Dr Lutz Harnisch, MD, Pfizer, Sandwich, UK
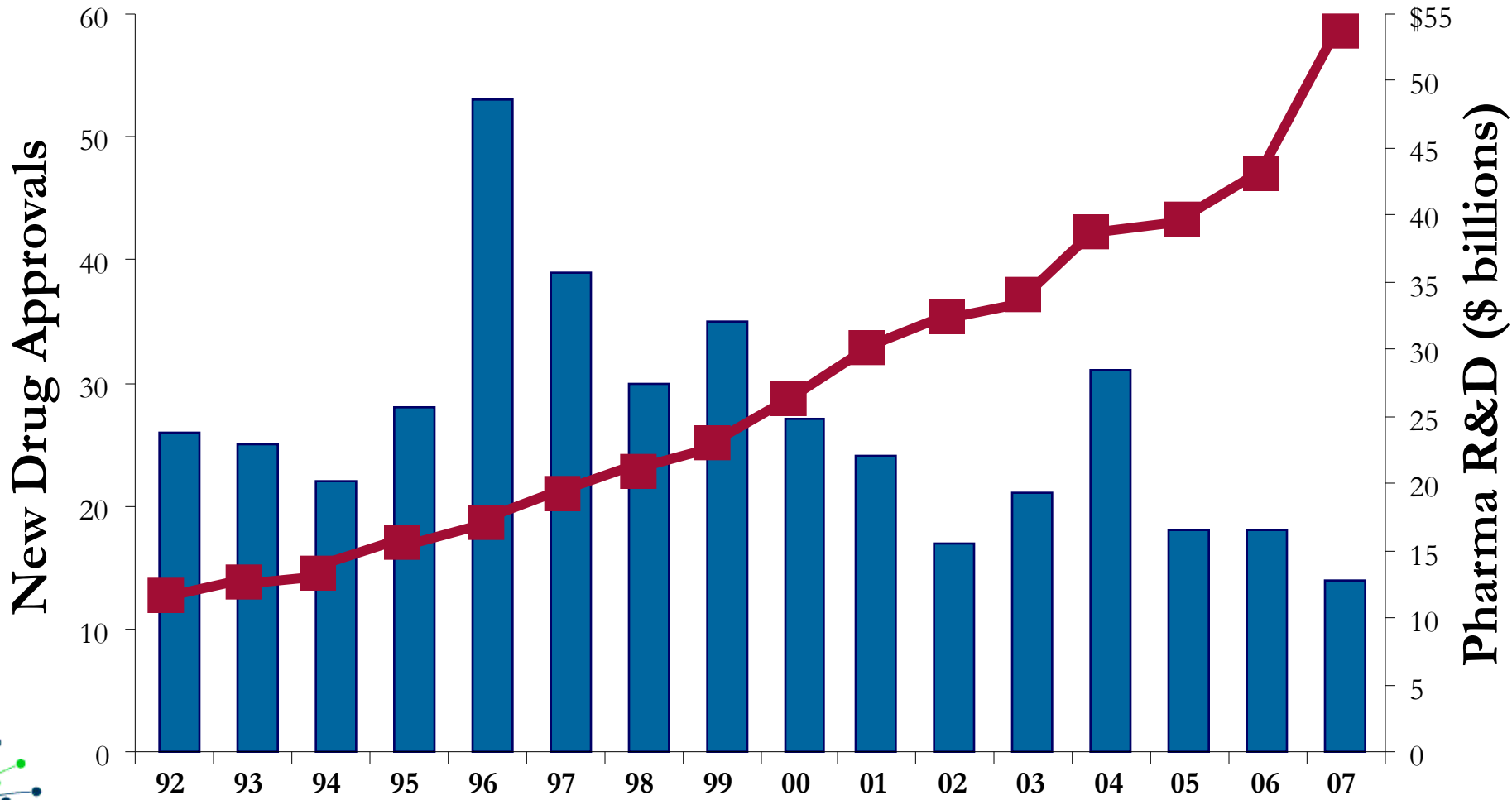**Coordinator**
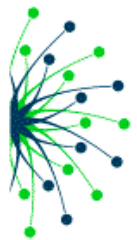
The Productivity Gap in Pharma R&D

