Innovative Medicines Initiative

New Drugs for Bad Bugs (ND4BB)
Topic 4
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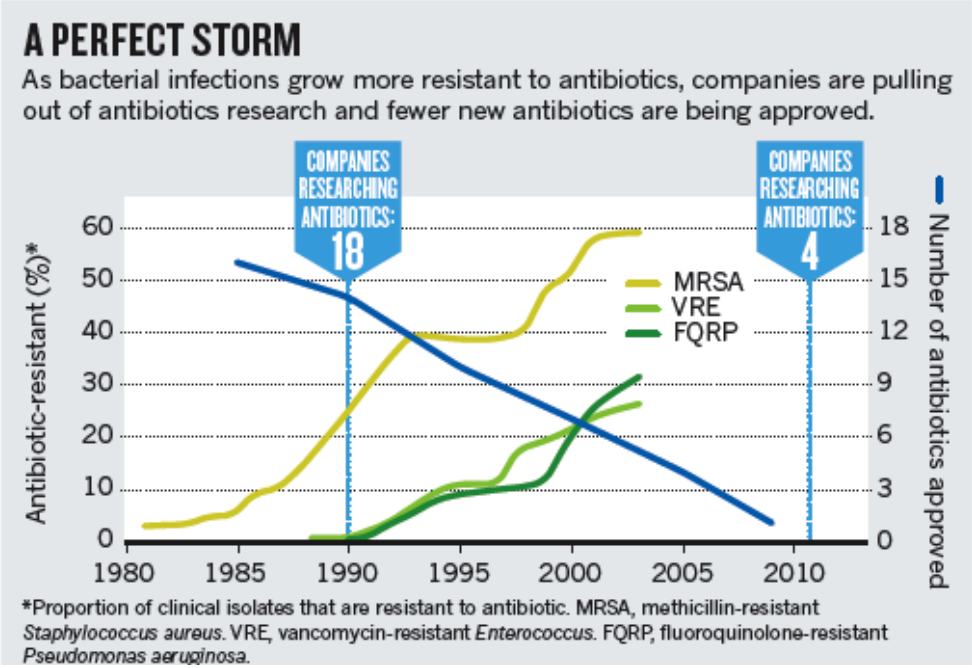
efpia

ND4BB: Need for public-private collaboration

- *The overall vision of ND4BB is to create an innovative collaborative Public-Private Partnership (PPP)-based approach that will encompass all aspects from the discovery of new antibiotics to Phase 2 and 3 clinical trials with the aim of reinvigorating antibiotic R&D*

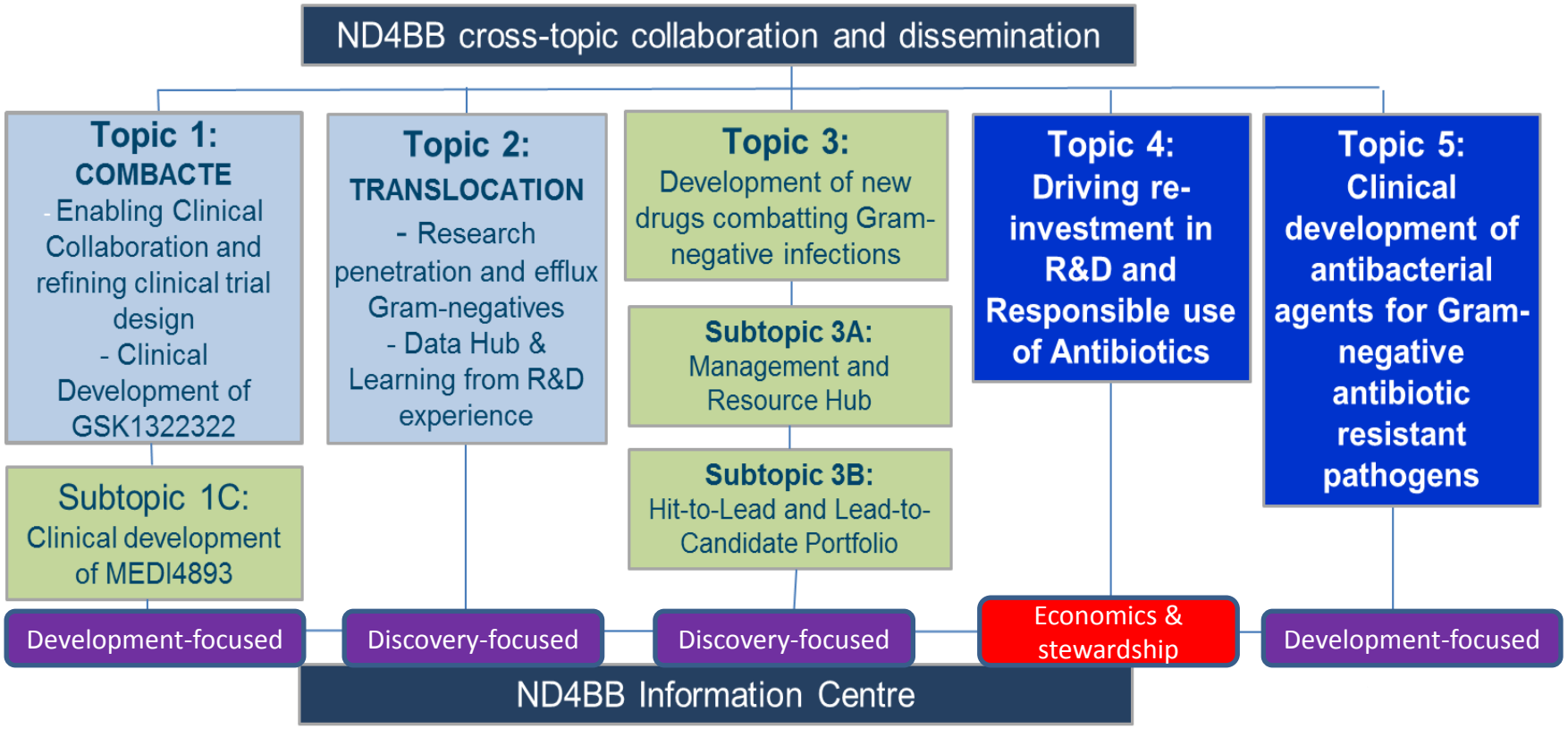
Three key challenges in antibiotic R&D:

1. **Discovery:** Unique scientific bottlenecks
2. **Development:** Challenging regulatory environment
3. **Economics:** Low return on investment



Graph adapted from reference sources:
- http:/ ec.europa.eu/research/fp7/pdf/antimicrobial_resistance_fact_sheet.pdf Accessed on line 4 July 2013
- Boucher H.Talbot G. Benjamin Jnr D. et al. Clinical Infectious Diseases (2013) doi: 10.1093/cid/cit152
- Infectious Diseases Society of America. Bad Bugs, No Drugs. July 2004

New Drugs for Bad Bugs



ND4BB Topic 4: The challenge of *Economics*

- The ND4BB Topic 4 aims to develop options for a new **sustainable commercial model** that will ensure future R&D investment in antibacterials leading to new products to combat emerging resistance **while supporting the appropriate use of all antibiotics, both old and new**.

  - There is a disconnect between the contribution that therapies to treat infection make to public health and the value attributed to antibiotics by public and payers.

  - There is a misalignment of economic incentives: a pharmaceutical company aims to generate returns through sales volumes contrasted with the public health goals of minimising resistance by limiting use through antimicrobial stewardship initiatives.

High-level concept for Topic 4

- **Create a multi-disciplinary, multi-stakeholder community** with an in-depth comprehension of the complexities of antibacterial R&D and the challenges of the current model.
  - This group will meet serially over a 3-year period to review progress, commission new research, and update stakeholders
  - Involved: Public health, payors, HTAs, academic, Industry, patients

