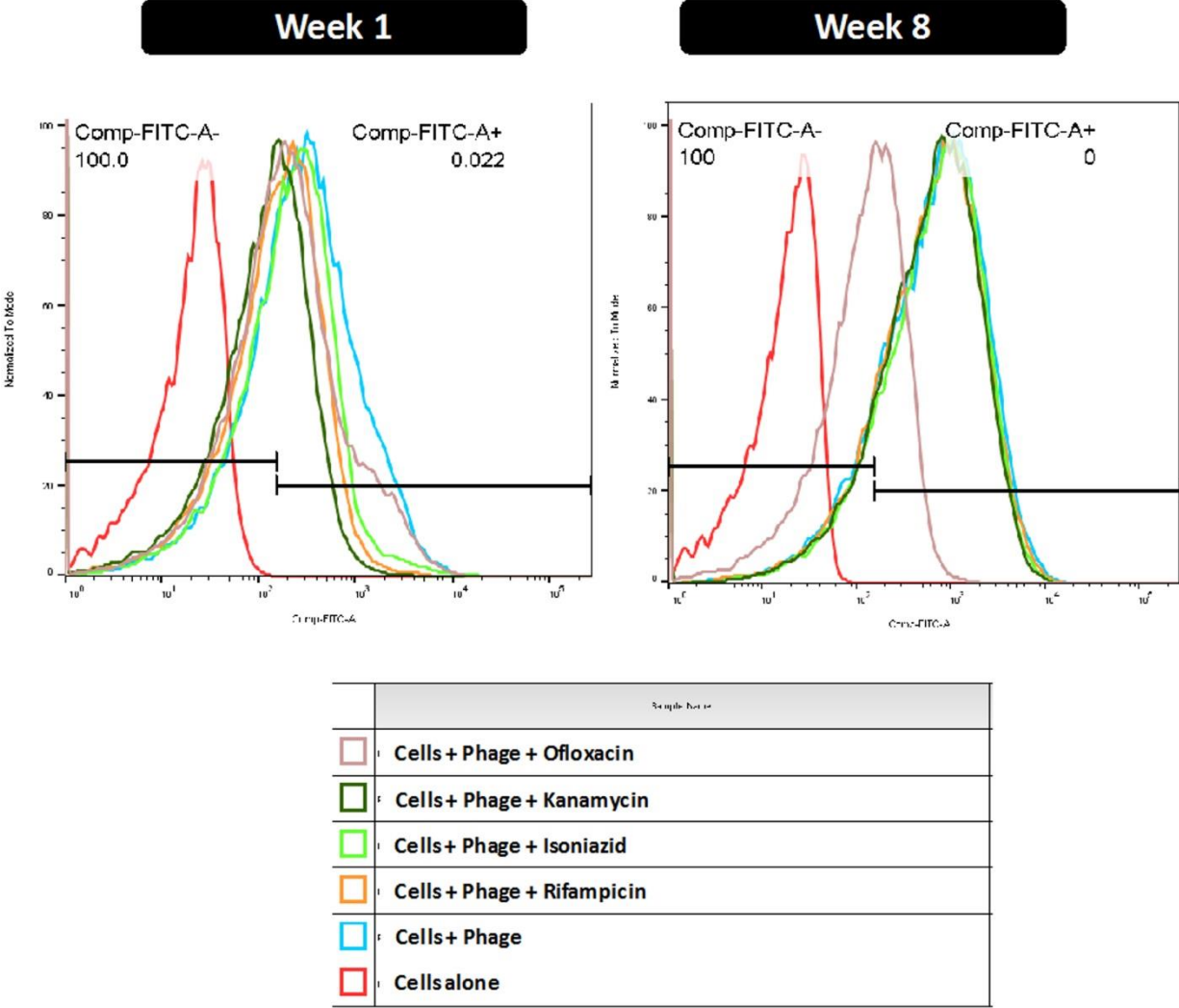


Figure S1. Phage infection demonstrates emergent drug resistance to Ofloxacin, Kanamycin, Isoniazid, and Rifampin during treatment



Supplement Figure 1. Flow cytometry (FACS) analysis of MTB isolates from clinical sputum samples from a patient (PID151) with initial drug-susceptible tuberculosis who developed emergent extensively drug-resistant tuberculosis (XDR-TB) during treatment. Isolates from week 1 and week 8 after TB treatment initiation are shown. MTB isolates were incubated with Φ^2 GFP10 and the indicated antibiotics simultaneously for 12 h and examined by flow cytometry. FACS plots show number of events (y axis) plotted against green fluorescence protein (Log GFP) (x axis). Failure to fluoresce in the presence of antibiotic indicates sensitivity, and a fluorescence signal in the presence of a specific antibiotic indicates resistance to that antibiotic.

In this figure we detected lower levels of fluorescence in the presence of Ofloxacin, Isoniazid, Rifampicin, and Kanamycin (mean percentage of fluorescent event per antibiotic condition=28.5% SD 5.3) concordant with whole genome sequencing data showing mixed infection with an XDR-TB strain at this early treatment time point. After week 8 of treatment MTB isolate showed higher levels of fluorescence in the presence of these drugs (mean percentage of fluorescent event per antibiotic condition=61.7% SD 24.3) consistent with positive selection for the XDR MTB during treatment.