Source: Burrill & Company; US Food and Drug Administration.
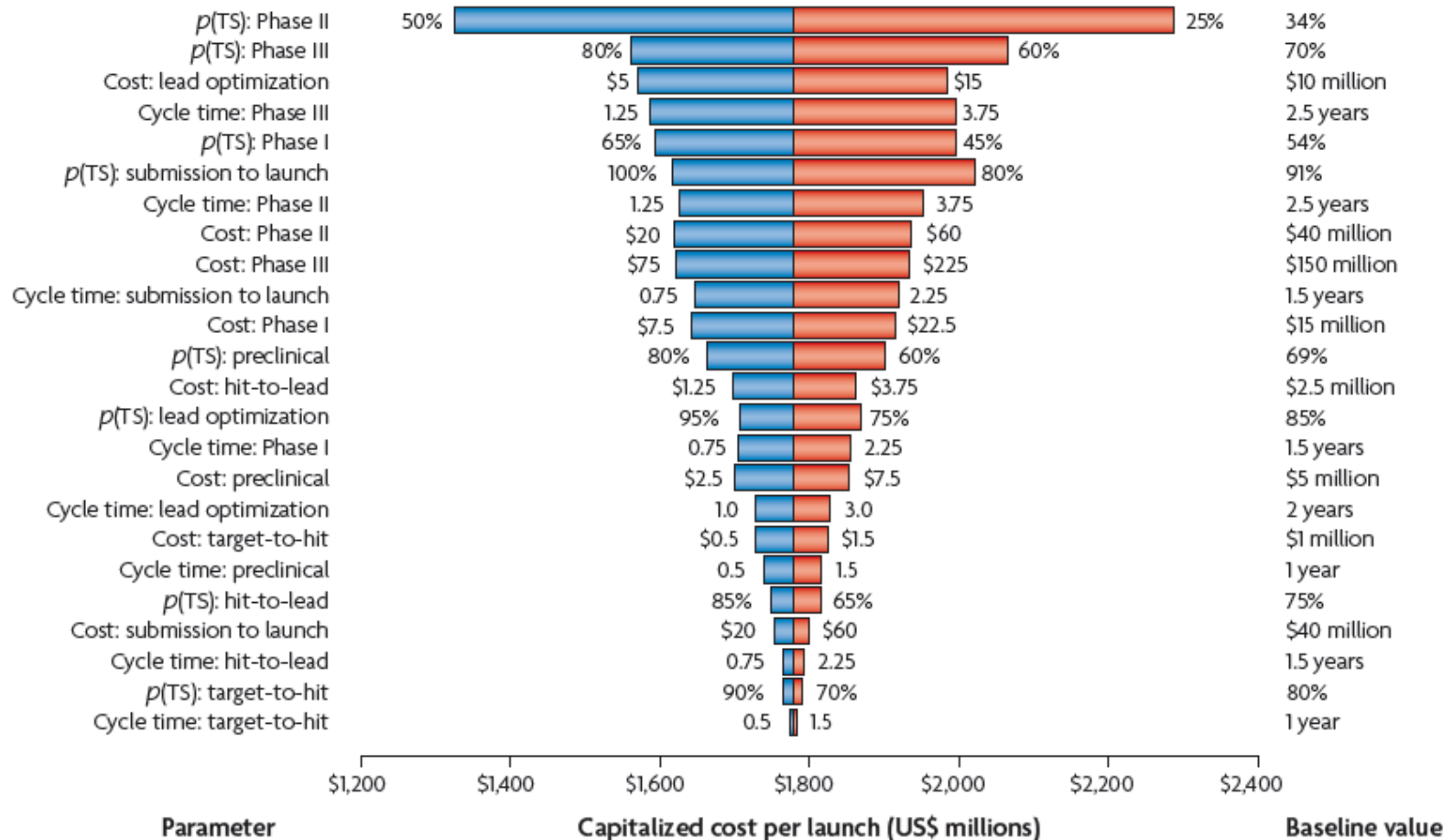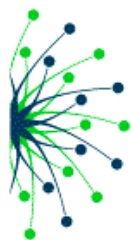
How to improve R&D productivity?

