Quo vadis Pharmaceutical Industry ?

R&D in the pharmaceutical industry - still a valid model?

Jochen Maas

SANOFI

Göttingen, May 30th, 2015

Agenda

The situation as it is today

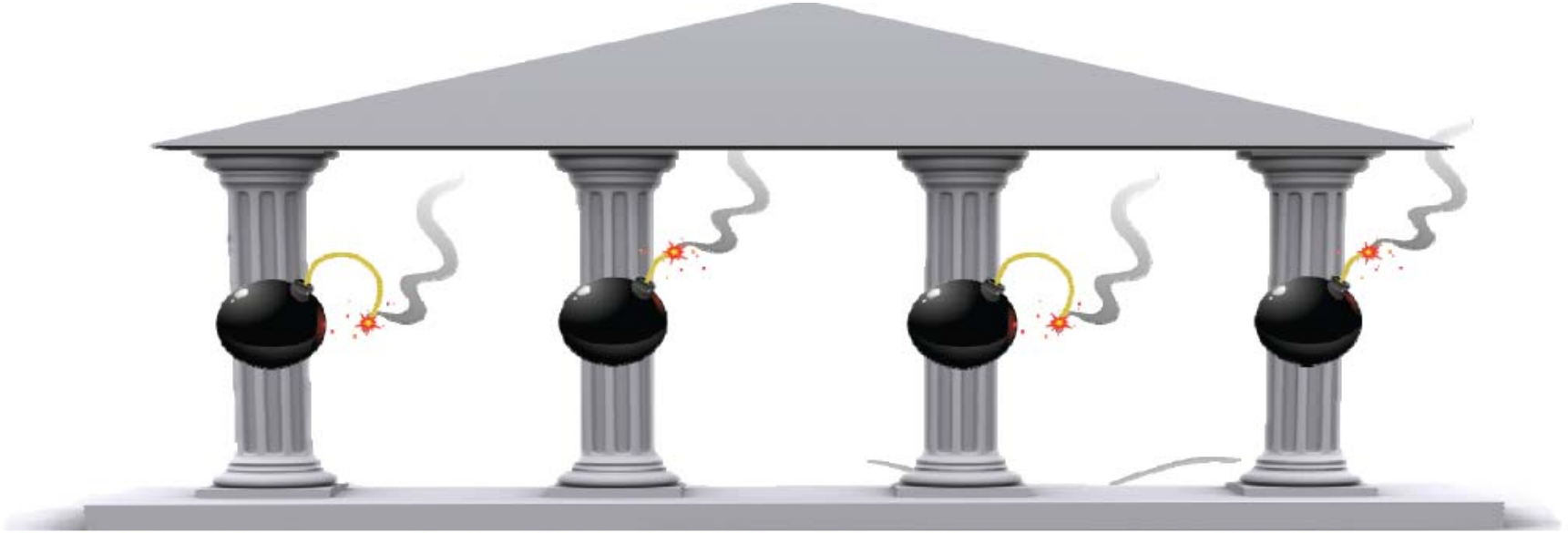
- What changed in the environment (external factors) ?
- What happened internally in big pharma (internal factors) ?
- What is the result, what the „lessons learned“ ?
- (What is the effect on external stake- and shareholders and on reputation?)

Ways out

- Open Innovation and external co-operations
- Integrated solutions for patients
- Translational medicine
- Personalized medicine
- Others

Overall conclusion

What Changed?
The Pharmaceutical industry is under pressure



Patient needs
- Acute to chronic
- Personalized
- Generics

Payer driven market
- Differential medical value
- Rise of formularies
- Payment restrictions
- Price controls

Regulation
- Regulatory burden
- Safety thresholds
- Postmarketing requirement
- Longer R&D cycles

Science
- Low predictibility in Humans
- Too concentrated on a few targets
- Low success rates
- Low overall efficiency

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The Fundamental problem

In spite of remarkable scientific progress, **our capacity to translate those advances into health benefits** has decreased

The number of biological targets has dramatically increased thanks to **progress made in the field of genomics**

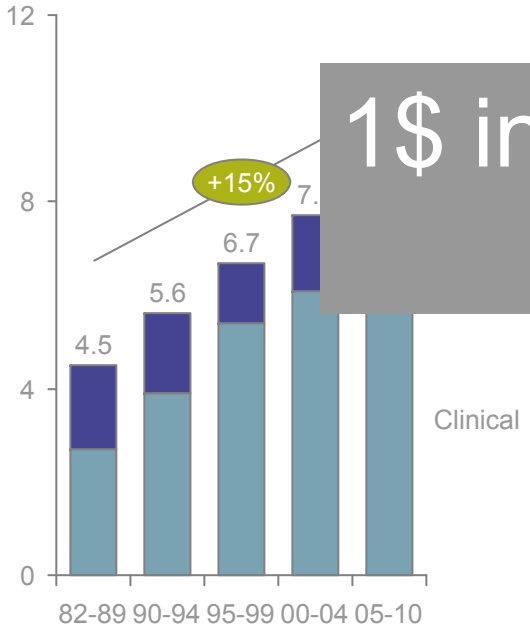
In the biopharmaceutical sector **success rate has dropped** from 1/8 to 1/14 and **the length of development has doubled**

