Academic Industry partnership

"*Various models, Various outcomes*"

Drug Discovery, Development and Commercialization
UCSD, Skaggs School of Pharmacy, *class 2013*
Feb 28th 2013

Remi Brouard, MD,
VP External Innovation,
Sanofi Recherche West Coast

Academic Industry partnership
"Various models, Various outcomes"
Summary

- **Changing landscape in Healthcare systems and pharma industry**
  - Healthcare cost, large vision of Healthcare
  - Innovation
  - Partnering with Academics, natural/obvious research partner.

- **Emergence of Various Models. Changing landscape of innovation and disease treatment**
  - Novel and emerging technologies
  - Growing area of innovation, potential game changer
  - Various field of Academic collaboration (when and how)

- **Model and outcomes of partnering**
  - Various experiences
  - Models most commonly used and emerging models
  - Human factor and outcomes

History & Changing Landscape

Historical Model

- **Public Sector**
  - Basic fundamental biological research

→

- **Private sector**
  - Discovery
  - Preclinical
  - Clinical testing
  - Regulatory approval
  - Manufacturing
  - Product distribution

Increase Scientific knowledge
Public health concerns
Economic challenge

= New Model

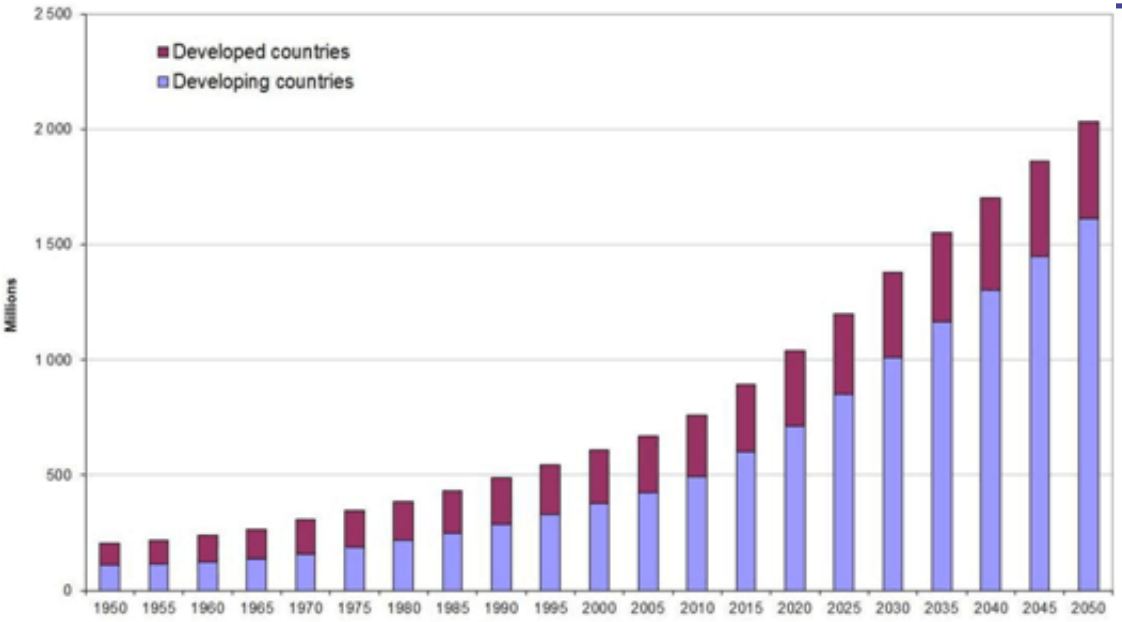
Emergence of partnership,Tech Transfer incentives,
(Bayh Dole act, EFPIA, harmonization collab…)

→

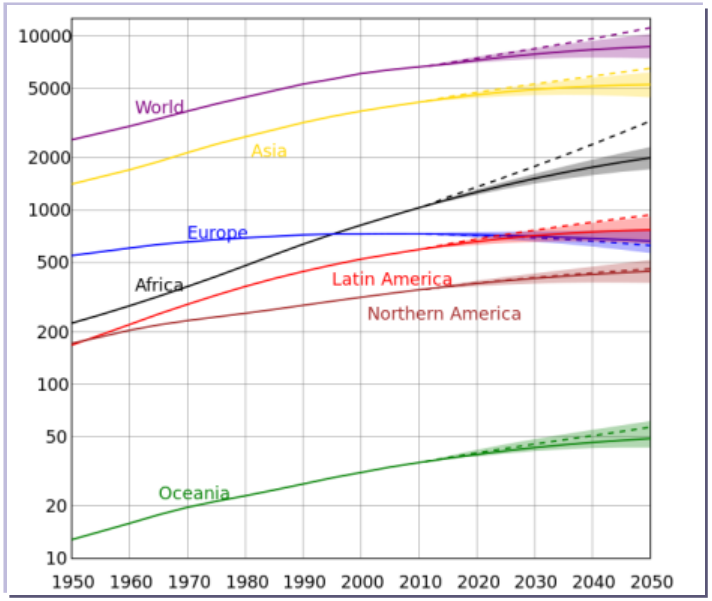
Private Public partnership

"Bringing together funds, scientific knowledge and centers of excellence"

Demography and Ageing impact



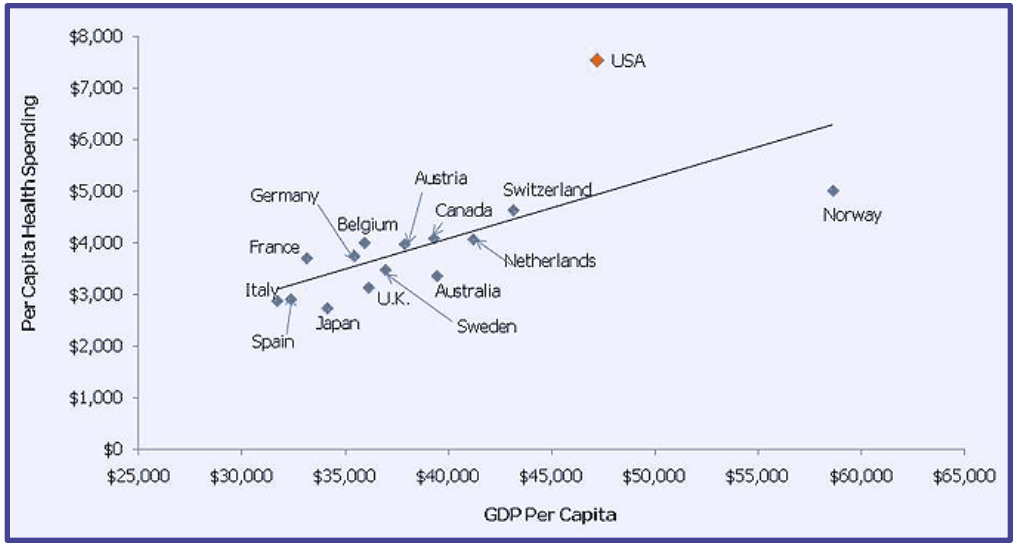
Source UNFPA 2012: Number of people aged 60 or over World, developed and developing countries, 1950-2050



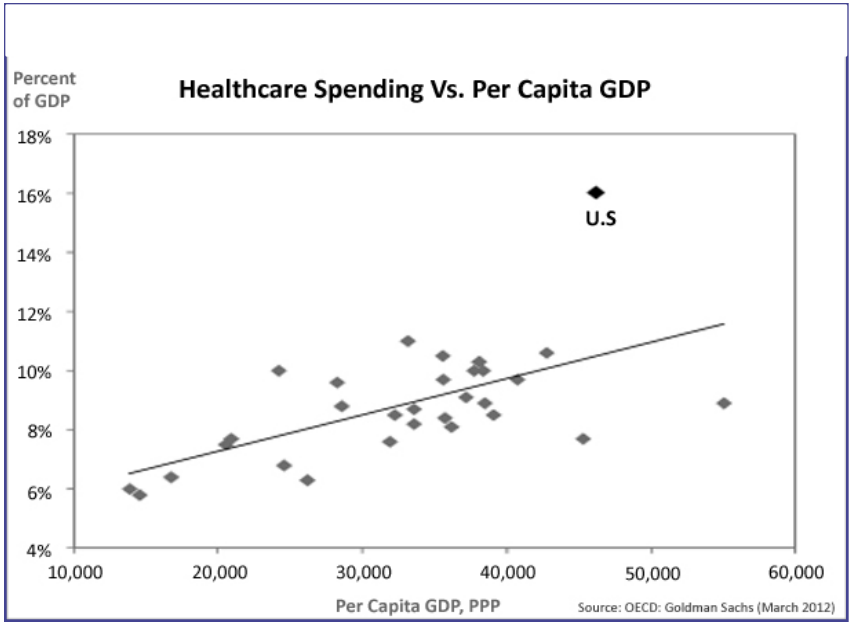
Source WHO 2011, United Nation's population projections by location. (millions of people)

