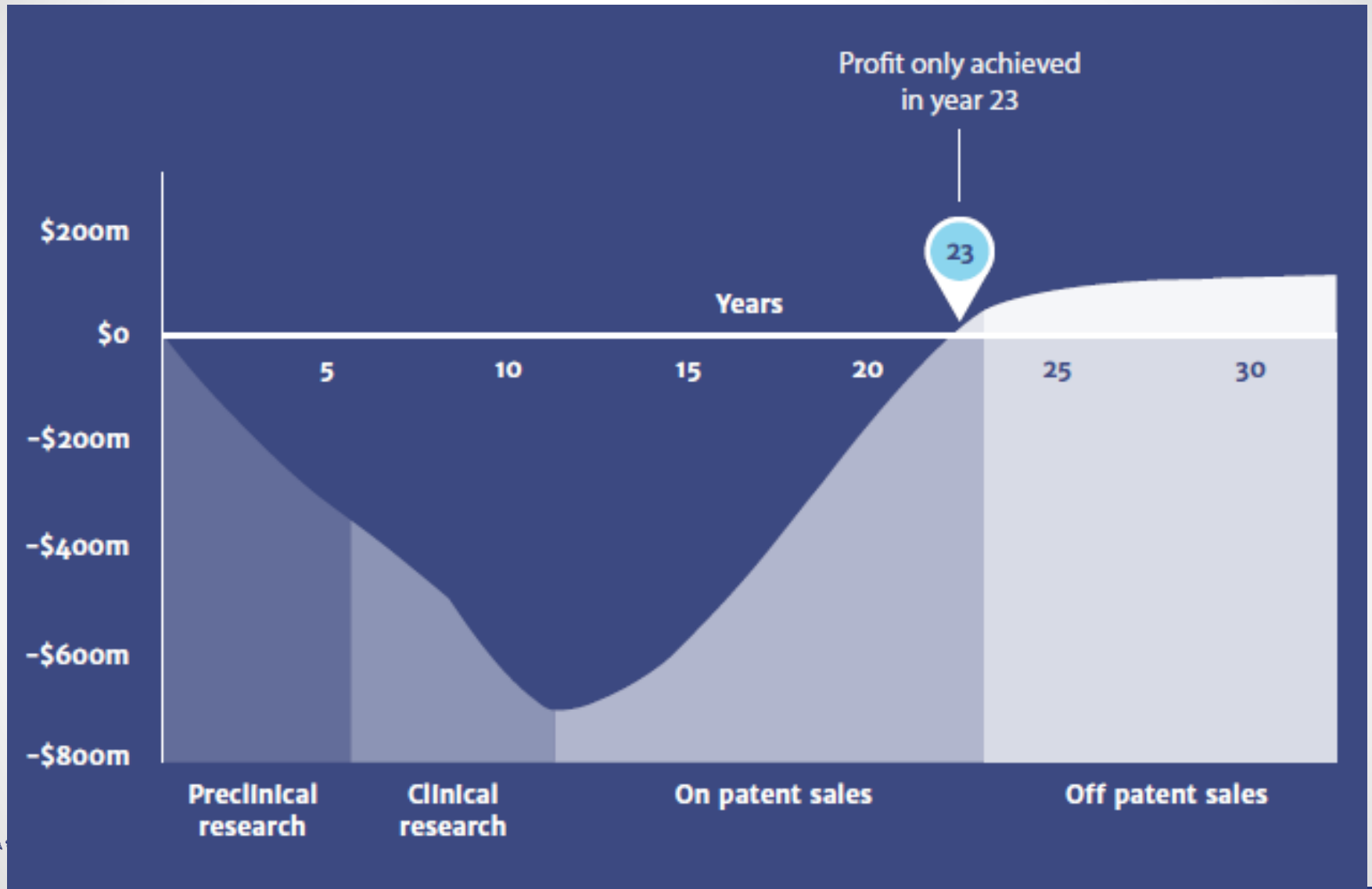




ECONOMIC INCENTIVES FOR ANTIBIOTIC DEVELOPMENT: AN OVERVIEW

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The Current Model...



Incentives to develop new antibiotics?

