Supplementary data

Table 1. Baseline characteristics and treatment details of the study patients (N=48)

Characteristic	Value
Baseline demographics and phenotype	
Age, *years*, median (range)	10 (4–17)
Sex, female, n (%)	28 (58)
Body weight*, *kg*, median (range)	38 (24–75)
Age 4-10 years	28 (24–55)
Age 11-17 years	52 (32–75)
Body mass index†, kg/m^2, median [IQR]	18 [15.5; 21.5]
Smoker : Non-smoker, n (%)	3 (6) : 45 (94)
Disease phenotype at baseline	
FEV_1 predicted, % (range)	
Age 4-10 years	85 (51-103)
Age 11-17 years	71 (47-96)
Rescue therapy	
TDM samples, n	205
Dose, mg per day	150
Sample time after dose, h (range)	1-28

Abbreviations: IQR, interquartile range; FEV1, Forced Expiratory Volume in 1 second. *Body weight was missing for two patients. †Body mass index was missing for three patients.

Table 2. Population pharmacokinetics model parameter estimates

	Final model estimates (%RSE) [%shrinkage]	Bootstrap median [95% CI]
Typical values		
CL/F (L/h)	7.95 (11)	8.05 [7.22; 11.01]
V/F (L)	190 (48)	200 [111; 389]
Ka (h^{-1})	0.17 (44)	0.15 [0.04; 0.32]
Covariate effects		
Baseline body weight on CL	0.75 (fixed)	0.75 (fixed)
Baseline body weight on V	1 (fixed)	1 (fixed)
Baseline body weight on Ka	-0.25 (fixed)	-0.25 (fixed)
Interindividual variability		
on CL (%CV)	39 (19) [25]	35 [26; 47]
Residual variability		
Proportional error (%CV)	32 (22)	34 [22; 48]
Additive error (mg/L)	0.18 (46)	0.19 [0.07; 0.39]

Abbreviations: CI, confidence interval; CL/F, apparent clearance; V/F, apparent volume of distribution; Ka, absorption rate constant; CV, coefficient of variation calculated as $CV=\sqrt{e^{\omega^2}-1}$ with ω^2 being the interindividual variability; RSE, relative standard error. The number of successful bootstrap runs is 1898 out of 2000 attempts.