Impact on Governments and allocation of resource for health

Healthcare cost impact (vs Gross Domestic Product)



Source OECD 2011



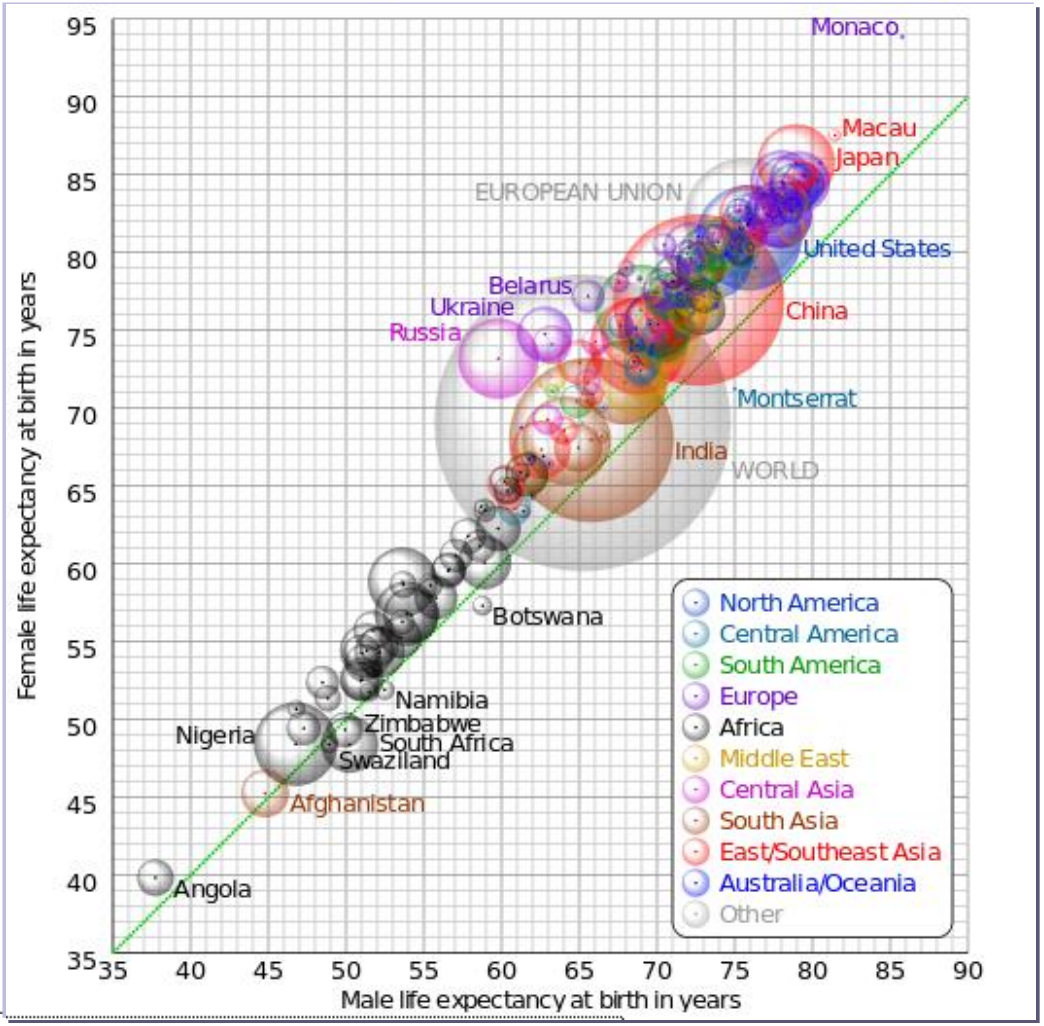
Source Goldman Sachs 2012

Impact on Payers, Pharma and Academics

Leading causes of Death and Life expectancy at birth

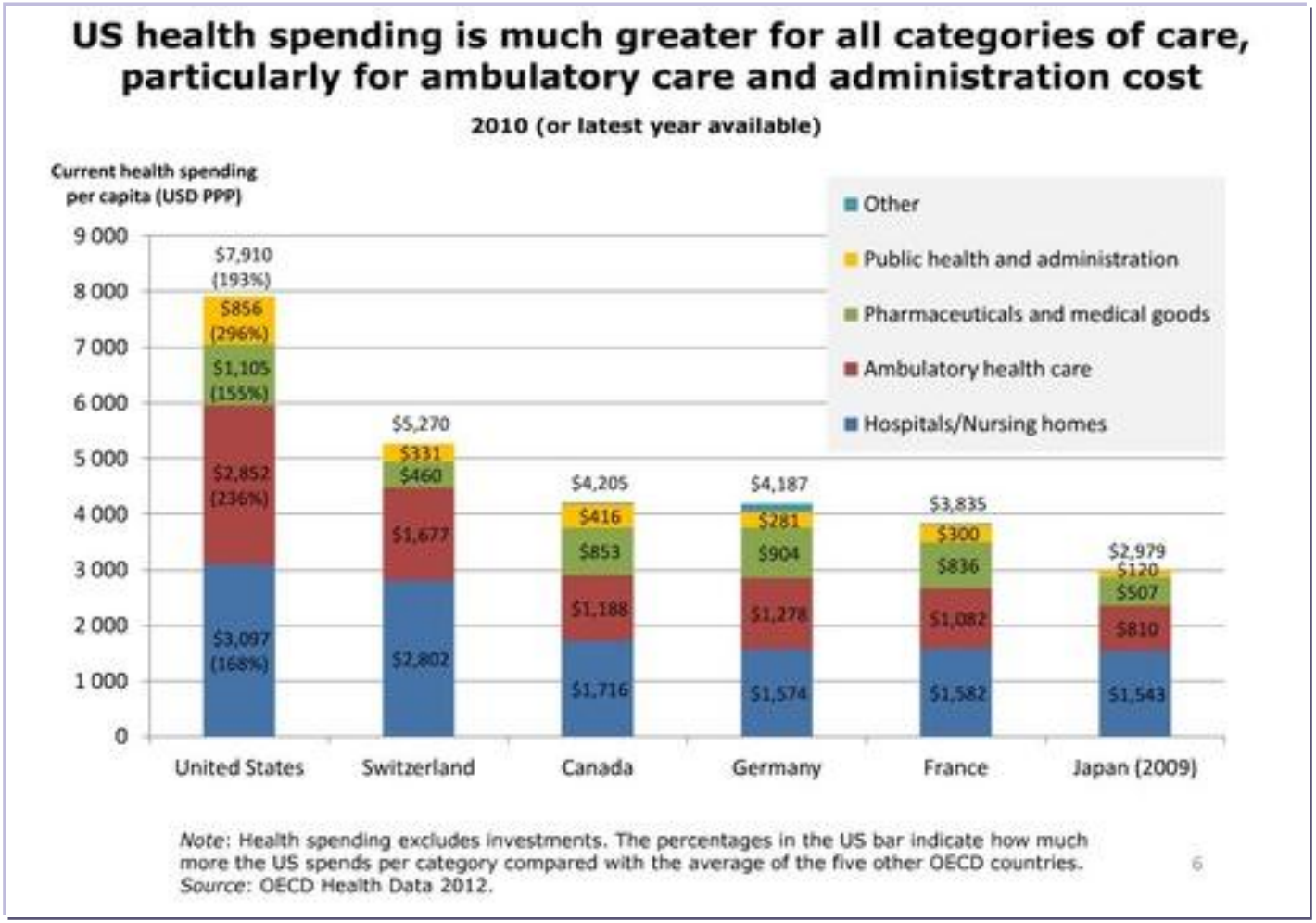
World			
Rank	Cause	Deaths (000s)	%
1	Ischaemic heart disease	3371	12.2
2	Stroke	3051	11.1
3	Lower respiratory infections	2014	7.3
4	COPD*	1405	5.1
5	Diarrhoeal diseases	1037	3.8
6	HIV/AIDS	1013	3.7
7	Diabetes mellitus	633	2.3
8	Prematurity and low birth weight	567	2.1
9	Neonatal infections**	546	2.0
10	Hypertensive heart disease	530	1.9

