



Innovative Medicines Initiative

# **A PPP Approach to boost antimicrobial resistance R&D : the ND4BB IMI platform**

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# The Problem



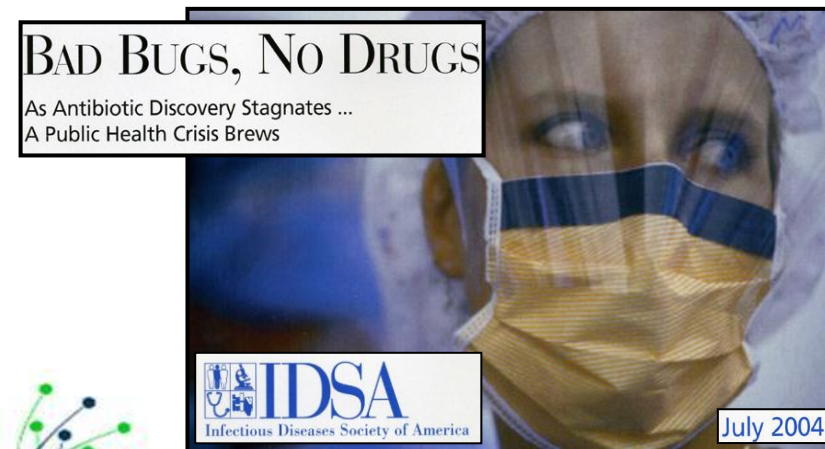
## Antibiotic-resistant infections spread through Europe

Superbug that moves faster than science

Antibiotics resistance 'as big a risk as terrorism' – UK medical chief -

Three million Europeans catch infections in hospital annually

Antibiotic resistance: we must act now, says WHO



*Le Monde*

17 Janvier 2008: La résistance des bactéries aux antibiotiques a atteint une dimension planétaire



# A solution ? : The New Drugs 4 Bad Bugs initiative

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13:56 17Nov11 RTRS-UPDATE 1-Europe kickstarts R&D fightback against superbugs

- \* Need to combat antibiotic resistance now "critical"
- \* EU to accelerate new drug approvals, ensure adequate pricing
- \* Plan to boost R&D collaboration via IMI initiative
- \* Drugmakers welcome fresh incentives for antibiotic research

# ND4BB



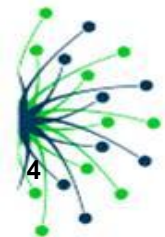
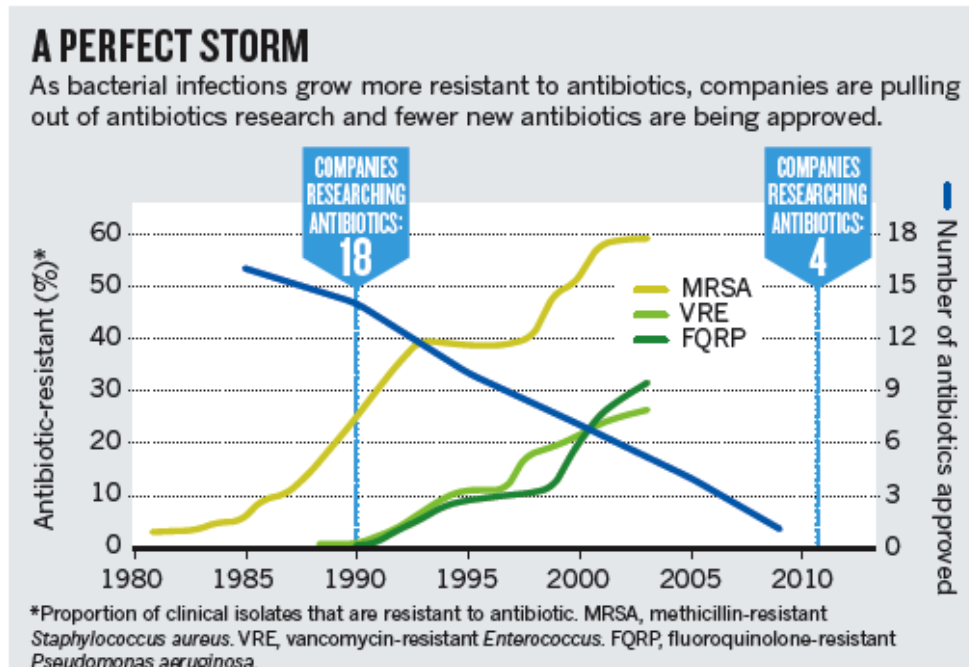
# ND4BB: Need for public-private collaboration