The Core issue

A spectacular drop in R&D productivity

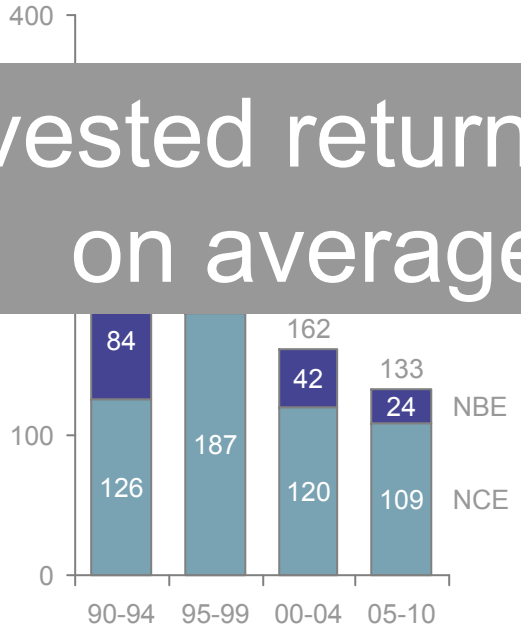
Clinical timelines increasing

Mean clinical development time (years)



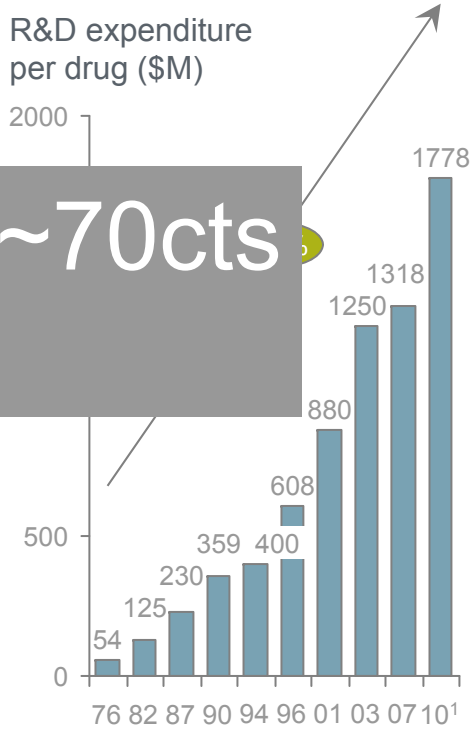
NME approvals by FDA decreasing

Number of NCEs and NBEs approved



Rising R&D costs

R&D expenditure per drug ($M)



1$ invested returns ~70cts on average!

NME: New molecular entity NCE: New chemical entity NBE: New biological entity
1 2010 data is from Paul et al Nature Feb-10, rest of data from Tufts
Source: FDA; EvaluatePharma; Tufts CSDD 2007; Parexel; CMR; Paul et al, 2010,

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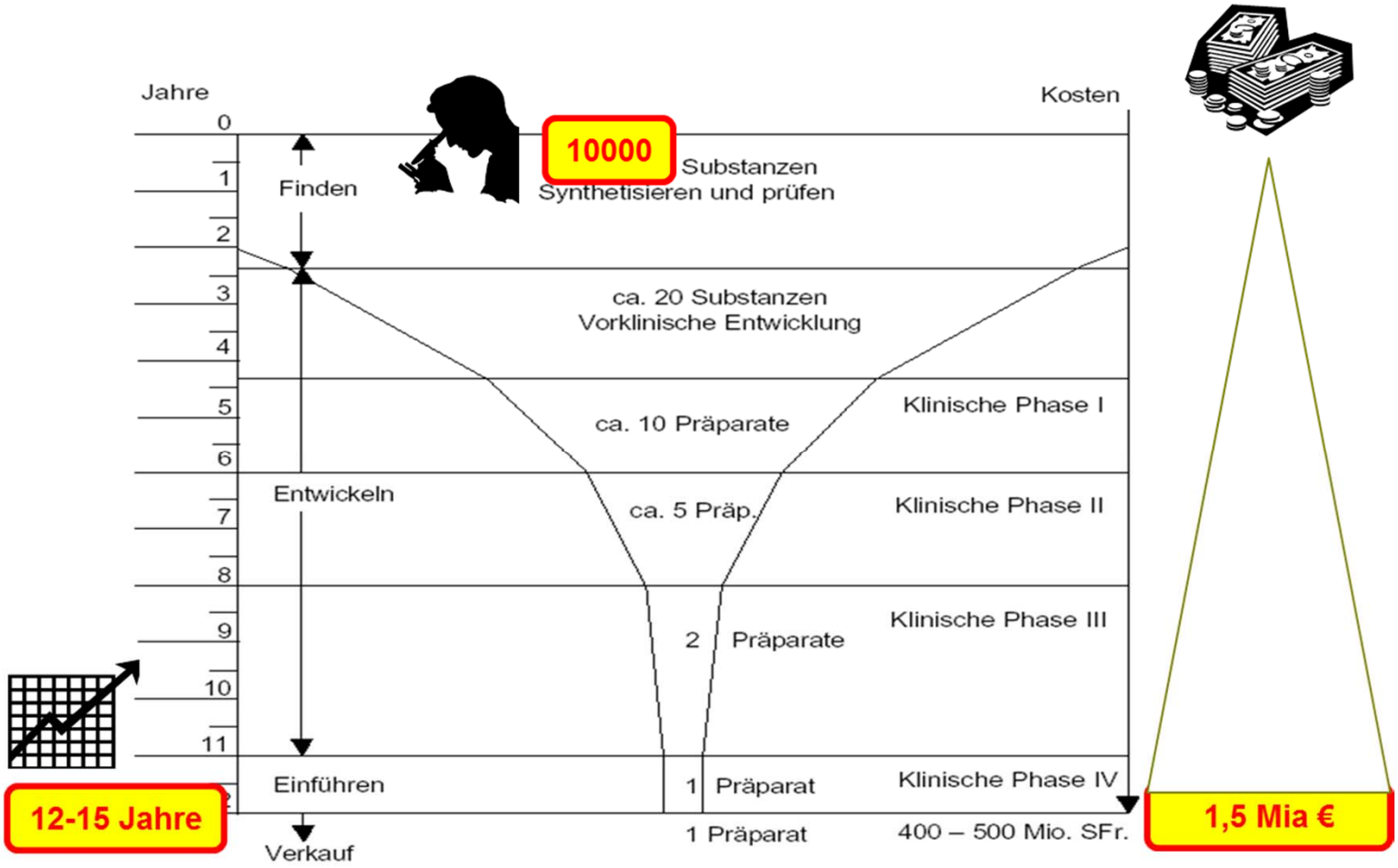
The Core issue

