



Innovative Medicines Initiative

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

Rob Stavenger for EFPIA partners (AstraZeneca,
Basilea, GlaxoSmithKline, & Sanofi)

17 December 2012



efpia

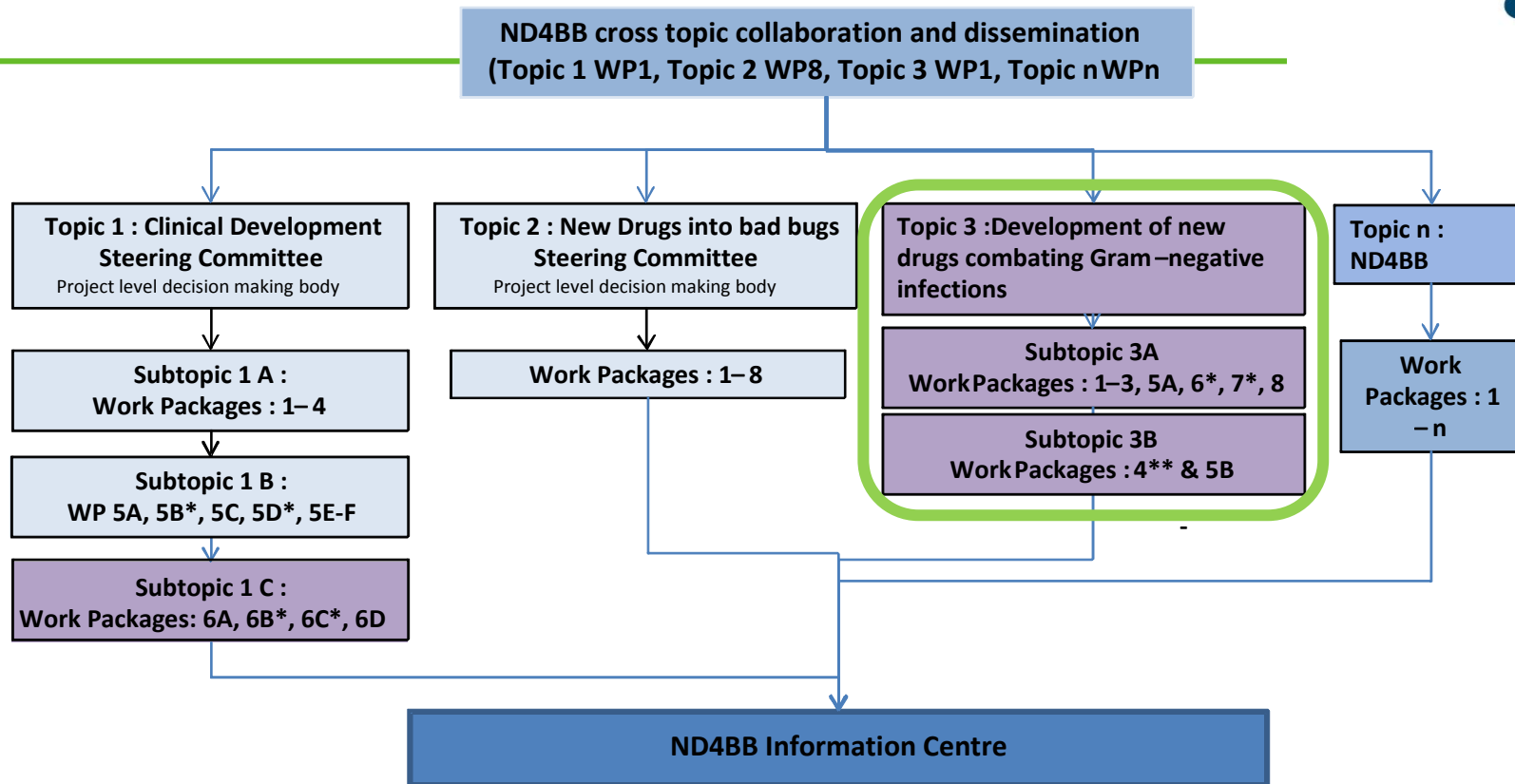
Antibiotic drug discovery & development – major challenges