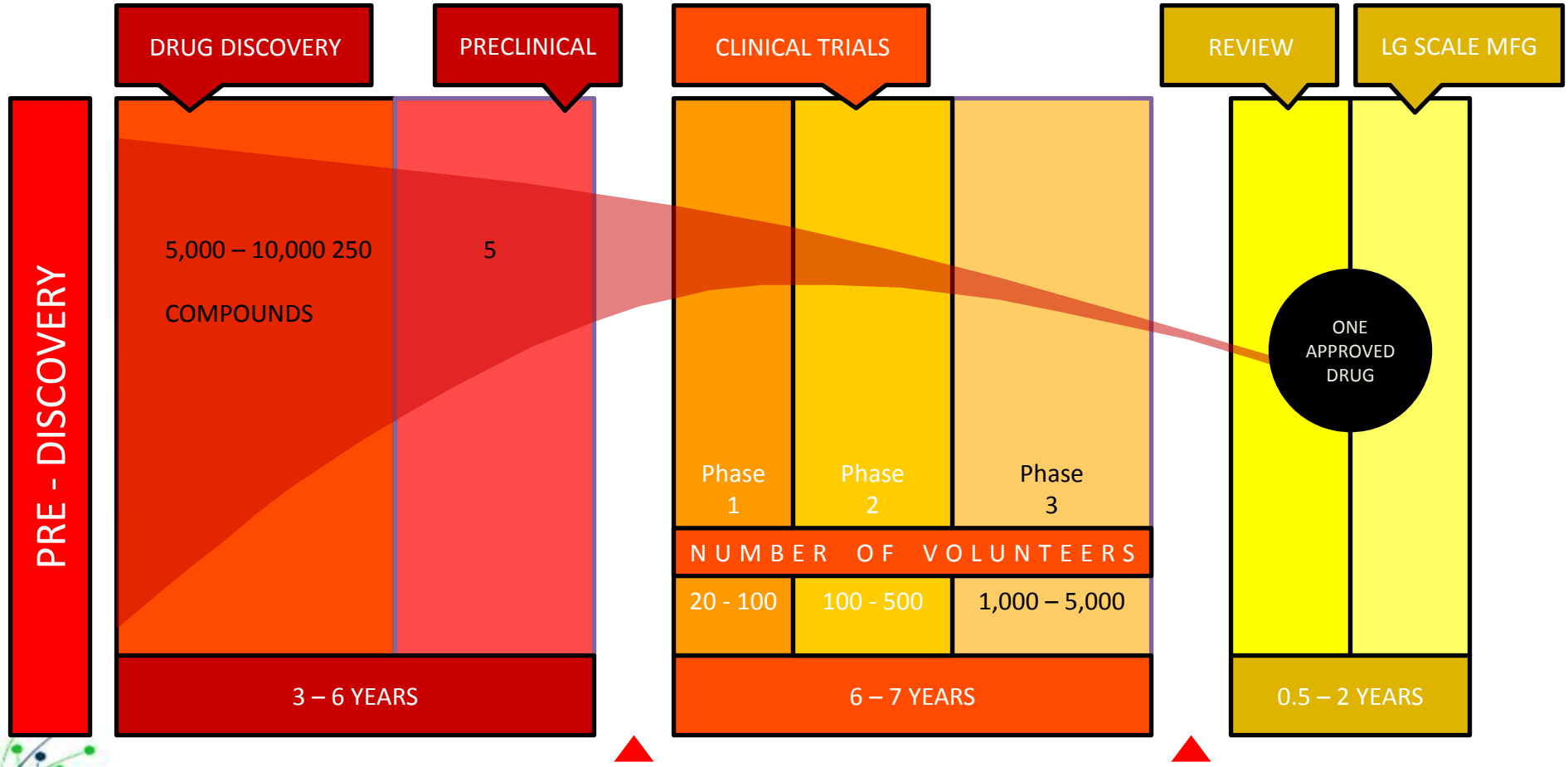
- **The multistakeholder community will conduct research** into the societal impact and cost of antibiotic resistance, and the predicted future cost to society now and into the future.

- The group will **define a research plan to define and explore alternative options**. The plan should address the need of multiple stakeholders, incentivise investment from the private sector, and provide a clear basis for action by policymakers.

- The group will **validate options through modelling** the effect on selected antibiotic case studies with recommendations for implementation. The plan will include metrics to use during implementation.

Why Topic 4? Well, one product takes 10-15 years…

… and an investment of $600-$1billion!



Adapted from a slide from Barry Eisenstein, Cubist Pharmaceuticals

And once approved, novel antibiotics are used initially as "last resort" treatment for small patient groups

Treatment usually starts with a broad-spectrum antibiotic

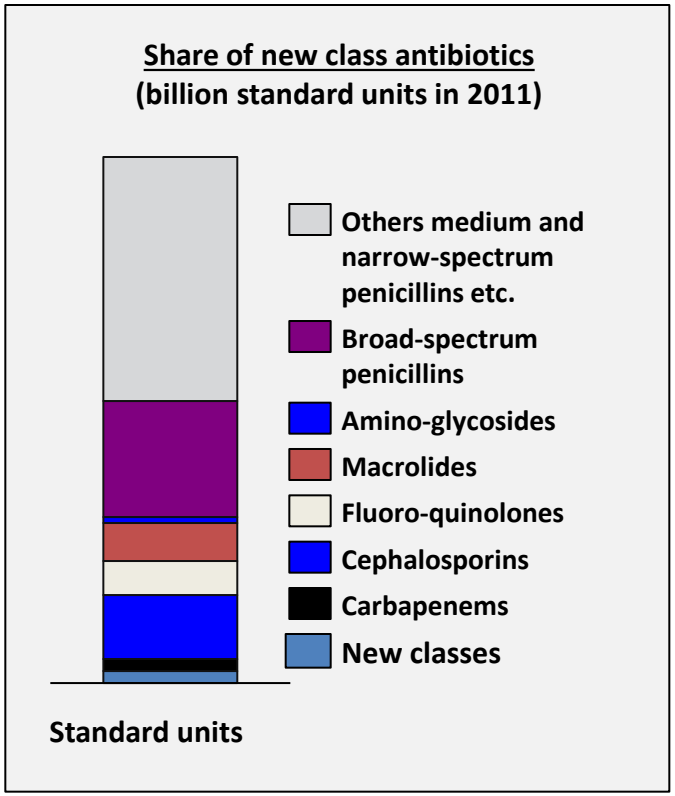
In serious infections where a delay in treatment could be fatal, a judgement is made as to which broad-spectrum antibiotic(s) are suitable