Low-income countries			
Rank	Cause	Deaths (000s)	%
1	Lower respiratory infections	1397	11.4
2	Ischaemic heart disease	1061	8.7
3	Diarrhoeal diseases	851	7.0
4	Stroke	749	6.1
5	HIV/AIDS	742	6.1
6	Maternal conditions	442	3.6
7	Neonatal infections**	426	3.5
8	Prematurity and low birth weight	405	3.3
9	Malaria	404	3.3
10	COPD*	404	3.3

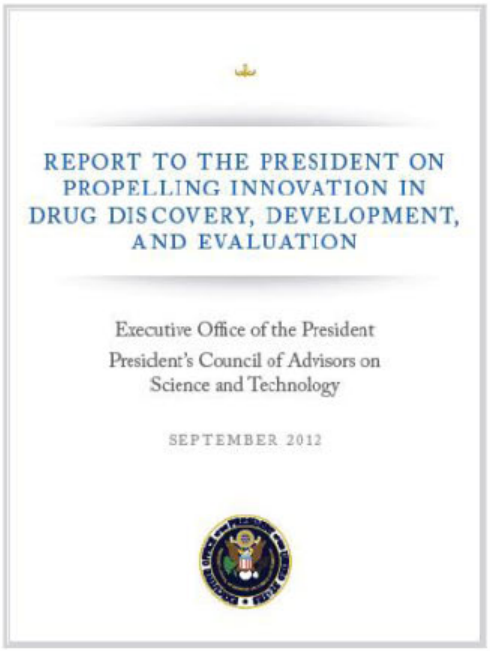


Source WHO, 2010

Contribution of categories of care in US health spending

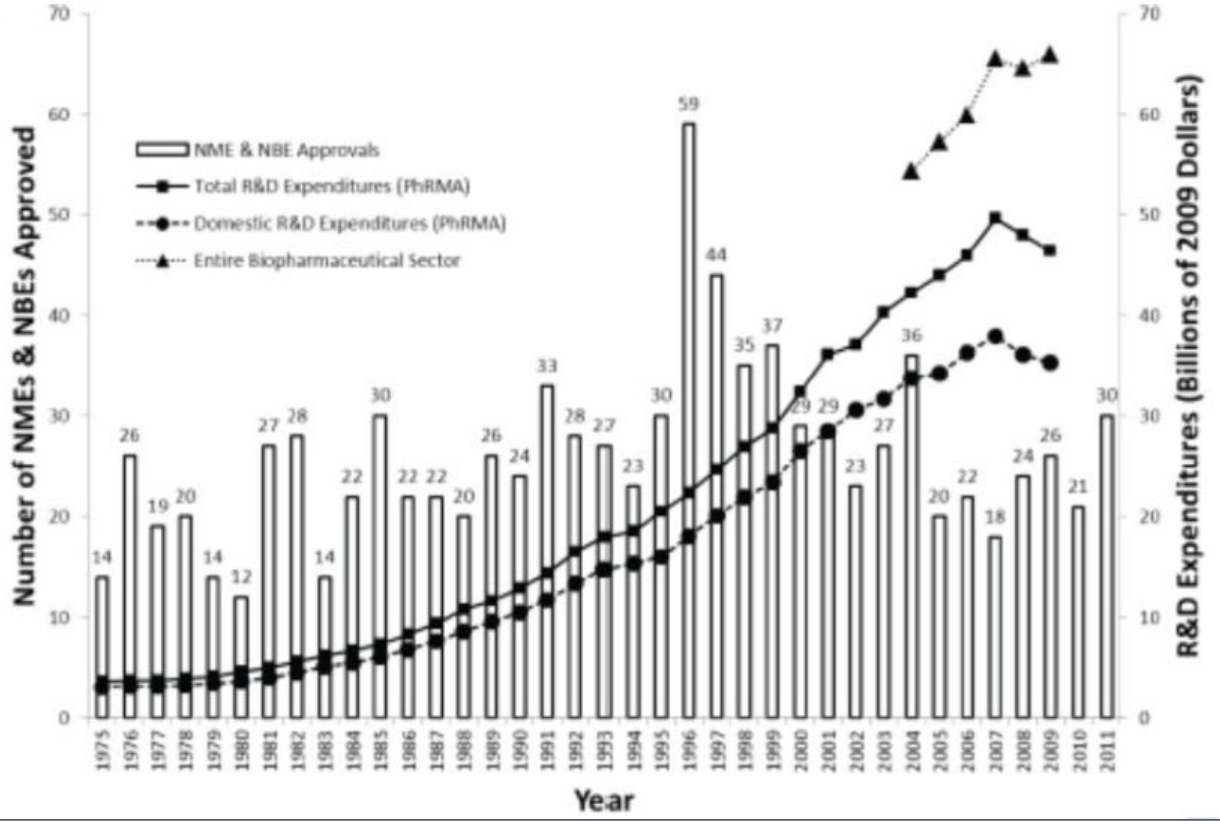


Changing Landscape in the Pharma Industry


REPORT TO THE PRESIDENT ON PROPELLING INNOVATION IN DRUG DISCOVERY, DEVELOPMENT, AND EVALUATION

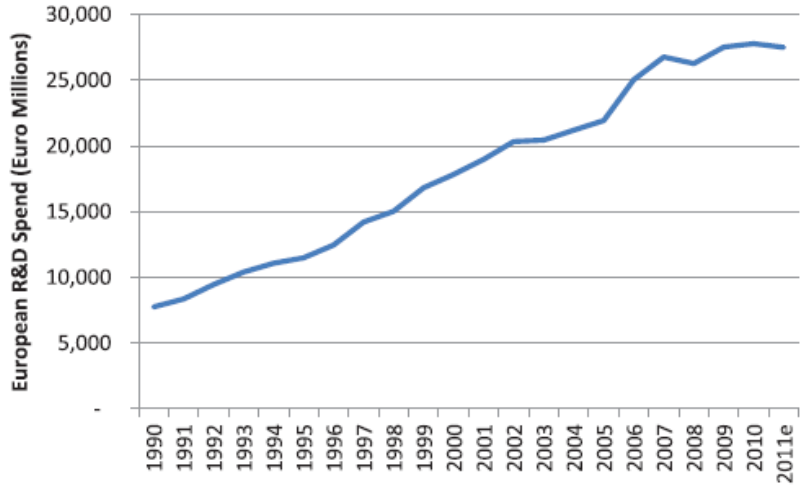
Executive Office of the President
President's Council of Advisors on Science and Technology

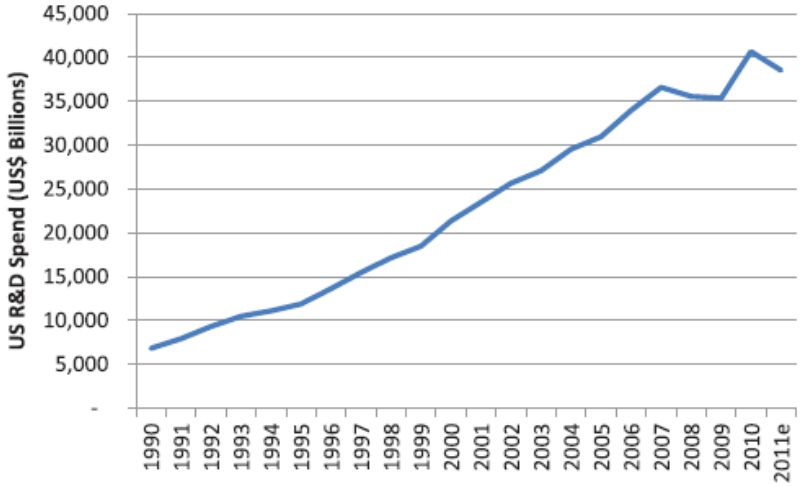
SEPTEMBER 2012



R&D spending reaching limits…

European and US R&D Spending





Source: EFPIA (2012)

