AFFORDABLE ORPHAN DRUGS: A ROLE FOR NOT-FOR-PROFIT ORGANISATIONS

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Overview

- Background
- Current situation and growing challenges
- Future opportunities and ideas

Background

- Between 5 000 and 8 000 distinct rare diseases exist
- Total number of people affected by rare diseases in the EU is estimated at between 27 and 36 million
- Medicines for rare diseases
  - Market failure of drugs for rare diseases
    - “High R&D costs
    - Very small market
    - Low return on investment
    - Commercial viability”

Orphan drug legislation

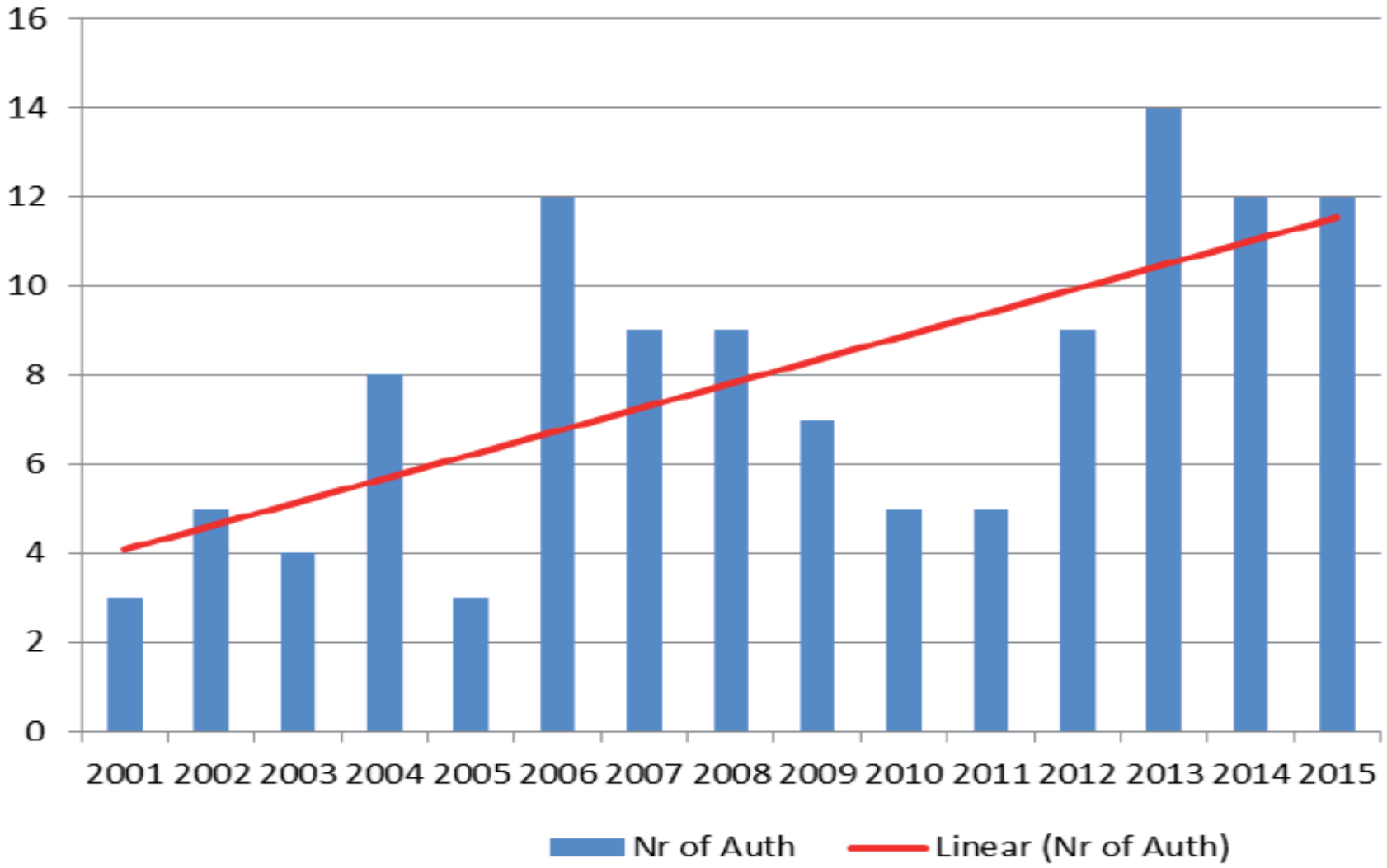
- To qualify for orphan designation, a medicine must meet **all** these criteria:
  - it must be intended for the treatment, prevention or diagnosis of a disease that is **life-threatening or chronically debilitating**;
  - the prevalence of the condition in the EU must not be more than 5 in 10,000 **or** it must be unlikely that marketing of the medicine would generate sufficient returns to justify the investment needed for its development;
  - no satisfactory method of diagnosis, prevention or treatment of the condition concerned can be authorised, or, if such a method exists, the medicine must be of significant benefit to those affected by the condition

EU: Regulation(EC) No 141/2000

Orphan drug legislation

- The main objective of the Orphan Regulation is to ensure that patients suffering from rare conditions have the same quality of treatment as any other patient in the EU
- Incentives:
  - marketing exclusivity in the EU for 10 years after approval
  - protocol assistance
  - access to the Centralised Procedure for Marketing Authorisation

Table 5: Number of marketing authorisations



http://ec.europa.eu/health/files/orphanmp/doc/orphan_inv_report_20160126.pdf

Example: elosulfase alfa for Morquio A syndrome

Elosulfase alfa - Vimizim

- Safety and efficacy assessed in a randomized, double-blind, placebo-controlled, Phase 3 clinical trial of 176 patients with Morquio A syndrome, ranging in age from 5 to 57 years
- The majority of the patients presented with short stature, impaired endurance, and musculoskeletal symptoms.