The R&D costs



The „Cost“ explosion – a different calculation...

- Costs for research and development increased dramatically over the years
- Development of a drug: >1 Bill. $ - is it the truth?
- Despite new technologies, still high failure rate during clinical phases

Company	Number of drugs approved	R&D Spending Per Drug ($Mil)	Total R&D Spending 1997-2011 ($Mil)
AstraZeneca	5	11,790.93	58,955
GSK	10	8,170.81	81,708
Sanofi	8	7,909.26	63,274
Roche	11	7,803.77	85,841
Pfizer	14	7,727.03	108,178
J & J	15	5,885.65	88,285
Eli Lilly	11	4,577.04	50,347
Abbott	8	4,496.21	35,97
Merck	16	4,209.99	67,36
BMS	11	4,152.26	45,675
Novartis	21	3,983.13	83,646
Amgen	9	3,692.14	33,229

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

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What went wrong?

The innovation model

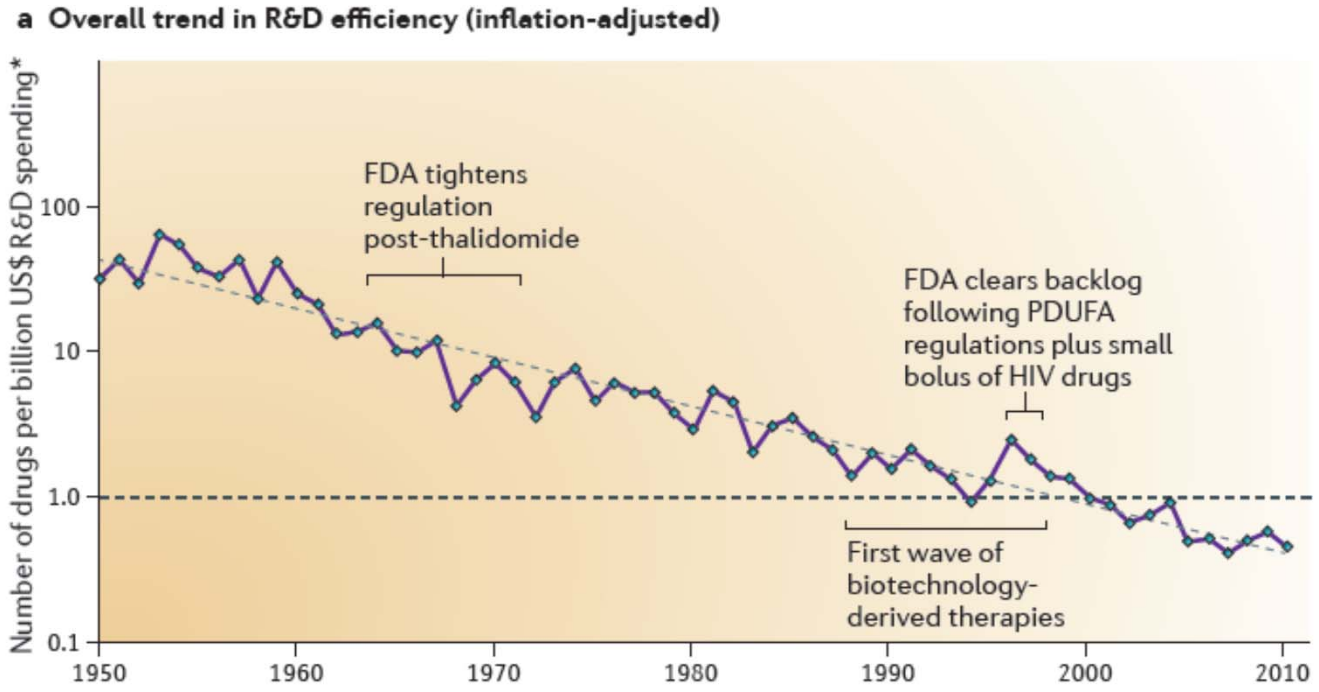
- Belief that advances in basic sciences could be easily translated to human disease
- Too many novel but not validated targets in humans
- A linear process from discovery to development to market with little interactions throughout the innovation cycle
- Number of research projects focused on « ME-TOO » drugs
- Quantity over Quality
- A strategy of « MANY SHOTS ON GOAL »