- The overall vision of ND4BB is to create an innovative collaborative Public-Private Partnership (PPP)-based approach that will encompass all aspects from the discovery of new antibiotics to Phase 2 and 3 clinical trials with the aim of reinvigorating antibiotic R&D

## Three key challenges in antibiotic R&D:

- Discovery:** Unique scientific bottlenecks
- Development:** Challenging regulatory environment
- Economics:** Low return on investment



# Antibacterials: The science is tricky

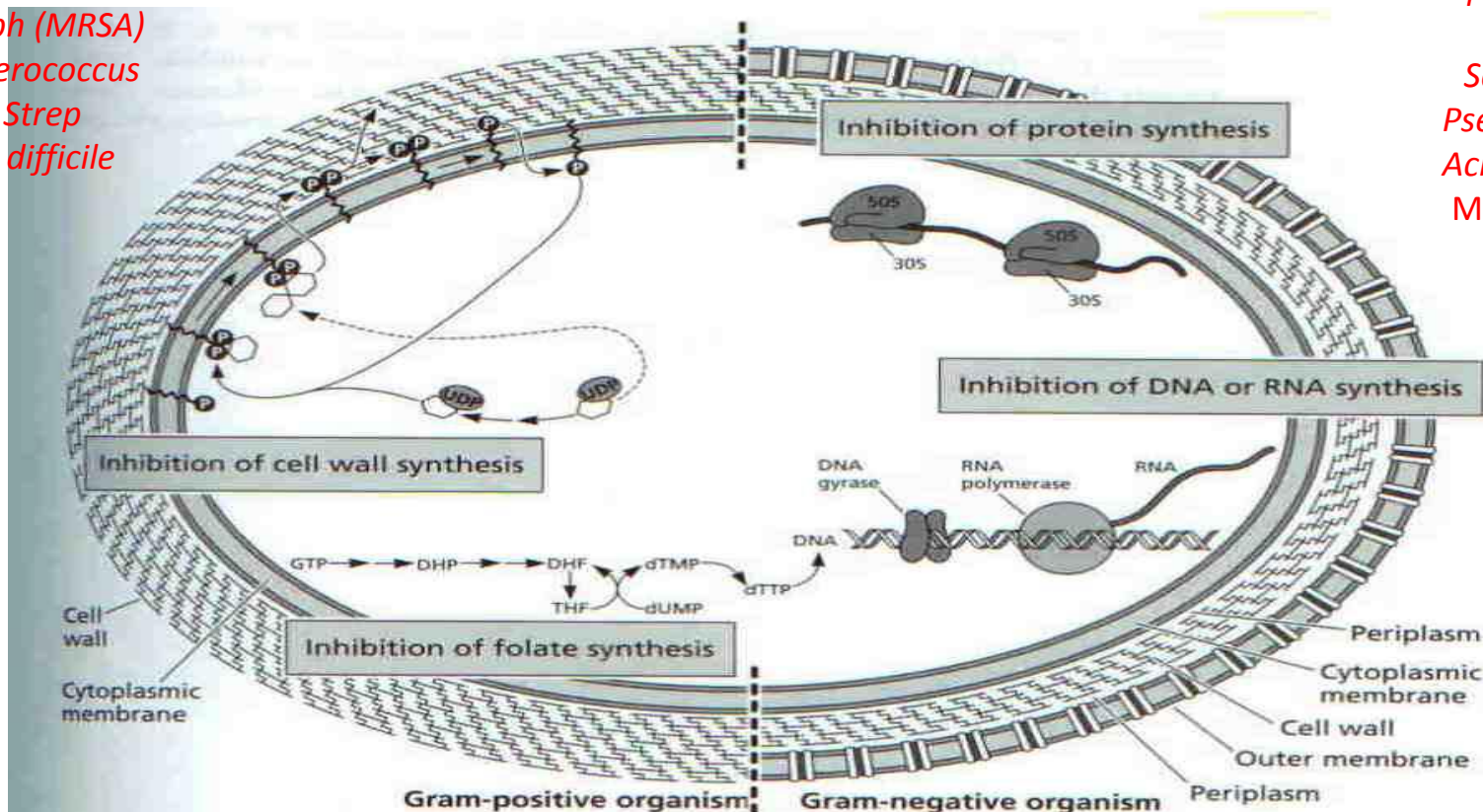
## - Validated Targets with Access Problems