Risk sharing, collaboration is becoming crucial

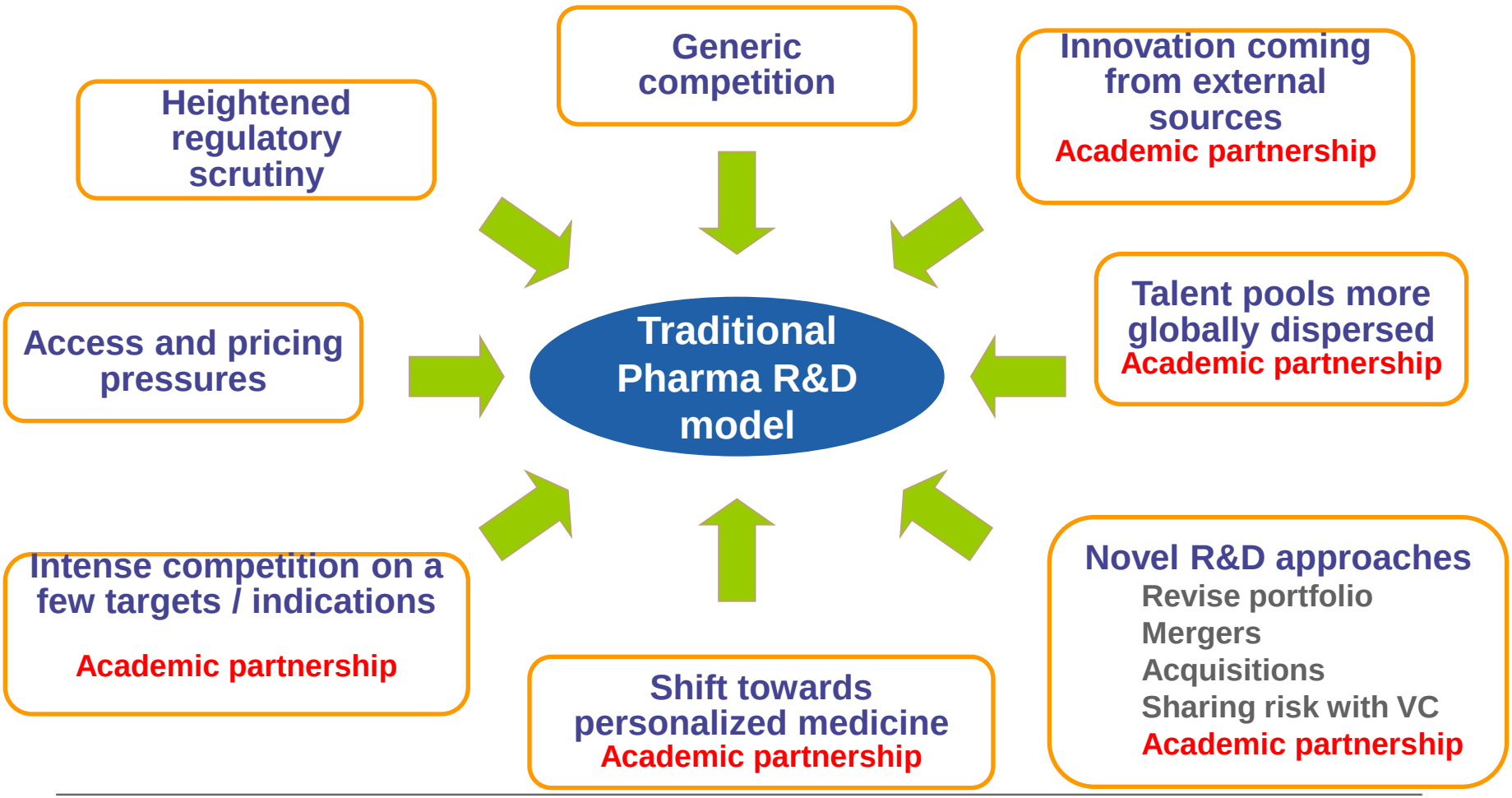
R&D spending reaching limits…

Research Spending Per New Drug

Company	Ticker	Number of drugs approved	R&D Spending Per Drug ($Mil)	Total R&D Spending 1997-2011 ($Mil)
AstraZeneca	AZN	5	11,790.93	58,955
GlaxoSmithKline	GSK	10	8,170.81	81,708
Sanofi	SNY	8	7,909.26	63,274
Roche Holding AG	RHHBY	11	7,803.77	85,841
Pfizer Inc.	PFE	14	7,727.03	108,178
Johnson & Johnson	JNJ	15	5,885.65	88,285
Eli Lilly & Co.	LLY	11	4,577.04	50,347
Abbott Laboratories	ABT	8	4,496.21	35,970
Merck & Co Inc	MRK	16	4,209.99	67,360
Bristol-Myers Squibb Co.	BMY	11	4,152.26	45,675
Novartis AG	NVS	21	3,983.13	83,646
Amgen Inc.	AMGN	9	3,692.14	33,229

Sources: InnoThink Center For Research In Biomedical Innovation; Thomson Reuters Fundamentals via FactSet Research Systems

Real challenges putting pressure on the traditional R&D model within Pharma



Collaboration with Academics
Obvious partner going beyond just funding

Examples of what could be attractive for Pharma

- Opportunity to diversify portfolio
- Access to leading research and disruptive science (potential game changer)
- Data exchange
- Target and new pathway expertise
- In vivo disease model expertise
- Access to database of patient
- …

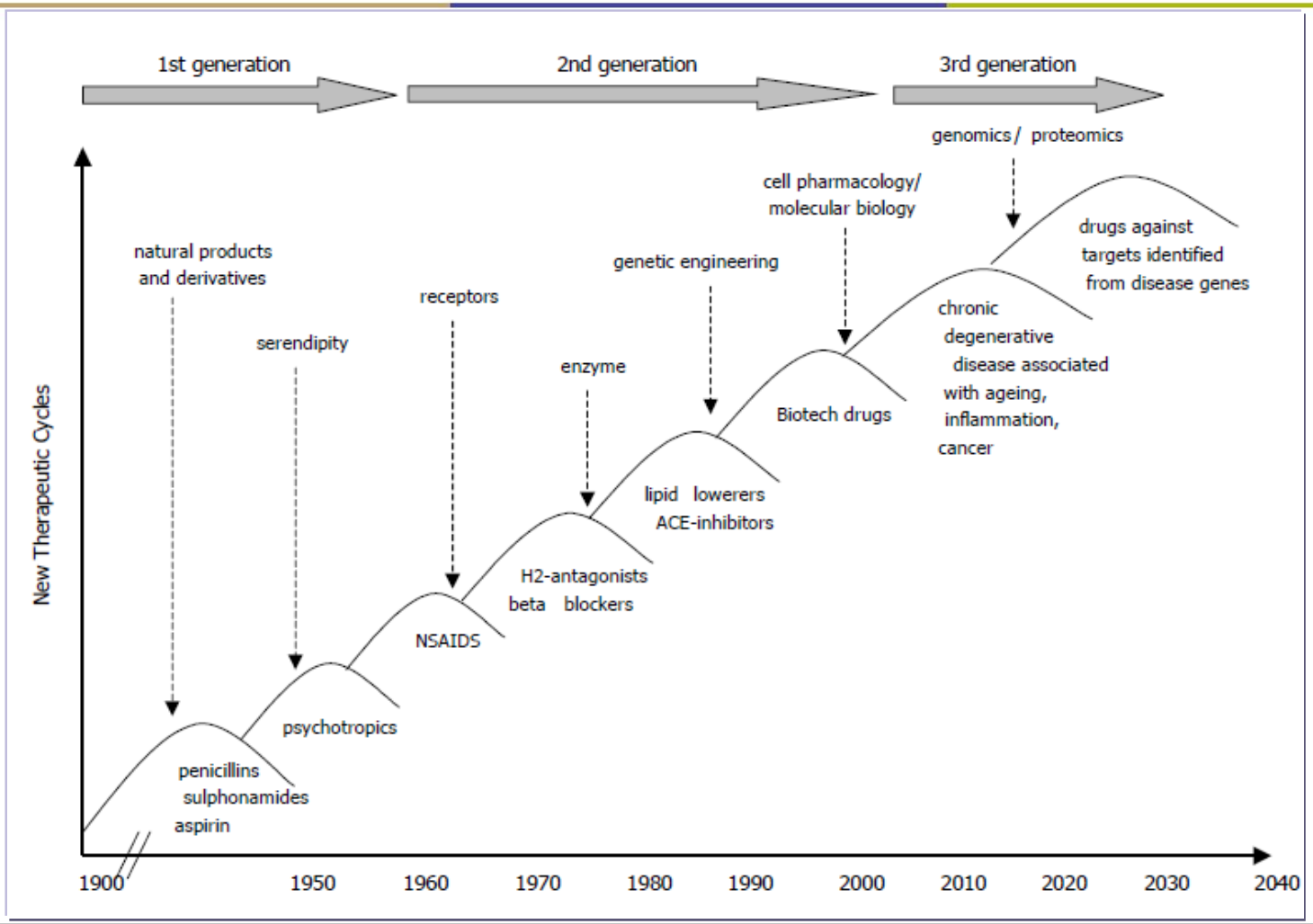
Examples of what could be attractive for Academics