Factors:

- Uncertainty in use at launch
- Stewardship means limited use
- Generics can be effective for most infections
- Lower returns generally than other therapeutic areas
- Increasing appropriate use limits use-impacts revenue
 - Need a different model



Net Present Value

- The pharmaceutical industry evaluates the overall risk/benefit and profitability of pursuing development utilizing a metric termed net present value (NPV).
- Net present value is the sum of all investment costs in development and expected present value of future revenues, considering discounted rate of the time value of money of a given development program.
- NPV for antibiotics: approximately \$50M*
- NPV for neurological or musculoskeletal drugs: \$720M-\$1.15B*
- Suggested that a ~\$200M NPV is appropriate to incentivize investment



Incentives need to:

- Improve Net Present Value
- Possess minimal disruptive effects
- Reward Innovation
- Ensure Conservation
- Not impact patient access



The Basics

- **Push Incentive:** A “push” incentive provides direct support and pays for the “effort” of developers, by underwriting the cost of that effort
 - Examples: Grants, contracts, PPPs, tax credits
- **Pull Incentive:** A “pull” incentive creates an incentive for private sector engagement by creating viable market demand or reward for success
 - Examples: Advanced market commitments, prize/milestone payments, tax credits (that pay off at some defined milestone), and regulatory incentives (market exclusivity, priority review vouchers, tradable patent vouchers)



Economic Incentives for Antibacterial Drug Development

- Growing consensus globally that they are needed
- The US government has not taken a formal position on this issue
 - Funds and supports push incentives
 - GAIN Act-additional market exclusivity (limited pull incentive)
- Pull incentives not a major component of our current package of incentives



De-linkage Model

- Antibiotics are one of the only class of drugs whose use diminishes utility
- How do we ensure antibiotics are available while not driving inappropriate use?
- De-linkage models seek to “delink” profit of antibiotics from the number of units sold
 - Allow a known return on investment (ROI)
 - Can build in provisions for stewardship and conservation



De-linkage Models

- **Full De-linkage Models:** A financial model where the intellectual property or license is purchased from the drug developer by the government or a third party at some point during development or at regulatory approval
- Payments would need to be large: \$1-2B
- Distribution and access could be challenging
- Sustainability of funds to make these payment is also a challenge



Delinkage Models

- **Partial Delinkage Model:** A financial model where the drug developer is rewarded for success through milestone payments. The drug developer retains all intellectual property and has responsibility for approval, manufacturing, and sales of the antimicrobial. Restrictions may be placed on marketing, promotion, volume sold
- Payment would be smaller than full delinkage
- May be easier to sustain since companies still allowed to sell

Allow for targeted use of incentive



Consensus is growing on this
issue



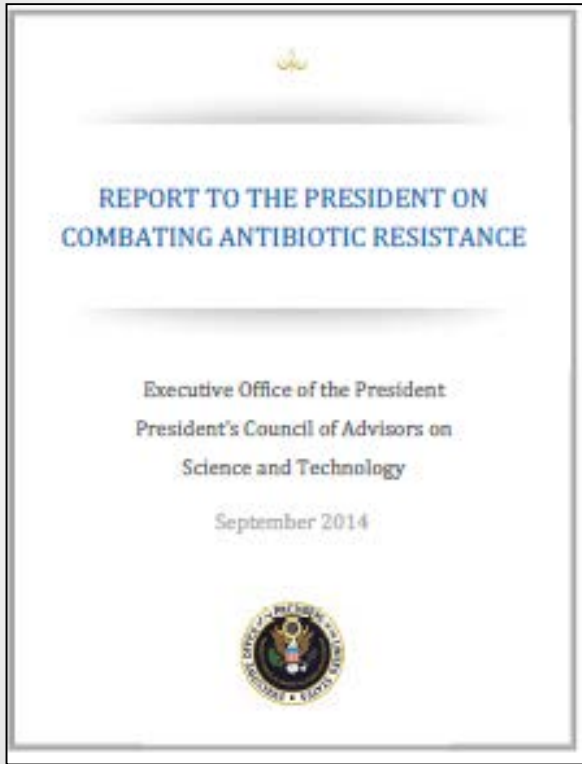
Davos Declaration

- January 2016, the *Declaration by the Pharmaceutical, Biotechnology and Diagnostics Industries on Combating Antimicrobial Resistance* was launched at an event at the World Economic Forum in Davos, Switzerland.
 - 85 companies and 9 industry associations
- Call on governments to work with them ***to develop new and alternative market structures*** that provide more dependable and sustainable market models for antibiotics, and to commit the funds needed to implement them.
- One recommendation-purse novel payment models that reduce the link between the profitability of an antibiotic and the volume sold