Fig.3: R&D productivity model: parametric sensitivity analysis. From Paul S, et.al., Nature Review, 2010(9)
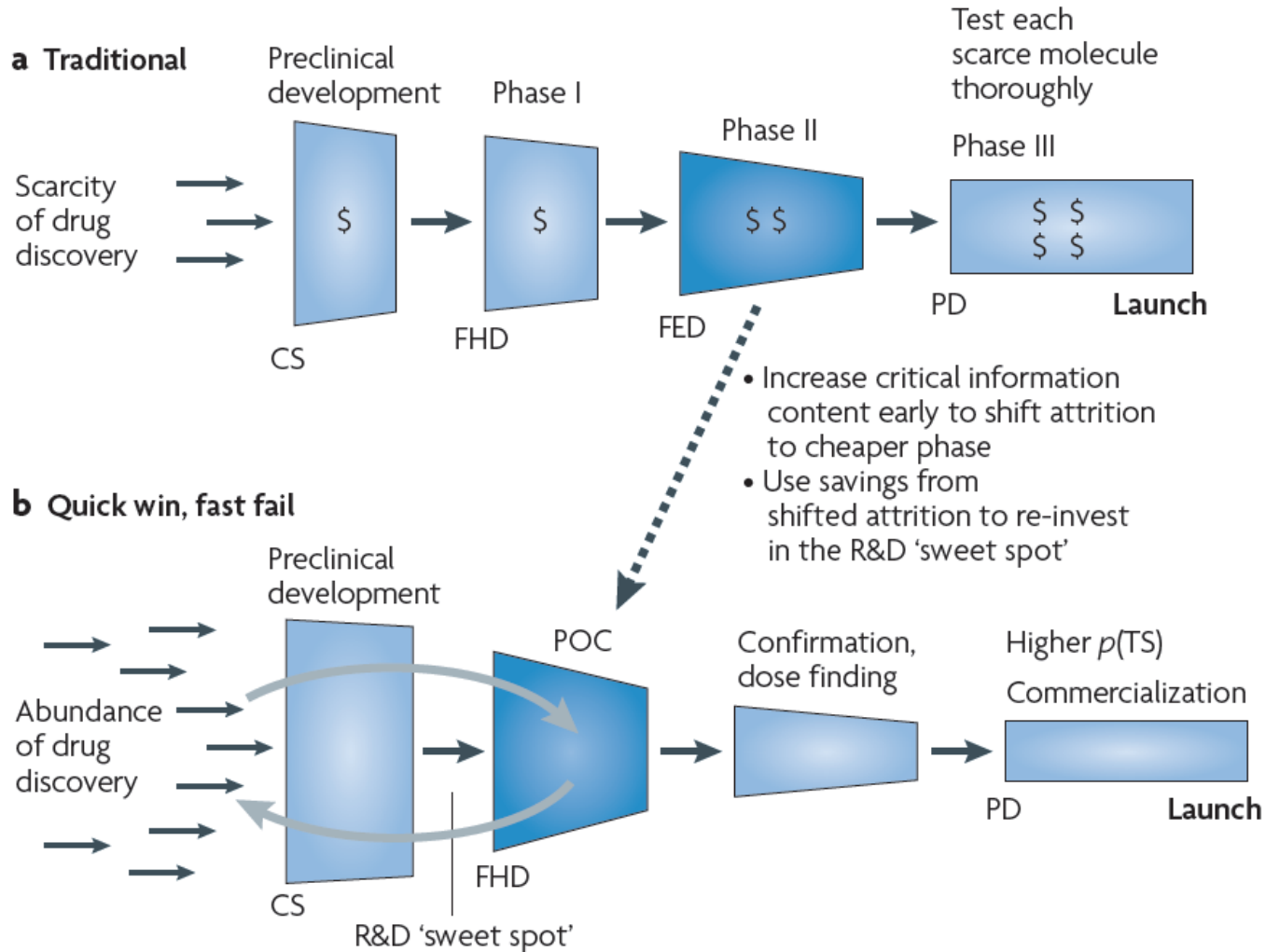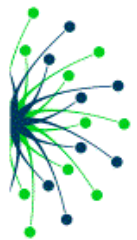
How to improve R&D productivity?

Fig 5: The quick win, fast fail drug development paradigm. From Paul S, et.al., Nature Review, 2010(9)