Switch antibiotic upon availability of culture results or treatment failure

Where the pathogen is identified, specialists may switch to antibiotic(s) more appropriate for that pathogen

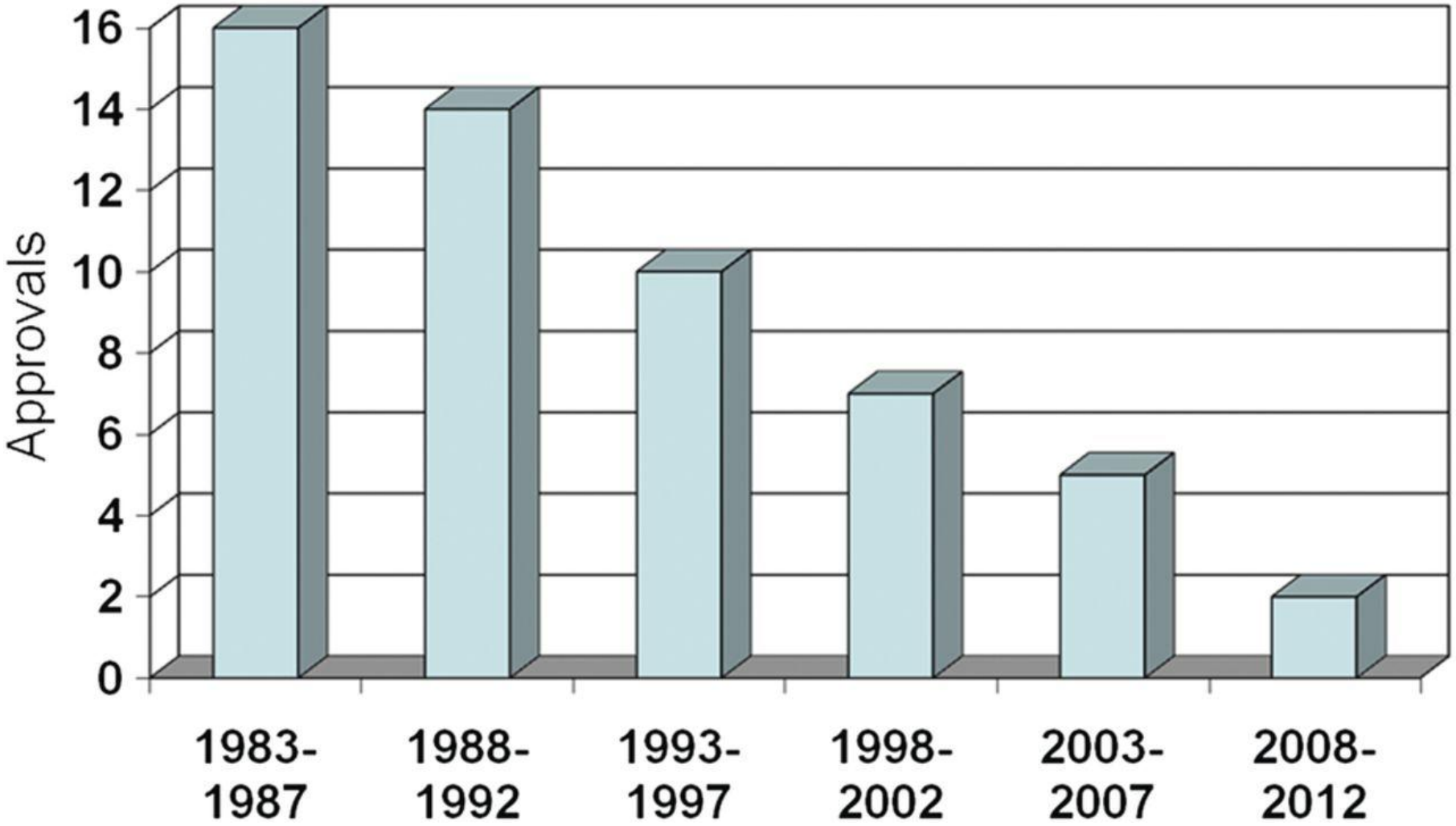
Innovative antibiotic

New and innovative products tend to be reserved as last option to ensure appropriate use and minimize risk of resistance



Source: IMS Consulting Group report for AstraZeneca from December 2011

This has contributed to the declining antibacterial pipeline



Boucher HW et al. Clin Infect Dis. 2013;cid.cit152

If we want a diverse, vibrant pipeline…

- We must find ways to fund / reward / incentivise this work
- We can't *make* companies do this work … we have to make them *want* to do this work[1]
- Topic 4's goal: Explore, define, and refine the diverse ways we might balance incentive and stewardship

[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.

