Bacteria continue to develop resistance to currently available antibacterial agents. These multidrug-resistant pathogens are responsible for considerable morbidity and mortality in the clinical setting. This burden is increasingly prevalent in infections caused by Gram-negative bacteria, especially non-fermenters like *Pseudomonas aeruginosa* and *Acinetobacter baumannii*, as well as, more recently, by carbapenem-resistant Enterobacteriaceae (CRE). Because of this, there is an ongoing need for the identification of new antibiotics that employ unique and effective mechanisms of action. Unfortunately, there has been a steady decline in the number of such promising agents in the clinical development pipeline. One contributor to this situation is the generally difficult prospect of finding new antibiotics. The reasons for this this will be discussed and some possible strategies/solutions advanced.