Report	Push Incentives	Pull Incentives	De-linkage	Global Threat Assessment	Global Funder
BEAM Alliance	Yes	Yes	Yes	No	Yes
BCG report for G7	Yes	Yes	Yes	Yes	Yes
Carlet and LeCoz 2015	Yes	Yes	No	No	Yes
Chatham House Report	Yes	Yes	Yes	Yes	Yes
DNDi GARD PDP	Yes	Yes	Yes	No	Yes
EU Plan 2011-2015	Yes	Yes	No	No	No
IMI ND4BB: DRIVE AB	Yes	Yes	Yes	Yes	Yes
Jackson CSIS 2016	Yes	Yes	Yes	No	Maybe
OECD	Yes	Yes	Yes	Yes	Yes
O'Neill Review	Yes	Yes	Yes	No	Yes
PCAST Working Group	Yes	Yes	Yes	No	No
Renwick et al., 2015	Yes	Yes	Yes	No	No

PCAST Recommendations



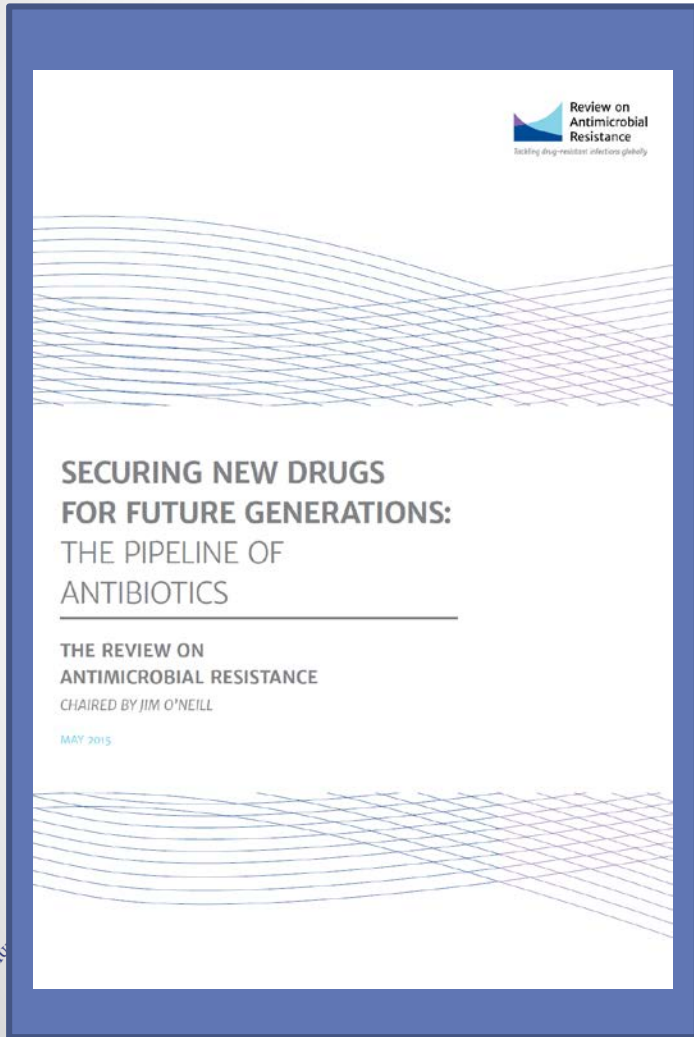
5.2 'Push' mechanisms: Direct Federal partnership in antibiotic development

- Recommended expansion of additional support for subsidizing research and development costs

5.3 'Pull' mechanisms: Economic rewards for drug developers

- Substantially higher reimbursement for antibiotics
- De-linkage models
- Mechanisms to extend patent life
- Antibiotic usage fee

O'Neill AMR Review



- AMR Innovation Fund (Push)
 - Early Stage Research
- Two broad approaches to delinkage (Pull)
 - Global Purchaser
 - Hybrid (Partial) Model

A systematic review and critical assessment of incentive strategies for discovery and development of novel antibiotics

Matthew J Renwick¹, David M Brogan^{1,2} and Elias Mossialos¹

- Analyzed 47 different incentives
- Conclude that a combination of multiple incentives necessary to be effective
- “The ideal incentive package would include incentives that facilitate cooperation and synergy throughout the market; ***one or two research and development linked push incentives and a large pull incentive rewarding successful development.***”
- “Suggest first developing a single incentive package that addresses market failures and subsequently enhance the package to address public health objectives with transition to more complex international business models.”



