OECD, October 11th 2016

DRIVE-AB –

DRIVING RE-INVESTMENT IN R&D AND RESPONSIBLE ANTIBIOTIC USE

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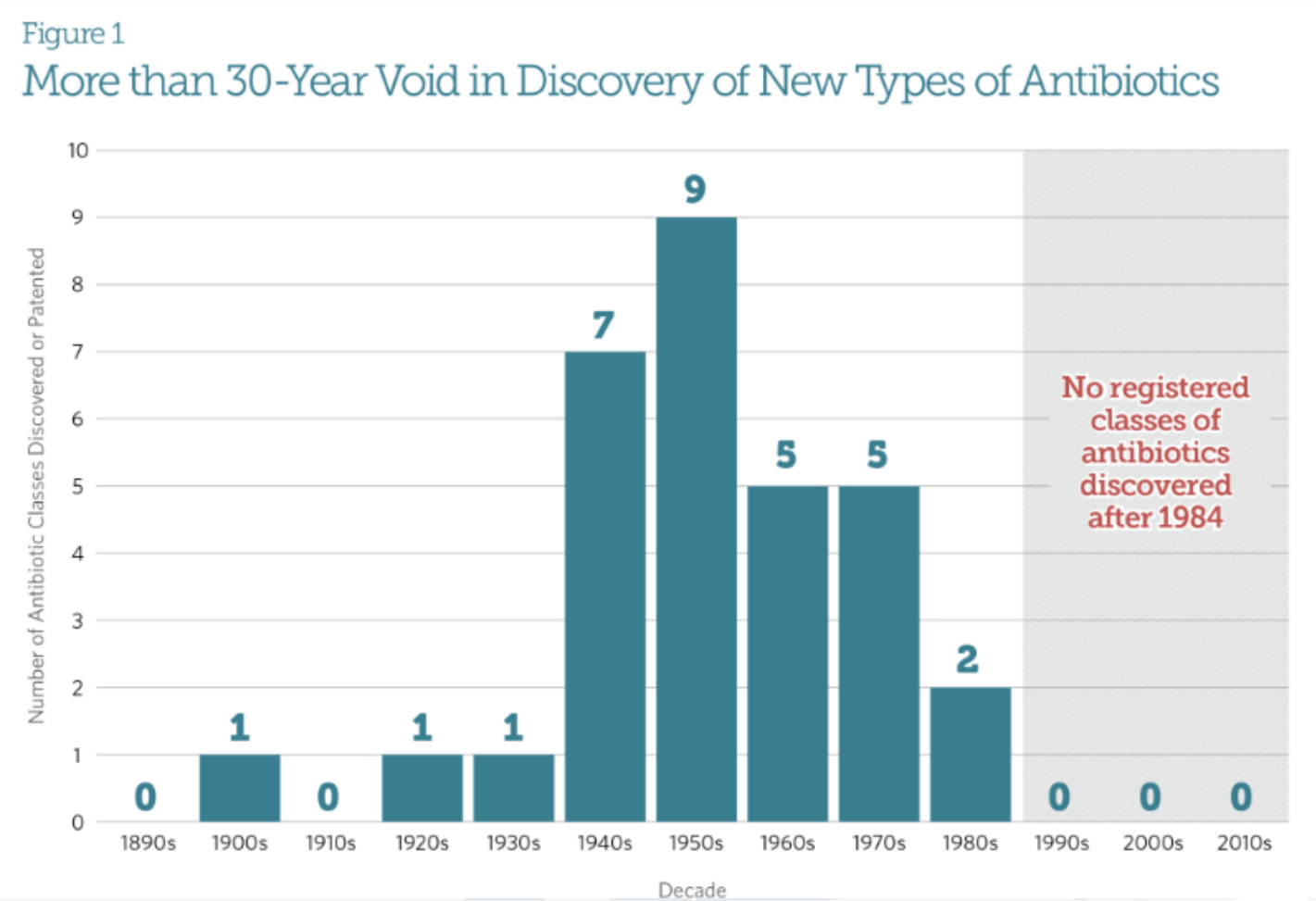
Antibiotic discovery void



Source: Pew Charitable Trusts. A Scientific Roadmap for Antibiotic Discovery. 2016.

