Oxidative stress arises from an imbalance between the excessive accumulation of reactive oxygen species (ROS) and a cell’s capability to readily detoxify them. Although ROS are spontaneously generated during the normal oxygen respiration and metabolism, the ROS generation is usually augmented by redox-cycling agents, membrane disrupters, and bactericidal antibiotics, which contributes their antimicrobial bioactivity. It is noted that all the bacteria deploy an arsenal of inducible antioxidant defense systems to cope with the devastating effect exerted by the oxidative stress: these systems include the antioxidant effector enzymes and the master transcription factors. The bacterial oxidative stress response is not essential for normal bacterial growth, but critical to survive the oxidative stress conditions that the bacterial pathogens may encounter due to the host immune response and/or the antibiotic treatment. Based on these, the ROS-inspired antibacterial strategies have been defined, which are to enhance the oxidative stress of ROS generation and/or to compromise the bacterial response against the oxidative stress. Topics discussed will include our recent data on quinone-based drug redirecting and metal-based drug repurposing, which are based on the well-defined ROS-generating pharmacophores.