Session V: Sustainability and Maintenance of Business Models to Ensure Rapid and Nimble Response to Emerging Threats of National Security Concern

John H. Rex, MD
SVP & Head of Infection Global Medicines Development, AstraZeneca
Non-Executive Director & Consultant, F2G Pharmaceuticals
john.rex@astrazeneca.com

The opinions expressed herein are my own.

Slides happily shared – just drop me a note.

Theme for this session

- Discuss the *business* of developing MCMs
  - Opportunities for companies to collaborate in pre-competitive areas
  - Use of public-private partnerships (PPPs)
  - Next steps to coordinate a rapid response
    - Look for common elements across threats
    - Discuss sustainability of business models

Five speakers

- Rex: Pharma antibacterial developer
- Larsen: US Government (BARDA)
- Garry: University-based consortium
- Majorowski: Re-imagining social change
- Hanna: PPP model from the TB world

Antibacterials as a parallel

- The efficacy of antibacterials is threatened by a rising tide of antimicrobial resistance (AMR)
  - 23,000 deaths/yr in the US (one jumbo jet/week)[1]
- An empty pipeline
  - # of active companies in 2013 = # in 1960[2]
- Why?
  - Hard to discover
  - Hard to develop
  - Economics are poor (despite dual MCM use!)

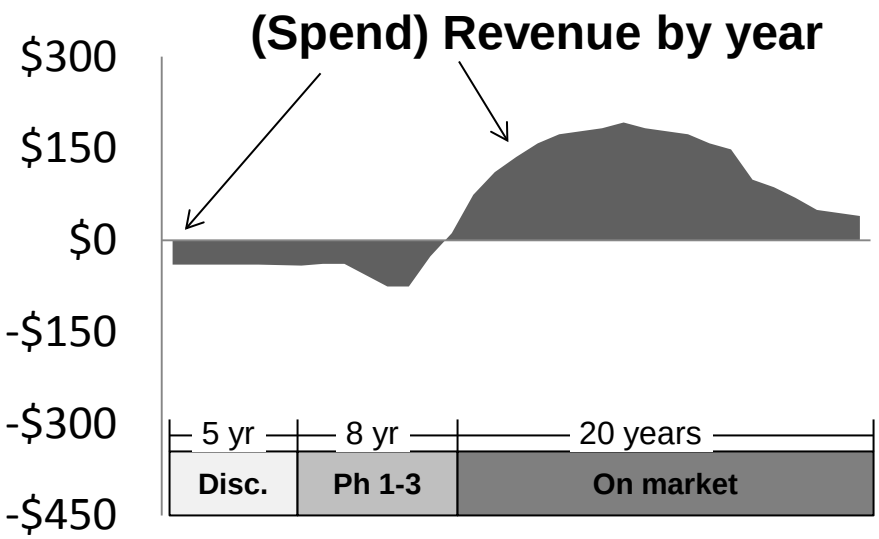
[1]CDC: Antibiotic Resistance Threats in the United Stated, 2013. [2]Kinch MS et al. Drug Discovery Today, July 2014.

What motivates companies?

- We can't *make* companies do this work … we have to make them *want* to do this work[1]
- We must address several basic tensions
  - We want to minimize use of *all* antibiotics
  - We want to have new(er) antibiotics available on demand
  - We want those antibiotics developed before the epidemic
- How can we do this?
  - Noting that "All models are wrong, but some are useful"[2]…
  - … let's now look at a model that may be instructive

[1]Spellberg B. The antibacterial pipeline: Why is it drying up, and what must be done about it? Appendix A in Antibiotic Resistance: Implications for Global Health and Novel Intervention Strategies: Workshop Summary, Institutes of Medicine, 2010. Accessed online at http://www.nap.edu/catalog/12925.html on 11 July 2013. [2]GEP Box and NR Draper in *Empirical Model-Building and Response Surfaces*, 1987, John Wiley & Sons, New York, NY.