Model Based Drug Development
a continuum of Learn/Confirm at each decision point

Pre-clin

PoC

Confirmation Dose finding

Registration Commercialisation

Disease Area Knowledge Gain

Academia / Public Health
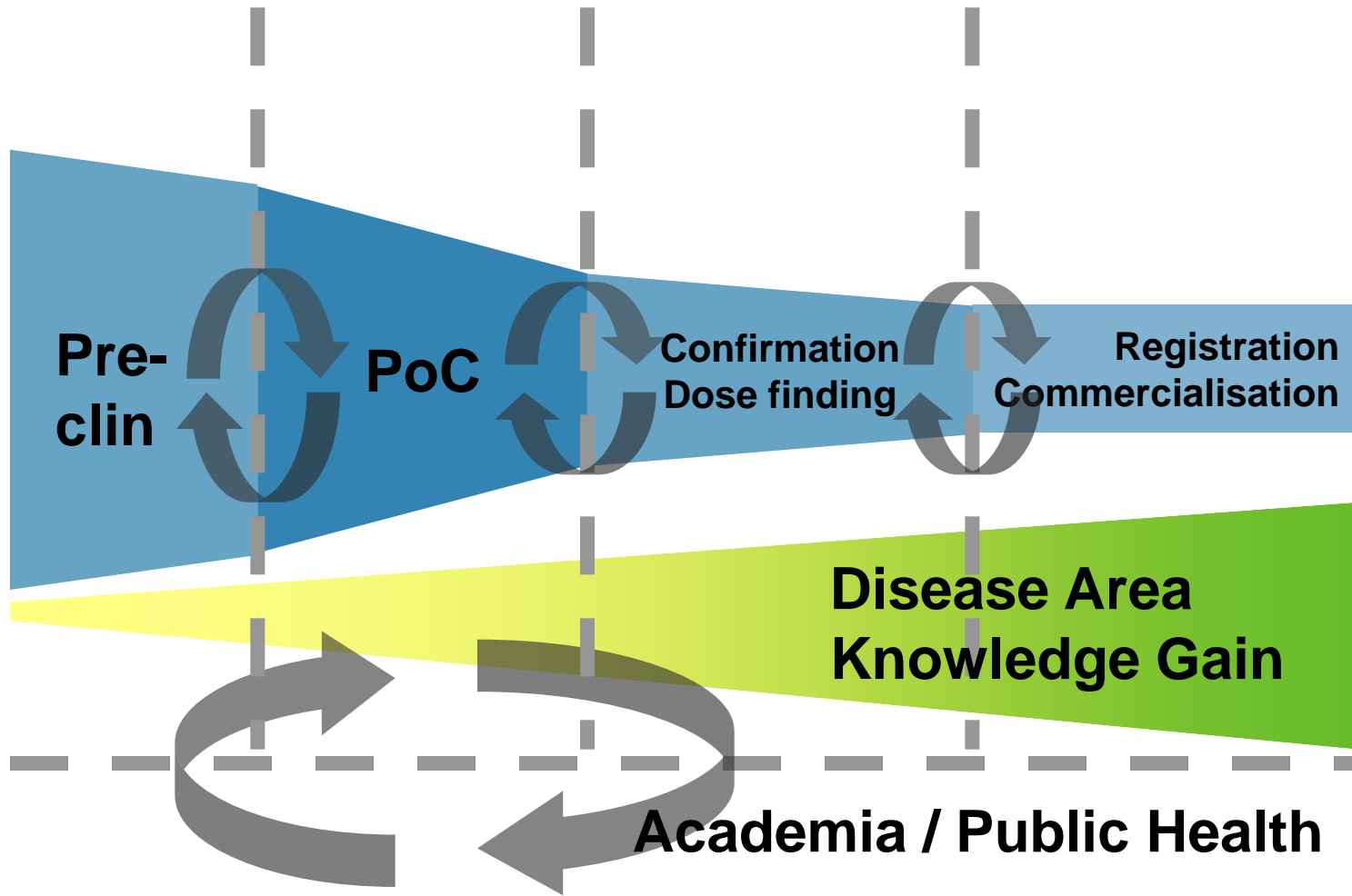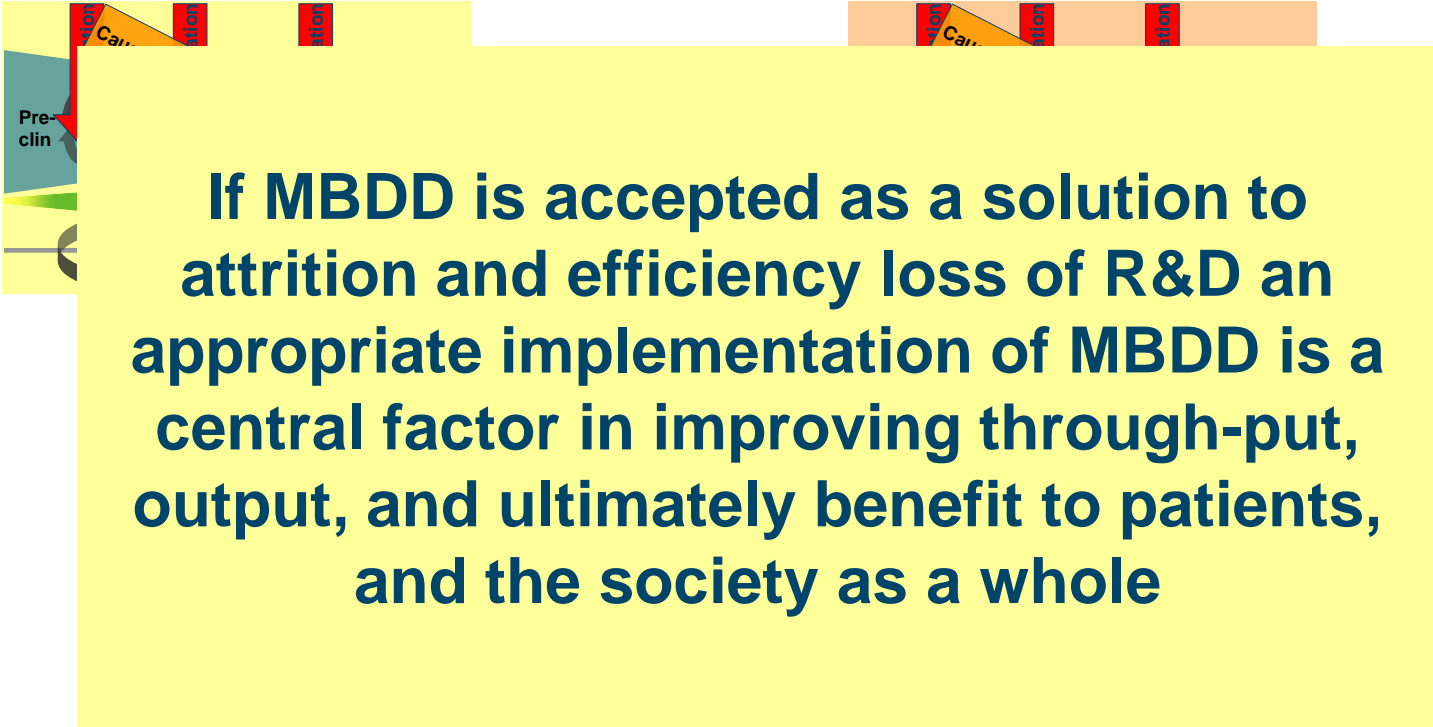
Model Based Drug Development
in reality fragmented and unsustainable
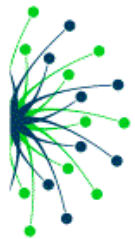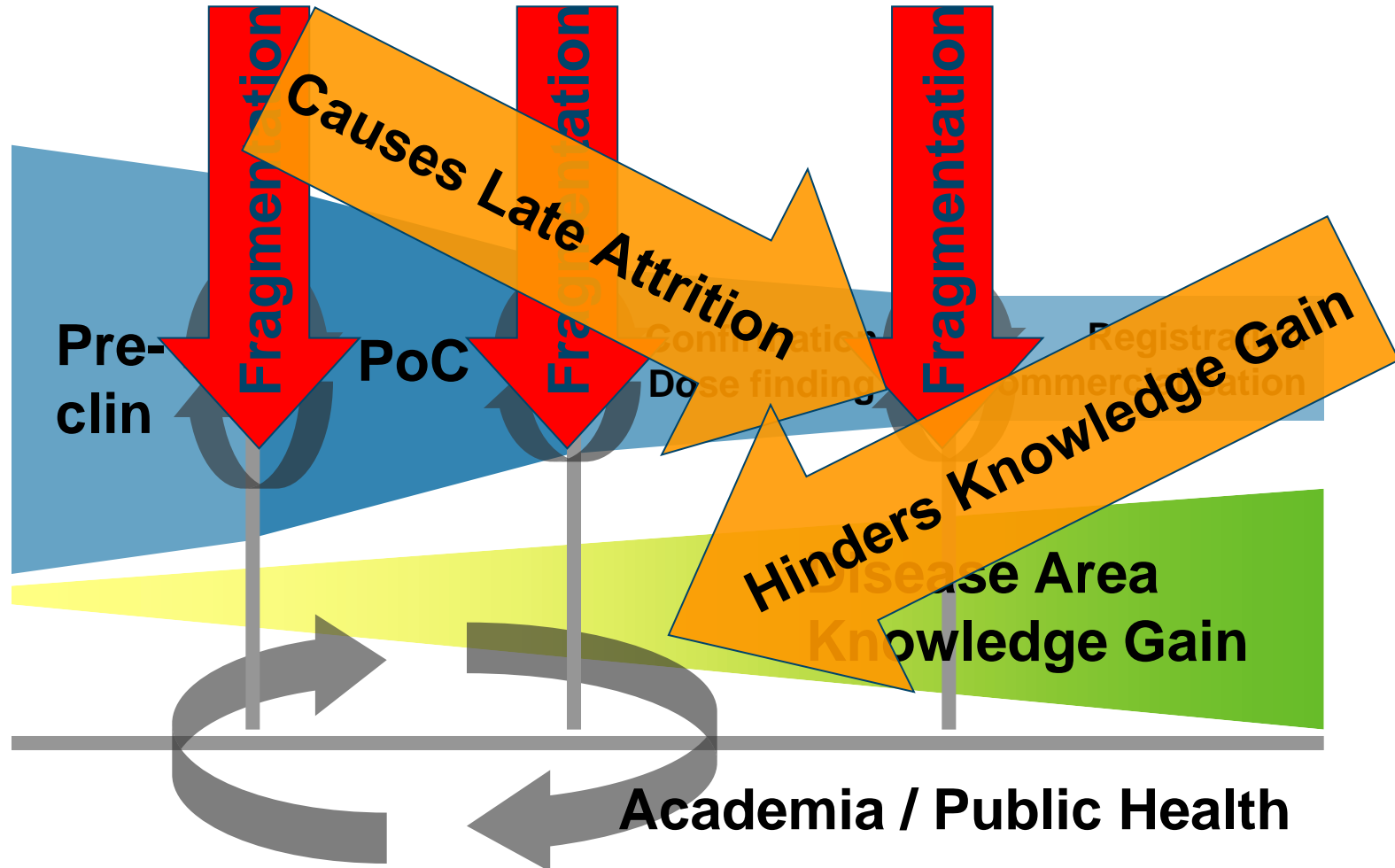
Fragmentation