- Translational applications of discovery
- Synthesis capacity + scale up
- Capacity to run parallel development
- Access to multidisciplinary development team
- Ability to move forward new investigational compounds, assay development.
- Access to chemistry library, HTS
- …

What should always be mutually discussed and agreed :

- **Ownership of intellectual property**
- **Financial return arrangement**
- **Resource manpower**
- **Team contribution**
- **Deadlines**
- **Budget**
- **Deliverable**

Historical contribution of Academics
Cycles of innovation



Growing area of Innovation
Potential game changer with Academic partners

- **MAbs.**
  - Cancer, infectious disease, as well as inflammation and immune disorders. MAbs have also revolutionized our ability to diagnose disease
- **Biomarkers technologies, Pharmacogenomics**
  - Technology breakthroughs are accelerating the pace of biomarker discovery based on proteomics, genomics, metabolomics and imaging
    - Improved read-out of drug action
    - Companion diagnosis
    - Ability to segment a drug to the right patient population…and obtain reimbursement
- **Stem Cells**
  - **Beyond cell therapy:** Disease in a dish. Using various sources of stem cells that have been induced to differentiate into the specific type of cell required to repair damaged or destroyed cell populations or tissues. Deeper understanding of physiological & pathological control mechanisms
- **RNA Interference**
  - Using a cellular pathway to silence specific genes by preventing the translation of the proteins they encode

Growing area of Innovation
Emerging Technologies with Academic partner

- **Microfluidics, Nanotechnology**
  - "From Lab in a chip, to lab in the body" : smaller sample volumes enabling more to be done with less (biopsies, electrolytes, protein, …)
  - Single cell highly multiplexed omic and phenotypic analysis
  - Drug delivery system

- **Next generation DNA sequencing**: nanopore/ nanochannel, electronic detection, …

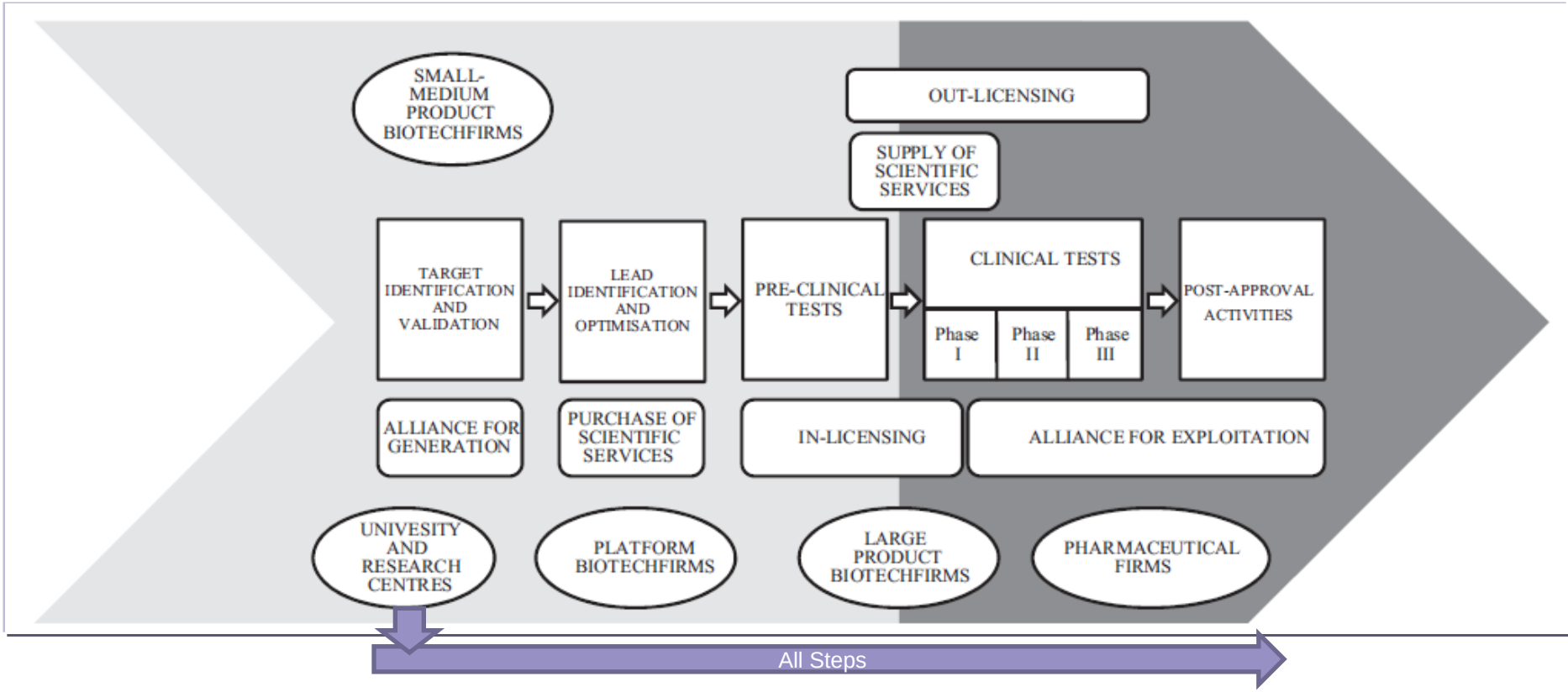
- **Imaging technologies:** in vivo molecular analyses for interaction as well as temporal and spatial dynamics, medical imaging understanding of pathophysiology

- **Analytical tools**, computational science, big data integration, emergence of multiple predictive models, decision support system

- **Drug Devices**
  - Diagnostic tools, E medicine, Non invasive devices
  - Combination: Two or more regulatory-approved components as a single entity (coated stent)

Collaboration between Academic and Pharma

Any step during devlpt are possible



Open innovation modes & partners along the phases of the drug discovery and devlpt process

Source : Technovation 2011, 31: 22-33

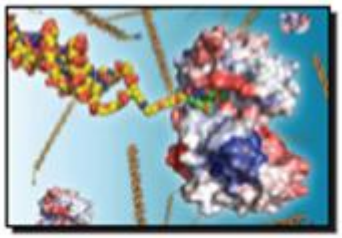
Preclinical large various fields of collaboration

Large scale protein production

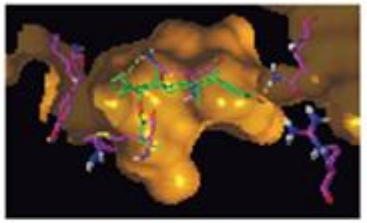
HTS capacity

Flexible, high tech assay platforms

"From target identification / physiological proof of concept to optimization"



Encoded Library technology



Medicinal chemistry and computational molecular design

Clinical collaboration with Academics

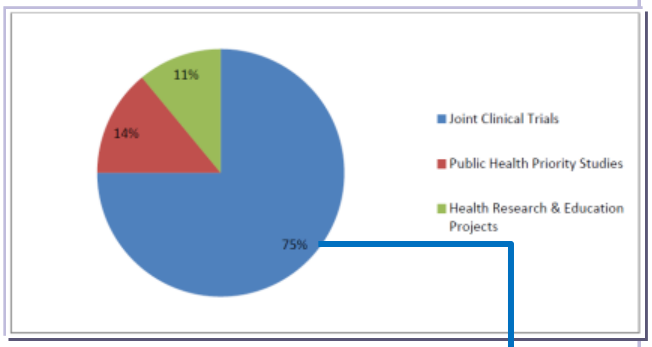
Translational application is mandatory
Access to patients / database

