Adaptive Licensing: Industry Perspectives

**Workshop 2: Innovation and Adaptive Governance in Biotechnology
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Risk Governance
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Cost of new drugs continues to escalate at an unsustainable rate for the industry…..or healthcare ecosystem
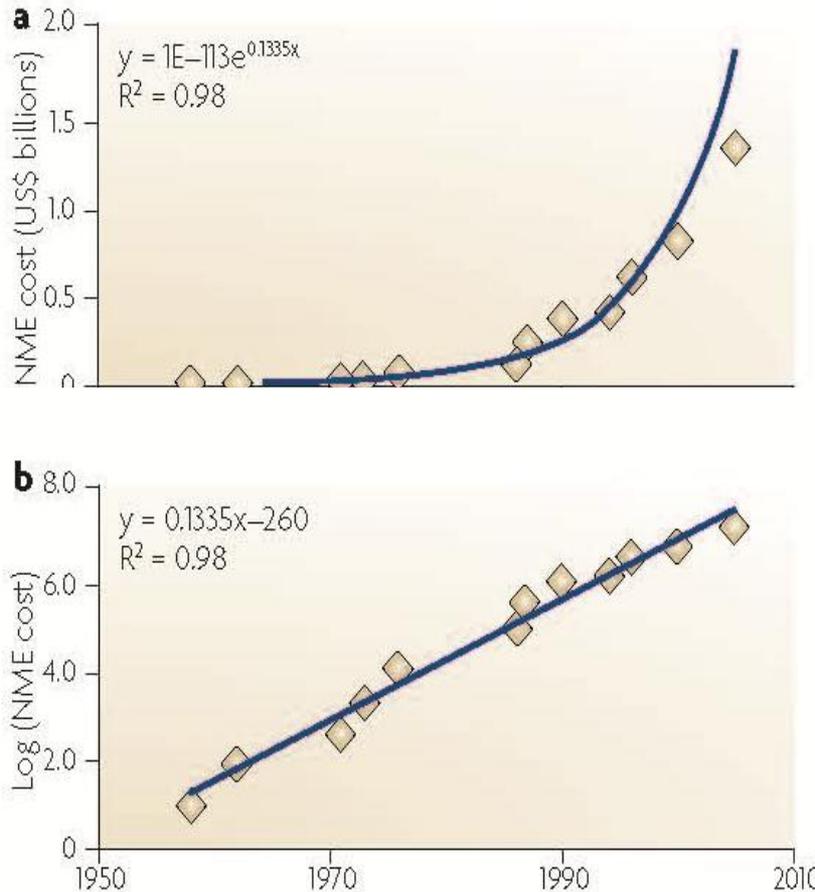
- A plot of twelve independent estimates of the cost of an NME spanning 48 years.

- The same data plotted on a logarithmic scale.

- The exponent in the line equation in part a and the gradient of the line in part b show that the **cost per NME has grown at an annual compound rate of 13.35% since the late 1950s.**

Source: *Nature Reviews: Drug Discovery, Lessons Learned from the Pharma Industry, December 2009*

