

8 Nov 2013 Workshop: Best of use new medicines legislation to bring new antibiotics to patients and combat the resistance problem



Innovative Medicines Initiative

Session 3 (R&D): Industry perspective on PPPs and the link between new business models and the regulatory framework

John H. Rex, MD, *on behalf of EPPIA and its Industry partners*



efpia

Three themes



- The economics of antibiotics
 - We can't *make* companies do this work
- What would make a difference?
 - It's not a single, simple thing. Here are 4 ideas.
 - Pediatrics; HTA & Payor; Global harmonization; Early authorisation
- The added power of the PPP: IMI & ND4BB
 - Discovery & development tools
 - Best evidence standards & harmonisation
 - New business model project



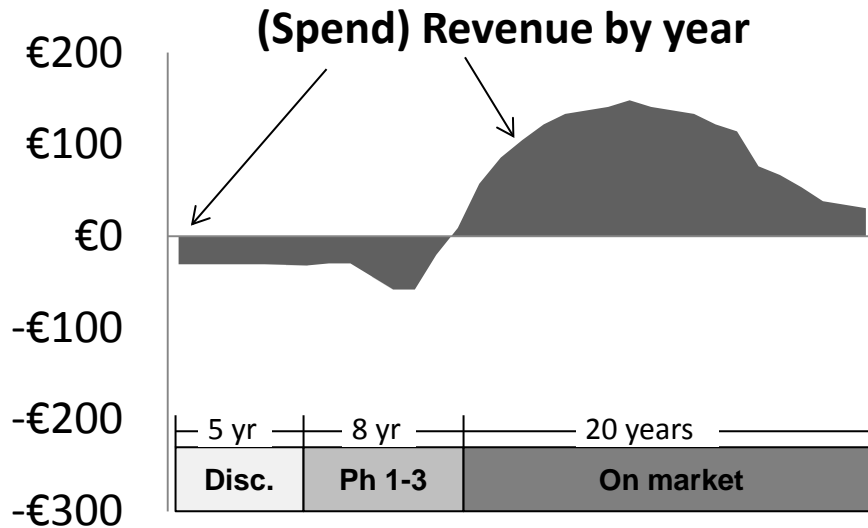
If we want a diverse, vibrant pipeline...



- We must find ways to fund & incentivize this work
 - “We can’t *make* companies do this work ... we have to make them *want* to do this work”¹
- Our answer 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

¹Spellberg 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. ²GEP Box and NR Draper in *Empirical Model-Building and Response Surfaces*, 1987, John Wiley & Sons, New York, NY.

The cost of creating an antibiotic



- The typical antibiotic lifecycle can be modeled from start to finish¹
- The model allows for failed drugs
- Spend and revenue by year are best 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 spend (years 1-13): €450m
- Approximate sales (next 20 years) : €1900m
- **But, we've forgotten about NPV!**

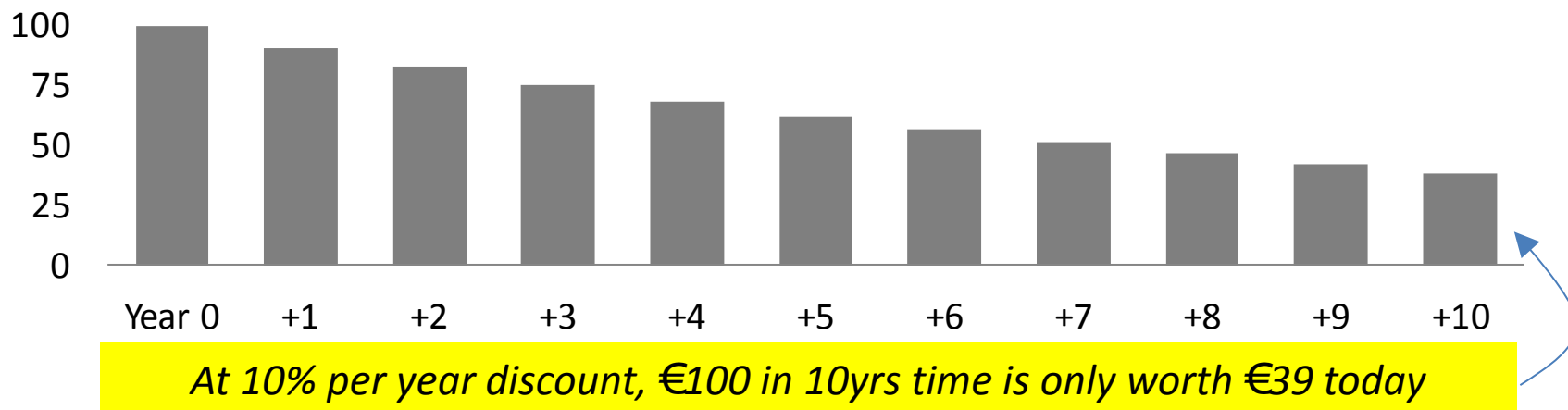
¹Sharma, P. & Towse, A. New drugs to tackle antimicrobial resistance: analysis of EU policy options. OHE website, 2011; Spellberg et al. Nat Rev Drug Discov 11: 168., 2012