… as well as the organizational model

- Large complex organizations inherited from successive mergers
- All research focused on internal research with few interactions with larger world of external innovation
- Resource allocations driven by functions rather than specific projects and programs
- A disconnect between R&D strategies and the rapid changes in the Scientific, Medical and Market environments

… and what was the result?

Eroom‘s law in pharmaceutical industry



Aus:

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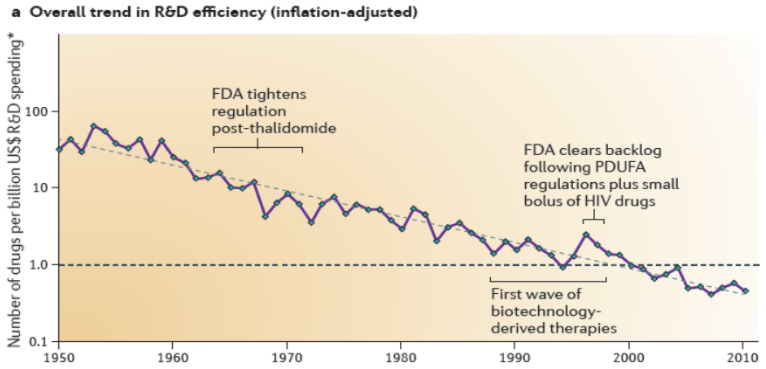
… and the learning?

Two general learnings for the pharmaceutical industry can be discussed



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„Positive“ message:

Even tremendous disasters (Thalidomide, Lipobay, Vioxx) did not significantly modify the tendency

Negative message:

Whatever the pharmaceutical industry tried to overcome the negative tendency (retroplanning, productivity models, mergers, acquisitions) did not significantly modify the tendency

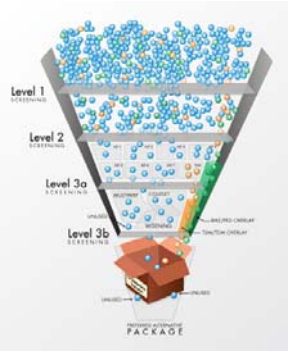
Why most of the approaches failed?

The „*better than the Beatles*“ problem

The „*cautious regulator*“ problem

The „*throw money at it*“ tendency

The „*basic research-brute force*“ bias



Scannel et all (2012): Diagnosing the decline in pharmaceutical R&D efficiency; Nature Reviews, Drug Discovery, Vol 11, March 2012

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Pharmaceutical industry under pressure