Decline in R&D Productivity – the major development is the lack of efficient development
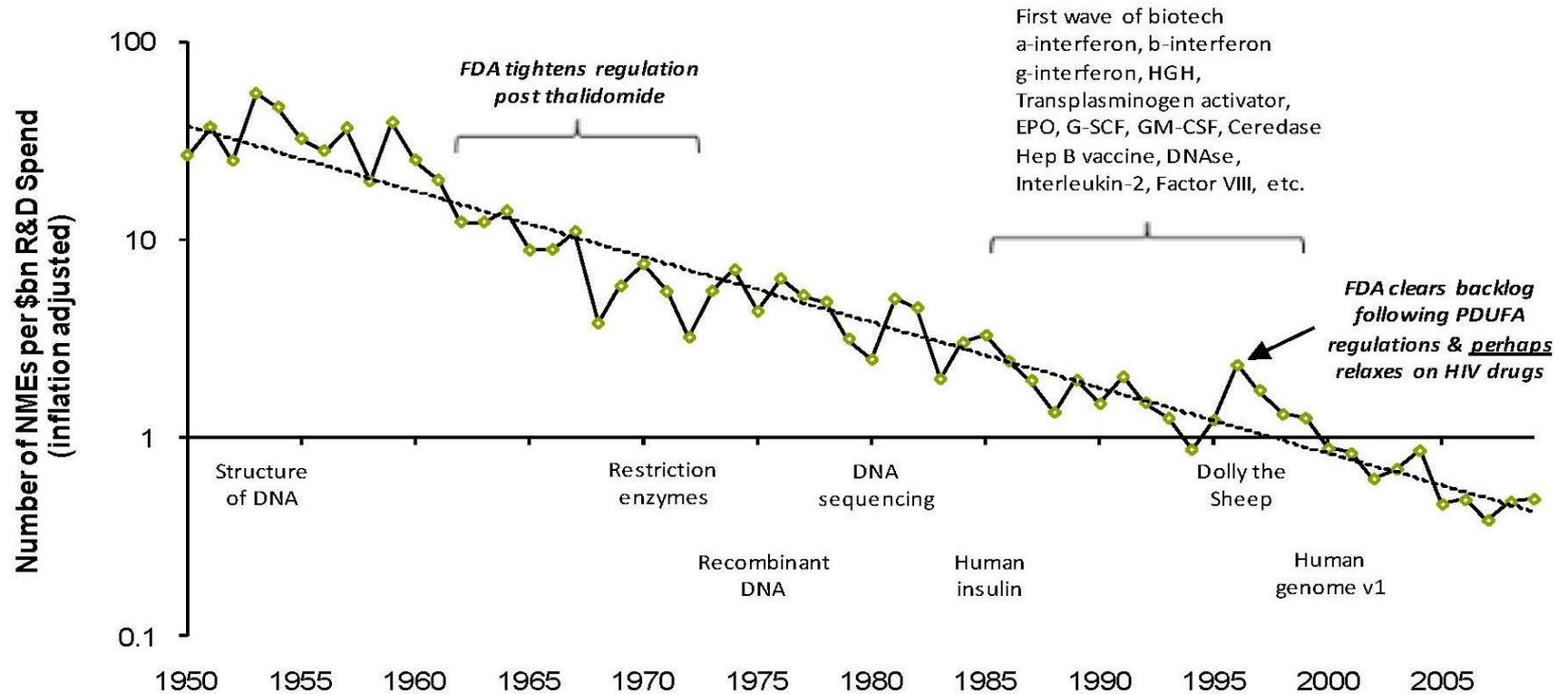
Source: *Nature Reviews: Drug Discovery, Lessons Learned from the Pharma Industry, December 2009*

Industry R&D productivity as assessed by 5th-year sales/ $1B R&D spend has dropped more than 70%

NMEs Approved per Year	x	Average 5th-Year Sales per NME (millions)	=	5th-Year Sales per Year (billions)	÷	R&D Spend per Year (billions)	=	5th-Year Sales per $1BN R&D Spend (millions)

Values shown:
- NMEs Approved per Year: 36 (1996–2004), 22 (2005–2010)
- Average 5th-Year Sales per NME: $515, $430
- 5th-Year Sales per Year: $18.3, $9.4
- R&D Spend per Year: 65, 125
- 5th-Year Sales per $1BN R&D Spend: $275, $75 — More than 70%