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

Sidebar: NPV (Net Present Value)

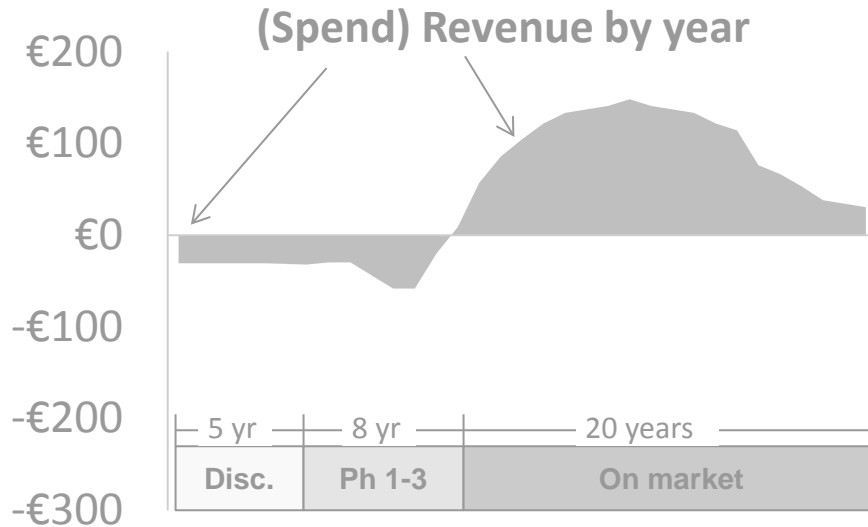
How much is an investment worth in today's terms?

- 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 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**

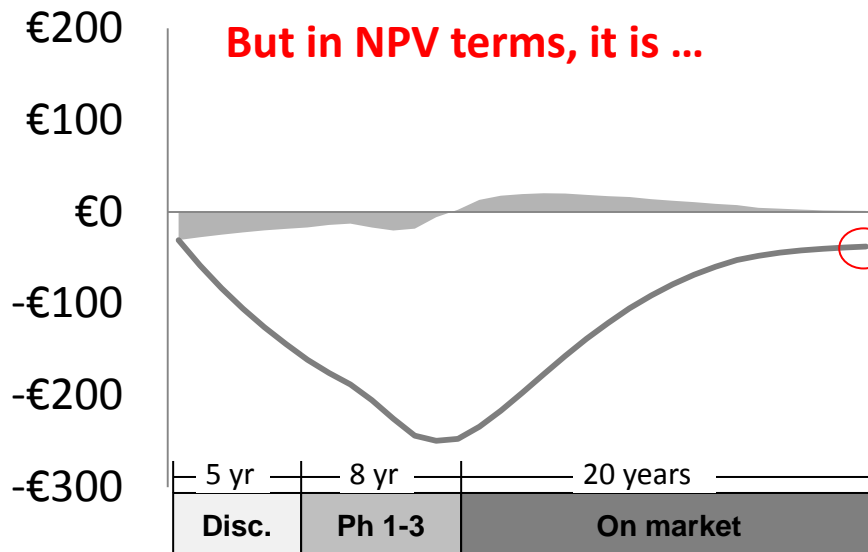
The very real effects of NPV math



- **Now, consider this in NPV terms**

- From the standpoint of year 0 (the day you decide to start discovery), the graph shows spend & revenue discounted 10%/year

- The grey line is the cumulative NPV



- It adds up to a loss (-38m euros)

- To restore vitality to the pipeline and ensure we have the life-saving drugs we will need in the future, we have to move this model back into positive territory.