The cost of creating an antibiotic
An EU-based analysis



- The typical antibiotic lifecycle can be modeled from start to finish[1]
- The model allows for failed drugs
- Spend and revenue by year are based on industry average data
- Note the Phase 3 bump in spend
- And then a sales curve: ~10 years of protected sales and then ~10 years of declining sales

- Approximate total spend (years 1-13): $600m
- Approximate total sales (next 20 years): $2,500m
- **But, we've forgotten about NPV!**

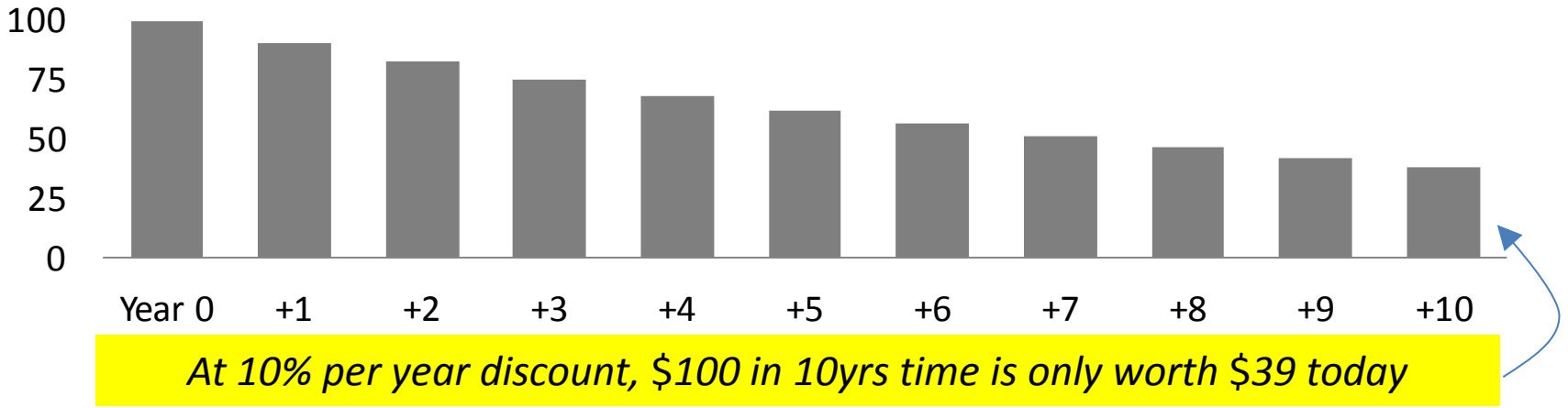
[1]Sharma, P. & Towse, A. New drugs to tackle antimicrobial resistance: analysis of EU policy options. OHE website, 2011; Spellberg et al. Nat Rev Drug Discov 11: 168., 2012

Before we go further, we interrupt this presentation...

Sidebar: NPV (Net Present Value)

How much is an investment worth in today's terms?

- Cash today is worth more than a promise of cash tomorrow (or in ten years)
- Based on cost of capital, risk, etc., it is typical to discount 10% per year
- The math is the inverse of interest on a loan:
  - $100 today = $100; $100 in a year = $90; $100 in two years = $81, etc.[a]