Legend: 2005–2010, 1996–2004

Sources: Drugs@FDA database, EvaluatePharma, Oliver Wyman analysis

Source: Oliver Wyman 2011

Evolution of drug regulation
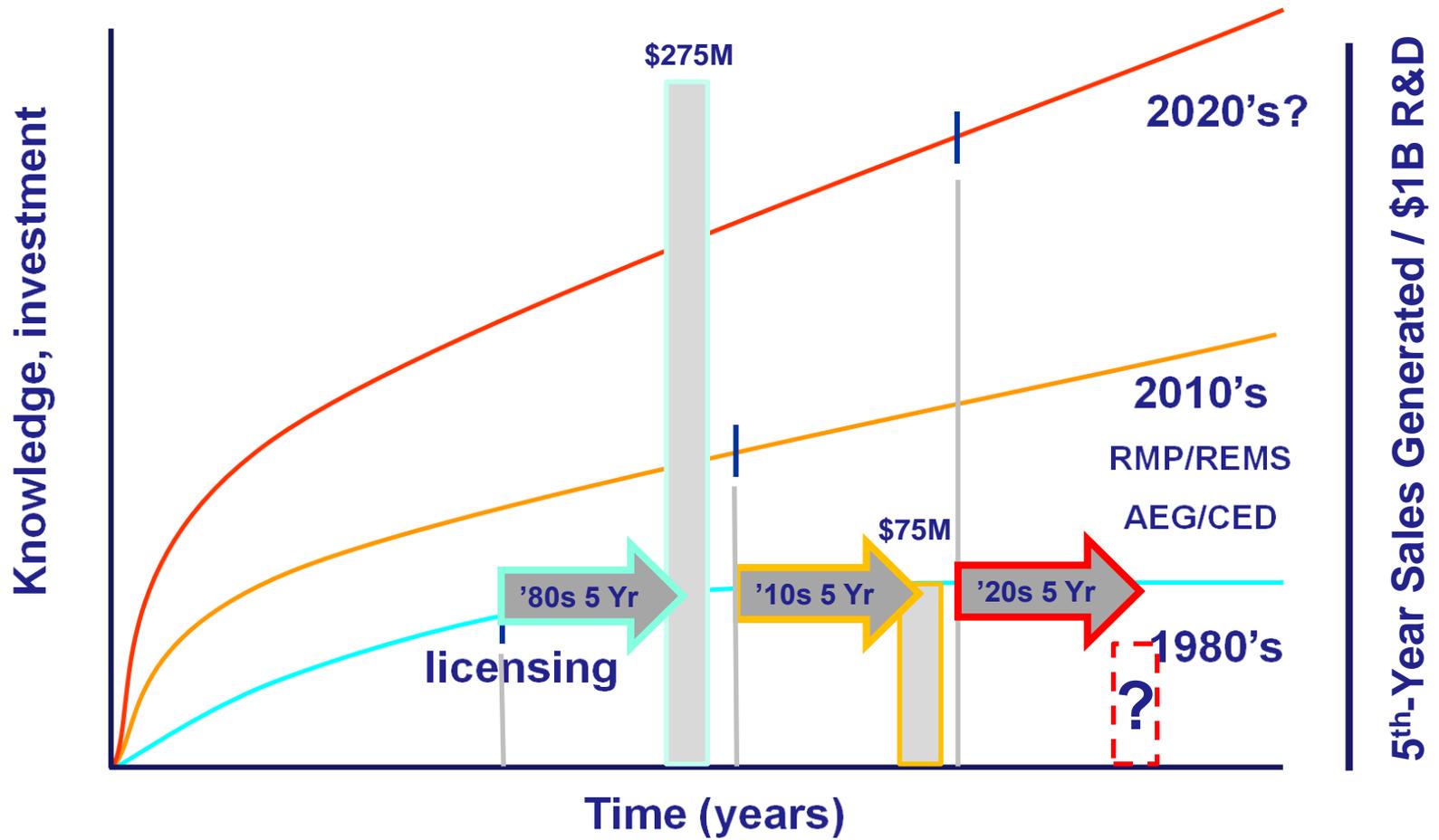
Source: HG Eichler, Oliver Wyman 2011

Are we effectively learning about new therapeutics being developed?

Medco Study Finds Many Patients on Newer Oncology Treatments Are at Risk for Drug Interactions
Oral Cancer Drugs Need Added Monitoring to Prevent Safety Risks, Impaired Effectiveness
Mar 16, 2012

WASHINGTON, March 16, 2012 /PRNewswire/ -- Oral cancer drugs that target key enzymes in tumor cells have made significant contributions to oncology care, freeing many patients from spending long hours at infusion centers to receive their chemotherapy treatments. But new research shows that many patients using these oral medications are also on other drugs that may prevent patients from getting the full benefit from their cancer treatment, or increase the risk of side effects.

(Logo: http://photos.prnewswire.com/prnh/20100609/MEDCOLOGO)

The study by the Med...
presented today at th...

The research found th...
potential to reduce the...
known as oral kinase i...
cause drug-drug intera...
antifungal agents.

- "The research found that 23-74 percent of patients taking one of nine oral oncology medications were also on a drug that had the potential to reduce the effectiveness of the cancer treatment or increase its toxicity."

State of drug development

- R&D productivity continues to decline
- Value of drugs has declined
- Time, cost and complexity of approvals increasing
- Despite an attempt to improve the quality of knowledge of approved drugs, the state of knowledge of a drug post approval, under current drug development approaches, must improve

What is adaptive decision making?