Antibiotic candidates in clinical trials

A data table from THE PEW CHARITABLE TRUSTS | May 2016

Antibiotics Currently in Clinical Development

As of March 2016, an estimated 37 new antibiotics[1] with the potential to treat serious bacte
success rate for clinical drug development is low; historical data show that, generally, only 1
clinical trials) will be approved for patients.* Below is a snapshot of the current antibiotic pip
external expert. It will be updated periodically, as products advance or are known to drop ou
numbers may not be sequential. Please contact abxpipeline@pewtrusts.org with additions o

37 potential antibiotics

Drug name	Development phase[2]	Company	Drug class	Expected activity against resistant Gram-negative ESKAPE pathogens?[3]	Expected activity against a CDC urgent threat pathogen?[4]	Potential indication(s)?[5]
WCK 4873[15]	Phase 1	Wockhardt Ltd.	Second-generation ketolide	No	No	Bacterial infections
MGB-BP-3	Phase 1[10]	MGB Biopharma Ltd.	DNA minor groove binder			
OP0595 (RG6080)	Phase 1[10]	Meiji Seika Pharma Co. Ltd./Fedora Pharmaceuticals Inc. (Roche licensee)	Beta-lactamase inhibitor			
BAL30072	Phase 1	Basilea Pharmaceutica Ltd.	Monosulfactam			
CRS3123	Phase 1	Crestone Inc.	Methionyl-tRNA synthetase (MetRS) inhibitor			
LCB01-0371	Phase 1[10]	LegoChem Biosciences Inc.	Oxazolidinone	No	No	Bacterial infections
TD-1607	Phase 1	Theravance Biopharma Inc.	Glycopeptide-cephalosporin heterodimer	No	No	**Acute bacterial skin and skin structure infections,[6] hospital-acquired pneumonia/ventilator-associated bacterial pneumonia,[6] bacteremia[6]**
WCK 2349[15]	Phase 1	Wockhardt Ltd.	Fluoroquinolone (WCK 771 pro-drug)	No	No	Bacterial infections
WCK 771[15]	Phase 1	Wockhardt Ltd.	Fluoroquinolone	No	No	Bacterial infections
Zidebactam+Cefepime	Phase 1	Wockhardt Ltd.	Novel beta-lactamase	Possibly	Possibly	Complicated urinary tract infections,[6] hospital-acquired bacterial pneumonia/

Only one novel class against Gram-negatives (Macrocycle LptD inhibitor), yet 16 against CDC urgent pathogens

Source: Pew Charitable Trusts and Morgan, ICID, 2016.

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Significant global attention

Convergence of principles:

- Need for both “push” and “pull” mechanisms
- Delinkage (i.e., revenues delinked from volumes sold)
- Access and sustainable use are integral
- Global collaboration and financing necessary

What is DRIVE-AB?

- **DRIVE-AB** is the EU's Innovative Medicines Initiative project in "New Drugs for Bad Bugs" (ND4BB) programme focusing new economic models to stimulate greater antibiotic innovation
- **16 public and 7 private partners from 12 countries**
- **Project duration**: 3 years (Oct 2014 – Sept 2017)

- DRIVE-AB's vision is **to transform the way policymakers stimulate antibiotic innovation and to ensure that new antibiotics are used sustainably and available equitably**

DRIVE-AB's principles

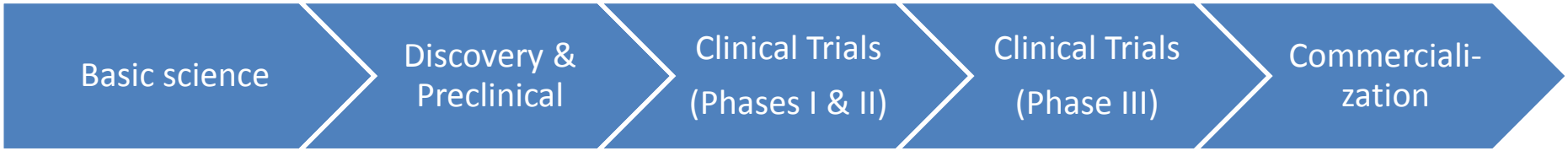
Access for patients in need

Innovation towards creating new antibacterials

Sustainable use of novel antibacterials

Hoffman et al. (2015)

