ND4BB Topic 3: Discovery and development of new drugs combatting Gram-negative infections

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Antibiotic drug discovery & development – major challenges

1) **Scientific challenge**: screening approaches often fail, difficult to obtain needed spectrum & safety—challenge increased for Gram-negative pathogens due to inherent penetration barriers

2) **Regulatory challenge**: large trials needed, non-inferiority designs, etc.

3) **Economic challenge**: (low Return on Investment) ABs expensive to develop, often give cure in days, new ABs will be used only when truly needed
Architecture of the overall ND4BB project

ND4BB cross topic collaboration and dissemination (Topic 1 WP1, Topic 2 WP8, Topic 3 WP1, Topic n WPn)

Topic 1 : Clinical Development
Steering Committee
Project level decision making body

Subtopic 1 A :
Work Packages : 1–4

Subtopic 1 B :
WP 5A, 5B*, 5C, 5D*, 5E–F

Subtopic 1 C :
Work Packages: 6A, 6B*, 6C*, 6D

Topic 2 : New Drugs into bad bugs
Steering Committee
Project level decision making body

Work Packages : 1–8

Topic 3 : Development of new drugs combating Gram–negative infections

Subtopic 3A
Work Packages: 1–3, 5A, 6*, 7*, 8

Subtopic 3B
Work Packages: 4**, & 5B

Topic n : ND4BB

Work Packages : 1–n

ND4BB Information Centre

Topics launched under Call 6
Topics to be launched under Call 8

* Subject to milestones approval and potentially Call for additional beneficiaries

** Potentially subject to Call for additional beneficiaries if needed to provide additional Hit-to-Lead efforts

Future Topics to be launched

Subject to milestones approval and potentially Call for additional beneficiaries
Objectives of ND4BB Topic 3

• Provide a **unique platform for collaboration** and exchange between private and public partners
• Establish a vibrant **drug discovery hub** across Europe with the resource, skills and expertise to optimize and progress “Leads” and “Development Candidates”
• Discover **up to three novel-mechanism antibacterial Leads**
• Identify **up to two novel-mechanism Development Candidates**
• Progress **at least one** novel-mechanism Development Candidate into **preclinical and Phase 1 clinical studies**
• Focuses on systemic **Gram-negative infections** only
  • *E. coli, K. pneumoniae, A. baumannii & P. aeruginosa*
Expected impact on the R&D process

• Sharing drug discovery strategies and tactics will make antibacterial R&D more efficient
• Creation of the Drug Discovery Platform team
  • Enhance drug discovery capabilities and know how
  • Opportunity for public partners to receive assistance in early stage efforts
• Progression of a portfolio of assets
  • Larger overall pipeline of antibacterial for Gram-negative infections arising from multiple sources
ND4BB Topic 3—concept of merged group

Subtopic 3A

- med chem, microbiology, biochem, dmpk, etc. (WP3)
  - from EFPIA (expertise/advice), academia, SME

Subtopic 3B

- Programmes with novel mechanisms (WP4 & WP5B)
  - From public and private partners

- GSK/Sanofi collaboration

- Portfolio Management Committee (WP2)

- European Antibiotic Drug Discovery Centre of Excellence
  - Hit-to-lead
  - Lead-to-Candidate
  - Candidate-to-Phase 1
  - Phase 1 clinical trial

- WP4
- WP5A
- WP6*
- WP5B
- WP7*

* Subject to future Calls

4 hit-to-lead programmes running in parallel, max. 8 total

2 lead-to-candidate programmes running in parallel, max. 3 total
Expected contributions of the applicants—Subtopic 3A

• Expertise in project management and communication (WP1)
• Expertise in portfolio management (WP2)
• Expertise and capacity to form Platform group (WP3)
  • Synthetic and medicinal chemistry, microbiology (in vitro and in vivo), biochemistry, pharmacokinetics, etc.
  • Indicative capacity to run 4 Hit-to-Lead and 2 Lead-to-Candidate efforts in parallel
• Expertise around topoisomerases to support aspects of WP5A
Expected contributions of the applicants—Subtopic 3B

• Hit-to-Lead and potentially Lead-to-Candidate programmes acting through:
  • Novel targets
  • Known targets with novel Mechanism of Action (MoA)
  • Known targets with known MoA

• To ensure a quality portfolio, Hits* will demonstrate:
  • MIC ≤ 32 ug/mL vs. a key Gram negative pathogen
  • Evidence that activity is not due to a non-specific mechanism
  • Proven chemical structure, preliminary SAR
  • Favourable properties (e.g. clogP <4, reasonable synthetic route or source if a natural product)

* Indicative criteria for a Lead can be found in the Call text
Expected (in kind) contributions of EFPIA members

- Expertise and advice in all phases of antibacterial drug discovery
- Project / portfolio management
- Robust Lead and Development Candidate criteria
- Leads from GSK/Sanofi collaboration
  - Drug discovery resources (e.g. medicinal chemistry, microbiology, dmpk, biochemistry, etc.) to support the GSK/Sanofi collaboration program
ND4BB—Topic 3: Projected merging of Subtopics 3A and 3B

- Anticipated that applicant consortia for Subtopics 3A and 3B will merge following Stage 1 review
  - 3A group—drug discovery management and resource
  - 3B group—small molecules in need of optimisation

- Full Topic 3 consortium—a powerful drug discovery group with the expertise and resource to optimise multiple starting points in parallel
What is the value for Europe?

• As part of ND4BB, Topic 3 will continue to:
  • respond to the European Strategy to combat antibiotic resistance
  • create a leadership position for Europe in addressing antibiotic resistance
  • increase investment in European healthcare institutions & academia
  • encourage companies to set up more research in Europe on antibacterial drug discovery
Questions?

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