- Many tractable targets exist in bacteria, but getting drugs to them is difficult

Staph (MRSA)  
 Enterococcus  
 Strep  
 C. difficile

K.pneumoniae  
 E. coli  
 Salmonella  
 Pseudomonas  
 Acinetobacter  
 Many others



**Figure 2.2** Major targets for antibacterial action. (Adapted from a poster on Mechanisms of Antibiotic Action and Resistance, C. Walsh, J. Trauger, P. Courvalin, and J. Davies [2001], *Trends in Microbiology*, *The Lancet Infectious Disease*, *Current Opinion in Microbiology*, *Trends in Molecular Medicine*.)





# Antibiotic resistance is increasing : Europe

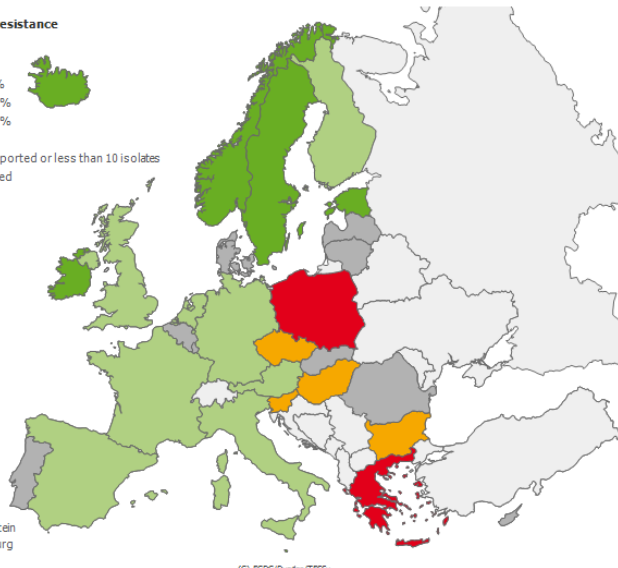
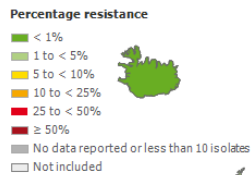
## Multi-drug resistant *Klebsiella pneumoniae*