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Pediatrics; HTA & Payor Requirements



- Pediatric programs
 - Reduced requirements would speed access
 - Example: Ceftaroline is a recently registered antibiotic
 - Its FDA + EMA pediatric commitments entail studies of ~750 patients over a 6-year period and at a global cost of > \$80m
- Evidence vs. access¹: HTA and payor requirements
 - These data packages will necessarily be smaller
 - Our clinical trials by design cannot routinely seek superiority outcomes
 - Untreated infections are lethal, we must always use a fully dosed comparator, and we must *exclude* the patient if the pathogen is resistant!
 - Reimbursement criteria must be adapted (more on this later)

¹Woodcock J. Evidence vs. access: Can twenty-first century drug regulation refine the tradeoffs? Clin Pharm Ther 91:378-80, 2012.

Global Harmonization; Early Authorisation



- Global harmonization
 - Regulatory clarity and simplicity are helpful in and of themselves: Reductions in uncertainty are very powerful
 - Tier B and Tier C can shrink trial programs
 - As we begin to use these ideas, we need to be consistent
- Early / earlier authorisation may be possible
 - Conditional approval with PK-PD data in patients?
 - Exceptional circumstances? Tier C¹ programs may fit here

¹Rex JH et al. The Lancet Infectious Diseases Volume 13(3):269 – 275, 2013

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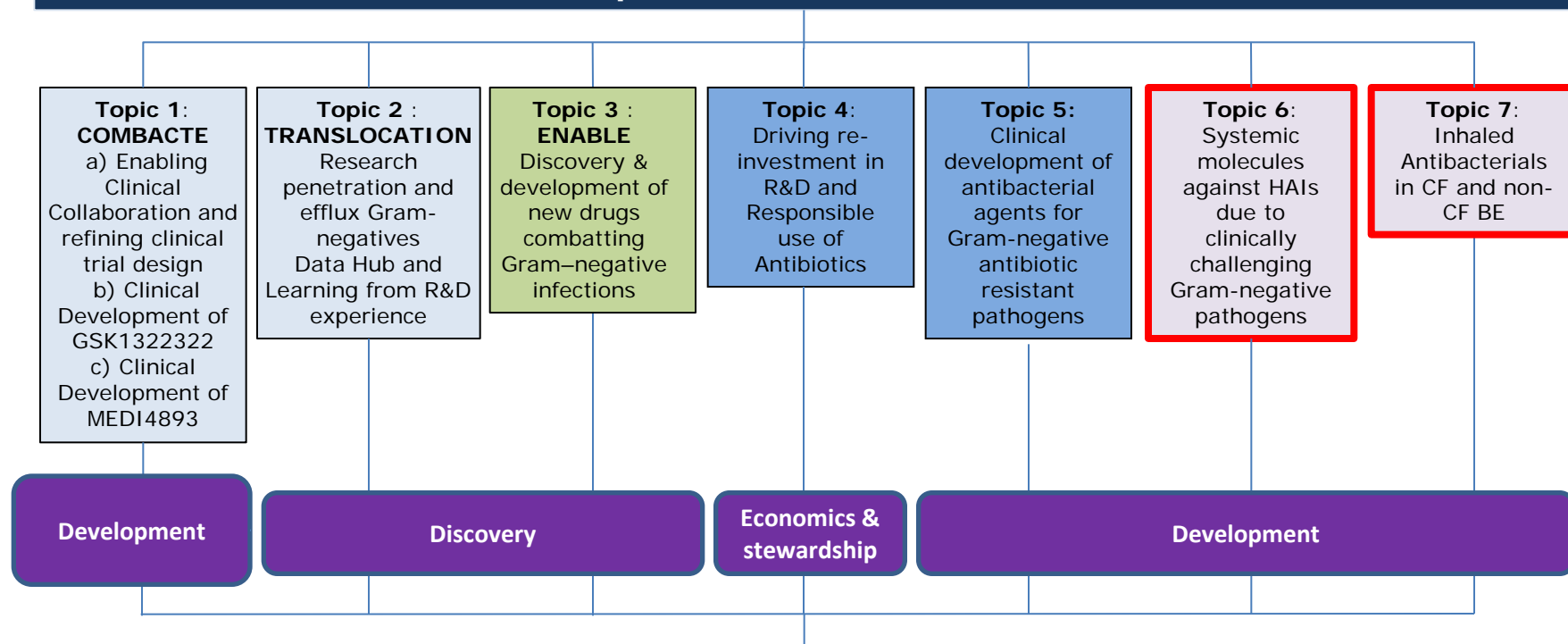


Happy Second Birthday on 17 Nov 2013!

