

**Figure S1. Inhaled carrier deposition and macrophage uptake functions. (a)** Snapshot of the granuloma model, a hybrid multi-scale agent-based model, showing an example inhaled dose depositing on the simulation grid. Carriers are denoted as yellow squares and an estimate of the granuloma border is shown in red. (b) Unscaled probability function describing the dependence of macrophage uptake on carrier zeta potential <sup>1-3</sup>. (c) Unscaled probability function describing the dependence of macrophage uptake on carrier diameter <sup>1-3</sup>. (d) Unscaled probability function describing the dependence of macrophage uptake on carrier targeting-ligand density <sup>1-3</sup>.



Figure S2. Comparison of an inhaled RIF formulation given every two-weeks with an oral RIF formulation given daily. (a) Total CFU per granuloma for the first 14-day dosing window.
(b) Average RIF concentration in the plasma compartment for the first 14-day dosing window.
(c) Average RIF peripheral AUC for the first 14-day dosing window. (d) Average RIF granuloma AUC for the first 14-day dosing window. Red = Oral, Blue = Inhaled. Solid lines indicate average values while dotted lines represent SD. Inhaled (N = 83), Oral (N = 87).



**Figure S3. Comparison of an inhaled INH formulation given every two-weeks with an oral INH formulation given daily. (a)** Total CFU per granuloma for the first 14-day dosing window. **(b)** Average INH concentration in the plasma compartment for the first 14-day dosing window. **(c)** Average INH peripheral AUC for the first 14-day dosing window. **(d)** Average INH granuloma AUC for the first 14-day dosing window. Red = Oral, Blue = Inhaled. Solid lines indicate average values while dotted lines represent SD. Inhaled (N = 81), Oral (N = 87).

## References

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