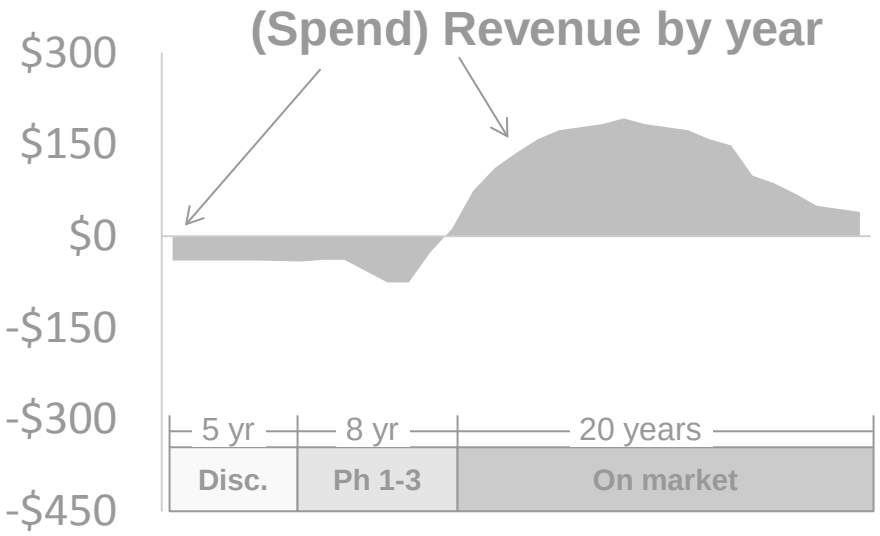


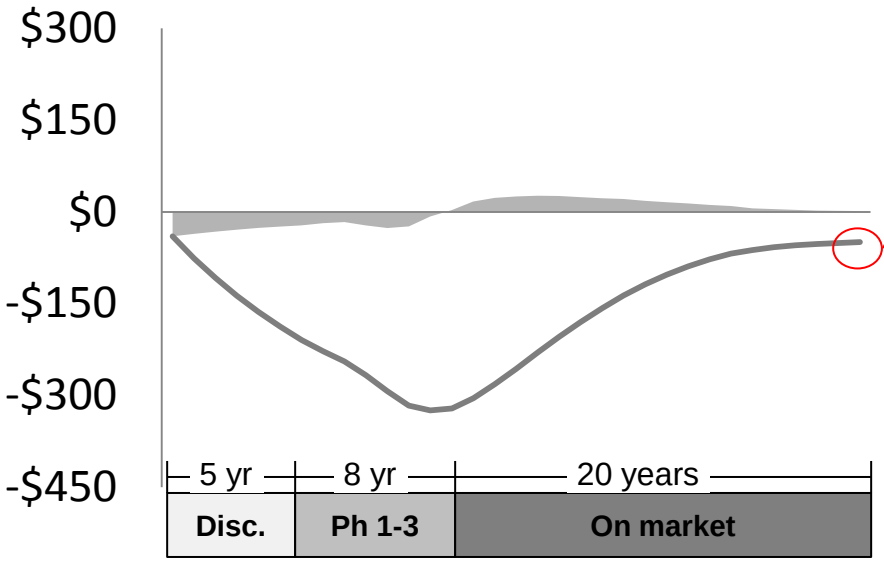
- A project's NPV is calculated by
  - Computing sales less costs for each year (Annual Net Cash Flow)
  - Each future year's Cash Flow is discounted to today
  - The total across all years is the **Net Present Value**
- **Any NPV > 0 means you've created (at least some) value**

a. Actually, I've simplified a bit here – the actual values are $91, $83 … but this simpler way of thinking about it is close enough for illustrative purposes

Now, back to the story…

The very real effects of NPV math





- **Now, consider this in NPV terms**
- From the standpoint of year 0 (the day you decide to start discovery), the graph below shows spend & revenue discounted 10%/year
- The line below is the cumulative NPV
- But in NPV terms, it totals to a loss of around $50m
- And think about the capital at risk and the timeline to the return. Even at +$50m, this would be unattractive

Recent US-based analysis: same result

- Comprehensive model for drugs for 6 key indications (ABOM, ABSSSI, CAP, cIAI, cUTI, HAP-VAP)[1]
- NPV of the new drug always < $40 million
  - All 90% confidence intervals on estimate went below zero
- Value to the patient was MUCH higher
  - Just based on the value of days of work and life restored, the value to society ranged from $500m to $12 billion
- Thus, these EU- and US-based models show that
  - Starting antibacterial R&D is not financially rational, at least not with traditional R&D costs and approaches
  - We (society) undervalue these drugs

[1]Sertkaya A, Eyraud J, Birkenbach A, Franz C, Ackerley N, Overton V, Eastern Research Group. Analytical framework for examining the value of antibacterial products. Report to US DHHS. http://aspe.hhs.gov/sp/reports/2014/antibacterials/rpt_antibacterials.cfm

That's a problem we must solve

- To restore vitality to the pipeline and ensure we have the life-saving drugs we will need in the future,

- We have to move these models back into consistently positive territory

And, we're trying now to do just that…

Global Leadership: A partial list

2003 et seq: IDSA: “Bad Bugs, No Drugs”