Stewardship: What is *Responsible Use*?

- This is surprisingly hard to define
  - It's not zero use: It is *appropriate* use
  - But, like beauty, is this in the eye of the beholder?
  - Or, can we make this idea more concrete?

- One set of ideas for "millennium development goals"
  - All antibiotics to be given by prescription or algorithm
  - A diagnostic is used some (high!) % of the time
  - Outpatient respiratory illness receives an antibiotic a (low!) % of the time

- That's but one set of ideas
  - Topic 4 would explore other possibilities
  - Developing good language and concepts would be invaluable

Economics: Investment follows return

True in all walks of life! The importance of NPV…

- The tension between stewardship and financial reward can be viewed in economic terms
- A commonly used approach is to consider the value of an investment using a tool called NPV (net present value)
- Projan (2003)[1] estimated that other therapy areas are as much as 10x more attractive in NPV terms
- To understand this, we need to review the idea of NPV

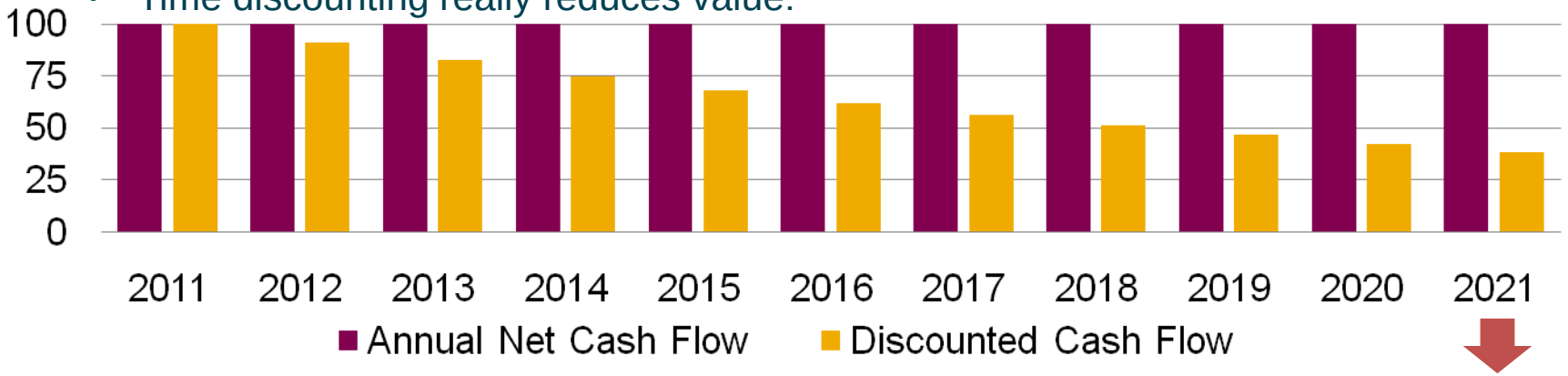
[1]Projan S: Curr Opin Microbiol 6:427-30, 2003

We interrupt this presentation to review a key idea…

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, and other factors, it is typical to discount by 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.
  - Time discounting really reduces value:

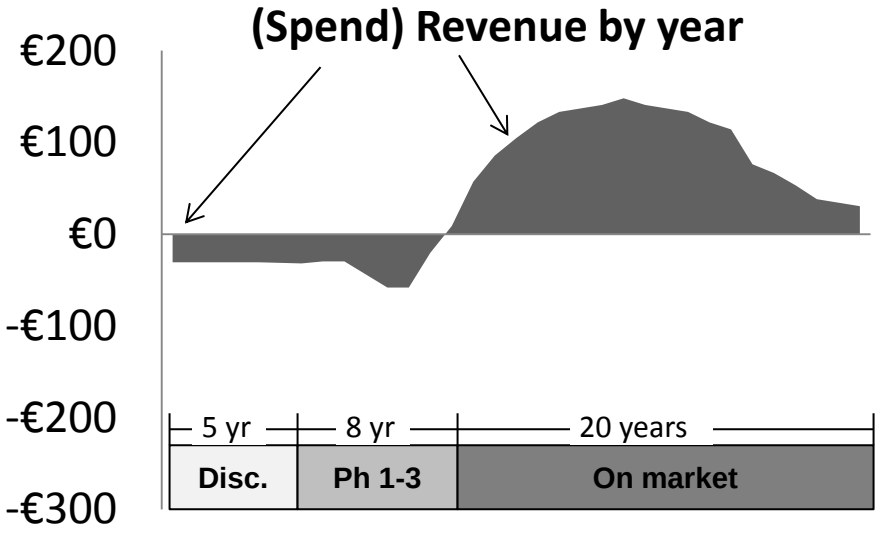


At 10% per year discount, €100 in 10yrs time is only worth €39 today

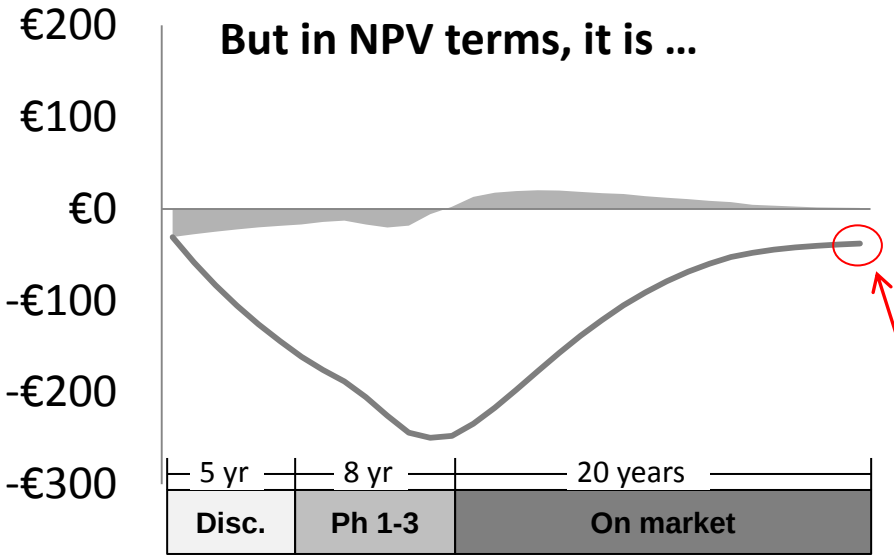
- A project's NPV is calculated by
  - Computing sales less costs for each year (Annual Net Cash Flow)
  - Each future year's Cash Flow is discounted to today, thus giving the Present Value (PV) of that future year's Cash Flow. PV is also called Discounted Cash Flow (DCF).
  - The total across all years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

Now, back to the story…

The very real effects of NPV math

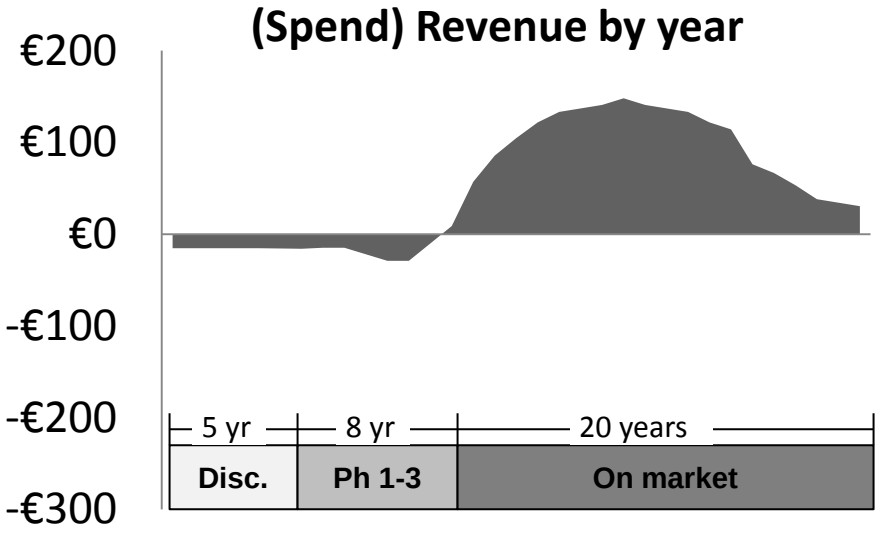


- The typical antibiotic lifecycle can be modeled from start to finish
  - Sharma, P. & Towse, A. New drugs to tackle antimicrobial resistance: analysis of EU policy options. OHE website, 2011.
  - Spellberg et al. Nat Rev Drug Discov 11: 168., 2012
- Spend and revenue by year for an average antibiotic are shown
- Note the Phase 3 bump in spend
- And then note the sales curve

