Title: The missing piece in the puzzle:
APC148 – a safe, selective and efficient metallo-β-lactamase inhibitor

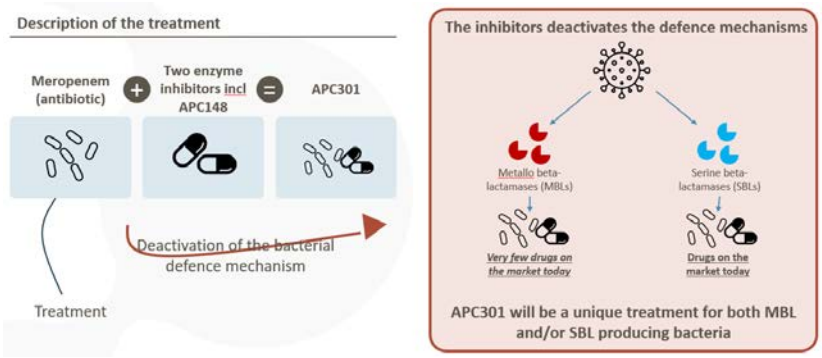
Authors: Veronika Smidt [1], Bjørn Klem [2], Bjørg Bolstad [2], Ole Andreas Økstad [1], and Pål Rongved [1,2].
Affiliations: [1] Dep. of Pharmacy, The University of Oslo, Norway. [2] Adjutec Pharma AS, Oslo, Norway.

The problem
WHO defines antimicrobial resistance (AMR) as one of the top 10 public health threats today and features of a post-antibiotic era today influence many healthcare settings. AMR is directly caused by the misuse, use and over-use of antibiotics. The β-lactamases (**BLs**) like **serine β-lactamases (SBL)** and **metallo-β-lactamases (MBL)** are bacterial enzymes destroying today's antibiotics. Drugs that inhibit the effect of SBLs (SBLi) are available, but ***there are currently no approved drug that selectively inhibit MBLs (MBLi) in a safe way.***

The solution – APC148
AdjuTec Pharma develops the selective and effective MBL inhibitor APC148 [1], which is already in clinical development [2]. Collective microbiological (MIC) studies show that APC148 in combination with available double combinations of SBLi and antibiotics is a missing piece in the puzzle. APC148 in different combinations was efficient against broad spectrum of clinical isolates harboring both MBL and SBL.

Methods
Antimicrobial susceptibility testing (AST) by broth microdilution was performed according to The European Committee on Antimicrobial Susceptibility Testing. Reading guide for broth microdilution. Version 4.0, 2022 (see: http://www.eucast.org).

Results and conclusions
A number of double combinations on the market, in development or described in literature, in general show low performance above EUCAST breakpoints for the antibiotics in the double combinations. Adding APC148 brings the MIC below EUCAST breakpoints. Further, FICI calculations show that in the triple combinations with APC138, the MIC performance shows a true synergy between the compounds in the combinations. These preliminary results show a promising outlook for the future of drug development against AMR.



1. Samuelsen, Ø., et al. "ZN148 Is a Modular Synthetic Metallo-β-Lactamase Inhibitor That Reverses Carbapenem Resistance in Gram-Negative Pathogens In Vivo." Antimicrobial Agents and Chemotherapy **64**(6): e02415-02419.
2. ClinicalTrials.gov ID NCT06360640. Abstract submitted to ECSMID 2025.