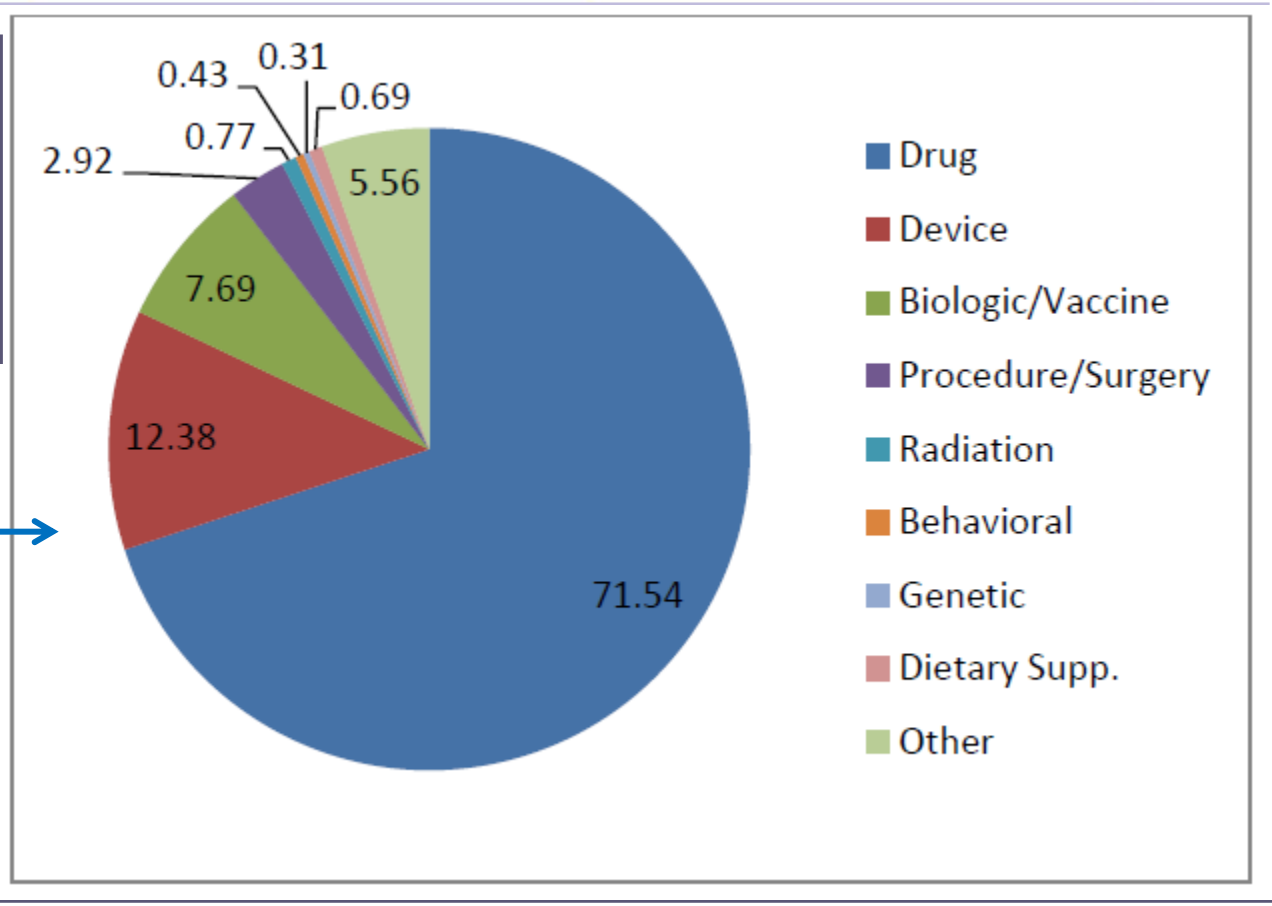
- **Clinical investigation (Drug devlpt)**
  - **Investigational drug phase (directly monitored Phase 1 or 2 or via CRO)**
    - Sponsor IND Principal investigator, multi-centric trial,
    - Investigator IND
  - **Registry of special population (long term follow-up)**
  - **Compassionate access**

- **Clinical investigation (Basic Medicine)**
  - **Prospective or retrospective cohorts, pharmaco-economic studies**
  - **Translational Medicine (Biological target identification, Phase 0, Biomarker identification/validation)**
  - **Exploratory trial (Proof of concept)**
  - **BioBanking investment : Clinical sample management can accelerate discoveries, lower the costs of research, identify disease mechanisms, and reduce the length and size of clinical trials**

- **Educational grants**
  - **Fellowship programs, workshop, conference, exchange of scientists**

Categories of collaboration



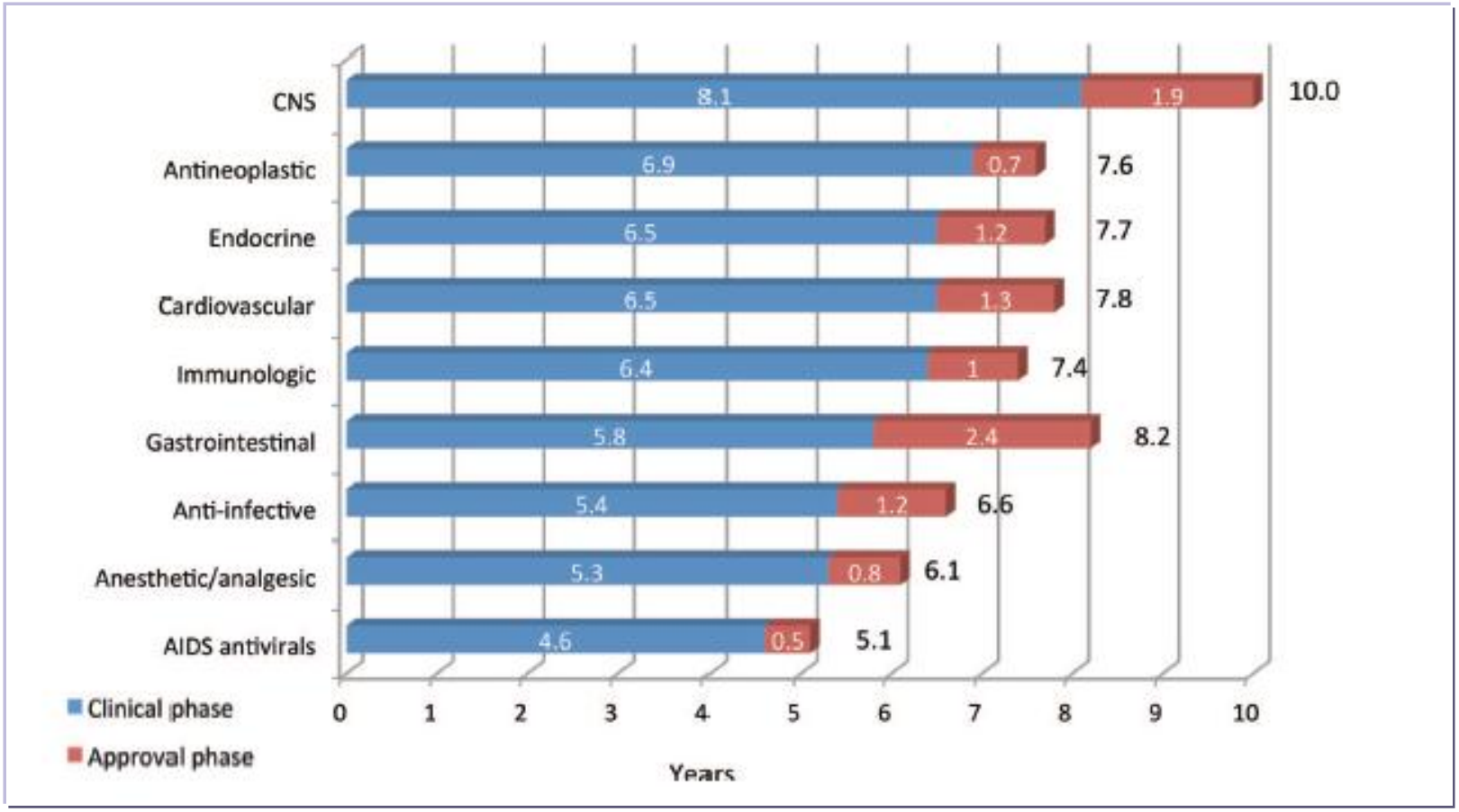


Type of clinical projects between Pharma and Academic Report on 3278 grants in the US, Period 2008-2010

(Source Academic-Industry Partnerships for biopharmaceutical Research and Devlopment, Tuft University, 2012)