External factors

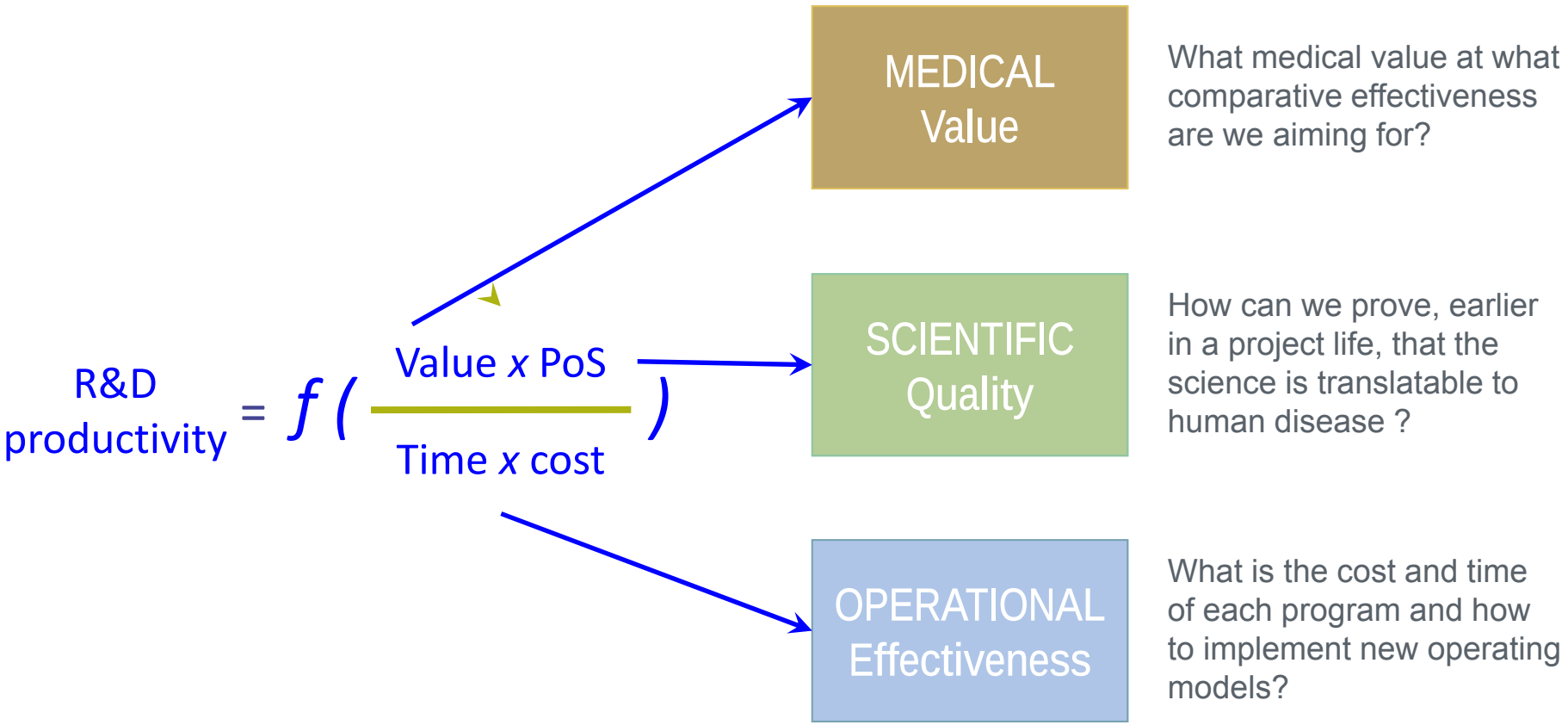
- Patient needs
- Payer driven market
- Regulation

- „Saturated“ market
- Reputation/Image
- Shareholder pressure

Internal factors

- Science
- Productivity
- Strategic decisions
- Reputation/Image

The new textbook of R&D in pharmaceutical industry



… and what are the (potential) detail solutions?

- Cost flexibility by increasing variable costs and decreasing fix costs
- Open innovation and external co-operations
- Integrated organisatorial solutions
- Integrated solutions for patients
- Early regulatory contacs
- Translational medicine
- Operational excellence and regionalisation
- Personalized medicine
- CDDO‘s

Open innovation and external co-operations (1)

THE WALL STREET JOURNAL.

Saturday 28 June 2008

"The pharmaceutical industry likes to depict itself as a research-based industry, as the source of innovative drugs," says Dr. Marcia Angell, author of "*The Truth About the Drug Companies*."

"Nothing could be further from the truth," she claims.

"Innovation comes mainly from NIH-supported research in academic medical centers."

"The drug companies do almost no innovation now."

Open innovation and external co-operations (2)

What is an innovation?

An innovation is ……

…. a new idea
…. its translation into a „prototyp“
…. its optimizationto a marketed product
…. and – last but not least – its realisation