- The primary endpoint was the change from baseline in 6 minute walking distance compared to placebo at week 24

- Secondary endpoint 3-minute stair climb test

6-minute walk test (metres)

	Baseline	Week 24	Change	Difference
Vimizim	204m	243m	+37m	22.5 (p=0.017)
Placebo	212m	225m	+14m	

3-minute stair climb test (stairs/minute)

	Baseline	Week 24	Change	Difference
Vimizim	30	35	+4.8	1.1 (p=0.49)
Placebo	30	34	+3.6	

£198,000
per patient per year

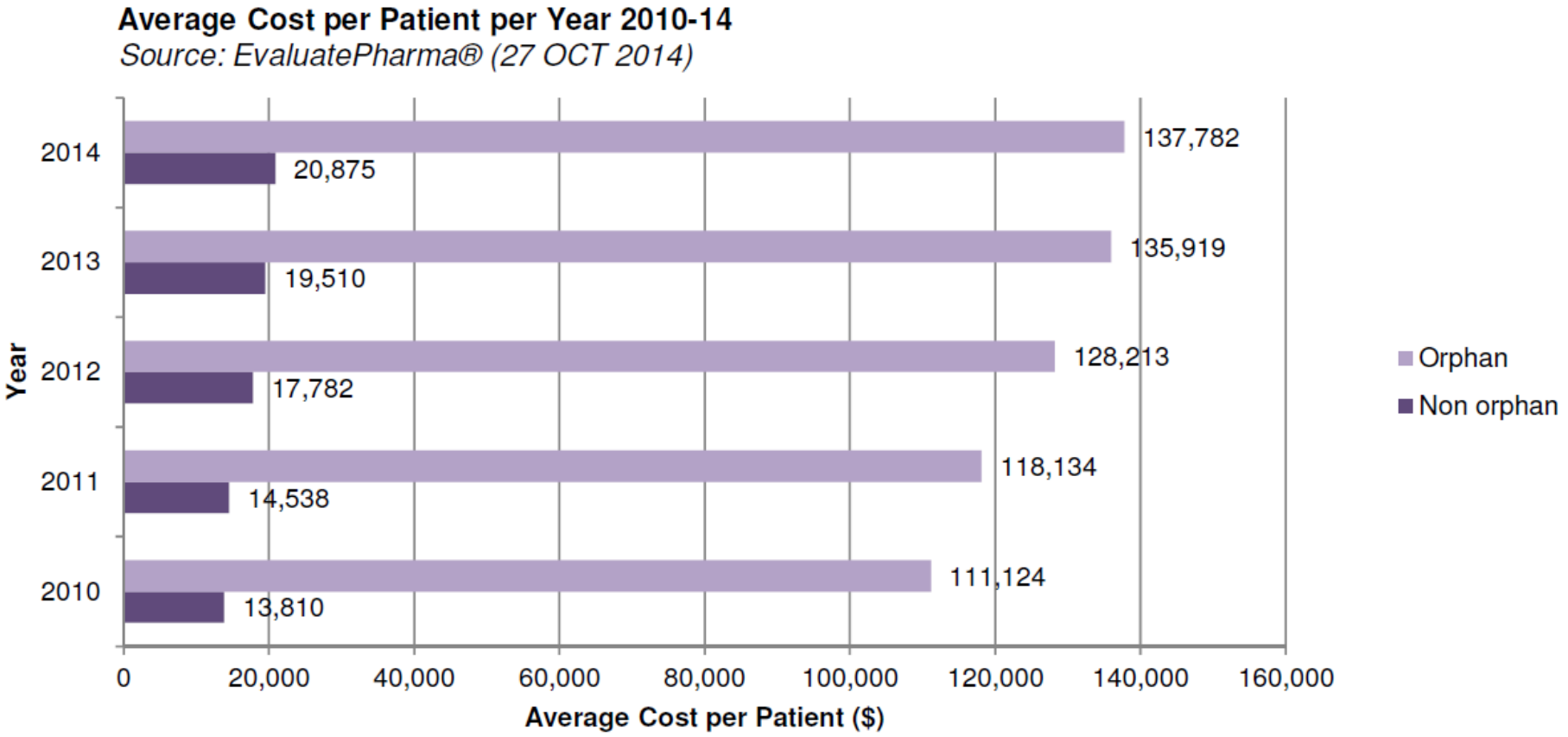
Example: marathon for Duchenne Muscular Dystrophy

Emflaza (deflazacort)

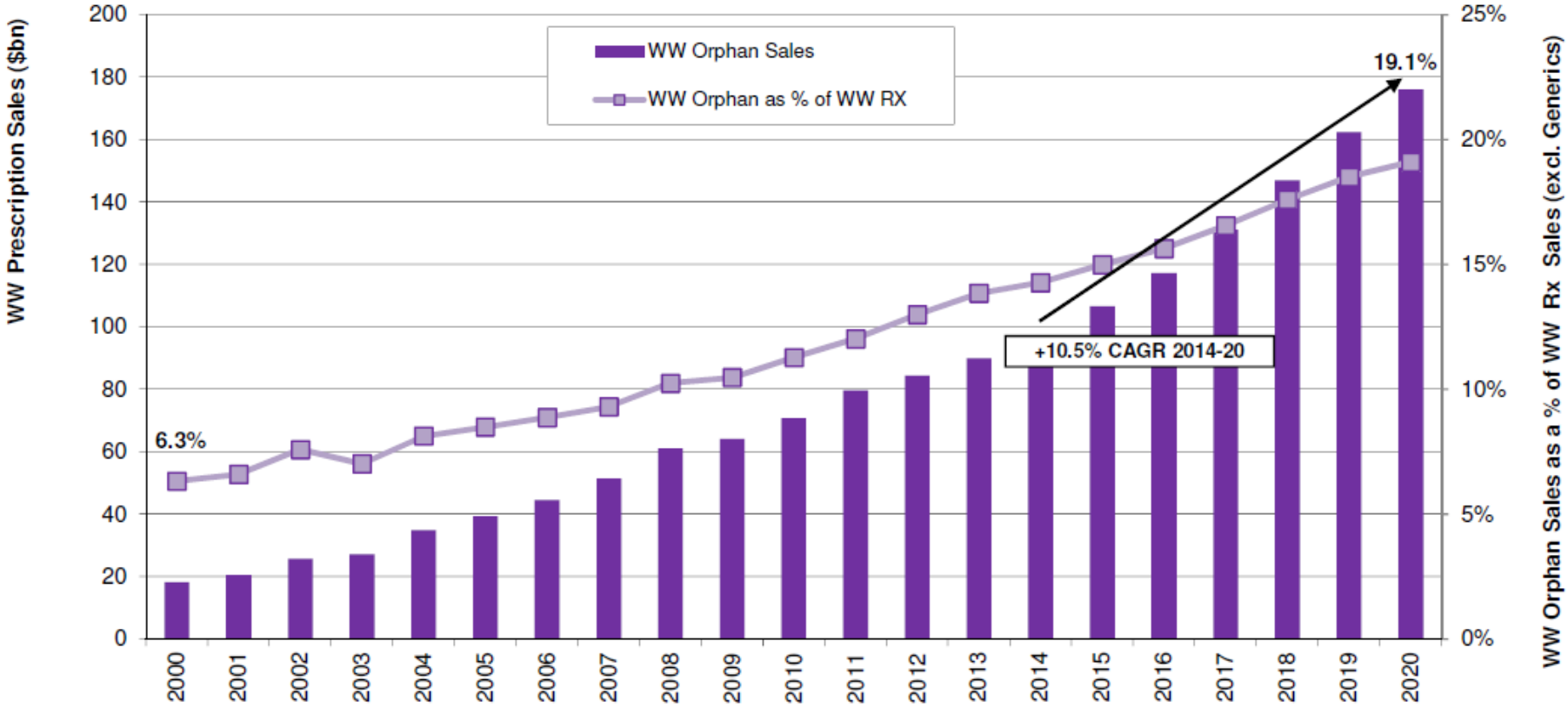
- Marathon Pharmaceuticals LLC, got FDA approval for a steroid to treat Duchenne Muscular Dystrophy (DMD), a rare and deadly muscle-wasting disease.
- This approval also got the company a valuable FDA voucher it can use to accelerate the review process for a different future drug, or sell to another company for millions of dollars.
- The steroid is available for less than **$2,000 a year** in other countries.
- Marathon tried to charge **$89,000 a year** for it in the U.S. - even though it didn't invent the drug and won FDA approval based in part on trial data from the 1990s that others produced.

