Supplementary Table S1a. Parameter estimates including precision (RSE) for study C110 (bedaquiline drug-drug interaction with ritonavir-boosted lopinavir)[a]

Study C110			
Fixed effects[b]	**Value (RSE)**	**Random Effects**	**Value [CV%] (RSE)**
MTT [h]	1.02 (18.6%)	BOV F	13.4 (28.6%)
NN [-]	5.77 (41.8%)	BSV F	9.40 (60.0%)
KA [1/h]	0.0983 (11.2%)	BOV MTT	71.1 (20.1%)
CL/F [L/h]	3.09 (17.3%)	BSV CL	39.2 (18.3%)
V/F [L]	16.1 (22.8%)	BSV CLM2	40.5 (20.5%)
Q1/F [L/h]	5.97 (4.6%)	BSV CL~BSV CLM2[c]	77.4 (23.6%)
VP1/F [L]	4890 (17%)	BSV EFF1, scaled BSV EFF2	34.6 (17.2%)
Q2/F [L/h]	3.52 (9.3%)	BSV V	47.5 (18.9%)
VP2/F [L]	174 (27.2%)	BSV Q1	14.0 (30.7%)
CLM2/F/fm [L/h]	14.6 (16.6%)	BSV VM2	52.0 (20.6%)
VM2/F/fm [L]	746 (25.1%)	BSV VP1M2	38.5 (40.5%)
Q1M2/F/fm [L/h]	75.5 (17.7%)		
VP1M2/F/fm [L]	3140 (19.5%)	Prop error TMC	17.1 (6.9%)
EFF1 LPV/r BDQ CL	0.347 (9.3%)	Prop error M2	14.5 (6.7%)
EFF2 LPV/r M2 CL	0.578 (8.7%)	Error correlation[c]	54.3 (12.2%)
Error wt TAD < 6 h	1.89 (7%)		
Scale ETA EFF M2 CL	0.335 (84.5%)		

[a] Abbreviations: MTT, mean transit time; NN, number of transit compartments; KA, absorption rate constant; F, bioavailability; CL, clearance, V, volume of distribution; Q, intercompartmental clearance; VP, volume of distribution of peripheral compartments; fm, fraction BDQ metabolized to M2; EFF, interaction effect; TAD, time after dose; BOV, between-occasion variability; BSV, between-subject variability; Prop, proportional; RSE, relative standard error; CV%, percent coefficient of variation.

[b] Disposition parameters for a typical individual of 70 kg, allometric scaling with body weight and fixed coefficients 0.75 for CL and 1 for V applied

[c] Correlation between errors for BDQ and M2

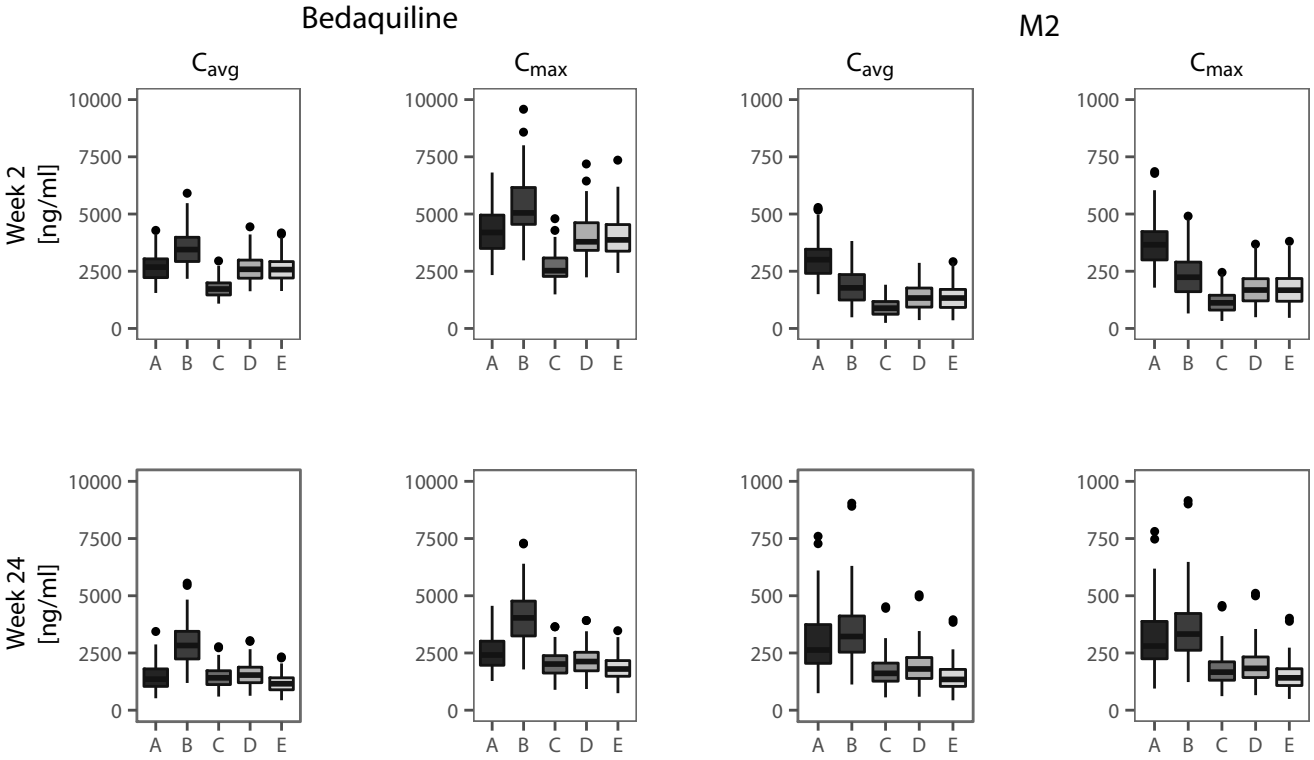
Supplementary Table S1b. Parameter estimates including precision (RSE) for study C117 (bedaquiline drug-drug interaction with nevirapine) [a]