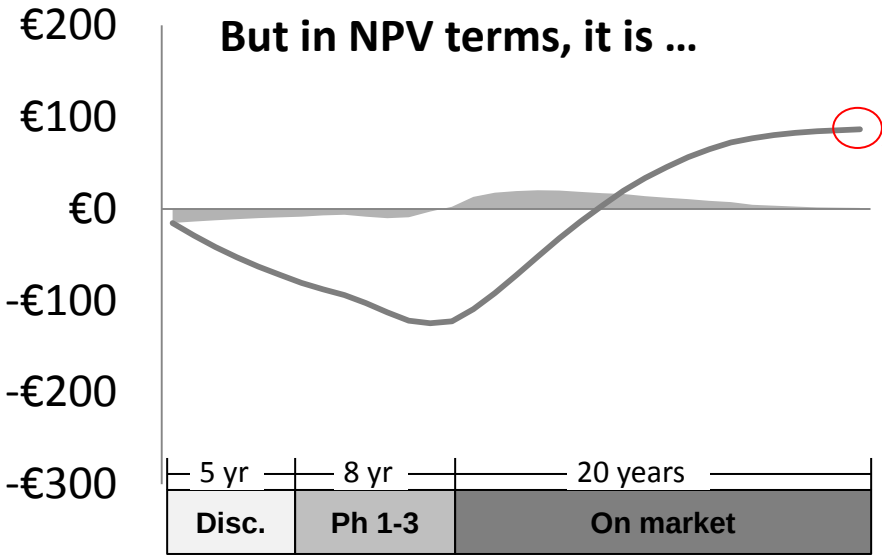


- **Now, consider this in NPV terms**
- From the standpoint of year 0 (the day you decide to start discovery), the graph shows spend & revenue discounted 10%/year
- The grey line is the cumulative NPV
- It adds up to -38m euros

Ways to change this: Alter early costs (Push)

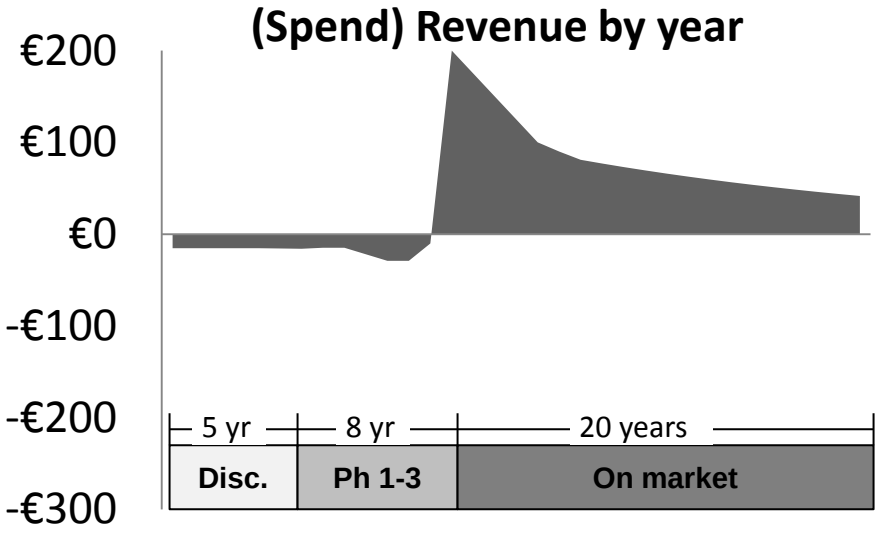


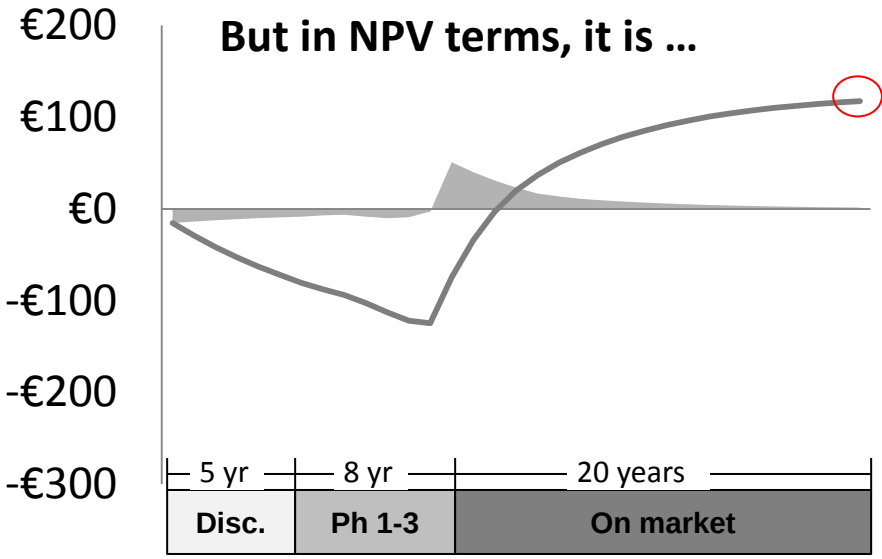
- Noting that early money is more expensive in NPV terms
- **What happens if we simply reduce the cost of the Discovery and Phase 1-3 by 50%?**
- No other changes
- Perhaps a grant or a tax credit