DRIVE-AB's shortlist of incentives



Grants

Non-Profit Antibiotic Developer

Market Entry Rewards

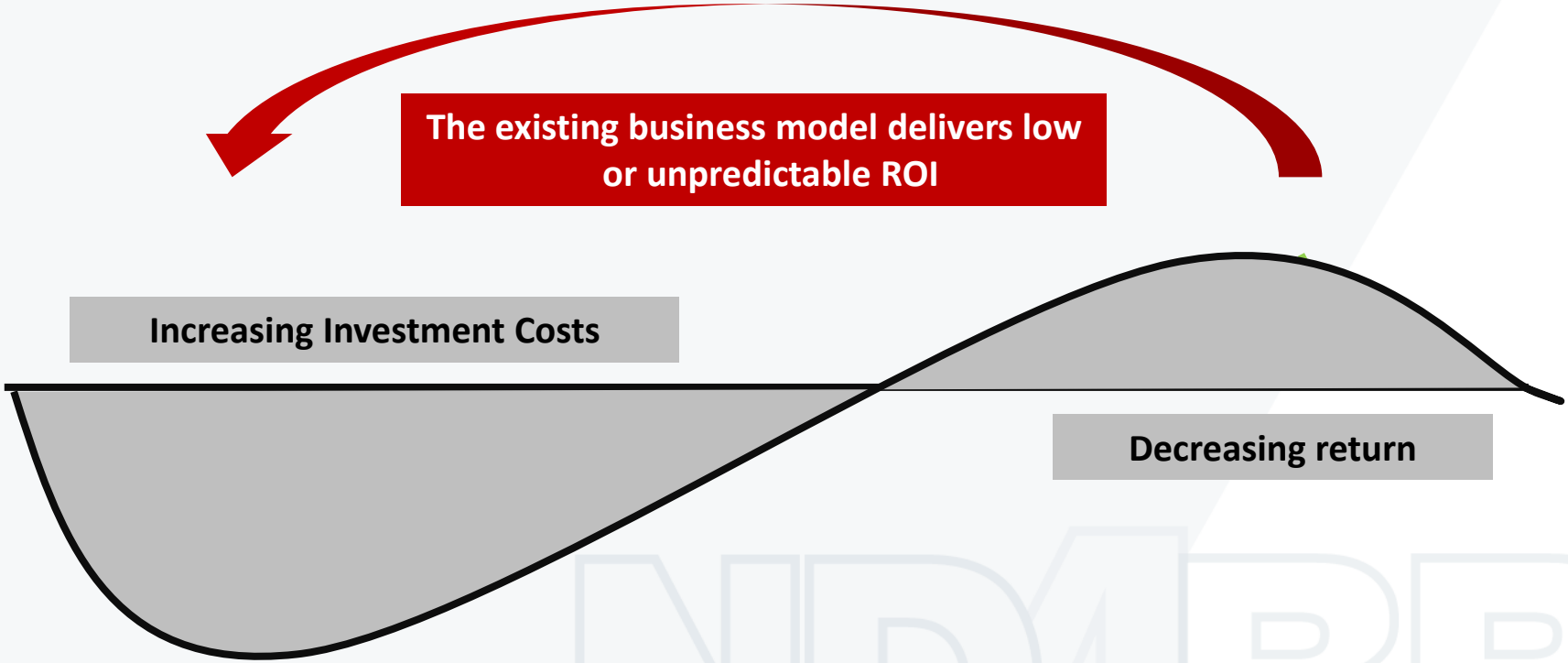
Insurance Licenses

Diagnosis Confirmation Model

one example

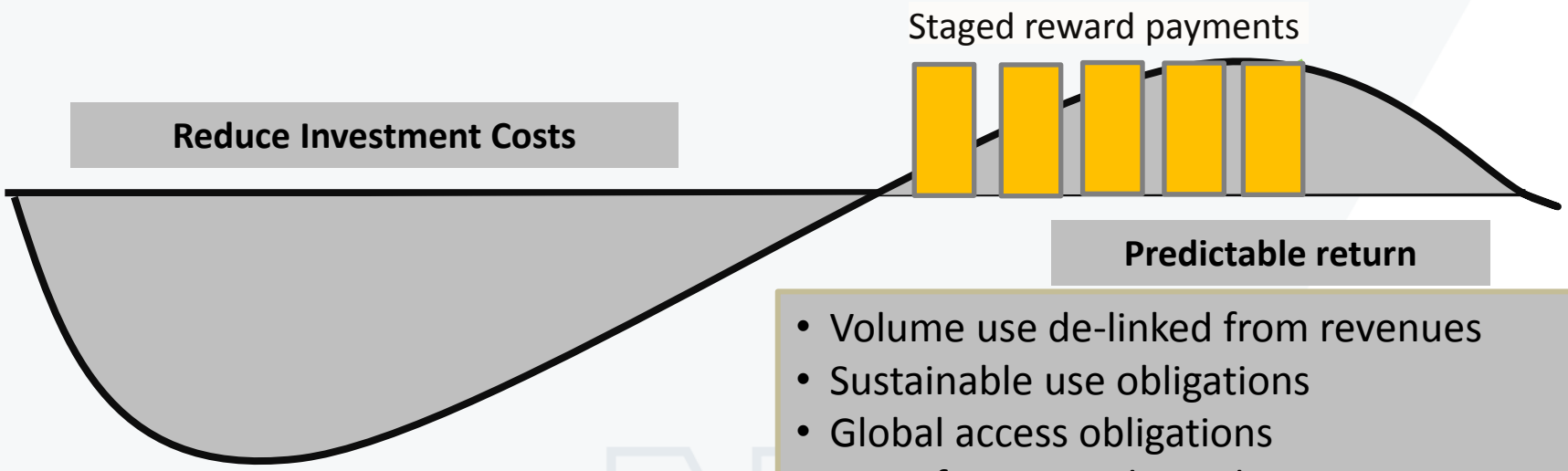
MARKET ENTRY REWARDS

Traditional antibiotic business model



Source: Adapted from Payne D et al, Phil Trans R Soc B 370:20140086

Market entry reward model



- Development risk/complexity remains

- Volume use de-linked from revenues
- Sustainable use obligations
- Global access obligations
- Manufacture and supply at cost
- Many details to be defined requires case studies /pilot antibiotics

Source: Adapted from Payne D et al, Phil Trans R Soc B 370:20140086

What type of R&D will it stimulate?

- Most pressing public health threats, i.e., high-priority, global pathogens, due to potential high price tag
  - However, only one novel class against Gram-negatives right now, so may not apply in the near future
  - Discovery needs continued support (JPIAMR, IMI, NIH, CARB-X, UK/China Global Innovation Fund, and more)

How will it promote access?

- Affordable prices for countries in compliance with sustainable use policies
- Innovator is required to seek regulatory approval (which may include other certifications like WHO prequalification)

How will it promote sustainable use?

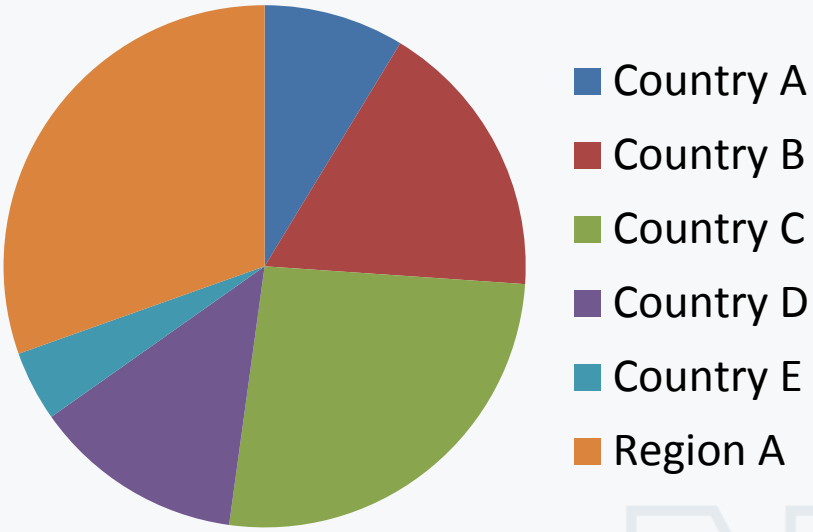
Innovator's obligations:

- No promotion
- Transparency of consumption figures including a warning system alerting when sudden significant increases in consumption occur
- And more

Countries who access the antibiotic at affordable prices:

- Restrictions on physician types or settings where the antibiotic can be used
- Surveillance systems
- And more

How might it work?



- Global Fund or
- National/regional contributions in line with common principles regarding financing amounts, priority pathogens, design of reward
  - Initial payment at regulatory approval
  - Access obligations after a threshold is met

DRIVE-AB continues to research…

Particularly for Market Entry Rewards

- How much does the total reward need to be to incentivize private sector to remain and new actors to enter anti-infective space? How can other incentives be used to reduce the overall price tag but achieve the same benefit?
- How to set unit prices in order to encourage sustainable use but not create out-of-reach pricing?
- What conditions would stop payments?
- What happens after patent expiry, when generic products can enter the market?
- And more…

Discussion questions

- A large pull mechanism, like a Market Entry Reward, will require **multi-country collaboration**. Is there sufficient interest for countries to commit to finance these rewards, given that they are well designed and aimed at the greatest public health threats?
- Can financing countries agree to a **priority list of the greatest public health threats** which are tied to rewards?
- In order to ensure the maximum longevity of R&D investments, **sustainable use policies** should be put in place. Can **multi-country norms** be adopted? For example, restrictions that certain antibiotics are only used for human health.