Causes Late Attrition

Hinders Knowledge Gain

Pre-clin

PoC

Confirmation
Dose finding

Registration
Commercialisation

Disease Area
Knowledge Gain

Academia / Public Health

Across Industry pre-competitive exchange happens only occasionally

The economic problem of society … to put it briefly, is a problem of the utilization of knowledge not given to anyone in its totality Friedrich von Hayek, 1960

Across Industry pre-competitive exchange happens only occasionally

If MBDD is accepted as a solution to attrition and efficiency loss of R&D an appropriate implementation of MBDD is a central factor in improving through-put, output, and ultimately benefit to patients, and the society as a whole

The economic problem of society … to put it briefly, is a problem of the utilization of knowledge not given to anyone in its totality Friedrich von Hayek, 1960

IMI Research Agenda defined DDMoRe's primary aims

The scientific and functional requirements for the KM Platform can be summarised as follows:

- **Data federation**: seamless search and navigation across heterogeneous data sources, both private and public;

- **Data integration**: the capacity to pool data from heterogeneous sources in a scientifically, semantically and mathematically consistent manner for further computation;

- **Shared services**: the development, sharing and integration of relevant and powerful data exploitation tools such as modelling and simulation.
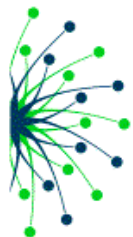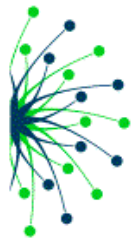
DDMoRe – The Vision
Major deliverables

Modelling Library
Shared knowledge

- Data contains raw information, which is difficult to share
  - IP, CDISC
- Models
  - represent an interpretation, understanding of the data (given experimental conditions)
  - allow to predict the future with uncertainty
  - are an *intellectual container of the knowledge*

DDMoRe – The Vision
Major deliverables

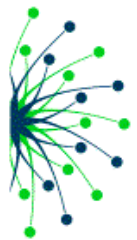**Standards** for describing models, data and designs

Modelling Library

Shared knowledge

… has standards at the core of its strategy …

Model Definition Language

...ystem interchange standards

DDMoRe – The Vision
Major deliverables

Standards for describing models, data and designs

Modelling Library
Shared knowledge
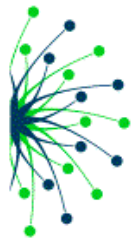
Modelling Framework
A modular platform for integrating and reusing models; shortening timelines by removing barriers

Model Definition Language

System interchange standards

… but the framework will put the system into life

DDMoRe – The Vision
Major deliverables

Standards for describing models, data and designs

Model Definition Language

Modelling Library
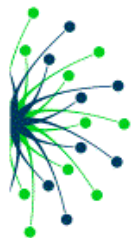**Shared knowledge**

Specific disease models
Examples from high priority areas

Modelling Framework
A modular platform for integrating and reusing models; shortening timelines by removing barriers
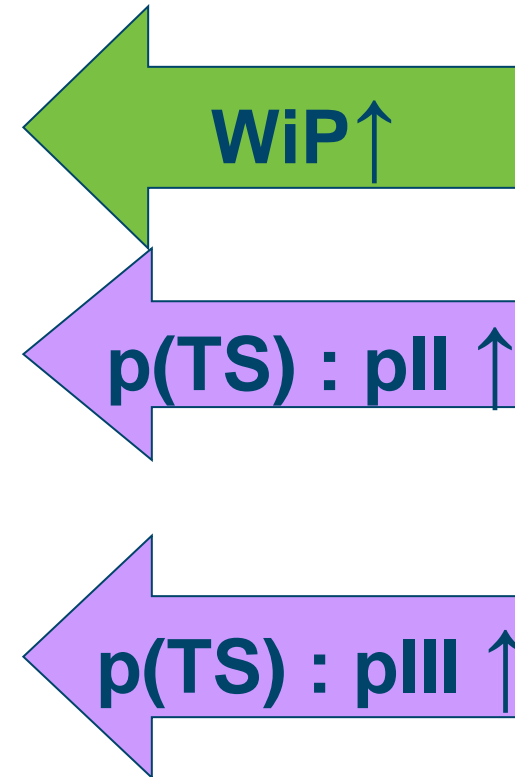
System interchange standards

