

Groningen, May 2016

New economic models for antibiotic R&D

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Where is innovation coming from?

- **Basic research:** Universities
- **Drug discovery**
 - Universities
 - SMEs
 - Publicly funded research institutes (Institute Pasteur, Fraunhofer, Deutsches Zentrum für Infektionsforschung,...)
 - Public-Private-Partnerships (Bioaster, IMI Lead factory,...)
 - Big Pharma
 - Research groups at GSK, Novartis, Merck, Genentech
 - Discovery partnerships with Roche, Sanofi-Aventis

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Where is innovation coming from?

Source and developing companies for antibiotics in Phase 2 or 3 clinical development:

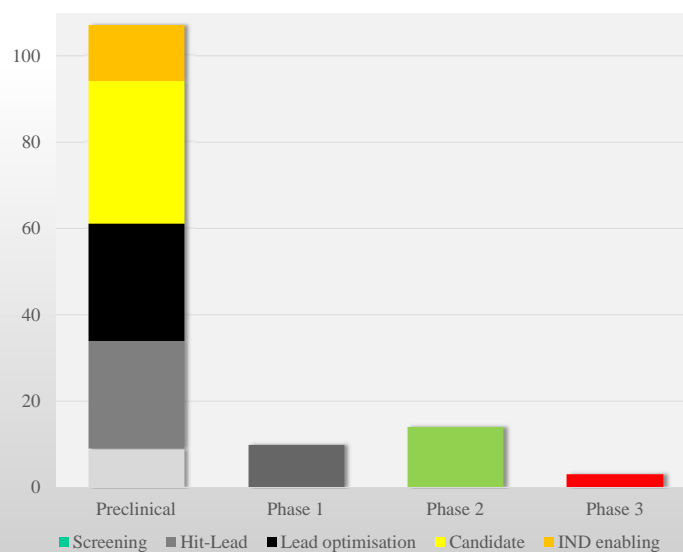
Antibiotic	Source	Developing companies			
Eravacycline	Harvard Univ	Tetraphase			
Plazomicin	Isis	Achaogen			
Brilacidin	Univ of Pennsylva	Polymedix	Cellceutix		
Debio 1450	Univ of Toronto	Affinium	Debiopharm		
Solithromycin	Optimer	Cempra			
Delafloxacin	Wakunaga	Abbott	Wakunaga	Rib-X=Melinta	
Omadacycline	Paratek	Paratek/Bayer	Paratek/Merck	Paratek/Novartis	Paratek
Nemonoxacin	TaiGen	Procter&Gamble	Warner Chilc	TaiGen	
Radezolid	Yale University	Rib-X=Melinta			
Lefamulin	Sandoz/Novartis	Nabriva	Forest/Actavis*	Nabriva	
Acorafloxacin	J&J (Janssen)	Furiex	Forest/Actavis*		
POL7080	Univ Zürich	Polyphor	Roche	Polyphor	
Carbavance (+Meropenem)		Rempex	The Med Comp		

*Allergan
 University/Small company
 Mid-sized company (>500 employees)
 Global pharmaceutical corporation

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Antibacterial projects of European SMEs



