Novel thiopeptides to target intractable bacterial infections

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There are clear unmet medical needs for more effective treatments for intractable bacterial diseases, such as *Clostridioides difficile* and nontuberculous mycobacteria (NTM), such as *Mycobacterium avium* (MAC) complex.

AJ-024 has shown promising activities against various *C. difficile* strains, and has promising traits to target *C. difficile* ribotype 027. It compares favorably to vancomycin and fidaxomicin *in vivo* with no sign of recurrence. This is attributed to AJ-024's ability to exert minimal impact to gut microbiota, and to enhance the faster recovery of gut microbiota. The restoration is faster than that of fidaxomicin.

AJ-099 and AJ-206 exhibit comparable *in vitro* activity profile compared to clarithromycin against *Mycobacterium avium* complex. Their enhanced antibacterial activity in macrophage infection is noteworthy and both show synergistic effect with clarithromycin and clofazimine. They do not show cross-resistance to clarithromycin.