Cost of orphan drugs and company profits

- Market exclusivity = monopoly
- Monopoly = no price competition
- No price competition = high prices!



Worldwide Orphan Drug Sales & Share of Prescription Drug Market (2000-20)
Source: EvaluatePharma® (27 OCT 2014)



The global orphan drugs market is expected to reach **US$176bn** by 2020, and account for **19%** of total branded prescription drug sales

Orphan adoption

- “Companies are flocking to orphan drugs partly because of the difficulty in finding significantly better treatments for common diseases that already are well supplied with medicines”
- “Even when diseases are extremely rare, orphan drugs can still be profitable”

Nature 508, 16–17 (03 April 2014) doi:10.1038/508016a

- [in relation to disease segmentation] “Use of such artificial orphan populations to obtain orphan-drug designation and its related benefits would divert resources away from R&D of drugs for true orphan diseases and conditions” (FDA)

- "The Orphan Drug Act has been used by some manufacturers of drugs that are highly profitable to increase their profits and block competition" (Henry A. Waxman)

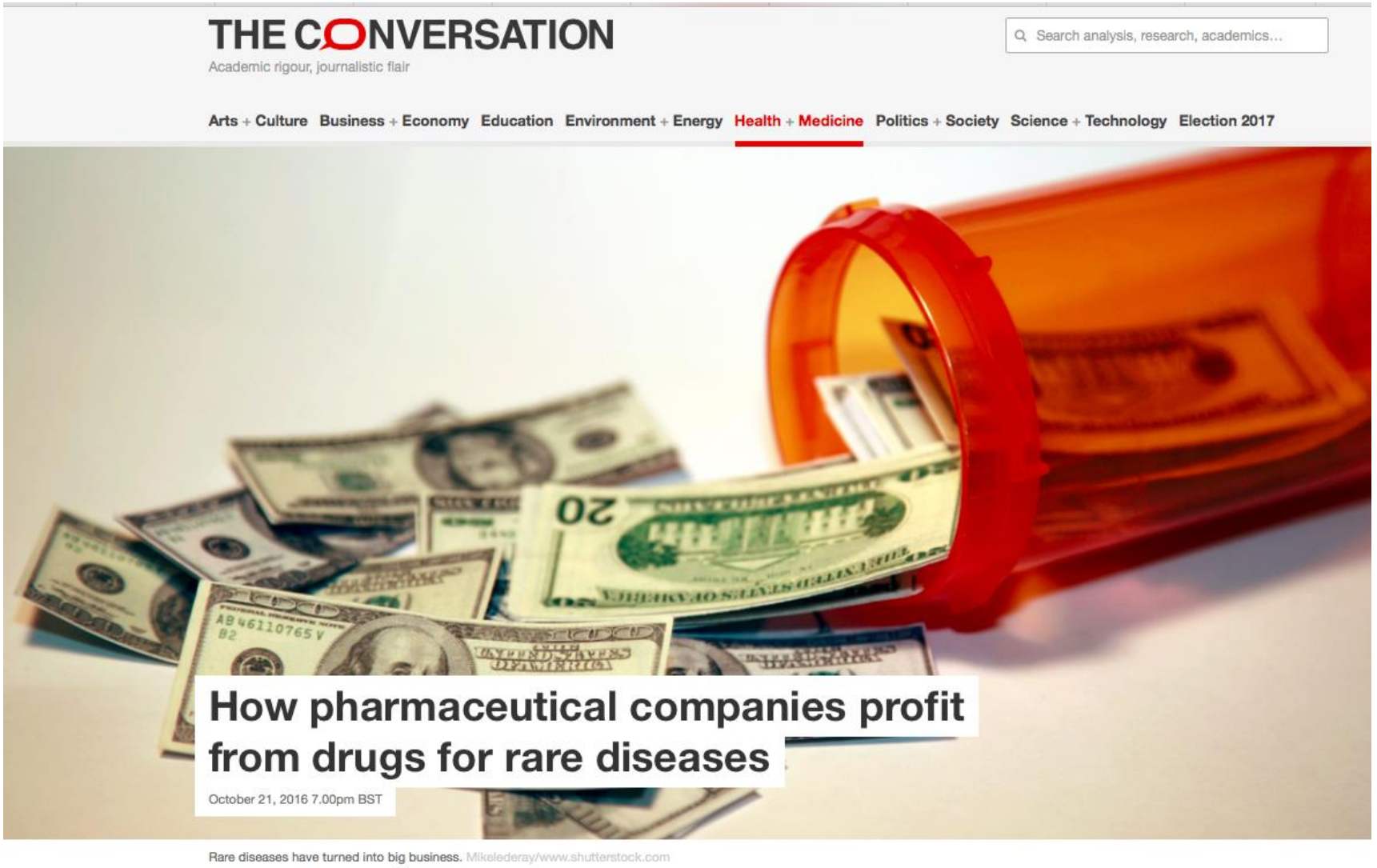
Orphan drug development: an economically viable strategy for biopharma R&D

Kiran N. Meekings[1], kiran.meekings@thomsonreuters.com, **Cory S.M. Williams**[2] and **John E. Arrowsmith**[1]

Drug Discovery Today • Volume 17, Numbers 13/14 • July 2012

- “the revenue-generating potential of orphan drugs is as great as for non-orphan drugs, even though patient populations for rare diseases are significantly smaller”

Hughes, D *et al*



Hughes, D *et al*

RESEARCH ARTICLE

Profitability and Market Value of Orphan Drug Companies: A Retrospective, Propensity-Matched Case-Control Study

Dyfrig A. Hughes[1]*, Jannine Poletti-Hughes[2]