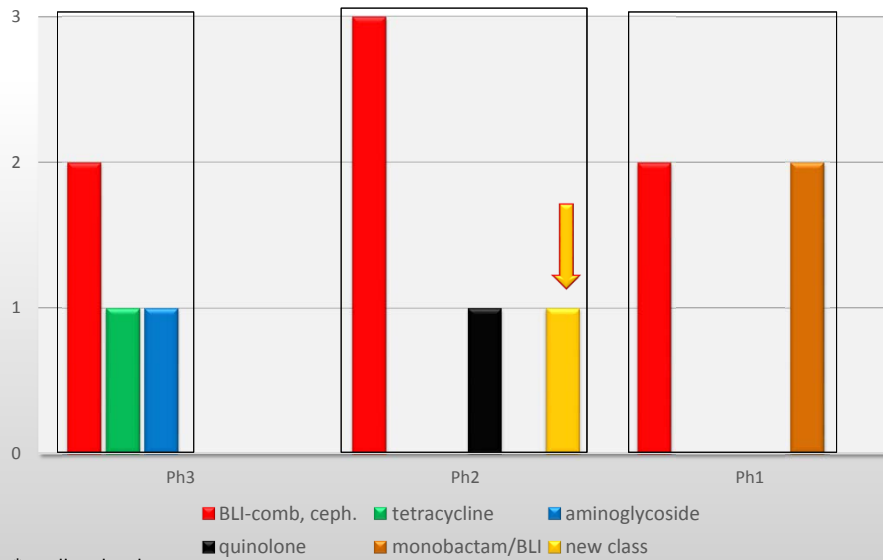
93 project in 81 companies

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Systemic antibiotics in clinical development

Clinical development pipelines for Gram-negatives*



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What to expect?

▪ Adjunctive therapies

- Require an active antibiotic
- Virulence factors, biofilm formation, persisters
- Immune system stimulation, microbiome modifying
- Phages

▪ Potentiators

- Resistance determinants (e.g. beta-lactamase-inhibitors, efflux pump inhibitors)
- Facilitating penetration
- Changing the sensitivity of the bacterial cell

▪ Targeted therapies

- Traditional antibiotics, antibodies
- Single pathogen, especially *S. aureus* or *P. aeruginosa*

▪ Prevention

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Pipelines are inappropriate

Discrepancy between antibiotic R&D pipelines and public health needs



Scientific challenges



Economic model

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Scientific challenges


- **Expertise**
 - Diminished pool of experience
- **Basic research**
 - Less attractive to funders and academic institutions
- **Science**
 - Penetration and efflux
 - High protein binding
 - Poor solubility, compounds not amendable to medicinal chemistry
 - Toxicity
 - High mutation frequency

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WHO – Global Action Plan AMR


- Improve awareness and understanding
- Strengthen knowledge through surveillance and research
- Reduce incidence of infection
- Optimize the use of antimicrobial medicines
- Ensure sustainable investment in R&D




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Convergence of principles

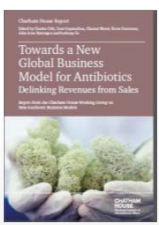


Review on Antimicrobial Resistance
Tackling drug-resistant infections globally





G7 GERMANY 2015






OECD
BETTER POLICIES FOR BETTER LIVES


- Need for both push and pull mechanisms
- De-linkage (i.e., revenues delinked from volumes sold)
- Clear priority setting
- Access and sustainable use are integral considerations for all mechanisms
- Global collaboration and financing necessary


World Health Organization **DNDi**
Drug for Neglected Diseases Initiative



European Parliament

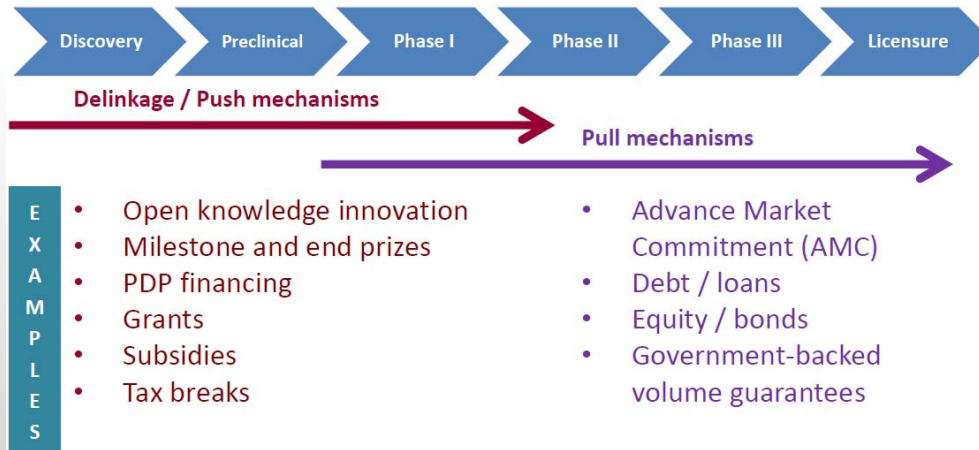


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R&D financing and incentive mechanisms