- Because that early spend is so significant for the NPV, this has a strong effect
- New cumulative NPV: +87m euros
- **This is kind of effect produced by IMI's R&D support**

Ways to change this: Alter revenue timing (Pull)





- Another approach?
- What happens if we combine reduced R&D costs with a revenue curve driven not by usage but by (for example) insurance-like purchase at the national or international level?
- Shown is an average of €150m/year x 5 years followed by a period of revenue declining at 10%/year
- Total revenue is ~10% less than on prior slides – but different timing

- This produces another increment
- New cumulative NPV: +117m euros

- **We don't yet know how to implement this type of incentive**
- Topic 4 would explore ways to do things such as this

Other change enablers to explore: Diagnostics

IMI has / is also supporting projects in this arena

Addressed clinical needs in antibiotics from diagnostics

- ✓ Identifies causative pathogen and resistance profile moving clinical preference away from empiric use to more personalized medicine
- ✓ Establishes higher likelihood of efficacy
- ✓ Alleviates fears of inappropriate use and concerns over resistance

Impact on model/approach generation

- **May justify** potentially higher drug cost and first line usage of novel agent when used **the right product is used in the appropriate patient**
- Adaptable to other novel models or approaches
- Stakeholders proposed coupling with the insurance model or in a portfolio approach to help select patients receiving most benefit
- Development of diagnostics helps align stakeholders efforts to appropriate use

Topic 4 would explore ways that diagnostic-guided usage might be used to change economics & improve stewardship for both development (more efficient trials) and on-market usage

Objectives

- This project should develop a vision for a new way for the public and private sectors to collaborate to ensure future generations aren't faced with untreatable infections.
- The project needs to develop new insights and collate data to inform the vision. Required outputs need to deliver clarity and agreed approaches to the following challenges:
  - Agreeing on a shared understanding of the responsible use of anti-infectives and how this can be delivered
  - Setting, communicating and acting on Public Health priorities
  - Agreeing the value of anti-infectives to society
  - Agreeing ways that investment in novel anti-infectives can be rewarded
- However, producing a vision is not sufficient. It needs to be turned into policy recommendations that are tested for implementability with those who need to turn them into practice. This will require a significant effort from the Project. The policy recommendations need to cover both current eventualities and likely future trends.

Deliverables

- Generate an analysis of the societal impact and cost of anti-infectives resistance, and the predicted future cost to society in 5, 10 and 20 years
- Create a multi-disciplinary, multi-stakeholder community with an in depth comprehension of the complexities of antibacterial R&D and the challenges of the current commercial model
- Develop concrete, implementable options for new commercial models that address the needs of multiple stakeholders, incentivize investment from the private sector and provide a clear basis for action by policymakers. These should be validated through modelling the effect on selected anti-infectives case studies.
- Provide recommendations on the implementation of any new model, both in terms of the areas to be prioritised and ensuring the understanding of stakeholders
- Improve linkage between public health perspectives on management of resistance and industry R&D programmes
- Define metrics to support and document progress towards the appropriate and sustainable use of all anti-infectives, incorporating the specific needs of developing countries.

Proposed Project Architecture: Big picture

- WP1: Creating the building blocks for a new economic model for antibiotic development and responsible use
  - WP 1A: Responsible use of antibiotics, both new and old
  - WP 1B: Setting, communicating and revising Public Health Priorities
  - WP 1C: Antibiotic valuation
  - WP 1D: Developing novel reward models
- WP2: Creation and testing of new economic models
  - Assemble these concepts into a set of coherent policy options, which tie together to address the full set of issues
  - Test these concepts for
    - Legal, political and regulatory feasibility
    - Geographical reach and differences (EU vs US vs rest of world)
    - Impact of evolving medical practice (eg use of diagnostics, novel forms of administration, etc) and other macro trends
    - Impact on real-life antibiotics in development by innovator companies
- WP3: Project management

Potential Project Partners

Function	Contribution
Public Health	Define the infectious disease priorities (including epidemiology and cost/disease burden) for antibacterials and initiatives to combat the development of resistance
Industry	Define the hurdles to current investment, describe the desired commercial landscape and input to the economic models. Provide specific data to support development of case studies
Academia	Provide expertise in economic modelling, other commercial model case studies and analytics
Clinical societies	Provide the clinical description of the need for new antibiotics and define guideline and antibacterial stewardship initiatives
Government/payers	Examines respective political, legislative, access and commercial systems in order to enable the delivery of a new commercial model

Industry Partners

- Astellas
- AstraZeneca (lead)
- Cubist
- GlaxoSmithKline R&D
- Merck
- Pfizer
- Rempex*
- Sanofi
-

**Not currently an EFPIA member*

Questions?

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