2005



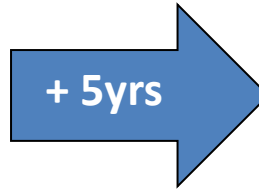
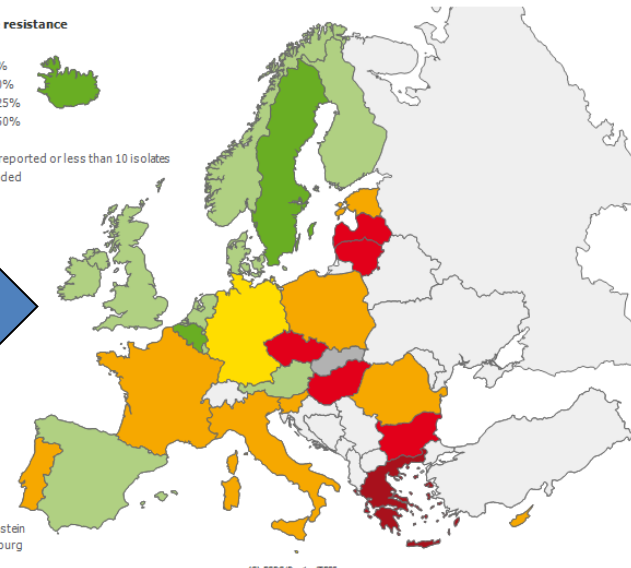
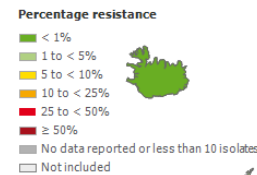
Multidrug-resistant *Klebsiella pneumoniae* Isolates in Participating Countries in 2005 (Resistant to Third-generation Cephalosporins, Fluoroquinolones and Aminoglycosides)



2010



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This report has been generated from data submitted to TESSy, The European Surveillance System on 2012-09-28. Page: 1 of 1. The report reflects the state of submissions in TESSy as of 2012-09-28 at 14:00

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- Numerous examples of rapid global spread of clones & resistances
- **Spread is unpredictable, heterogenous and can be sporadic**
- Takes 10+ years to make an AB
- Long term strategy needed for threats of today and the future



# The economic model?

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One product can take 10-15 years...

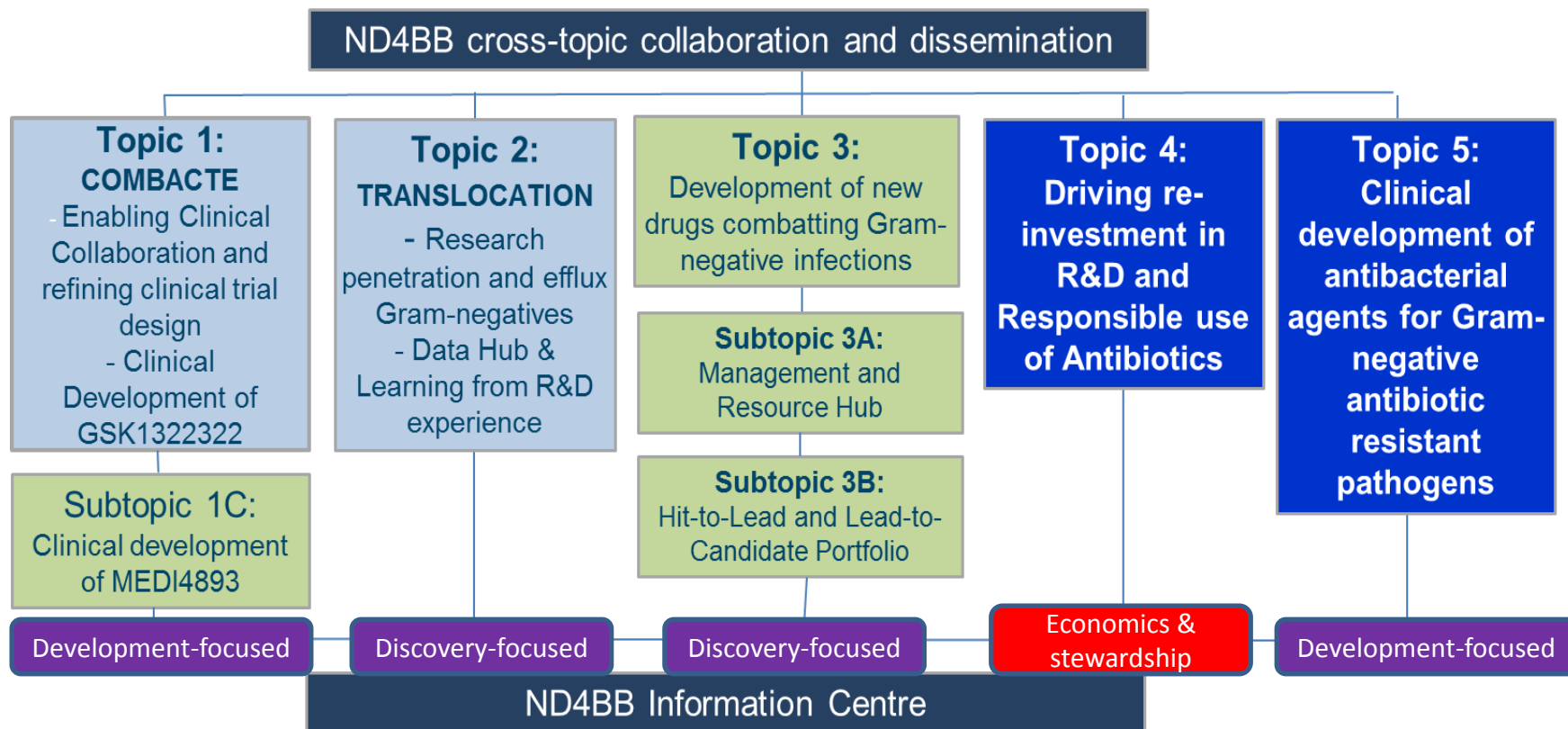
***... and an investment of \$600-\$1billion!***