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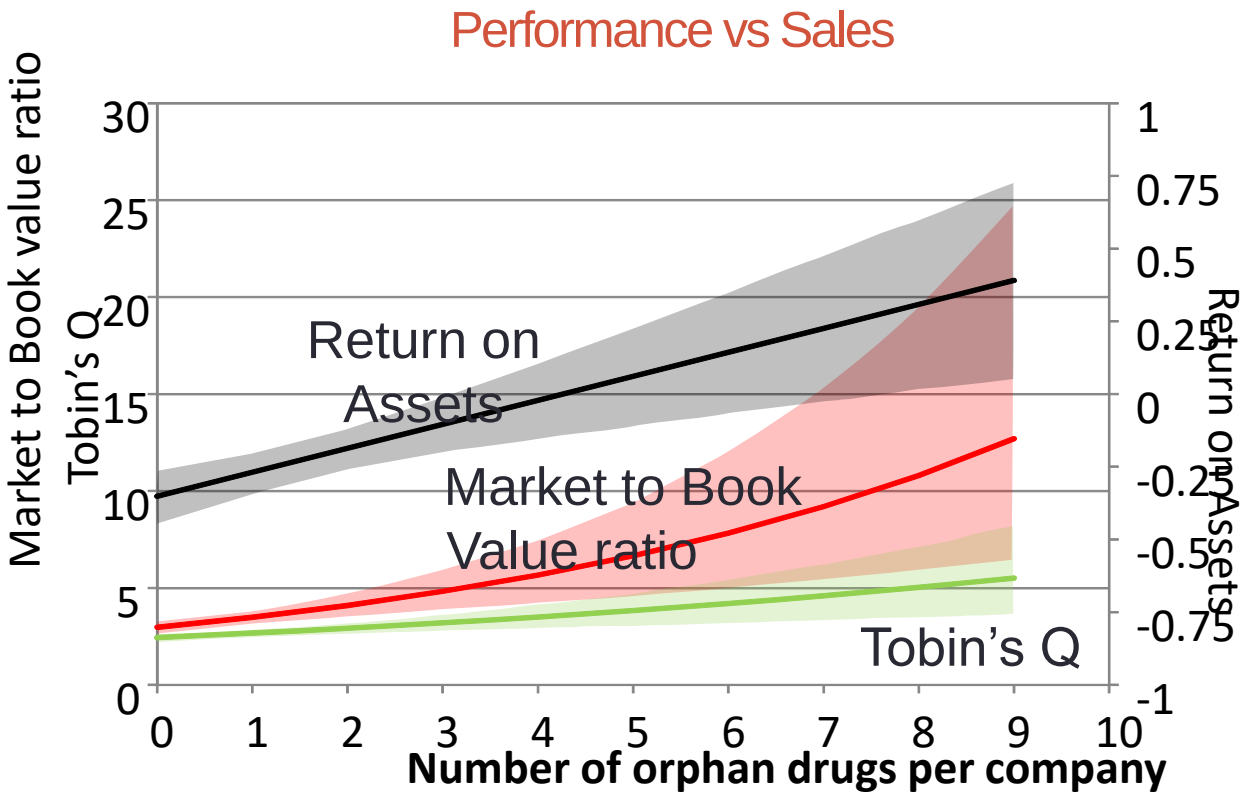
Methods

- Identified EU and US approved orphan drugs
  - 102 US and 21 EU companies with Orphan drugs approved between 2004-2012



Findings

- For orphan drug market authorization holders:
  - Return on assets **9.6% higher than non-orphan** drug companies; (95% CI, 0.6% to 18.7%)
  - Tobin's Q higher by 9.9% (1.0% to 19.7%); and
  - Market to book value ratio higher by 15.7% (3.1% to 30.0%)
- **Sales of orphan drugs increase the profitability of pharmaceutical companies**.
- For each additional orphan drug sold:
  - Return on assets increased by 11.1% (0.6% to 21.3%)
  - Tobin's Q by 2.7% (0.2% to 5.2%), and
  - Market to book value ratio by 5.8% (0.7% to 10.9%).

Conclusions

- Publicly listed pharmaceutical companies that are orphan drug market authorization holders are associated with **higher market value and greater profits** than companies not producing treatments for rare diseases
- EU and US orphan drug legislations should make provisions for incentives to be proportionate to the monetary success associated with marketing orphan drugs
- Continuation of the status quo will make orphan drugs less affordable and companies more profitable

Public preferences for funding of treatments of rare diseases

Health Economics 2013. DOI: 10.1002/hec.2872

Methods

- Cross sectional, web-based survey (n=4,118)
- Allocation of fixed funds between competing hypothetical patient groups
- 2 cohorts - following piloting
- Part A: All else being equal, common to both cohorts
- Part B: Trade-off in:
  - effectiveness (cohort 1)
  - costs (cohort 2)
- Preferences categorised

Health Economics 2013. DOI: 10.1002/hec.2872

Question format

Imagine two diseases - Disease A and Disease B. They affect the same age groups and are equally common. The only difference between the two diseases is that, without treatment:

- **Disease A** — is **common** (e.g. affects 500,000 patients in the UK)
- **Disease B** — is **rare** (e.g. affects 1000 patients in the UK)

Medicine A (for treatment of Disease A) and Medicine B (for the treatment of Disease B) both improve the health and well-being of patients by the same amount, and they cost the same.

As the NHS has a fixed amount of money, and there are no extra funds available, treatment of patients using either Medicine A or Medicine B may mean that other treatments or services for other patients have to be reduced.

Part A (Common to both cohorts):

If the NHS were able to pay for treatment for a maximum of:

- **100 patients with a rare disease**, or
- **100 patients with a common disease**, or
- **some combination** of the two,

How would you prefer NHS money to be spent? Please indicate using the scale below.

All money spent on Disease A					**Money divided equally**					All money spent on Disease B
100 patients Rare	90	80	70	60	50	40	30	20	10	0 patients Rare
0 patients Common	10	20	30	40	50	60	70	80	90	100 patients Common

Cohort 1

Cohort 2

Description – Part B (n=2,033):
Now imagine that treatment of

- **Rare disease will improve health a little**, whereas
- **Common disease will improve health considerably**

How would you prefer NHS money to be spent? Please indicate using the scale...

Description – Part B (n=2,085):
Now imagine that the costs of treatment differ so the NHS is able to pay for treatment for a maximum of:

- **50 patients with rare disease**, or
- **100 patients with common disease**, or
- **Some combination of the two**

How would you prefer NHS money to be spent? Please indicate using the scale...

