

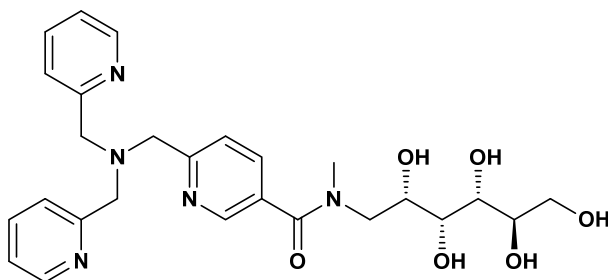
OVERCOMING METALLO- β -LACTAMASE MEDIATED RESISTANCE IN BACTERIA

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Antibacterial resistance represents one of the largest threats to public health worldwide.¹⁻⁴ The problem is getting worse due to the lack of new effective treatments being authorized over the past few years, which may lead to infections becoming more difficult to treat in the future. Probably the most important antibiotic resistance mechanisms in terms of distribution and clinical relevance are β -lactamases.⁵ β -lactamases are enzymes that hydrolyze β -lactam antibiotics compromising the efficacies of β -lactams, our largest group and mainstay of antimicrobial chemotherapy for more than 60 years.

This poster will outline a novel technology called ZinChel.⁶⁻⁸ The ZinChel technology aims to inhibit an important class of resistance enzymes found in gram-negative bacteria that render β -lactam antibiotics useless, thus restoring the effect of the β -lactam antibiotics. There are currently no clinical inhibitor against these enzymes, the metallo- β -lactamases, and there is an urgent need for new treatments. This poster will summarize the synthesis, *in vitro* and *in vivo* results from one of the best compounds, ZN148, shown below.



ZN148

[1] World Health Organization (W.H.O), "Infectious disease report: Removing obstacles to healthy development"; 1999.

[2] World Health Organization (W.H.O), "Global Strategy for Containment of Antimicrobial Resistance"; 2001.

[3] World Health Organization (W.H.O), "The evolving threat of antimicrobial resistance: Options for action"; 2012.

[4] World Health Organization (W.H.O), "Antimicrobial resistance: global report on surveillance"; 2014.

[5] Drawz et al., New β -Lactamase Inhibitors: a Therapeutic Renaissance in an MDR World. *Antimicrob Agents Chemother* **2014**, 58 (4), 1835-46.

[6] Åstrand et al., Synthesis and biological evaluation of new dipicolylamine zinc chelators as metallo- β -lactamase inhibitors, *Tetrahedron*, **2019**, 75 (11), 1525-1540.

[7] Åstrand et al., Synthesis and biological evaluation of zinc chelating compounds as metallo- β -lactamase inhibitors, *Med. Chem. Commun.*, **2019**, 10, 528-537

[8] Åstrand et al., Synthesis and Preclinical Evaluation of TPA-Based Zinc Chelators as Metallo- β -lactamase Inhibitors, *ACS Infect. Dis.* **2018**, 4, 9, 1407-1422