DDMoRe DA Prototypes: Oncology
Tumour size – survival model
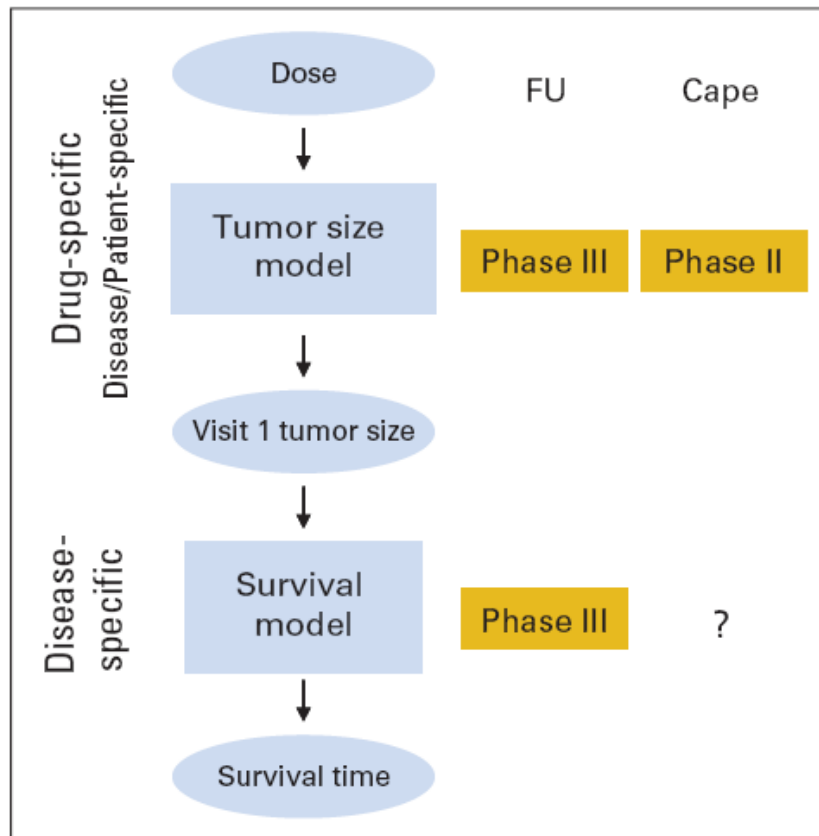
Fig 1. Scheme for simulating a phase III study on the basis of phase II data of an investigational agent (here, capecitabine [Cape]) and historical phase III data of a reference drug (fluorouracil [FU]).

WiP↑

p(TS) : pII ↑

p(TS) : pIII ↑

Claret L, Girard P, Hoff PM, Van Cutsem E, Zuideveld KP, Jorga K, Fagerberg J, Bruno R. J Clin Oncol. 2009; 27:4103-8.

DDMoRe DA Prototypes: Diabetes
a variety of models describe experimental and patient outcome data
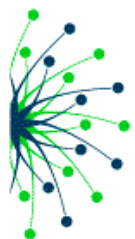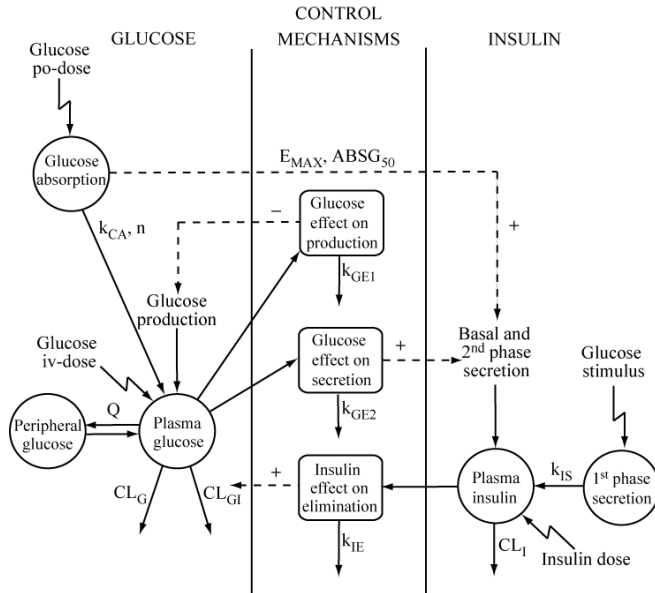