Results

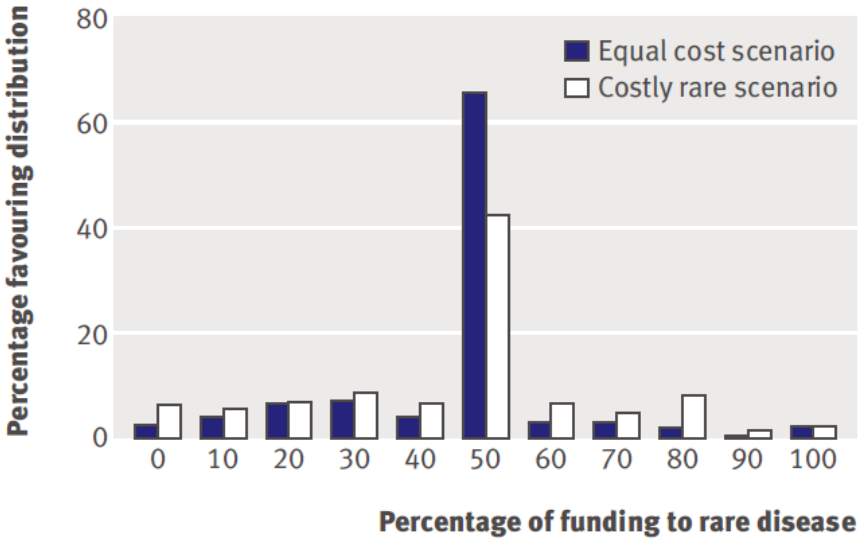
Choice	Prioritise Medicine for rare disease	Equal allocation to both populations	Prioritise Medicine for common disease	Choice
All else being equal	15.1 (14.0 to 16.2)	43.2 (40.5 to 45.9)	41.7 (38.2 to 45.3)	**All else being equal**
Little health improvement	10.4 (9.1 to 11.8) RR 0.45; p<0.0001	32.4 (30.3 to 34.4) RR 0.39; p<0.0001	57.3 (55.1 to 59.4) RR 5.54; p<0.0001	**Improves health considerably**
Twice the cost of population 2	23.7 (21.9 to 25.6) RR 3.00; p<0.0001	38.0 (35.9 to 40.1) RR 0.52; p<0.0001	38.3 (36.2 to 40.4) RR 0.82; p=0.0784	**Half the cost of population 1**

BMJ

RESEARCH

Societal views on orphan drugs: cross sectional survey of Norwegians aged 40 to 67

Arna S Desser, research fellow,[1] Dorte Gyrd-Hansen, professor,[2] Jan Abel Olsen, professor,[3] Sverre Grepperud, professor,[1] Ivar Sønbø Kristiansen, professor[1,2]



Conclusions Despite strong general support for statements expressing a desire for equal treatment rights for patients with rare diseases, there was **little evidence that a societal preference for rarity exists** if treatment of patients with rare diseases is at the expense of treatment of those with common diseases.

Interpretation

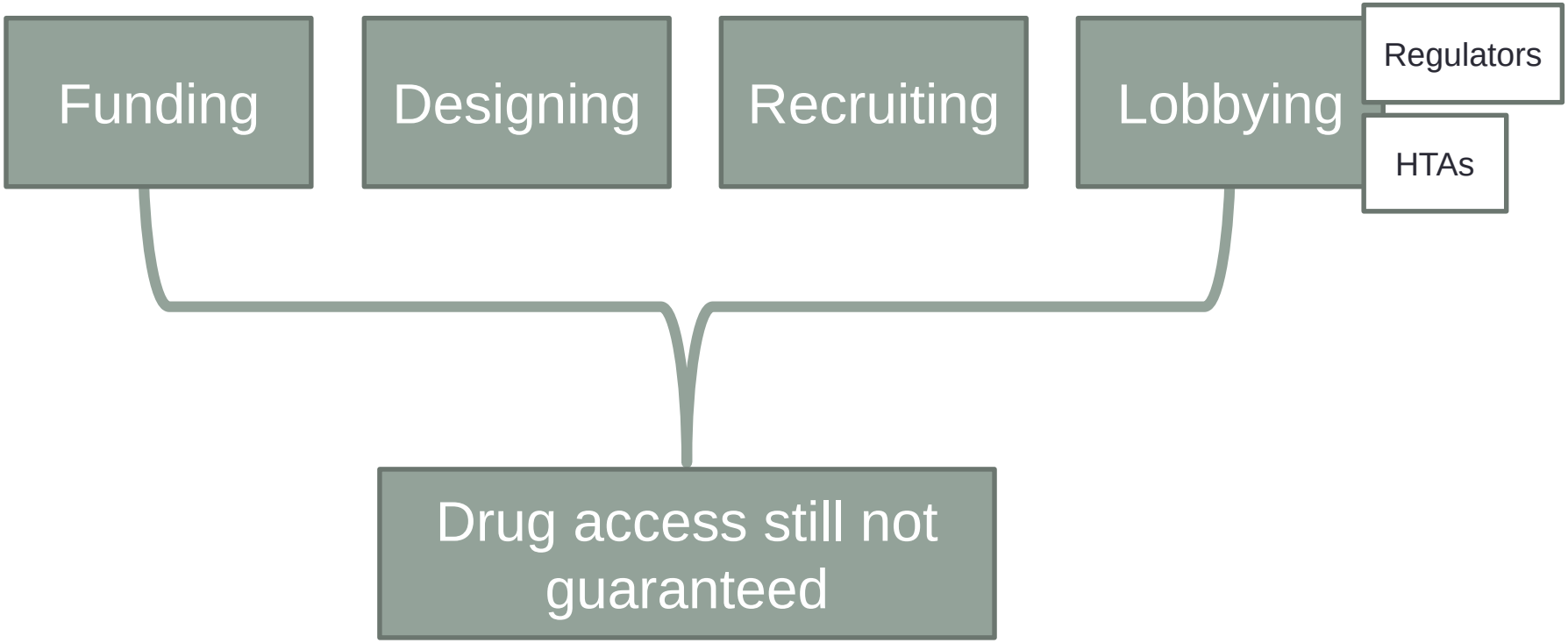
- Whether or not orphan drugs warrant special funding status would seem to rest on the value attached to rarity of disease
- No evidence of societal support for special funding status
- Specific policies that prioritise funding for rare diseases not supported