A systematic review and critical assessment of incentive strategies for discovery and development of novel antibiotics

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- *De-linkage models are favored* because it 1) provides developers with a definitive ROI, 2) removes the motivation for developers to market and oversell their antibiotic, and 3) allows access to antibiotics in patients who need them.

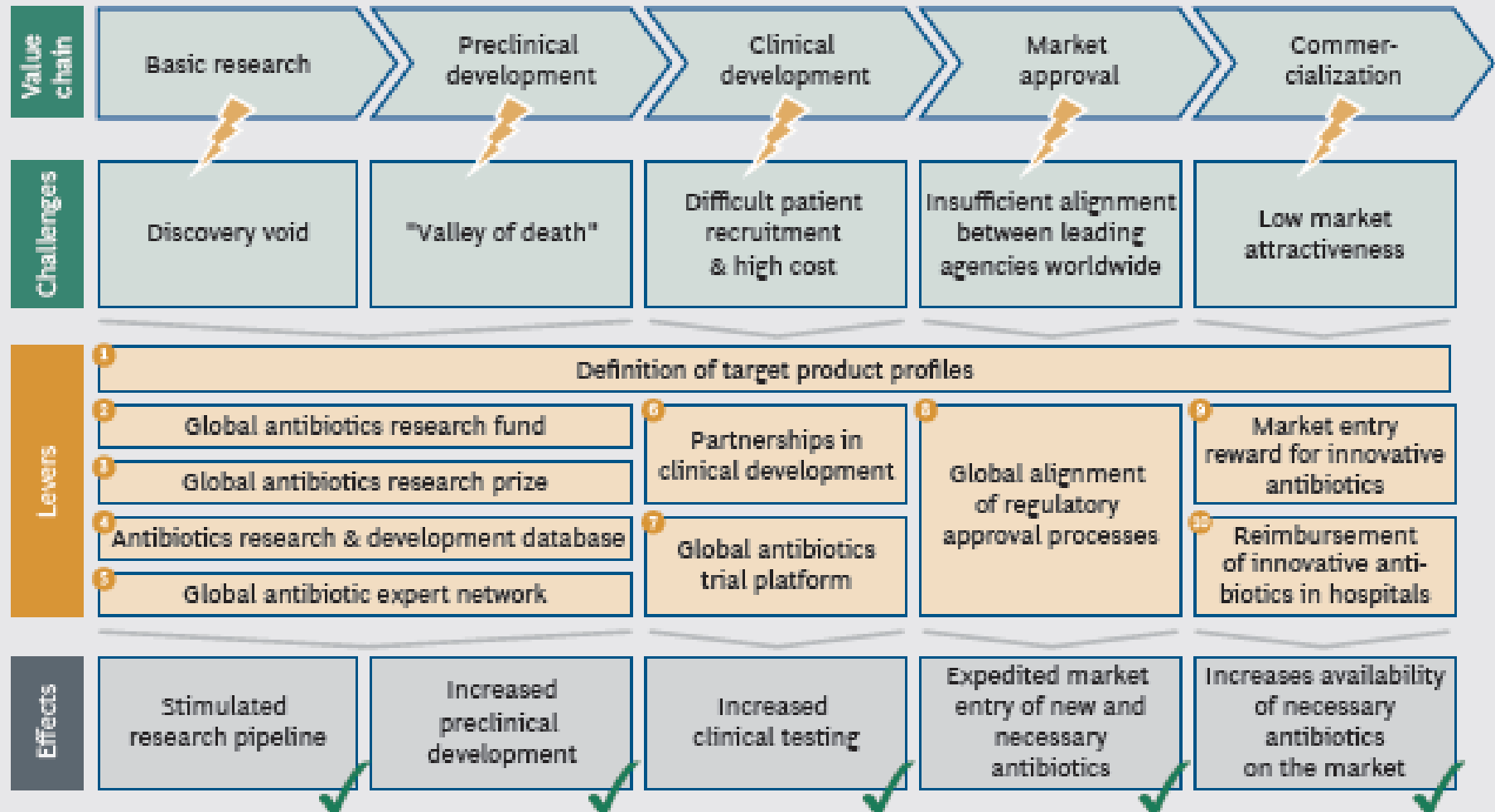


Boston Consulting Group: Report for the German MoH



BCG recommendations

FIGURE 1 | Overview of recommendations along the value chain



- **Lever 2: Global Antibiotics Research Fund**
Create a fund that supports basic research at academic institutions and small and medium-sized enterprises (SMEs). The priorities of the fund will be based on a strategic research agenda in-line with the Target Product Profiles. Priorities of the fund could be research into gram-negative bacteria and point-of-care diagnostics
- **Lever 3: Global Antibiotics Research Prize**
Establish an annual prize rewarding scientific advancements in antibacterial research in order to increase the attractiveness of the research area and awareness for certain research challenges.
- **Lever 6: Partnerships in Clinical Development**
Establish partnerships in clinical development in order to support research institutions and small and medium-sized enterprises in advancing the clinical development of promising antibiotic candidates. Partnerships in clinical development include financial support as well as in-kind support (e.g., access to experts and laboratories).
- **Lever 9: Market Entry Reward for Innovative Antibiotics**
Introduce a market entry reward for innovative antibiotics that meets the Target Product Profiles. The market entry reward has to be significant (i.e., in the order of €1,000 million) and will provide a reliable and predictable source of income that is delinked from sales volumes, thereby increasing the commercial attractiveness of antibiotics research and development.



Chatham House WG

Chatham House Report

Edited by Charles Clift, Unni Gopinathan, Chantal Morel, Kevin Outterson, John-Arne Røttingen and Anthony So

Towards a New Global Business Model for Antibiotics Delinking Revenues from Sales

Report from the Chatham House Working Group on
New Antibiotic Business Models

Main Recommendations

1. A new business model needs to be developed in which the return on investment in R&D on antibiotics is delinked from the volume of sales.
2. Increased public financing of a broad menu of incentives across the antibiotic life-cycle is required, targeted at encouraging the development of antibiotics to counter the greatest microbial threats.
3. The assessment of current and future global threats arising from resistance should be updated periodically in order to identify which classes of product are a priority for incentives.
4. The delinkage model should prioritize both access and conservation.
5. Domestic expenditures on the model need to be globally coordinated, including through the establishment of a secretariat, and global participation in the model is the ultimate goal