And once approved, novel antibiotics are used initially as “last resort” treatment for small patient groups

How do we reward value and innovation and ensure responsible use



# ND4BB Structure



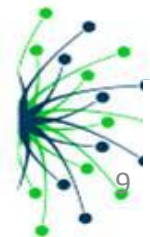
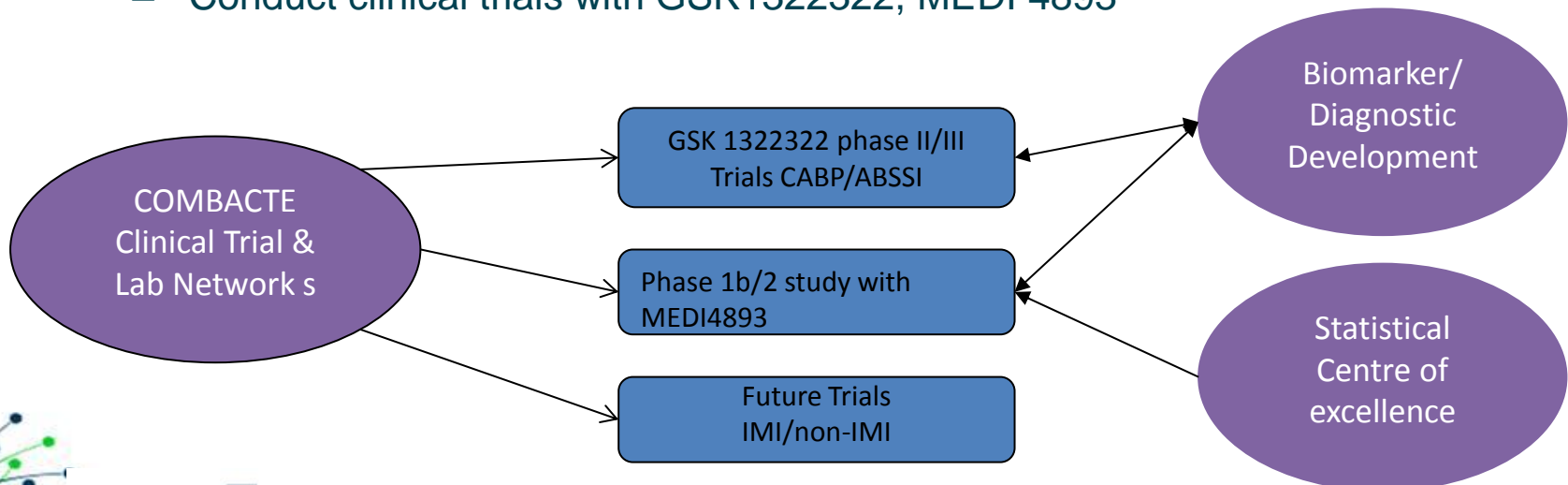
- Projects from Call 6 initiated 1/01/2013
- Topics launched under Call 8 (Dec 2012)
- Topics launched under Call 9 (July 2013)