- A structured, iterative process of optimal decision making in the face of uncertainty
- Aim to reducing uncertainty over time via system monitoring
- Simultaneously maximizes one or more resource objectives and, either passively or actively, accrues information needed to improve future management

- Adaptive decision making a long standing tool effective in management
  - Adaptive management is a tool which should be *used not only to change a system, but also to learn about the system* (Holling 1978)
  - Because adaptive management is *based on a learning process, it improves long - term management outcomes*
  - The challenge in using the adaptive management approach lies in finding the correct balance between gaining knowledge to improve management in the future and achieving the best short - term outcome based on current knowledge (Stankey & Allan 2009)
  - Adaptive management is particularly applicable for *systems in which learning via experimentation is impractical* (Elzinga et al. 1998; Alana & Michael, 2009
  - The achievement of these objectives requires an open management process which *seeks to include past, present and future stakeholders*

MIT/NEWDIGS Case Study*: Antibacterial Indication

Current Development Model

Submit NDA NDA Approved

Year 1	Year 2	Year 3	Year 4	Year 5	Year 6	Year 7	Year 8	Year 9	Year 10

AL Model

Year 1	Year 2	Year 3	Year 4	Year 5
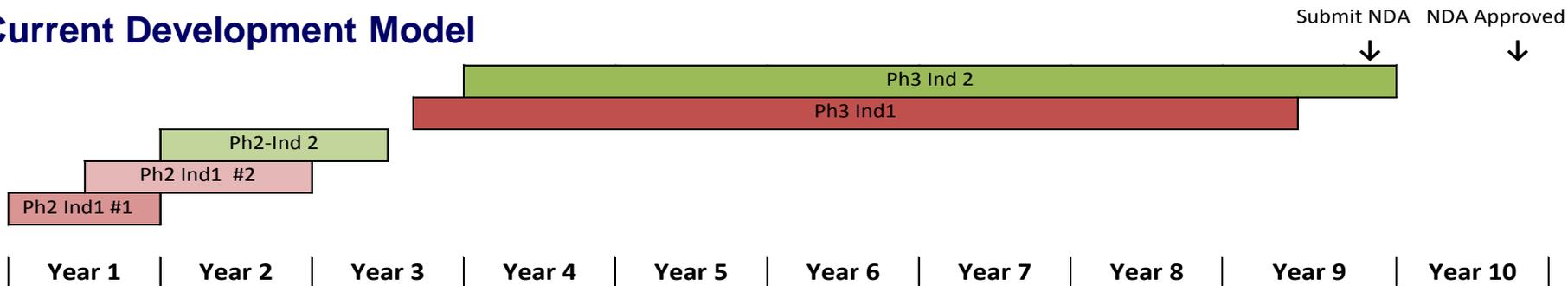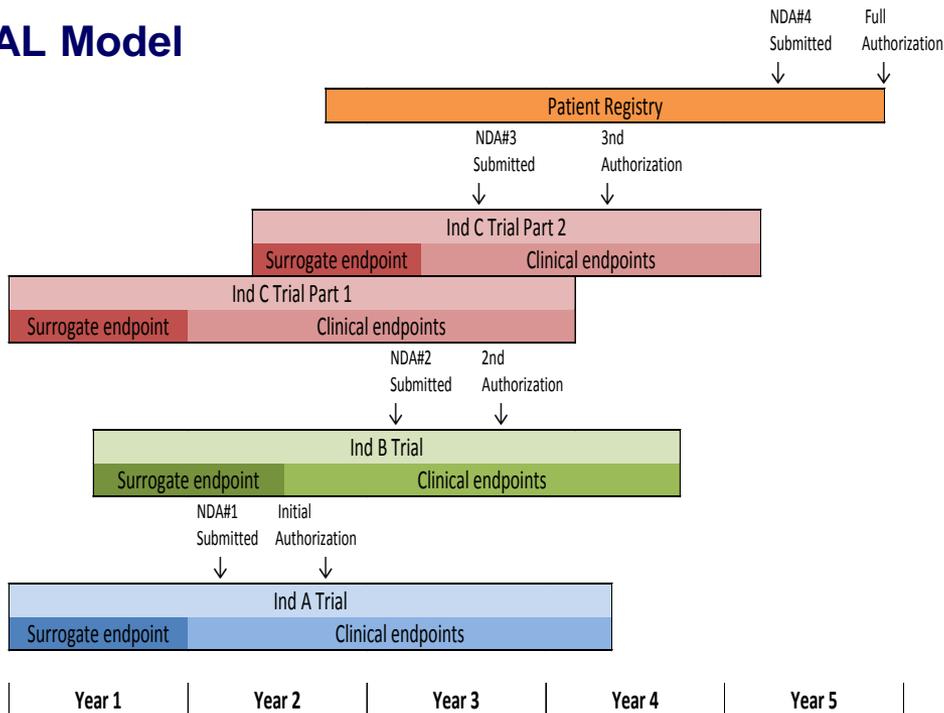
Key premises of Adaptive Licensing of drugs

