

An integrated multidisciplinary approach to **kill Gram-negative bacteria through existing antibiotics** by making their outer membrane permeable

## Background

Antimicrobial resistance has become a serious global health emergency. The growing number of drug-resistant pathogens is making common infections increasingly difficult to treat. Due to various barriers to development, no new antibiotic classes have been discovered since 1987. The current lack of innovation creates an urgent need for alternative solutions.

Targeting multidrug-resistant Gram-negative bacteria, one of the most alarming microbes, the BREAKthrough Doctoral Network aims to develop a new compound that will modify these bacteria in a way that makes them vulnerable to existing antibiotics.

## Research

Infections by multidrug-resistant Gram-negative bacteria are particularly hard to treat because their outer membrane cannot be infiltrated by most drug-like molecules. **The overall aim of the BREAKthrough research programme is therefore to disturb the structure of the outer membrane, enabling antibiotics to pass through and kill the bacterial cell.** For this purpose, it will develop novel molecules that can damage the outer membrane. More specifically, BREAKthrough will:

- develop and optimise biological tests that report on stress and permeabilisation of the outer membrane as well as on defects in three protein machineries that are of key importance to the membrane's sustenance
- develop an in vivo screening test for compounds that make the outer membrane permeable using a zebrafish infection model
- construct a data hub of at least 500 compounds that are able to pass the outer membrane based on an analysis of their properties
- optimise the most promising compounds in iterative tests

## Duration

01/01/2023 – 31/12/2026

## Budget

2.6 million euro

## Website

[www.breakthrough-project.eu](http://www.breakthrough-project.eu)

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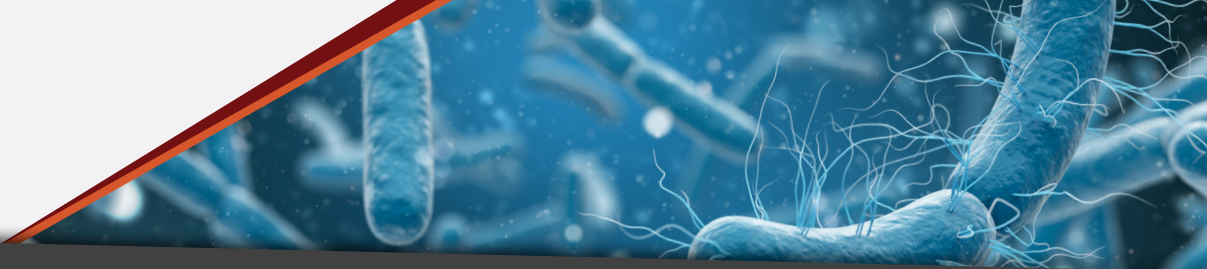
## Funding programme

Marie Skłodowska-Curie Actions,  
Horizon Europe



**Funded by  
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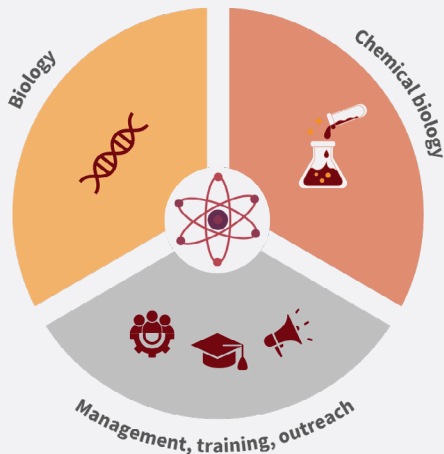
## Training

Designed to educate the next generation of scientists with expertise in antimicrobial resistance, the BREAKthrough Doctoral Network offers its 11 doctoral candidates (DCs) a varied and interdisciplinary training programme.

The programme will provide DCs with an extensive set of **scientific, business, and personal development skills**. In addition, each DC will have a minimum of two international secondments at other partners within the BREAKthrough network, improving their employability in both academic and industrial contexts.

## Consortium

The interdisciplinary BREAKthrough project integrates academic and research institutions with SMEs and industry, covering the entire chain of knowledge and innovation.



## Coordinator

Prof. Jean-François Collet  
Université catholique de Louvain, Belgium

## Participants

- Centre National de la Recherche Scientifique, France
- Università degli Studi di Milano, Italy
- Vrije Universiteit Amsterdam, Netherlands
- University of Ljubljana, Slovenia
- Amsterdam UMC, Netherlands
- Institute of Chemical Research of Catalonia, Spain
- NAICONS Srl, Italy
- ABAC Therapeutics SA, Spain

## Impact

BREAKthrough will tackle antimicrobial resistance, identified by the European Commission as one of the top three health threats that require immediate EU-level coordination.

The research outcomes will **not only open up new avenues for antibiotic development but also create new treatment options** through synergies with already existing antibiotics. Moreover, BREAKthrough will **strengthen R&I and the biopharma sector in Europe** by training a highly competent next generation of drug developers and scientists.



- accelopment Schweiz AG, Switzerland
- Symeres Netherlands B.V., Netherlands
- Roche Pharma AG, Switzerland
- Syngulon SA, Belgium
- University Rovira i Virgili, Spain
- University of Newcastle upon Tyne, UK
- University of Queensland, Australia