ND4BB: Proposed Program, from 2014



ND4BB cross topic collaboration and dissemination



ND4BB Information Centre –

All data generated is submitted and is accessible to all consortium partners

Development, Discovery, & Economics

Call 6

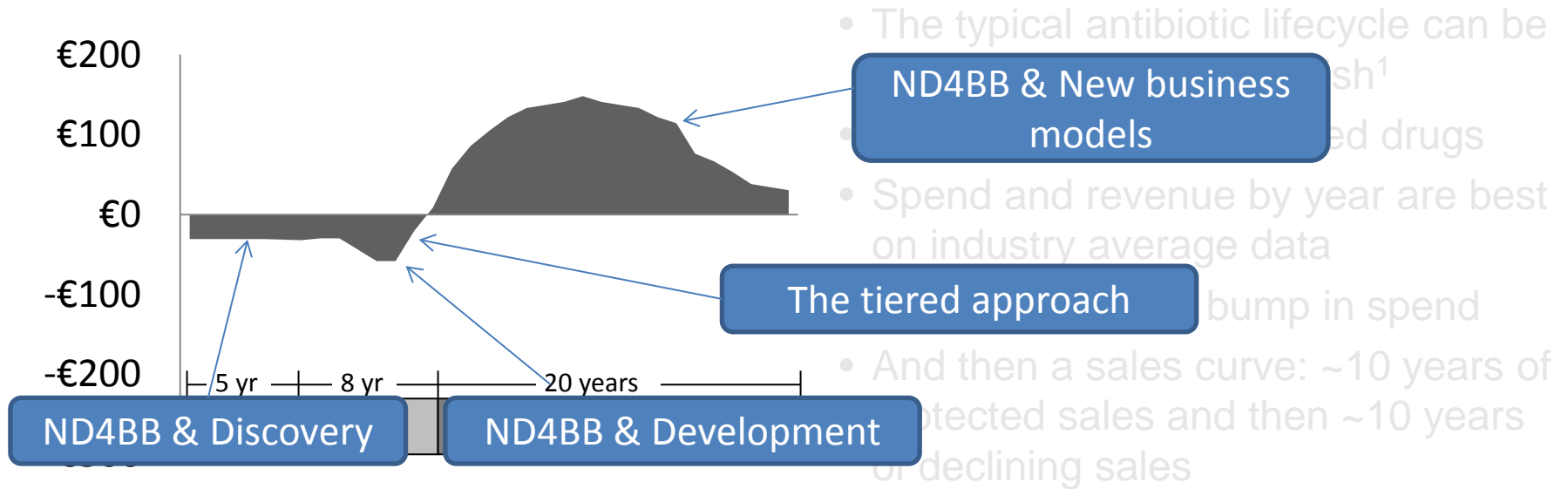
Call 9

Call 8

Call 11



We're now tackling the entire model!



- With ND4BB and tiered approach, we are truly taking a systems approach to this problem
- ND4BB's Discovery and Development support + the tiered approach is already having an impact
- And we're also pleased to be starting Topic 4...

Topic 4: Just now starting: Economics & Stewardship



- Just now starting, no catchy name yet
 - “Driving re-investment in R&D and Responsible use of antibiotics”
 - DRIIRADARUOA? A better name is coming, I promise
- Aim: Address the tension between economics & stewardship
 - Create a multi-disciplinary, multi-stakeholder community with an in depth comprehension of challenges
 - Develop implementable options for new commercial models that address the needs of multiple stakeholders,
 - Validate options through modelling
- We expect Topic 4 to explore a broad range of approaches
 - Fee-based approaches. Insurance-based approaches
 - We don't know how to do these ... yet!



In closing (1)



- Thank you for organizing this discussion
 - Antibiotics are the most life-saving drugs invented
 - But, a post-antibiotic era is now a real possibility
- The incredibly thin pipeline has many causes
 - A path to a diverse, sustainable pipeline must be found
- The solution will require many hands
 - Discovery: Difficult
 - Development: Difficult
 - Economics: Difficult



In closing (2)



- Thank you for organizing this discussion
 - Antibiotics are the most life-saving drugs invented
 - But, a post-antibiotic era is now a real possibility
- The incredibly thin pipeline has many causes
 - A path to a diverse, sustainable pipeline must be found
- **We've made a lot of progress! Thank you!**
 - Discovery: *ND4BB is opening doors*
 - Development: *Now improved! ND4BB will augment*
 - Economics: *Tiered framework; new business models*

A small graphic in the bottom left corner showing a network of green and blue dots connected by thin lines, resembling a molecular structure or a data network.

With many thanks to all who are part
of these amazing endeavours!