17 Sep 2009: (EU) Swedish presidency
- “Innovative Incentives for Effective Antibacterials”

7 April 2011: WHO World Health day on AMR
- “No action today, no cure tomorrow”

17 Nov 2011: (EU) ND4BB program
- PPP for Discovery & Development

2011 forward: (US & EU) FDA & EMA
- A steady stream of new guidances

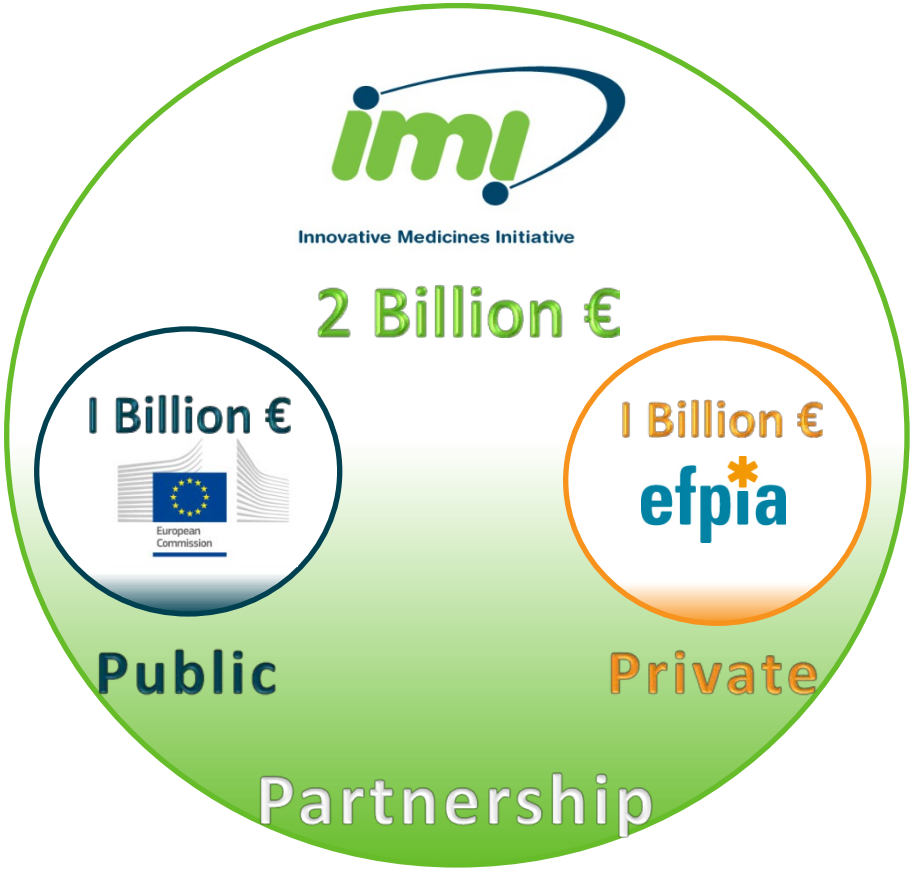
2012: (US) GAIN Act (see subsequent slide)

3-4 Oct 2013: (EU) Chatham House Conference
- “Antimicrobial resistance: Incentivizing Change Towards a Global Solution”