Risky and long process

Mean clinical and approval phase times for approved NMEs by Therapeutic Class

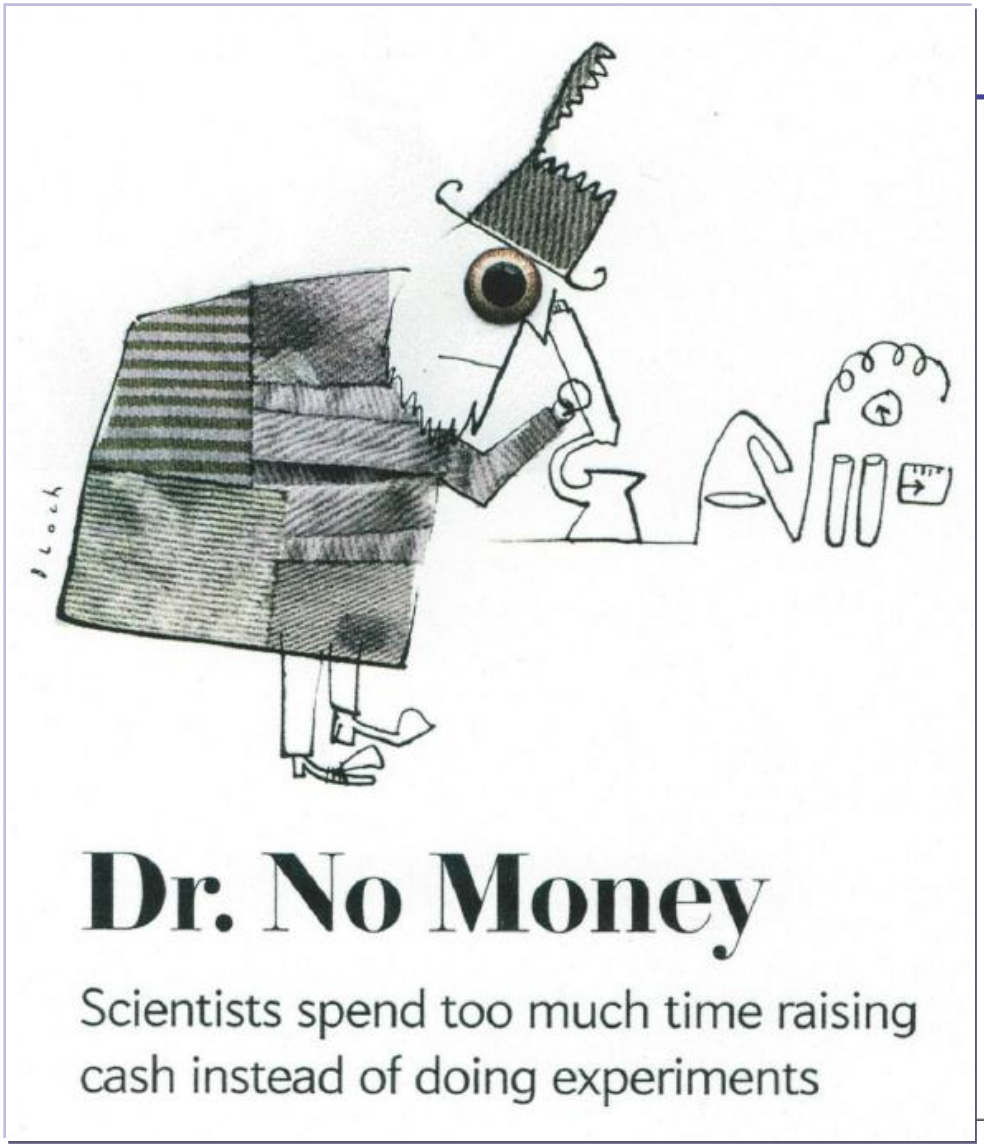


Source: Kaitin and DiMasi (2011)

Models widely used between Academic and Industry

- **Unrestricted research support**
  - High degree of independence of investigator
  - Unrestricted funds, less frequently used
  - High-risk, unpredictable return, dependence
  - Alliance based on trust and high level scientific full collaboration
- **Expert KOL exclusive relationship**
  - Expert generally participating to Company Board
  - Access to Company ressource
  - Specific to one domain. Short term in general
- **Fee for service**
  - Pharma to contract out specific project
  - Short term deal in general. Local expertise
  - Could be in a competitive way (RFP)

A Grants life…



Dr. No Money

Scientists spend too much time raising cash instead of doing experiments

10 Scientific American, May 2011

"In 2007 a US government study found that university faculty members spend about 40 % of their research time navigating the bureaucratic labyrinth for applying grants to the government agencies or private foundation….

…even for some of them it has a net negative value: they would not even pay for the time that applicants and peer reviewers spent on them"

Models widely used between Academics and Industry

- **Strategic Alliance with one University**
  - Several investigators or global deal focused on particular disease
  - Master agreement,
  - Sponsor Research Agreement,
  - Discovery award system and Request For Proposal system
  - High level of exchange of material
  - Human aspect , alliance manager aspect.
  - Joint steering committee
  - Long term commitment if high level of feedback and deliverable
  - Necessity of a win-win situation
  - Could include project team within Pharma with Academic leadership
  - Go /No-go decision should be anticipated

Models increasingly used between Academics and Industry

- Corporate Venture Capital (CVC)
  - **Company helps Academic experts to start company focused on specific problem or platform, with additional support of private investors (could by in kind or cash investment)**
  - **Need clear timelines and exit predefined terms**

- Corporate mini-lab within academic structure (biocluster)
  - **Specific specialized platform developed within university by academic scientist and Pharma.**
  - **Pharma can provide devlpt capacity and resource + eventually manpower.**
  - **Collaborative research agreement. Leverage academic expertise**
  - **Allow proximity research with daily interaction**

- Institute creation supported by Pharma
  - **Pharma provides large donation to establishes a new center within institute with multiple investigators addressing the same problem. Sponsor may additionally funds the team that solves problem first. Competitive mode. (Gilead-Yale School Med, cancer therapy; GSK –Harvard Stem Cell)**

Emerging models between Academic and Industry

- **Competition, challenging RFP**
  - Company solicits ideas/challenges from academic scientists, and selects most promising for further support (SRA or discovery award)
  - Competitive model
  - Award for possible drug candidate with a contribution of pharma to use computational molecule screen and to validate target based assays. (Eli Lilly Model; GSK Pharma in Partnership model)

- **Industry/Government funded research centers.**
  - Coalition Against Major Diseases (CAMD) a consortium under the Critical Path Institute. CAMD members (Academics, Pharma, Agencies, Patient advocacy group, & Research foundation contribute collectively)
  - Allow clarification of disease model, biomarker validation, and epidemiology (degenerative or rare disease)
  - CIRM model with Federal fund

Emerging models between Academics and Industry

- **Academic Drug Discovery Centers (ADDC)**
  - Industry entrepreneurs forming academic units, with commercial support. Mixed-ventures, scale down pharma model for small molecule discovery, synthetic chemistry, HTS, PK.
  - In general focus on orphan diseases (Moulder Center for Drug Discovery Research MCDDR Temple University).
  - Supports from Pharma are possible

- **Risk sharing models**
  - Companies and academic institutions share the control of a research project and split the contribution of resources and assets
  - Projects will involve co-development partners, such as contract research organizations (CROs), whose work will increase the technology probability of finding a corporate partner to bring the new products to market. (Evotec collab with Harvard and Howard Hugues Medical Institute to develop betacell regeneration program. All partners contribute financial resources or FTE/technology)

Outcomes depends on science and on human factors too…

- Effective Partnering Success Factors

  - **Matching Quality Science with Strategic Objectives**
    - Beyond science, never forget to include review of partner abilities, track records, facilities, management.
    - Anticipate reorganization, or at least be aware.

  - **Establishing Clear Expectations from both side**
    - Who is responsible for performing what tasks, by when, and at what cost
    - Anticipate turnover (Academics move as well !)
    - Re conduction of deals is rarely possible

  - **Respect Your Partner**
    - Shared vision, collaborative spirit, visible commitment by both sides
    - Communication is mandatory
    - Use your 5 senses, be physically present

