/15	---	---
Ammerman *et al.* 2018, Study 2	7.11 (0.10)	2RHZE/4RH	---	---	1/15	1/14
Ammerman *et al.* 2018, Study 3	7.73 (0.18)	2RHZE/2RH	---	5/14	---	---
		4RHZE	---	6/14	---	---
TOTAL RELAPSE			**30/30 (100%)**	**23/58 (40%)**	**4/30 (13%)**	**2/24 (8%)**

--- indicates not determined.

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Table S26. Preparation of drug suspensions/solutions for oral administration to BALB/c and C3HeB/FeJ mice. Isoniazid, pyrazinamide, and ethambutol were prepared in combination in one solution for administration. R, rifampin; H, isoniazid; Z, pyrazinamide; E, ethambutol; C, clofazimine; P, rifapentine.

Mouse strain and week of treatment	Average body mass (g)	Drug concentrations (µg/mL) to administer the following doses in 0.2 mL					
		R 10 mg/kg	H 10 mg/kg	Z 150 mg/kg	E 100 mg/kg	C 12.5 mg/kg	P 20 mg/kg
BALB/c mice							
Weeks 1-12	20	1.00	1.00	15.00	10.00	1.25	2.00
C3HeB/FeJ mice							
Week 1	25	1.25	1.25	18.74	12.51	1.56	2.50
Week 2	26.3	1.32	1.32	19.73	13.15	1.63	2.63
Week 5	27.8	1.39	1.39	20.85	13.90	1.74	2.78
Week 10	32.2	1.61	1.61	24.17	16.10	2.01	3.22