- 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



□ 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



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*



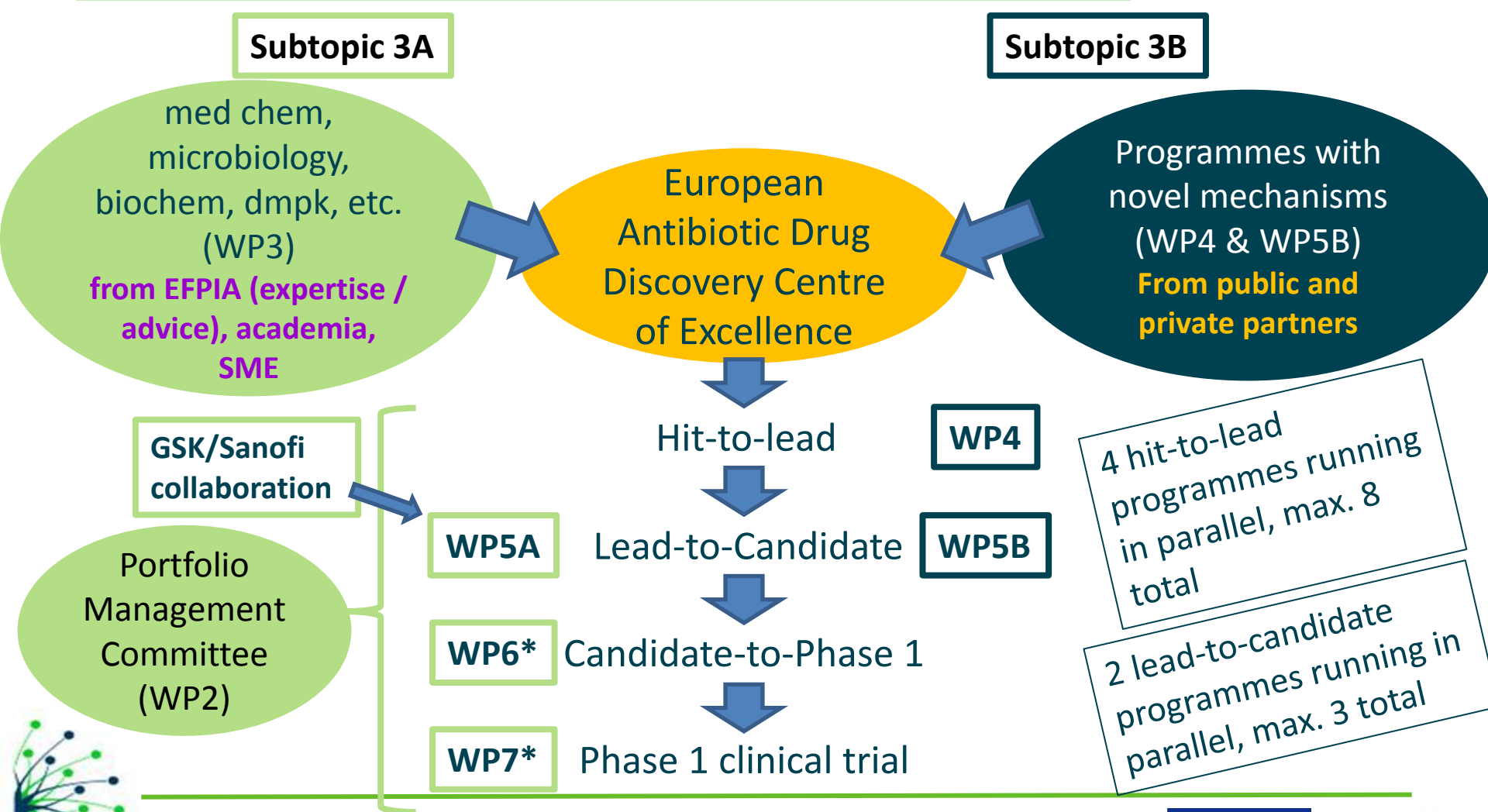
Expected impact on the R&D process



- 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 antibacterials for Gram-negative infections arising from multiple sources



ND4BB Topic 3—concept of merged group



* Subject to future Calls



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 \leq 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?



- Contact the **IMI Executive Office**

E-mail: infodesk@imi.europa.eu

Website: www.imi.europa.eu