Challenges we face today

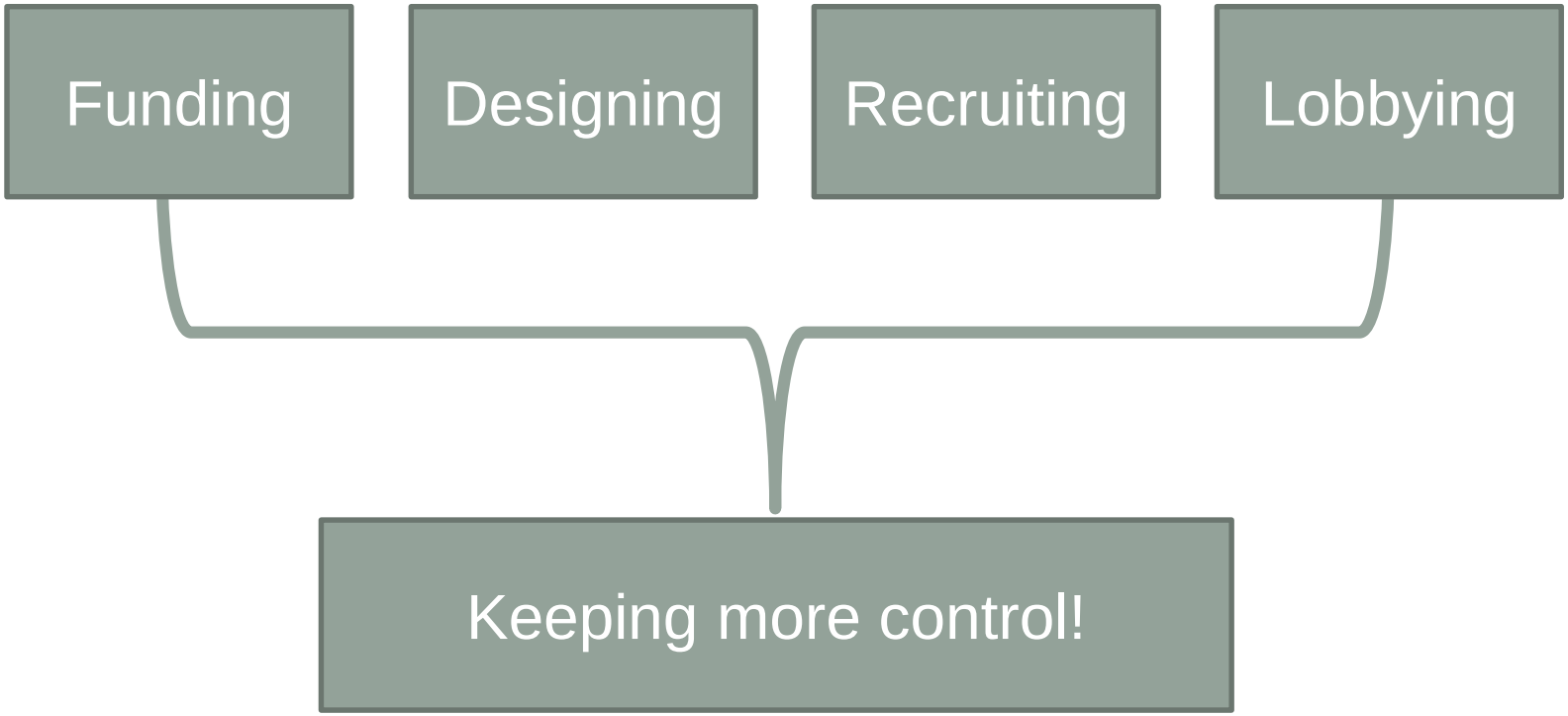
- Unsustainable drug prices (majority of rare diseases still without drug option)
- Controversial profits by pharma leads to bad feeling
- Resistance by HTAs increasing
- Public support not guaranteed

Future opportunities and ideas

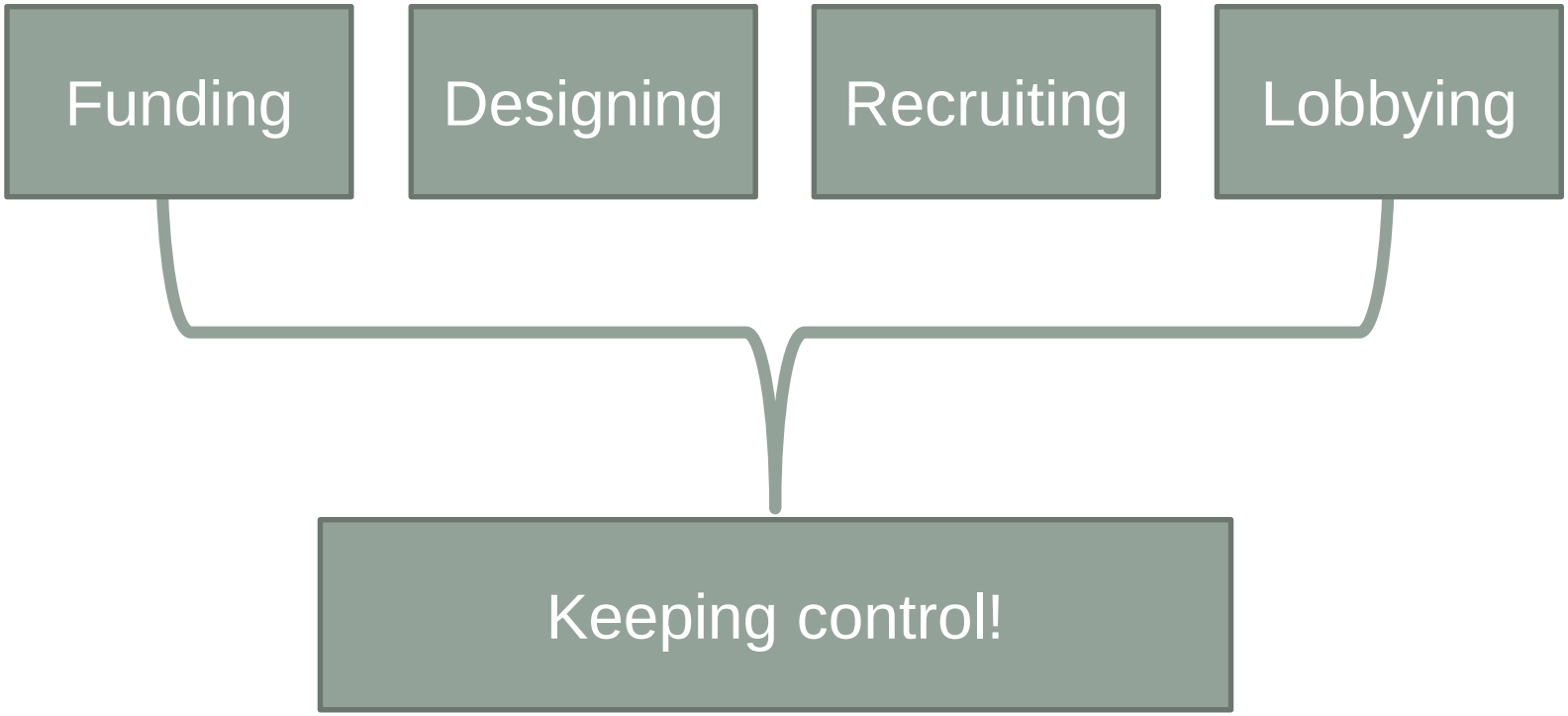
Patient Involvement in Drug Development Today