Study C117			
Fixed effects[b]	**Value (RSE)**	**Random Effects**	**Value [CV%] (RSE)**
MTT [h]	3.37 (7.7%)	BOV F	22.6 (35.1%)
NN	4.48 (9.3%)	BSV F	20.5 (37.5%)
KA [h^{-1}]	0.131 (9.8%)	BOV MTT	32.9 (13.1%)
CL/F [L/h]	3.34 (9.5%)	BSV CL	20.4 (18.0%)
V/F [L]	11.2 (42.0%)	BSV CLM2	22.6 (19.2%)
Q1/F [L/h]	7.03 (8.3%)	BSV CL~BSV CLM2[c]	24.2 (56.7%)
VP1/F [L]	4000 (11.4%)	BSV V	98.0 (35.8%)
Q2/F [L/h]	5.26 (19.2%)	BSV Q1	17.7 (20.9%)
VP2/F [L]	164 (8.2%)	BSV VM2	9.43 (152%)
CLM2/F/fm [L/h]	16.0 (9.9%)	BSV VP1M2	9.90 (75.8%)
VM2/F/fm [L]	824 (10.5%)		
Q1M2/F/fm [L/h]	131 (11.4%)	Prop error TMC	22.7 (8.4%)
VP1M2/F/fm [L]	3090 (8.3%)	Prop error M2	16.2 (9.0%)
EFF NVP on BDQ CL	0.915 (5.9%)	Error correlation[c]	54.2 (10.9%)
EFF NVP on M2 CL	1.05 (10.3%)		
Error wt TAD < 6 h	2.42 (9.3%)		

[a] Abbreviations: MTT, mean transit time; NN, number of transit compartments; KA, absorption rate constant; F, bioavailability; CL, clearance, V, volume of distribution; Q, intercompartmental clearance; VP, volume of distribution of peripheral compartments; fm, fraction BDQ metabolized to M2; EFF, interaction effect; TAD, time after dose; BOV, between-occasion variability; BSV, between-subject variability; Prop, proportional; RSE, relative standard error; CV%, percent coefficient of variation.

[b] Disposition parameters for a typical individual of 70 kg, allometric scaling with body weight and fixed coefficients 0.75 for CL and 1 for V applied

[c] Correlation between errors for BDQ and M2



Supplementary Figure S2. Simulation results presented as average concentrations (Cavg) and maximum concentrations (Cmax) of bedaquiline and its M2 metabolite during weeks 2 and 24 of treatment with bedaquiline administered alone or together with ritonavir-boosted lopinavir (400/100 mg dosed twice daily) for the full 6 months of TB treatment (Scenario 1).

A = 2 weeks 400mg daily, then 22 weeks 200mg thrice-weekly (no LPV/r)
B = 2 weeks 400mg daily, then 22 weeks 200mg thrice-weekly (with LPV/r)
C = 2 weeks 200mg daily, then 22 weeks 100mg thrice-weekly (with LPV/r)
D = 2 weeks 300mg daily, then 22 weeks 100mg thrice-weekly (with LPV/r)
E = 2 weeks 300mg daily, then 22 weeks 100mg twice-weekly (with LPV/r)