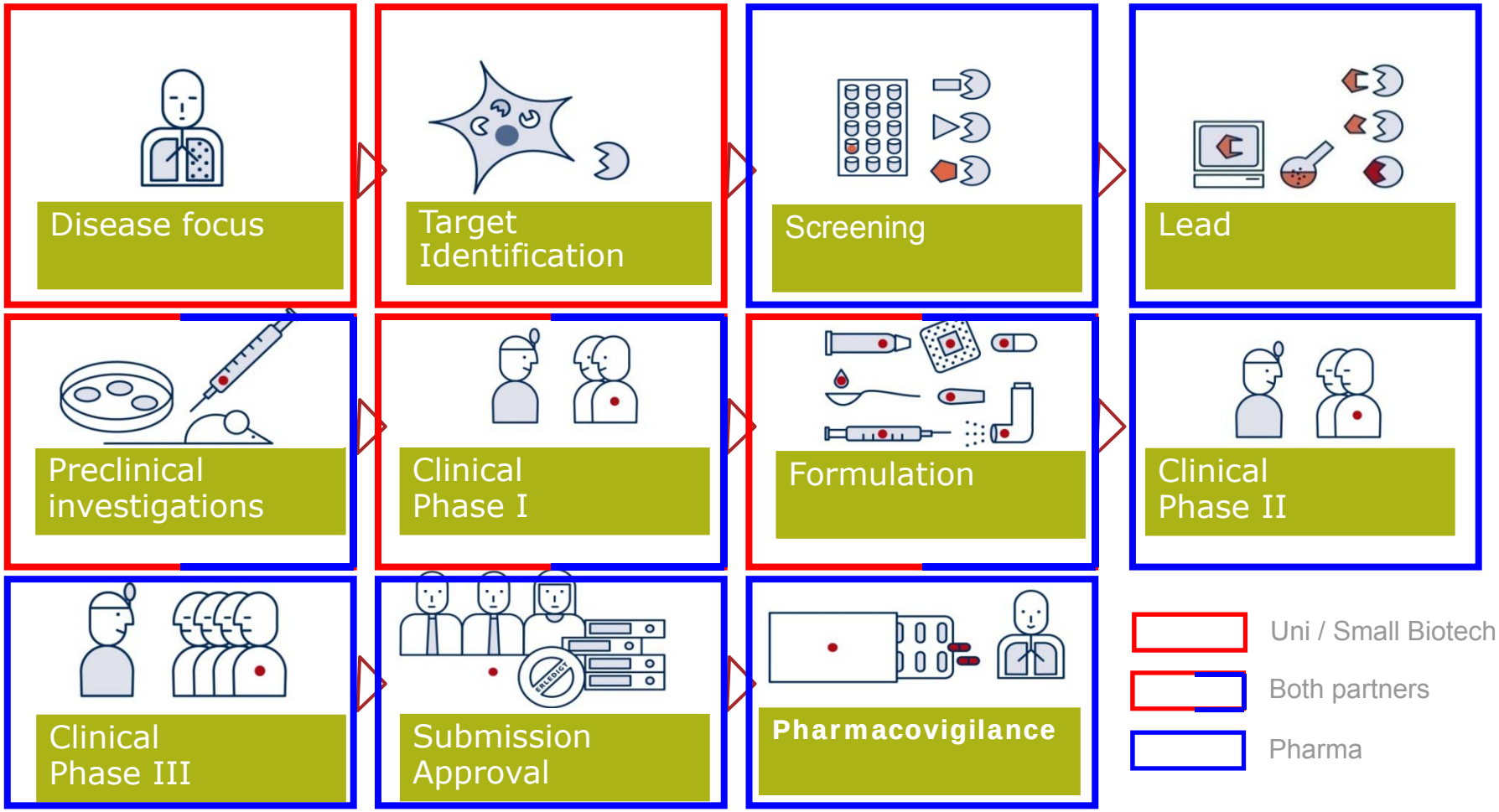
Translation into the Life-Science context?

…. The new idea is the new ***Target***
…. its translation results in a ***Lead-structure***
…. its optimization in a ***Development candidate***
…. and its realisation in a ***Drug***

Where are the real experts ?

Open innovation and external co-operations (3)

Individual strenghths along the value chain



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Open innovation and external co-operations (4)
Diverging interests?

„Currency "of Universities:

- Publications,
- Papers

„Currency" of Industry:

- Products
- Patents

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Open innovation and external co-operations (5)

It has already been started…..

Academic Partnerships

aviesan
alliance nationale pour les sciences de la vie et de la santé
CHARITÉ
SIBS
DANA-FARBER CANCER INSTITUTE
CALTECH
CRG Centre de Regulació Genòmica
imi Innovative Medicines Initiative
HARVARD UNIVERSITY
SALK INSTITUTE FOR BIOLOGICAL STUDIES
Massachusetts Institute of Technology
JOHNS HOPKINS UNIVERSITY
UCSF University of California San Francisco
THE ROCKEFELLER UNIVERSITY
Science for the benefit of humanity

Pharmaceuticals Partnerships

Dyax
EXELIXIS
micromet
ALOPEXX
KYOWA KIRIN 協和発酵キリン株式会社
bioMedica
IMMUNOGEN, INC.
REGULUS THERAPEUTICS
ascendispharma
ASCENTA THERAPEUTICS
REGENERON
AgaMatrix
MERRIMACK PHARMACEUTICALS
Glenmark A new way for a new world

Vaccines Partnerships

Naval Medical Research Center U.S. Navy
Syntiron
CSL
KaloBios
to therapeutics Vivalis

R&D Acquisitions

TargeGen
fovea PHARMACEUTICALS
SHANTHA BIOTECHNICS
BiPar sciences

Foundation Partnerships

JDRF Juvenile Diabetes Research Foundation International
dedicated to finding a cure
THE MICHAEL J. FOX FOUNDATION FOR PARKINSON'S RESEARCH
BILL & MELINDA GATES foundation

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Open innovation and external co-operations (6)

… but we need also new ways of working together

- **Common project teams from the beginning**
- **Common project identity**
- **Common visions**
- **Openess and confidence from start**
- **Common laboratories, daily co-operation**
- **Exchange of scientists and technicians**
- **Acceptance of „not invented here“ and other interests**
- **Clearly defined intellectual property**
- **Opening of „treasure chests“**
- **etc, etc……**

Integrated solutions for patients (1)

The principle

Figure 2. Examples of convergence

Device – Drug

- Drug-eluting stent that opens and prevents restenosis in coronary and peripheral arteries
- Bone grafting scaffold/sponge coated with a growth protein that promotes bone regeneration
- Implantable, programmable pump that delivers a drug or biologic in small, timely doses
- Implantable polymer wafer that releases a chemotherapy agent to a specific site
- Implantable neuromodulator that enables the targeted, regulated delivery of a drug or electrical stimulation
- Transdermal patch that transports drugs locally and systematically through the skin
- Pre-filled, metered dose syringe, injector pen, or inhaler