Outcomes depends on science and on human factors too…

- Effective Partnering Success Factors

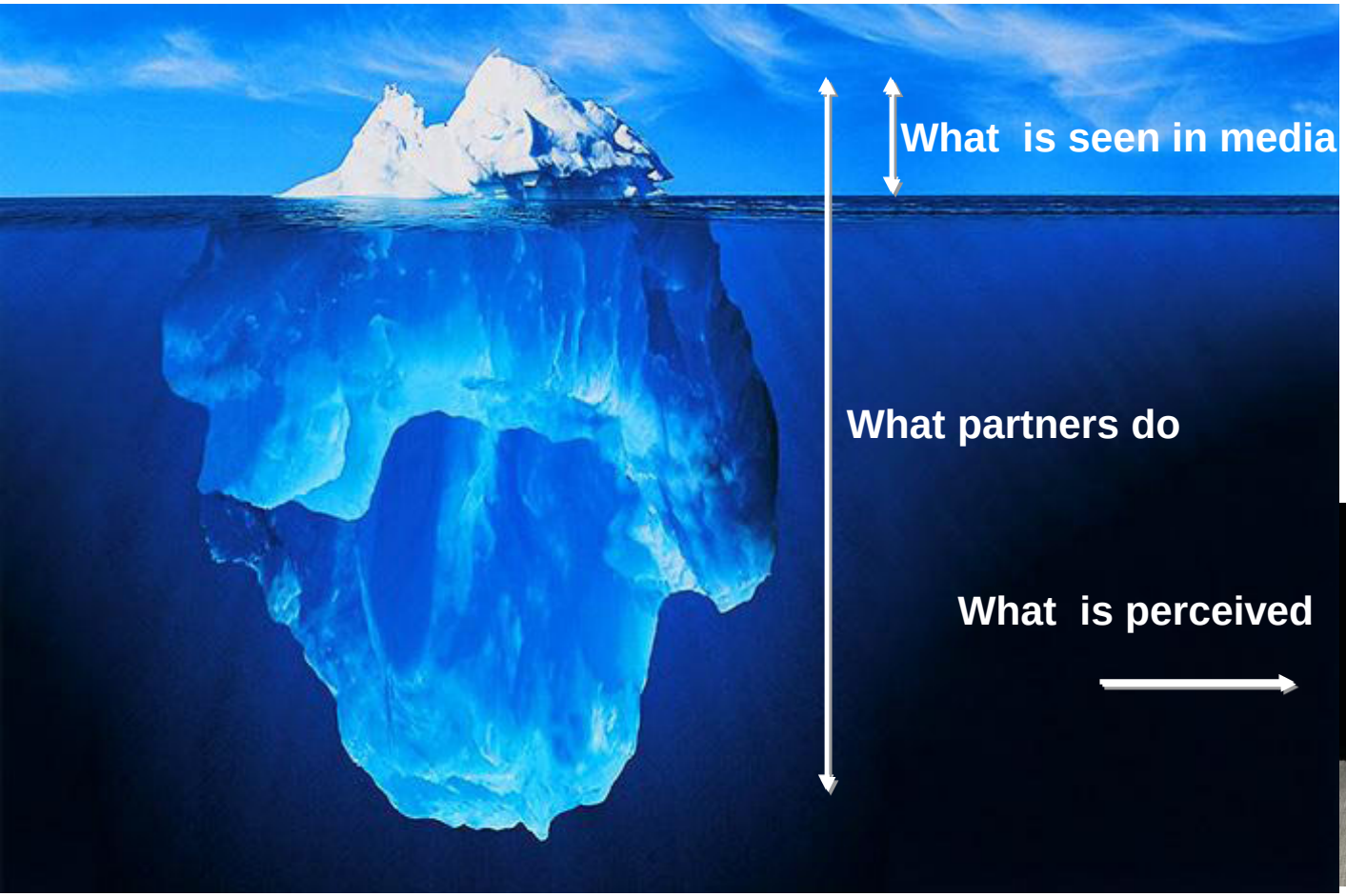
  - **Contract Negotiation**
    - Deal terms on intellectual property (access vs. ownership),
    - Publication rights (ensuring freedom to publish),
    - Liability, and confidentiality often can be balanced so that both sides achieve what they really need to get out of the collaboration

  - **Actively Manage the Collaboration**
    - Appropriate governance structures for strategic, scientific, and tactical decision making needs to be effective, fair, part of the contract, and clear to all

  - **Anticipate the Exit**
    - Anticipate success/failure : Exit of a deal (Startup, closure , ….)
    - Exit can be a Success

Partnering activities : Outcomes

Perception vs Judgment - What is perceived?

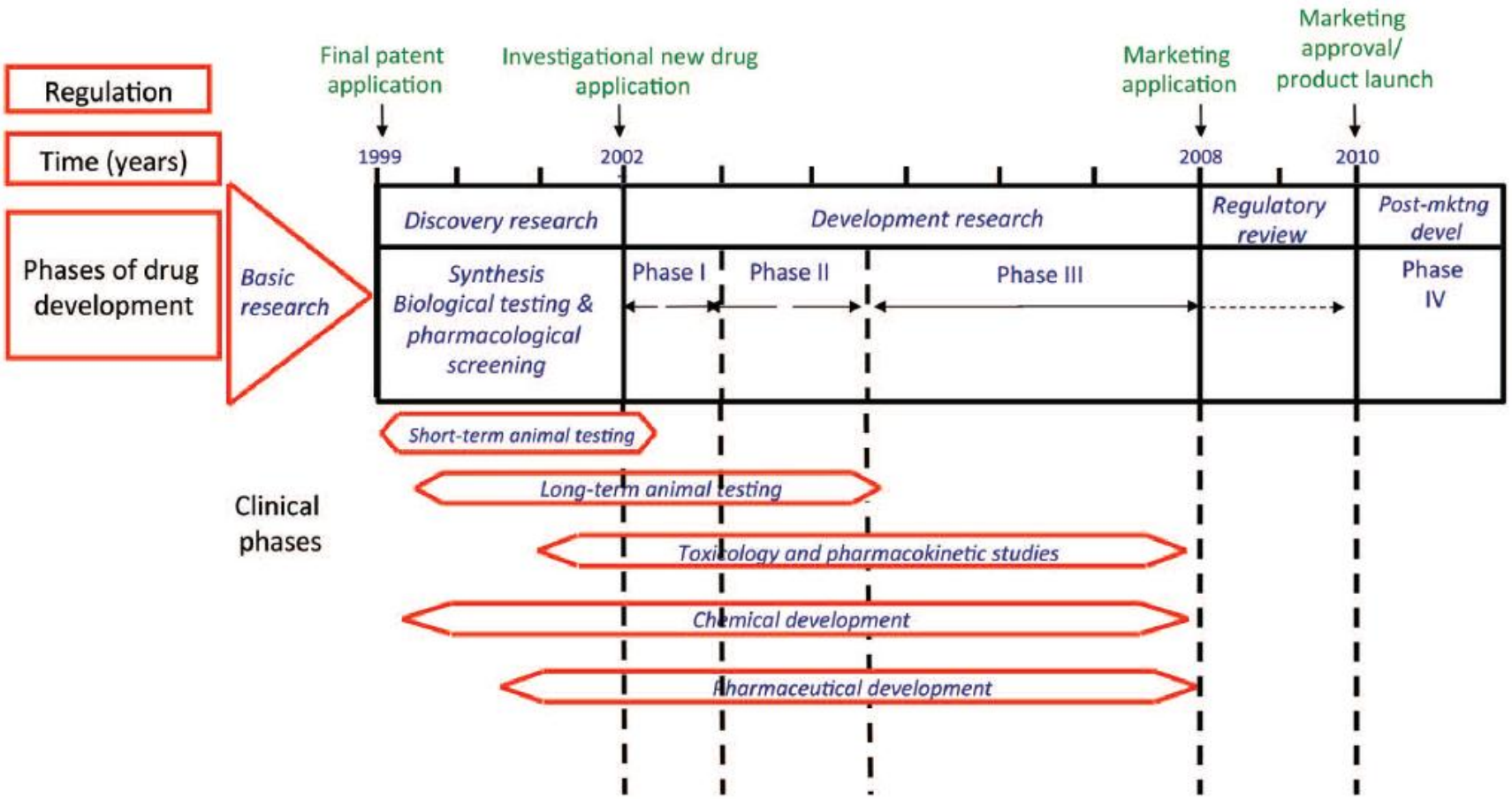


Take Home Messages

- **Traditional relationships between Academy and Industry are being re-defined**
- **Collaboration between Pharma and Academics is natural and necessary for the benefit of all, including the patient (yourself)**
- **Innovative partnership models allow both Pharma & Academics to better find a way to work together**
- **There is not only one model, but several adaptation of various models**
- **Alliance Management, timeline and deliverables are key in the development of the relationship**
- **Failure is part of research and not an issue. Exit is fine if anticipated.**
- **High level of communication with the partner facilitate flexibility and allow to move to a next level of model when the relationship develops.**

Back up

Reminder


Regulation
Time (years)
Phases of drug development
Basic research
Final patent application
Investigational new drug application
Marketing application
Marketing approval/ product launch
1999
2002
2008
2010
Discovery research
Development research
Regulatory review
Post-mktng devel
Synthesis Biological testing & pharmacological screening
Phase I
Phase II
Phase III
Phase IV
Short-term animal testing
Long-term animal testing
Clinical phases
Toxicology and pharmacokinetic studies
Chemical development
Pharmaceutical development