- Considers the totality of a plan over a lifecycle perspective
- Improves efficiency of obtaining data at key decision points, especially at earlier decisions
- Does not assume weakening of safety or efficacy standards
  - Decision making based on acceptable benefit/risk relevant to sub-populations
- In many cases imposes restrictions and conditions
  - Including informed consent, registries and restricted distribution
- Iterative data collection and reevaluation
  - Post approval data collection
  - Modifications based on evolving knowledge on benefit/risk/harm obtained from ongoing studies and real-world data
  - Controlled expansion
- Improved relevance to patients
- Not appropriate for all products
- Build upon best regulatory science methodologies

There are a number of critical question for industry to consider…

- **Understanding ideal use of Adaptive Licensing as a tool**
  - Narrow to wide expansion - marketplace dynamics
  - Data may require narrowing of the target population
  - Mechanism to contract label post initial or full authorization
- **How Adaptive Licensing fits into a global development strategy**
- **Understanding the financial and economic impacts**
  - Impact on NPV versus conventional approaches
  - Changes of risk profile by reduction of risk through earlier knowledge and real-world data
  - Intellectual property impact – product exclusivity
- **Pricing and reimbursement strategies**
  - Will there be sufficient early data at launch
- **Competitive strategy – validating mechanisms and fast followers**
- **Post authorization commitments**
  - Design and cost of programs; length of time required adequately fulfill requirements
  - Ability to access data in a timely manner to effectively support assessments
- **Benefit risk frameworks that are appropriate to inform decision point**

….and other requirements and potential implications

- Would restrictions on use appear that regulators are moving to regulate medical practice
- Acceptance and transition to a structured learning approach
- Changing mindset from large indications to more focused sub-groups
- Cost requirements to support front and back-end obligation
- Clear understanding and validation of required "enablers"
  - Benefit/risk framework
  - Registries
  - Restricted access
  - Active pharmacovigalence
  - Acquisition of required information – EMR/HER

- Pilots to fully understand dynamics and requirements

In appropriate cases, there can be many benefits for industry and regulators to consider Adaptive Licensing approaches

- Improve access to new therapeutics
  - Reduced time and costs at risk
  - Open up "lost" therapeutic areas where investment and risk seen as excessively high
- Shorter cycles of structured learning can improve knowledge for subsequent trials, authorization decisions and post approval utilization
- Improved focus on disease understanding across stakeholders
- More robust discussions and consideration of benefit/risk
  - Improved consideration of benefit or acceptable benefit and risks
  - Improved mechanism to decrease risk of a large populations
  - Tightly framed and relevant to patients
- Improved transparency and communication with others
  - Engaging patients and providers more effectively
  - Communication that knowledge of a drug is not binary
- Accelerate and augment post-approval data analysis and utilization
- Mechanism that is adaptive with evolution of technologies and medical science

In appropriate cases, there can be many benefits for industry and regulators to consider Adaptive Licensing approaches

- Parallel trials that can provide more actionable data during development
- Considers the totality of data for optimal decision making in the face of uncertainty
  - Not just based on surrogates, but proactive thorough assessment of efficacy and safety data – often with relevance to disease and to real world
- Impact on clinical trial designs and costs
  - Real-world aspects may improve rate of recruitment into trials - with higher front end costs?
- More informed adoption for following indications through decreased risk, adherence programs and improved understanding of outcomes
- Improve predictive value of early studies
- Generation and utilization of real world data
  - Improved awareness of polypharmacy issues
  - Increase prediction in real world population

- An opportunity to improve societal ROI on massive investments in health
- Address the changing tide of R&D investment – large pharma and venture community