Patients Leading Drug Development Tomorrow



Patients Leading Drug Development Tomorrow



LYSOGENE

SOLID BIOSCIENCES

Patient Leading Drug Development Tomorrow

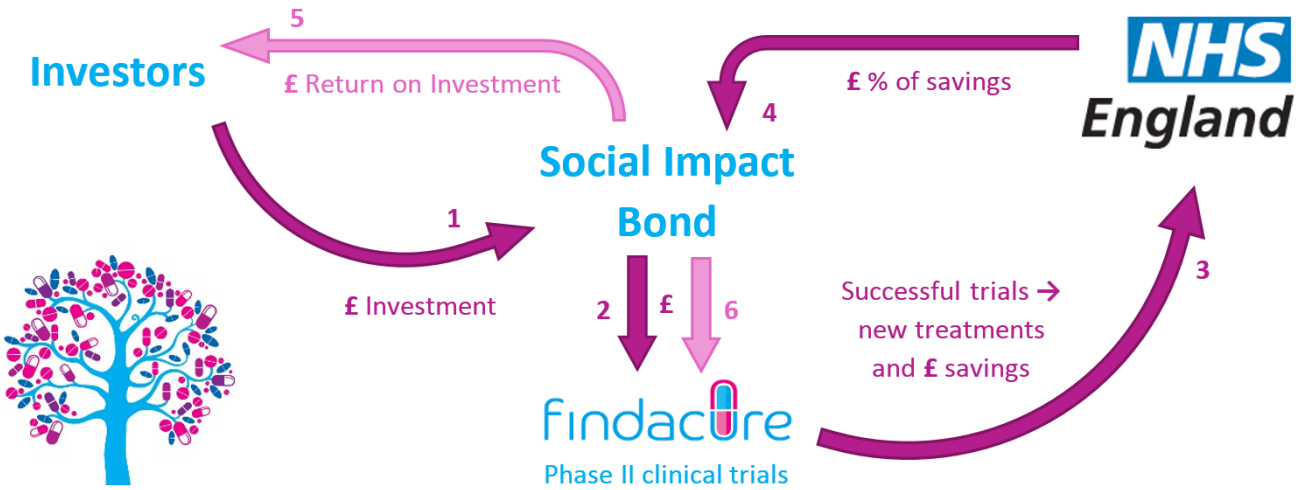
Funding

IP / patent

Pharma Company

Patients Leading Drug Development Tomorrow

Funding



Expert Opinion on Orphan Drugs

Taylor & Francis
Taylor & Francis Group

ISSN: (Print) 2167-8707 (Online) Journal homepage: http://www.tandfonline.com/loi/ieod20

Repurposing as a strategy for orphan drug development, evidence from European approvals

Peter Norman MBA PhD

Identifying drugs for the treatment of rare diseases requires cost-effective discovery approaches. As the prevalence or incidence of the disease decreases, the need for lower cost approaches becomes more important. The systematic use of repurposing provides better opportunities for meeting such goals, and can facilitate subsequent development of the resulting drug(s).

Analysis of the 78 orphan drugs approved for use in Europe indicates that that 38% resulted by repurposing drugs from either approved or originally intended indications.

Canolfan Economeg Iechyd a Gwerthuso Meddyginiaethau
CHEME
Centre for Health Economics and Medicines Evaluation

BJCP British Journal of Clinical Pharmacology

PHARMACOECONOMICS

Affordable orphan drugs: a role for not-for-profit organizations

Elin H. Davies, Emma Fulton, Daniel Brook, Dyfrig A. Hughes

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Abstract

Aims

The success of the Regulation on Orphan Medicinal Products in the European Union is evidenced by the 127 orphan drugs that have had market authorization since 2000. However, the incentives aimed at stimulating research and development have had the unintended consequence of increasing drug cost, resulting in many orphan drugs not being cost-effective. Orphan drugs command an increasing share of the pharmaceutical market and account for a disproportionate amount of healthcare expenditure. Orphan drug ownership by socially motivated, not-for-profit organizations may facilitate access to more affordable orphan drugs, for the benefit of patients and healthcare systems alike. This study aims to describe opportunities for such organizations to become orphan drug Market Authorization Holders.