Diagnostic – Drug

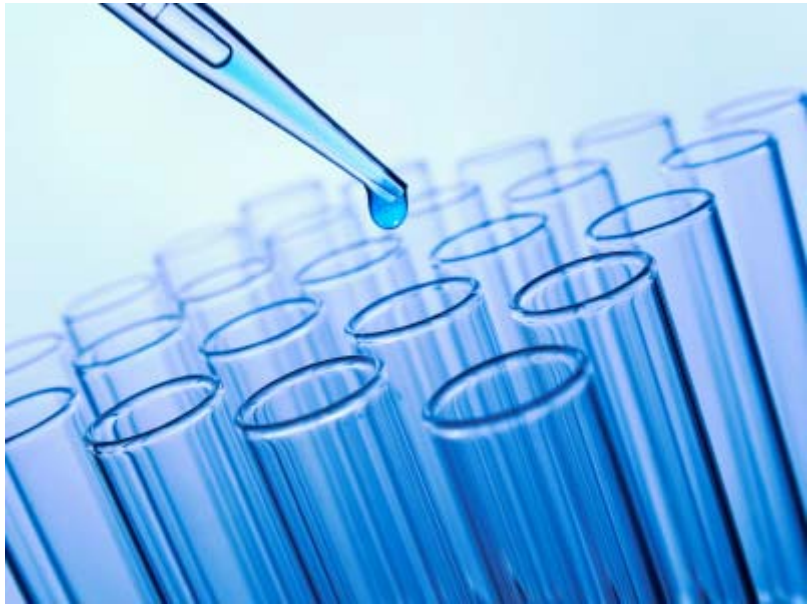
- Screening test for the presence of a specific gene or protein coupled with targeted drug therapy
- Use of passive pharmaceuticals and radiopharmaceutical tracers as contrast agents for positron emission tomography (PET) scanners