- The IGI model (Jauslin at al., JCP, 2007-11))
- The BIG model (Ribbing et al., JPP, in press)
- The FPG-HbA$_{1c}$ model (Hamren et al., CPT, 2008)
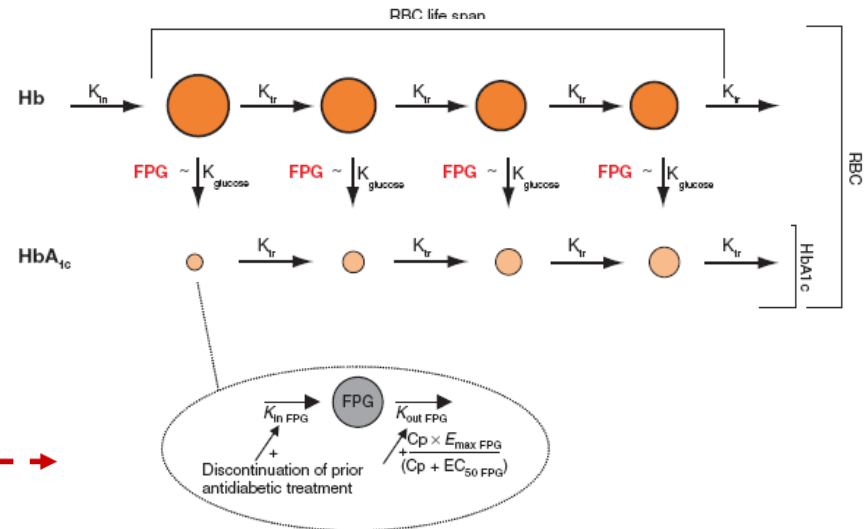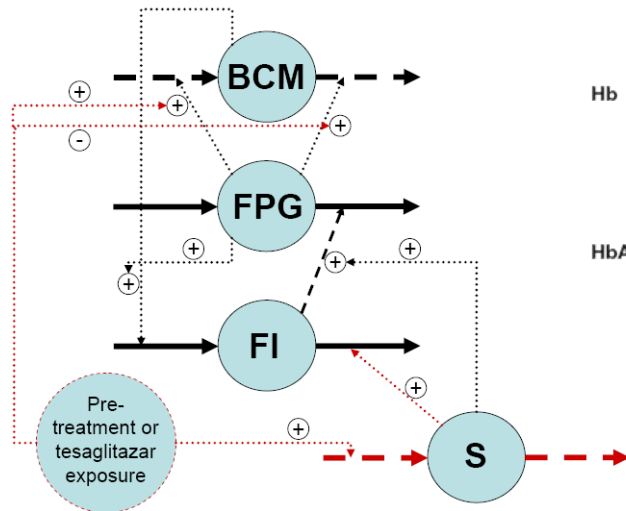
DDMoRe – The Vision
Major deliverables

Standards for describing models, data and designs

Modelling Li...

Shar...
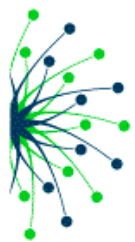
Modelling ...work

Public instance
http://www.ddmore.eu

Model Definition Language

Sp... disease models

Examples from high priority areas

...atform ...ng and ...dels; ...nelines ...ng barriers

System interchange standards

Education

Training

Time and money

- **Timing:**
    - **Starting Date:**   01/03/2011
    - **Duration:**   60 months

- **Financing:**
    - IMI funding: €   9.615.058
    - Other contributions: €   1.729.833
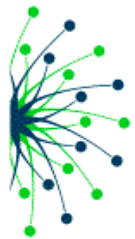   - EFPIA in kind contribution: €   9.820.120
    - **Total Project Cost:**   **€ 21.165.061**

Participants are a unique combination of model builders, model users, software developers and teachers

AstraZeneca

Eli Lilly

Université Paris Diderot-Paris 7

CNR-ISIB

Mango Solutions

Universita' degli Studi di Pavia

Cyprotex Discovery

Martin-Luther-Universität Halle-Wittenburg

Pfizer

EMBL-EBI

Merck

Roche

GlaxoSmithKline

University of Navarra

Servier

INRIA

Novartis

Simcyp

Interface Europe

Novo Nordisk

UCB

Universiteit Leiden

Optimata

Uppsala Universitet

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Roche

GlaxoSmithKline

University of Navarra

Servier

Interface Europe

Novo Nordisk

UCB

Universiteit Leiden

Optimata

Uppsala Universitet

- **Major European Pharma represented**

- **Major Academic Centres on Quantitative Drug Development involved**

- **SMEs with many yearlong exposure to tools, methods and applications in MBDD**

- **500 – 1000 years shared experience**

Further information

Project Coordinator:
Dr. Lutz Harnisch
Senior Director, Pharmacometrics
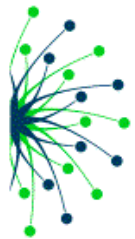Pfizer Ltd, UK
Email: Lutz.O.Harnisch@pfizer.com

Managing entity of IMI beneficiaries:
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Professor of Pharmacometrics
Uppsala University, Sweden
Email: Mats.Karlsson@farmbio.uu.se

Project website:

http://www.ddmore.eu

www.imi.europa.eu

Thank you!

The general who wins a battle makes many calculations in his temple ere the battle is fought. The general who loses a battle makes but few calculations beforehand. Thus do many calculations lead to victory, and few calculations to defeat: how much more no calculation at all! It is by attention to this point that I can foresee who is likely to win or lose.

– Sun Tzu