# Topic 1 : COMBACTE



- Create a self-sustaining premier antibacterial development network
  - Expanding research and laboratory networks
  - Optimal alignment of clinical trials with investigator sites
  - Clinical and epidemiologic data also supports stewardship
- Increase efficiency of antibiotic development
  - Align clinical trials with cutting edge molecular methodologies and trial design
  - Conduct clinical trials with GSK1322322, MEDI 4893



# COMBACTE partners





# Topic 2 : Translocation

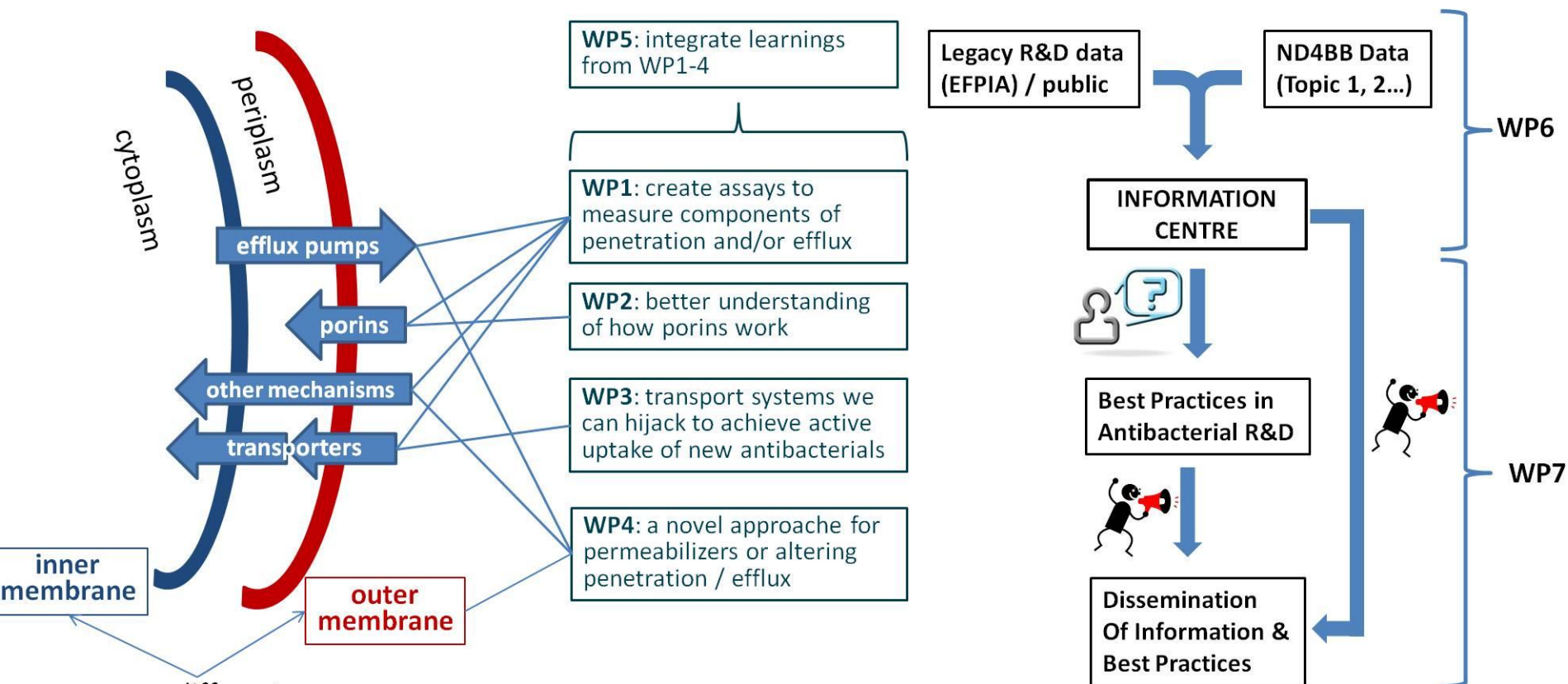


Discovery: improve understanding of penetration into Gram-negatives

Efficiency: creation of a data centre to compile and analyze AB and ND4BB information

