

**Call:** 6<sup>th</sup> transnational call for the JPIAMR within the ERA-NET JPI-EC-AMR:  
Innovations against antibiotic-resistant bacteria: New targets, compounds and tools

**Title:** Exploration of the TPP riboswitch as a new target for antibiotics

**Acronym:** Explore

#### Consortium composition

Type	Name	Institute	Country
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#### Abstract

In this project, we will explore the TPP riboswitch as a new drug target for antibiotics for key ESKAPE pathogens (*E. coli*, *K. pneumoniae*, *A. baumannii*, *P. aeruginosa*, *S. aureus*) and *Streptococcus pneumoniae*. The TPP riboswitch has already been validated as a drug target, however, potent and drug-like ligands with antibiotic activity are needed as starting points to develop novel strategies for anti-infective treatments. The goal of this proposal is to deliver such compounds. Using an innovative assay technology, we will develop a high-throughput assay that monitors simultaneously transcription efficiency and the regulatory activity of the riboswitch, which is crucial for its action, and use this assay to screen the CZ- and EU-OPENSOURCE libraries of lead-like compounds. The hits obtained will be thoroughly validated and the most promising hits will be optimised to improve their affinity. The advanced compounds will be evaluated for antibiotic activity against the key ESKAPE pathogens and *Streptococcus pneumoniae*. We will also assess the broad-spectrum potential of the compounds and carry out mode of action studies to ensure that the compounds act on target. If the TPP riboswitch holds up to its high promises, this project will pave the way for urgently needed new antibiotics.