

## Breaking the barrier - An integrated multidisciplinary approach to kill Gram-negative bacteria through existing antibiotics by making their outer membrane permeable

**Timeline** | 1/2023 to 12/2026



**ICIQ People** | [R. Martín Research Group](#)

**Overall Budget** | 2.627.056,80 €



**Website** | <https://breakthrough-project.eu/>

**ICIQ's Budget** | 251.971,20 €

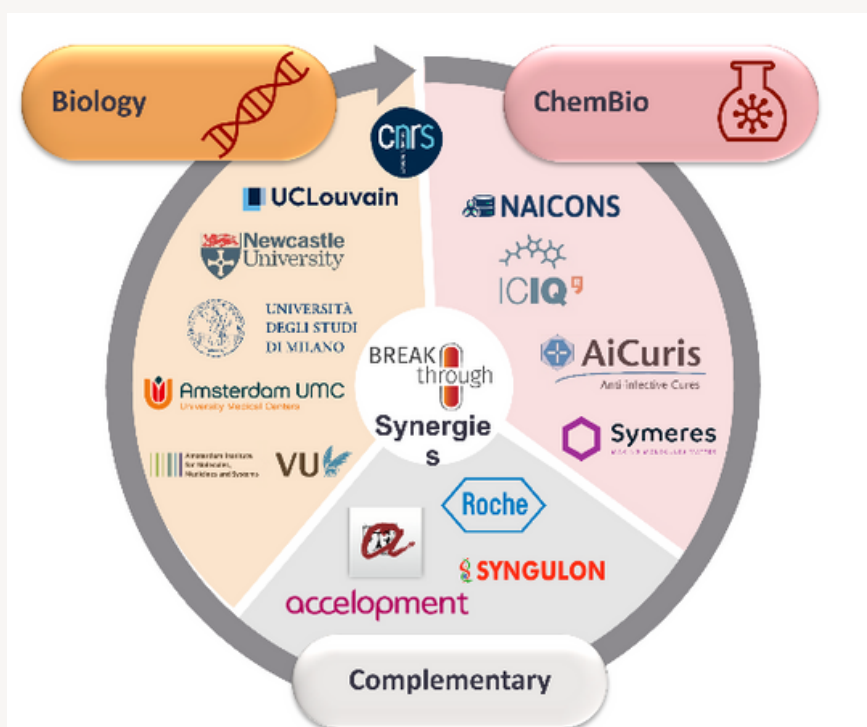


**Call** | HORIZON-MSCA-2021-DN-01

### SUMMARY

Antimicrobial resistance, which is caused by multi-drug-resistant bacterial pathogens is a global health emergency. Gram-negative bacteria (GNB) notably hinder effective treatment because of their impermeable outer membrane (OM). Consequently, many standard-of-care (SOC) antibiotics cannot access intracellular targets in GNB. The objective of the **BREAKthrough** European Training Network (ETN) is to sensitise GNB to these antibiotics by making their OM permeable. To this end, we will develop inhibitors of three protein machineries that are responsible for OM maintenance. Importantly, many known antibacterial agents have characteristics different from drugs that are directed against targets in mammalian cells. To define better rules for antibacterial drug development a data hub will be created to assemble information on the physico-chemical characteristics of molecules that can pass the OM. To achieve these goals, a multi-disciplinary academic-industrial consortium has been assembled with organic chemists, computational chemists and specialists in high-throughput drug screening, zebrafish infection models, bacterial morphogenesis and the molecular biology of the three targets. The expected outcomes of the **BREAKthrough** ETN include (i) the development of new chemical space rules for drugs that need to cross the OM, (ii) the discovery of new inhibitors that interfere with OM maintenance to overcome the insensitivity of Gram-negative pathogenic bacteria towards SOC antibiotics and (iii) providing 10 Early Stage Researchers with scientific, technical, business and transferable skills to become professional drug developers with a keen eye for the hurdles in the development of these drugs in an industrial context.

### CONSORTIA



#### UCLouvain

**Project coordinator**



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