Items for Consideration

- Whether there is a need for incentives and what do you want those incentives to accomplish
- Avoiding secondary disruptive effects
 - Patient Access
 - Cost to the health care system
 - Sustainability and political will
 - Role of the government
- Incentives related to pricing would only be felt in the U.S. market in the absence of global adoption
- Health care markets are different, you may need different sets of incentives for different markets



Pros to having the government administer the incentive

- Public health agencies could ensure appropriate targeting of the incentives
- Known system that is enforceable -i.e. government contracts
- Existing infrastructure, governance, processes could be leveraged-i.e. the Public Health Emergency Countermeasures Enterprise



Cons to having the government administer the incentive

- Bureaucracy
- Restrictiveness of Federal Contracting
- Political will and funding-incentives need to be stable and sustainable to be effective
- More versatile financing tools available in private sector
- Equity positions



A perspective

- A mix of general and targeted incentives are needed
- Expansion of push incentives across all phases of development
- General pull incentives-anyone gets Y if you develop X
 - Tax credit that is transferable, refundable and pays 50% of Phase II/Phase III clinical development cost at approval
 - Avoids the government picking winners and losers
- Targeted pull incentives-partial de-linkage
 - Government prioritizes products for unmet medical need
 - Provides milestone payments for a known ROI
 - Includes restrictions on marketing, volume sales caps, stewardship requirements



Summary

- There is growing consensus on the need for and types of economic incentives for antibacterial drug development
- A mix of push/pull incentives and models that delink profits from volumes sold are favored
- Market incentives will be market-specific
- It is time for the US government be involved in the discussion and take a position on this issue



Questions?



Figure 1 text version:

Value Chain	<i>Basic Research</i>	<i>Preclinical Development</i>	<i>Clinical Development</i>	<i>Market Approval</i>	<i>Commercialization</i>
Challenges	Discovery Void	“Valley of Death”	Difficult patient recruitment & high cost	Insufficient alignment between leading agencies worldwide	Low market attractiveness
Levels	1. Definition of Target product profiles				
	2. Global antibiotics research fund	6. Partnerships in clinical development	7. Global antibiotics trial platform	8. Global alignment of regulatory approval processes	9. Market entry reward for innovative antibiotics
	3. Global antibiotics research prize				10. Reimbursement of innovative antibiotics in hospitals
	4. Antibiotics research & development database				
5. Global antibiotic expert network					
Effects	Stimulated research pipeline	Increased preclinical development	Increased clinical testing	Expedited market entry of new and necessary antibiotics	Increases availability of necessary antibiotics on the market