Current paradigm characterized by periods of significant value loss based on inefficiencies
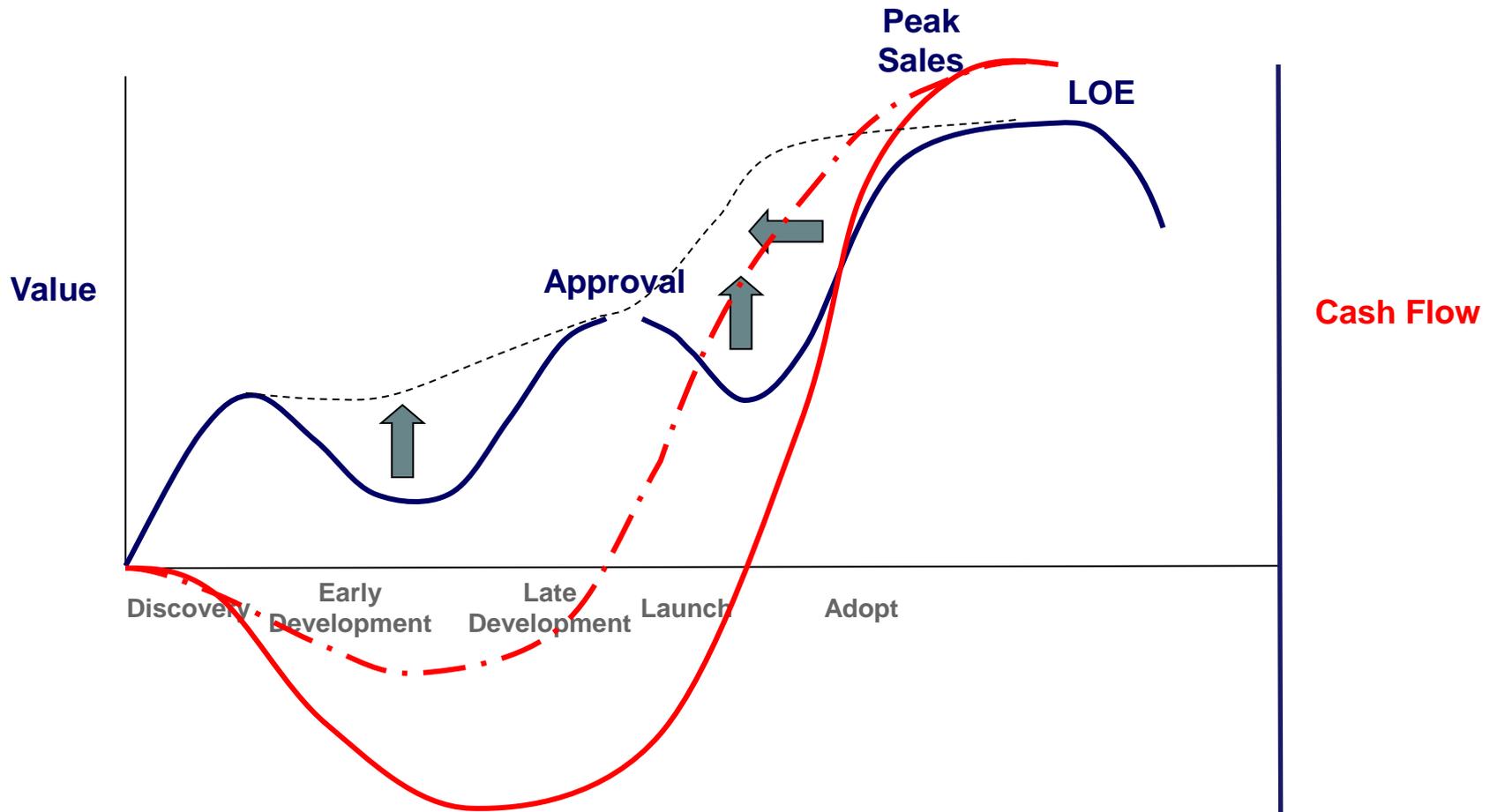
An approach worth exploring?

- A structured learning process built on existing and established ideas
- Mechanism that keeps pace with emerging knowledge and science
- May open lost therapeutic areas and improve access where no or unacceptable treatments exists
- Facilitates import communication of relevant benefit/risks with important communities
- Improving understanding in real-world populations
- Short-term and long-term benefits to generate therapeutics and improve the process of drug development
- Improve economics of drug development

- *Thank you*