Patients Leading Drug Development Tomorrow

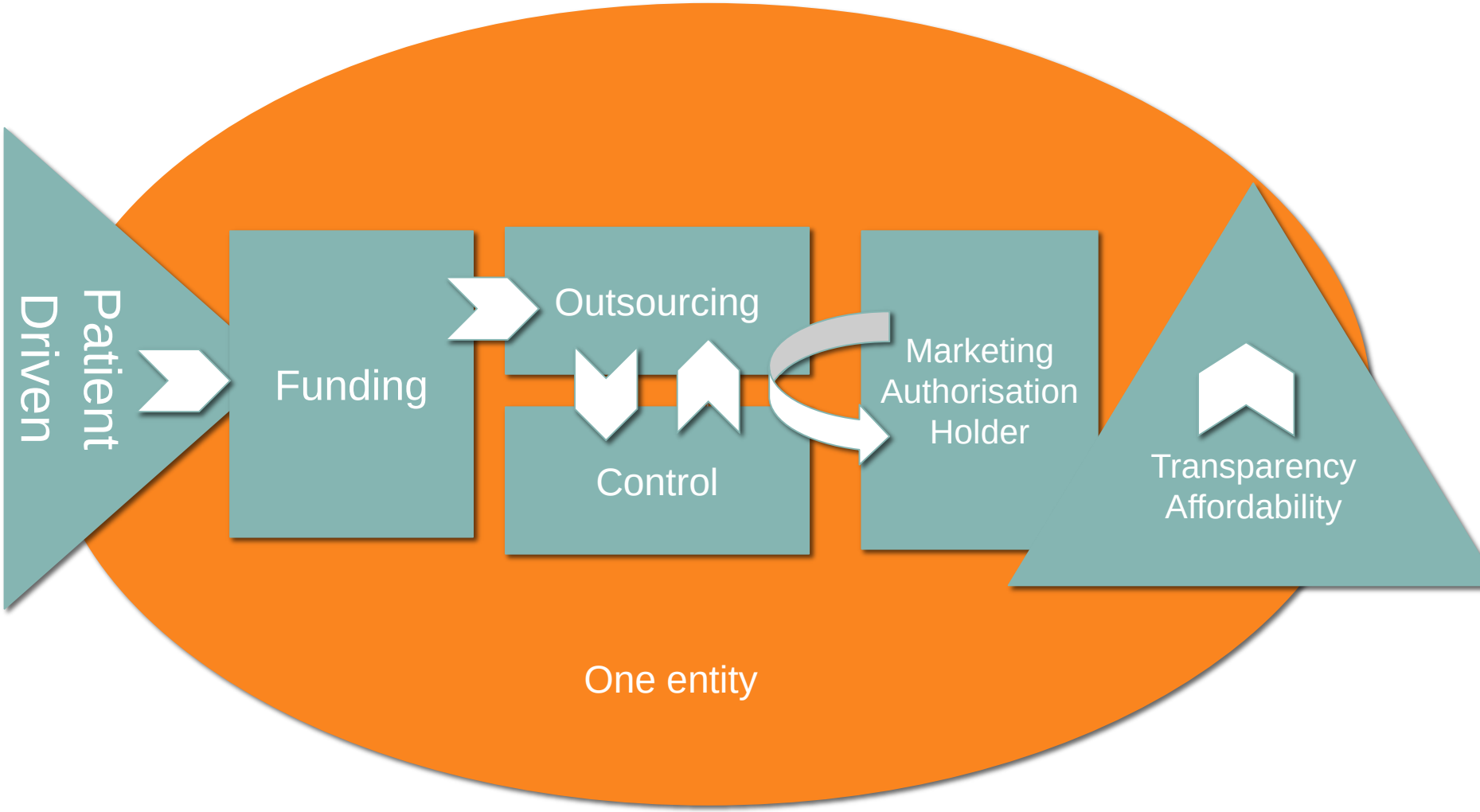
Funding

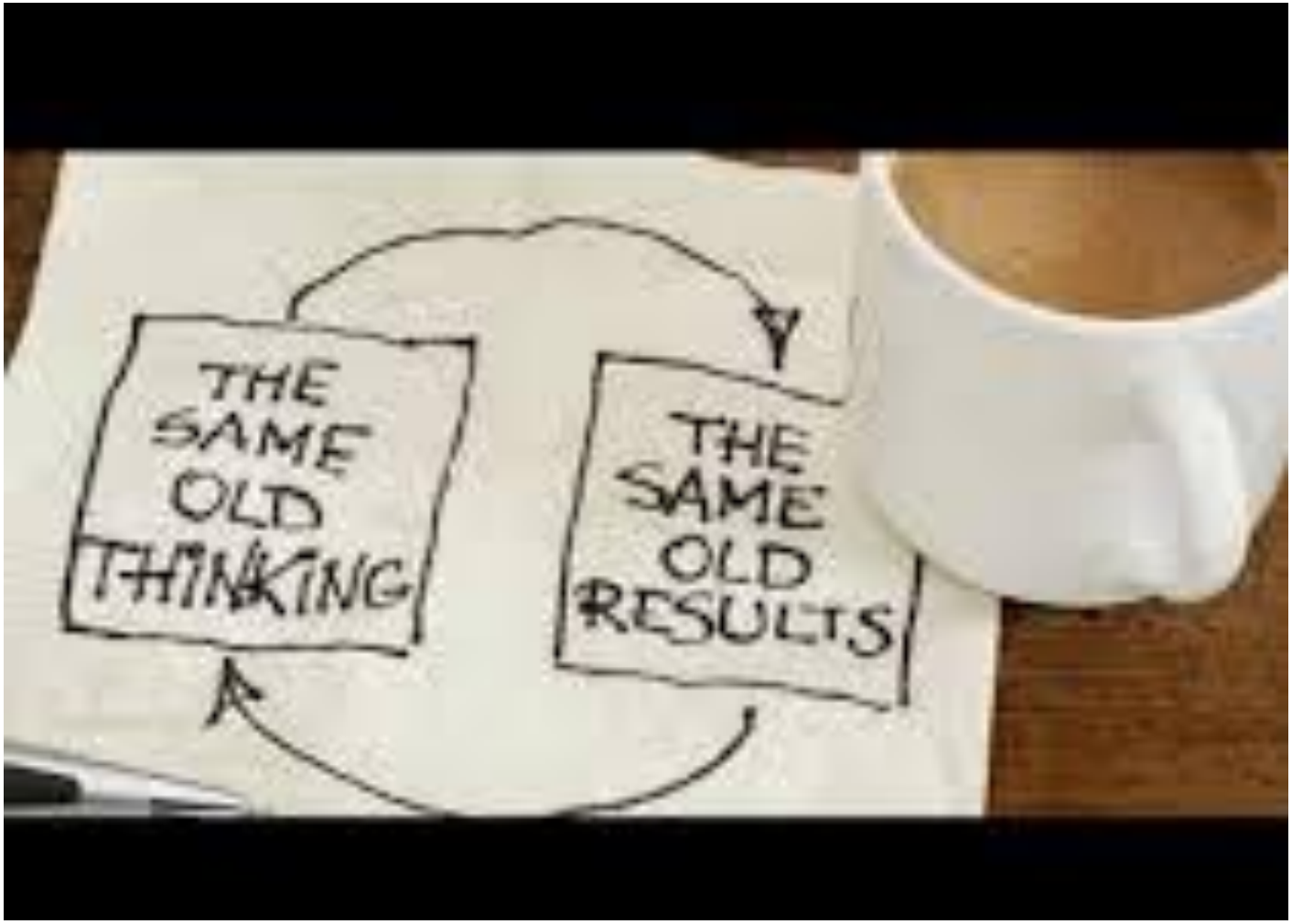
IP / patent

RECYCLE
REPURPOSE

Becoming a Marketing Authorisation Holder

Patients Leading Drug Development Tomorrow





Insanity is doing the same thing over and over again but expecting different results.

Treatment

Available

Appropriate

Adaptable

Affordable

A mindset of the willing

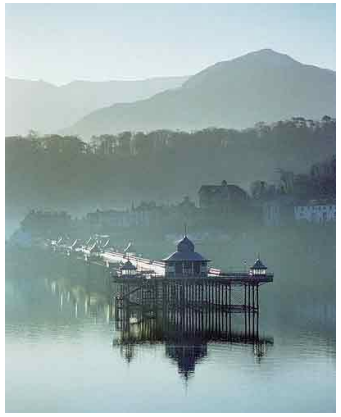
If you want to go fast, go alone.

If you want to go far, go together.

African proverb.

Acknowledgements

- Prof Dyfrig Hughes and colleagues at CHME



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