2014: (US) PCAST Report

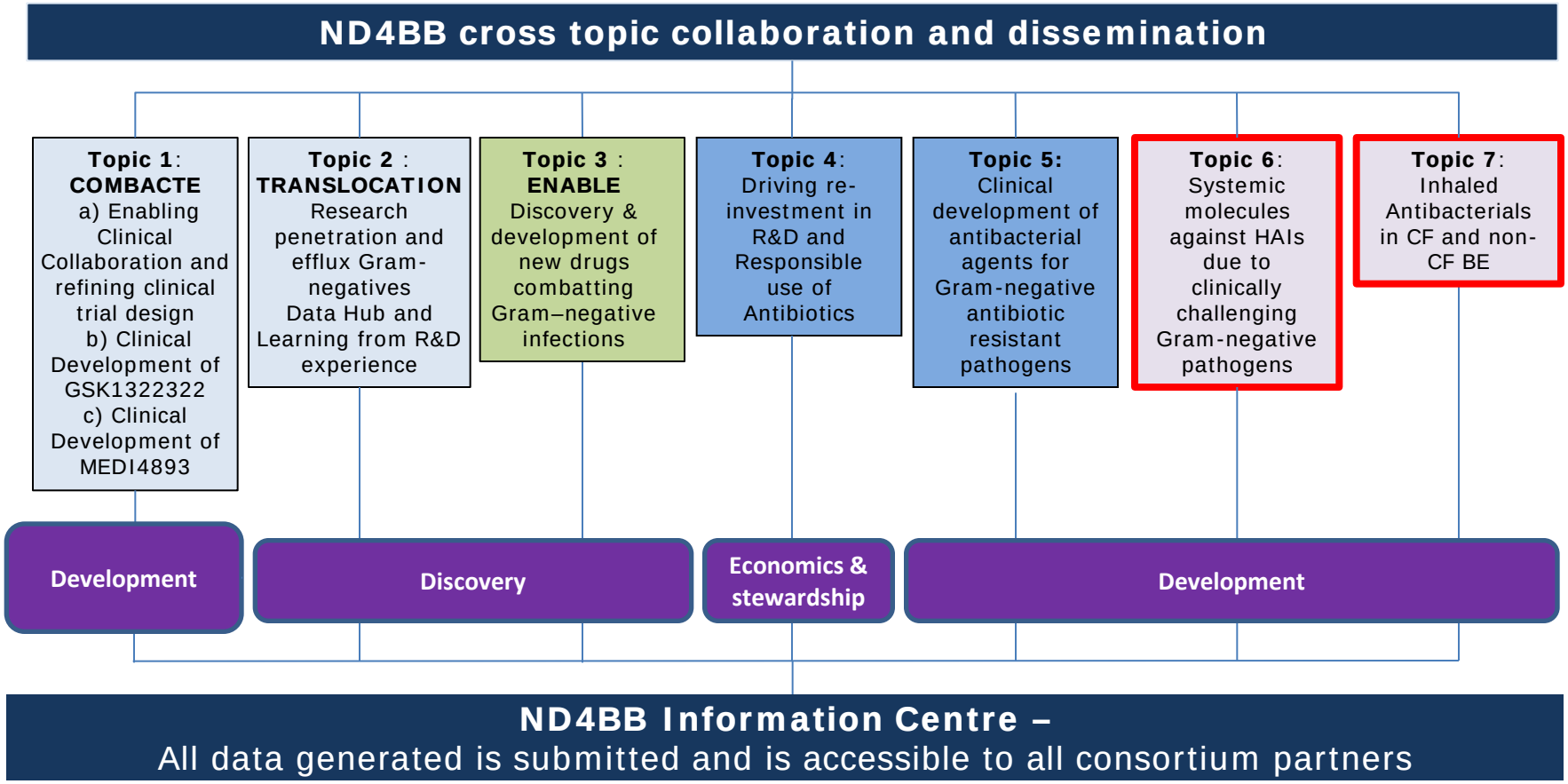
The Innovative Medicines Initiative

- A collaboration between EC and the EFPIA[1] companies
- Each provides €1b
  - EC: Contributes cash
  - EFPIA: Contributes effort
- Projects are
  - Proposed by EFPIA
  - Approved by consensus
  - And come alive as a group of academics, SMEs, and EFPIA companies
- All work is open & shared



[1]EFPIA is the trade organization for EU-based pharmaceutical companies. PhRMA is the equivalent organization in the US. IFPMA is the equivalent organization outside the EU and the US.