## Discovery

## Efficiency

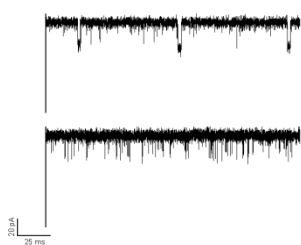




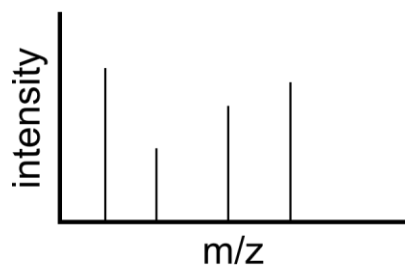
# ND4BB TRANSLOCATION: Discovery



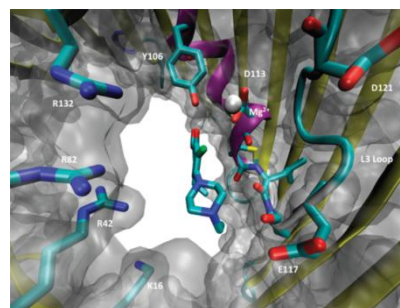
- *Challenge:* Making inhibitors of Gram negative targets is not a substantial challenge – **getting them into Gram negative bacteria is the bottleneck**
- *Goal:* Merging the best science of microbiology, structural biology and biophysics to bring **unprecedented understanding of penetration into Gram negatives, including novel assays and design concepts** increasing overall probability of success to deliver novel antibacterials across the industry



