SUPPLEMENTARY MATERIAL

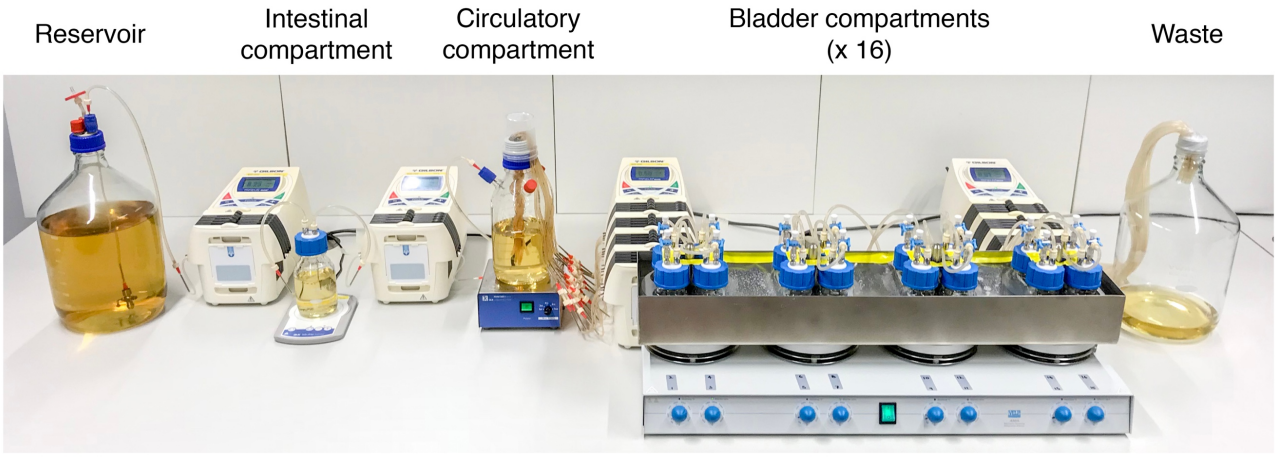

Figure S1. Bladder infection *in vitro* model design
Media pumped via autoclavable 1.01 mm PVC tubing (Gilson, UK) run through three sequentially arranged peristaltic pumps (Gilson, UK) delivering fresh media from the reservoir to the intestinal compartment, into which fosfomycin was administered, through to the circulatory compartment, and eliminated into the sixteen bladder compartments, which were run in parallel and held within a water-bath at 37°C ± 1°C. Automated and timed intermittent bladder compartment voiding was controlled by a fourth peristaltic pump.

(A) *In vivo* equations

Drug in G.I. tract:

$$X_{GI} = X_{dose} \cdot e^{-k_1 \cdot t}$$

Drug in blood:

$$X_{blood} = \frac{k_1 \cdot X_{dose}}{k_2 - k_1} \cdot \left(e^{-k_1 \cdot t} - e^{-k_2 \cdot t} \right)$$

Excreted drug:

$$X_{bladder} = X_{dose} - X_{GI} - X_{blood}$$

(B) *In vitro* equations

Drug in first compartment:

$$X_A = X_{A^\circ} \cdot e^{-(F/V_A) \cdot t}$$

Drug in second compartment:

$$X_B = \frac{\left(F/V_A \right) \cdot X_{A^\circ}}{F/V_B - F/V_A} \cdot \left(e^{-(F/V_A) \cdot t} - e^{-(F/V_B) \cdot t} \right)$$

Cumulative drug in third compartment:

$$X_C = X_{A^\circ} - X_A - X_B$$

Figure S2. Drug distribution equations informing target urinary fosfomycin concentrations
The dynamic amount of drug (X mg) in each respective compartment at time t (h) as a function of the first-order rate constants (absorption k_1; elimination k_2). The initial dose of fosfomycin (mg) is indicated by X_{dose} or X_{A°. In the *in vitro* equations the fluid volumes (V mL) in the respective compartments and flow rate of fluid (F mL/h) are the variables.