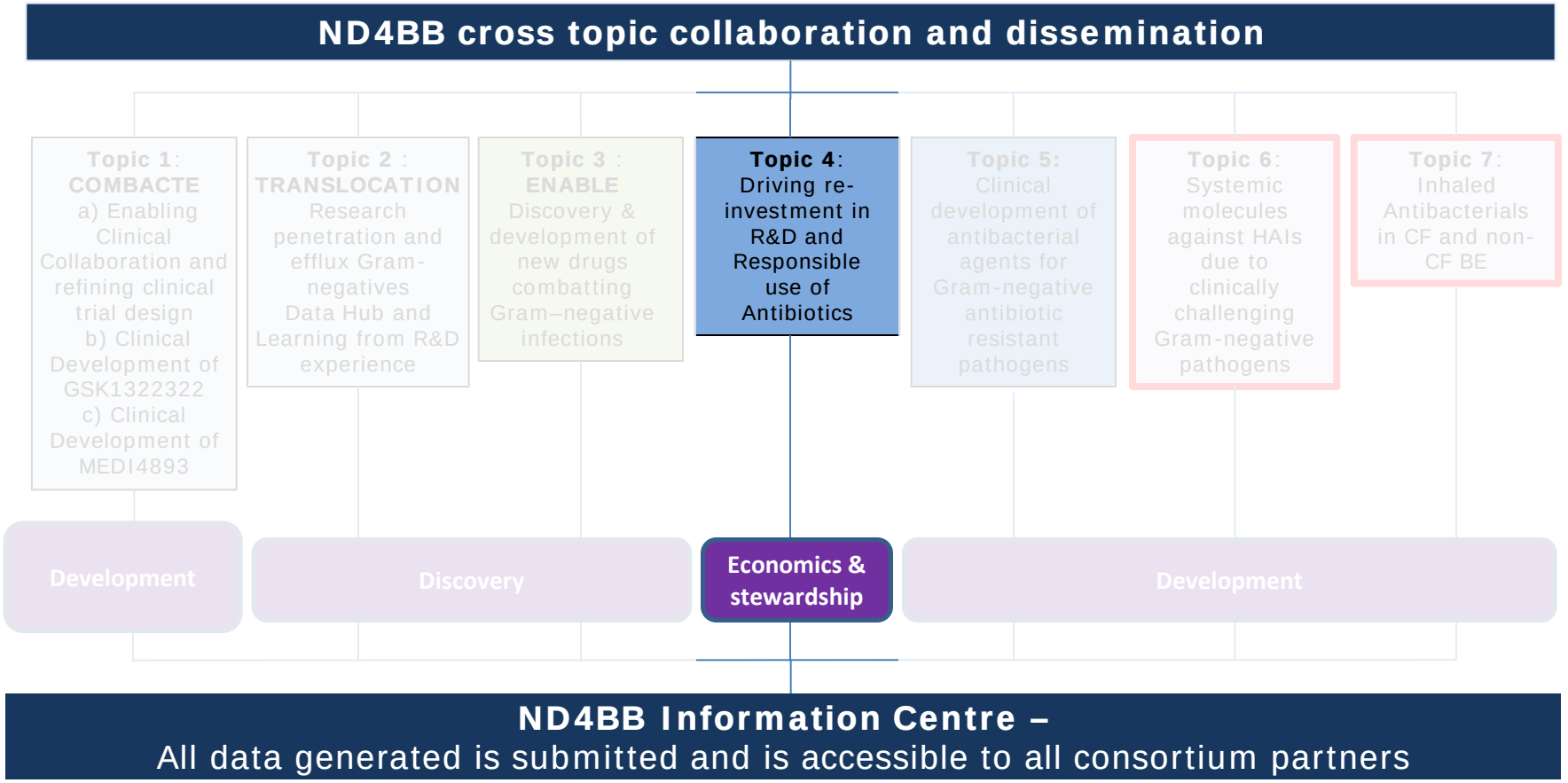
Under IMI, we created ND4BB (New Drugs For Bad Bugs)



IMI = Innovative Medicines Initiative

Call 6 | Call 9 | Call 8 | Call 11

In the EU: IMI's ND4BB program (New Drugs For Bad Bugs)



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And in the EU…
ND4BB Topic 4: The DRIVE-AB Project

- Launch meeting: 6 Oct 2014
  - "Driving re-investment in R&D and Responsible use of antibiotics"
- Aim: Address the tension between economics & stewardship
  - Create a multi-disciplinary, multi-stakeholder community (16 public partners and 7 private partners from 12 countries) with an in-depth comprehension of challenges of antibiotic development
  - Develop evidence-based measures for responsible antibiotic use
  - Create implementable options for new commercial models that address the needs of multiple stakeholders
  - Validate options through modelling
- We expect DRIVE-AB to explore a broad range of approaches
  - In particular, we hope to see ways to separate (delink) usage from reward to the innovator. That is, reward should not be sales-based
  - Let's look at two possible tools...

Two intriguing economic ideas

- (Push) Refundable tax credits
  - For some percentage (e.g., 50%) of qualified expenses, the company either gets a tax credit (if the company has income) or receives a payment of that amount
  - Has immediate impact on NPV while also ensuring the company has "skin in the game" that ensures delivery
- (Pull) Insurance-based approaches
  - National acquisition at a fixed, predictable rate (e.g., US buys $100m/year of a new antibiotic for 5 years)
  - Annual fee guarantees availability of a certain number of courses of therapy, whether used or not
  - We should be pleased to buy but not use the drug, just as we are pleased when our life insurance does not pay off

Questions for speakers

- How do we create business models that are resilient despite the uncertainty of MCM markets?
- What policies (regulatory or other) are needed?
- Do other industry offer relevant business models?
- How can we sustain
  - A discovery apparatus?
  - Registered products?
- How do we value new products?
  - How do we consider value to society?