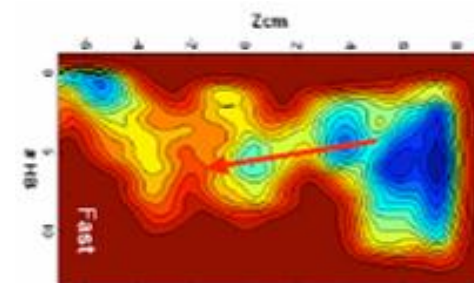
electrophysiology



mass spec



X-ray  
crystallography

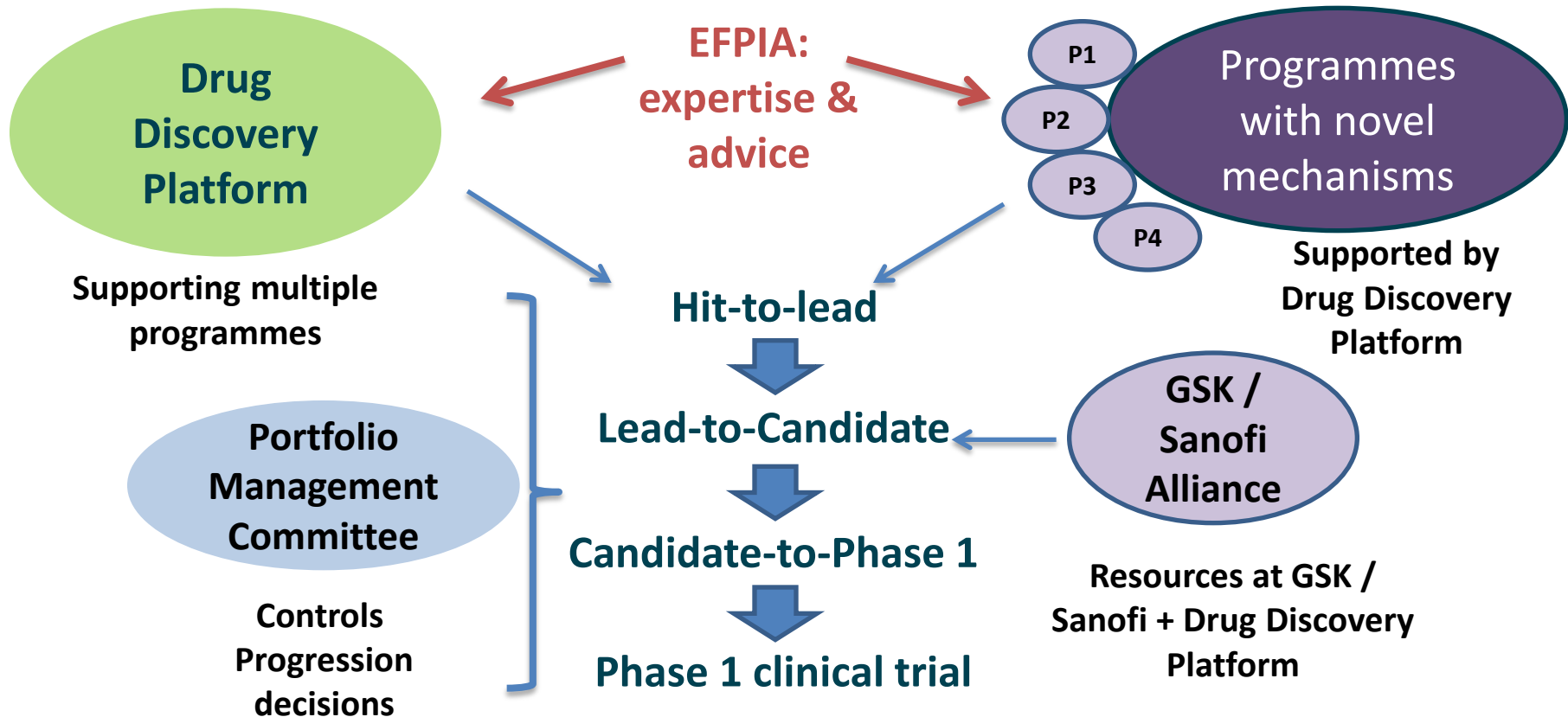


all atom kinetic  
modeling





# Structure of ND4BB Topic 3:



**Goal: create a drug discovery platform to optimize hits from public partners and GSK/Sanofi into Candidates and progress into Phase 1**



# New Topics : Deliverables - Topic 4

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## Topic 4 : Driving re-investment in R&D and Responsible use of antibiotics

Generate an analysis of the societal impact and cost of anti-infectives resistance

Create a multi-disciplinary, multi-stakeholder community with an in depth comprehension of the complexities of antibacterial R&D and the challenges of the current commercial model

Develop implementable options for new commercial models that address the needs of multiple stakeholders,

Validate options through modelling on selected case studies

Launched in IMIJU 9<sup>th</sup> Call – 09/07/2013

Deadline for expressions of interest - 09/10/2013



# New Topics : Deliverables - Topic 5



## Topic 5 : Clinical development of anti-bacterial agents for Gram-negative antibiotic resistant pathogens

Observational clinical and microbiological data sets to make recommendations for the development of novel antibiotic agents for MDR Gram-negative pathogens

Understanding of the clinical management and outcomes of patients with serious hospitalised infections to validate our understanding of the clinical outcomes for patients in areas of emerging and endemic antibiotic resistance.

Successful therapeutic clinical trials demonstrating the pharmacology, safety and efficacy of novel agents/combinations, in particular aztreonam-avibactam (ATM-AVI), directed towards treatment of infections due to priority pathogens.

Launched in IMIJU 9<sup>th</sup> Call – 09/07/2013

Deadline for expressions of interest - 09/10/2013



# ND4BB – Summary

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- Antibiotic resistance is a societal problem needing a societal response
- IMI ND4BB platform is a visible and growing European response
- Addressing the key barriers to new antibacterial agents
- Collaboration and sharing of success and failures is core to the approach.