John-Arne Rottingen 2015, DRIVE-AB

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New economic models

- Industry proposal
 - De-linkage
 - Value based pricing in developed countries

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IMI – ND4BB



Cross-project communication & collaboration

COMBACTE (Topic 1) Enabling clinical collaboration and refining clinical trial design- Clinical dev. of MEDI4893	TRANSLOCATION (Topic 2) Research on penetration and efflux in Gram-negative bacteria-Data hub and learning from R&D experience	ENABLE (Topic 3) Discovery and development of new drugs combatting Gram-negative infections	DRIVE-AB (Topic 4) Driving re-investment in R&D and the responsible use of antibiotics	COMBACTE CARE (Topic 5) Clinical development of antibacterial agents for Gram-negative, antibiotic-resistant pathogens	COMBACTE-MAGNET (Topic 6) Systemic molecules against Health-care-associated infections due to clinically challenging Gram-negative pathogens	iABC (Topic 7) Inhaled anti-bacterials (inhaled monobactam, tobramycin) in cystic fibrosis and non-cystic fibrosis bronchiectasis
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Development-focused




Discovery-focused

Economics & stewardship

Development-focused (Gram-negative infections)

ND4BB Information Centre


All data generated is submitted and made accessible to all partners

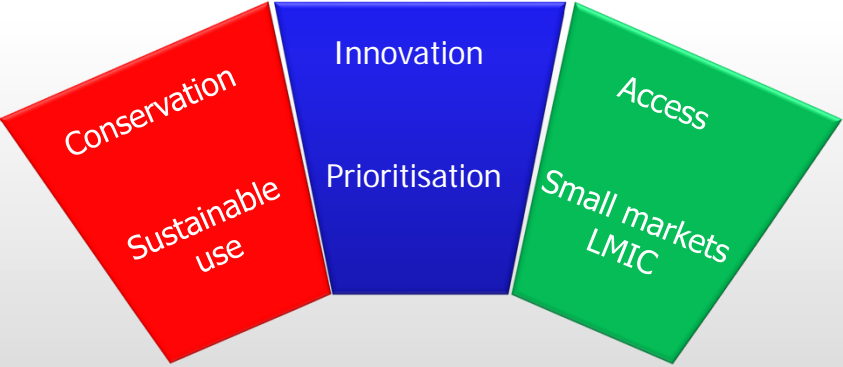





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New economic models

www.drive-ab.eu







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DRIVE AB RE-INVESTMENT IN R&D AND RESPONSIBLE ANTIBIOTIC USE

DRIVE-AB www.drive-ab.eu

- **Prioritising models**
- **Providing research data**
 - Defining challenges and bottlenecks, medical need
 - What does sustainable use mean, how to deal with equitable access?
 - Value of antibiotics
- **Testing models**
 - Fit high-level parameters? Mitigate a bottleneck?
 - How to pair with sustainable use and access?
 - Will it stimulate action? By whom? Cost/benefit?
 - How can it be implemented?
- **Stakeholder involvement, implementation plan**

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DRIVE AB RE-INVESTMENT IN R&D AND RESPONSIBLE ANTIBIOTIC USE

New economic models

- **Stimulate innovation + sustainable use + equitable access**
- **Models researched**
 - Grants
 - Determines research at universities, non-dilutive capital for companies
 - Product Development Partnerships
 - Non-profit entity (the PDP) and private sector industry to develop drugs on a not-for-profit basis. Innovation?
 - Post-approval payments (aka lump sum payments)
 - Structure of payments, source of funding, how much?
 - Payer licenses
 - Annual license fee and still charge unit costs, how much?


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- All incentives to stimulate innovation will be paired with
 - Sustainable use policies, conservation measures
 - Equitable access provisions

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THE WAY FORWARD
From discussion to testing and implementation

Conference on
Stimulating innovation, sustainable use and global access to antibiotics

Amsterdam, 2nd June 2016



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