Diagnostic – Device – Drug

- Glucose monitor with an insulin pump

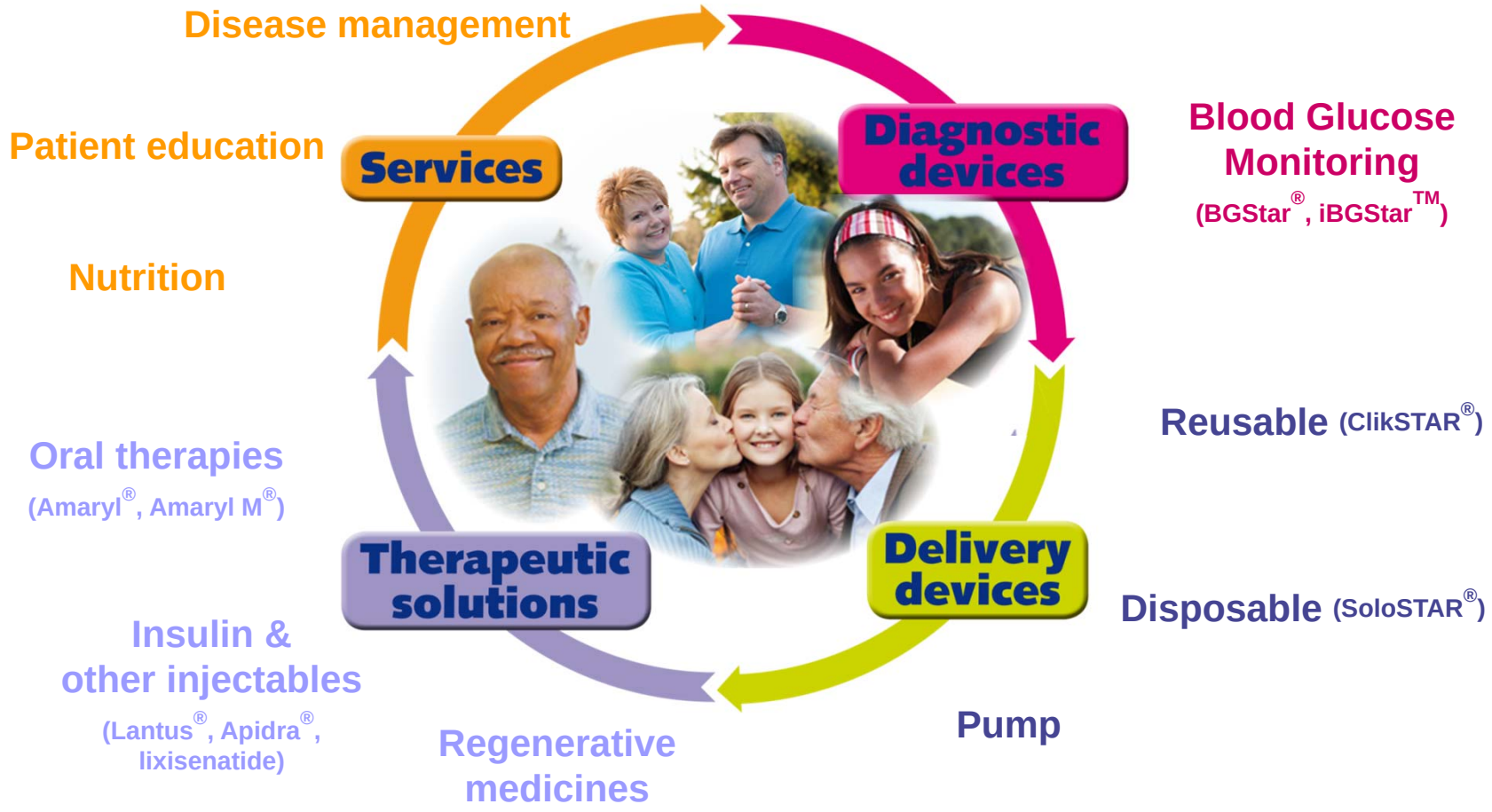
Source: Deloitte Research

Das 3D Paradigm (Drug/Device/Diagnostics)



Integrated solutions for patients (2)

The Diabetes example



Translational medicine

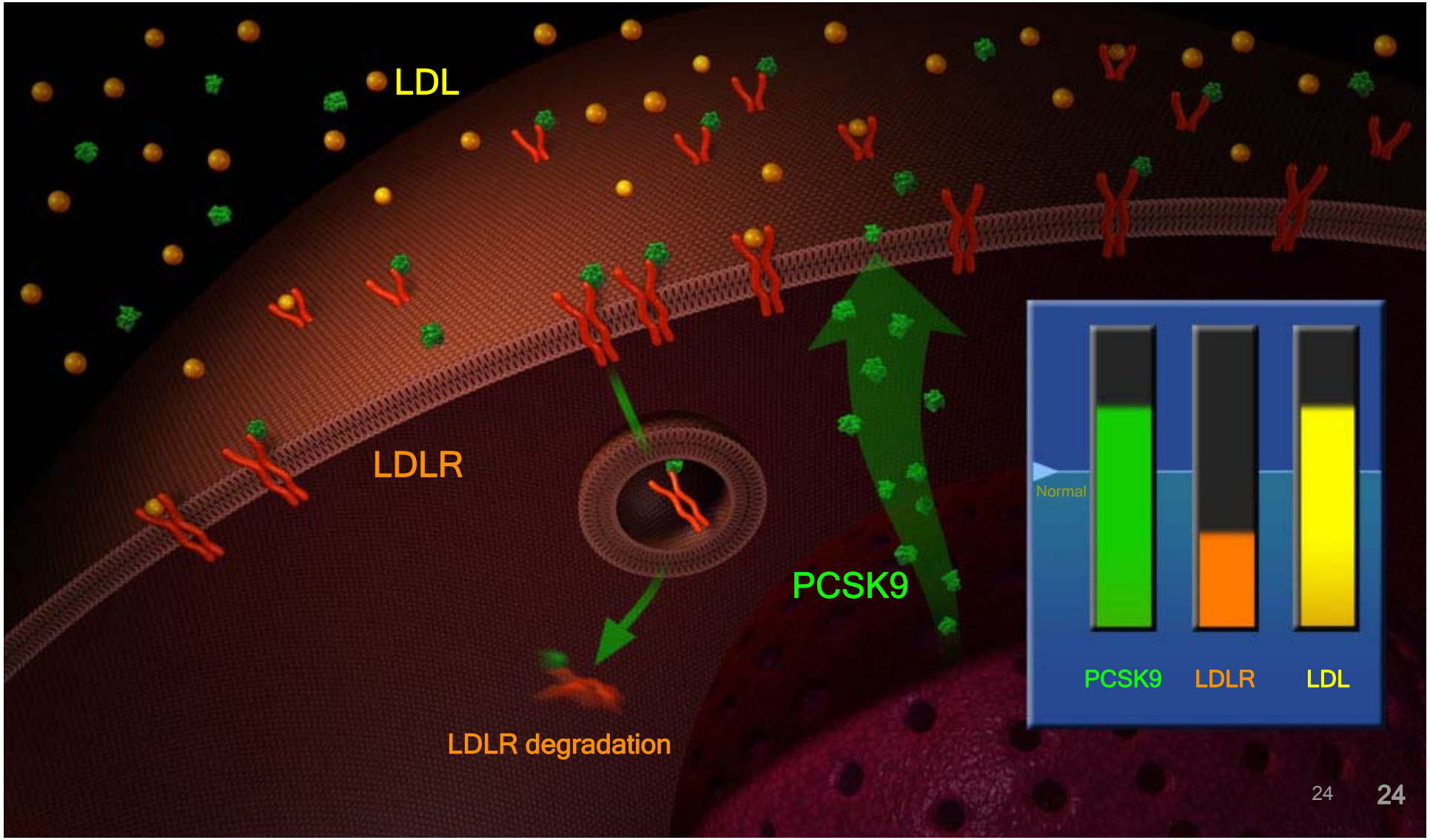
…. has „thousands“ of definitions

…. is the process of turning appropriate biological discoveries into drugs and medical devices that can be used in the treatment of patients.

But examples are better than explanations…..

Translational medicine (1) – The PCSK-9 example

Increased PCSK9 Leads To Lower LDLR



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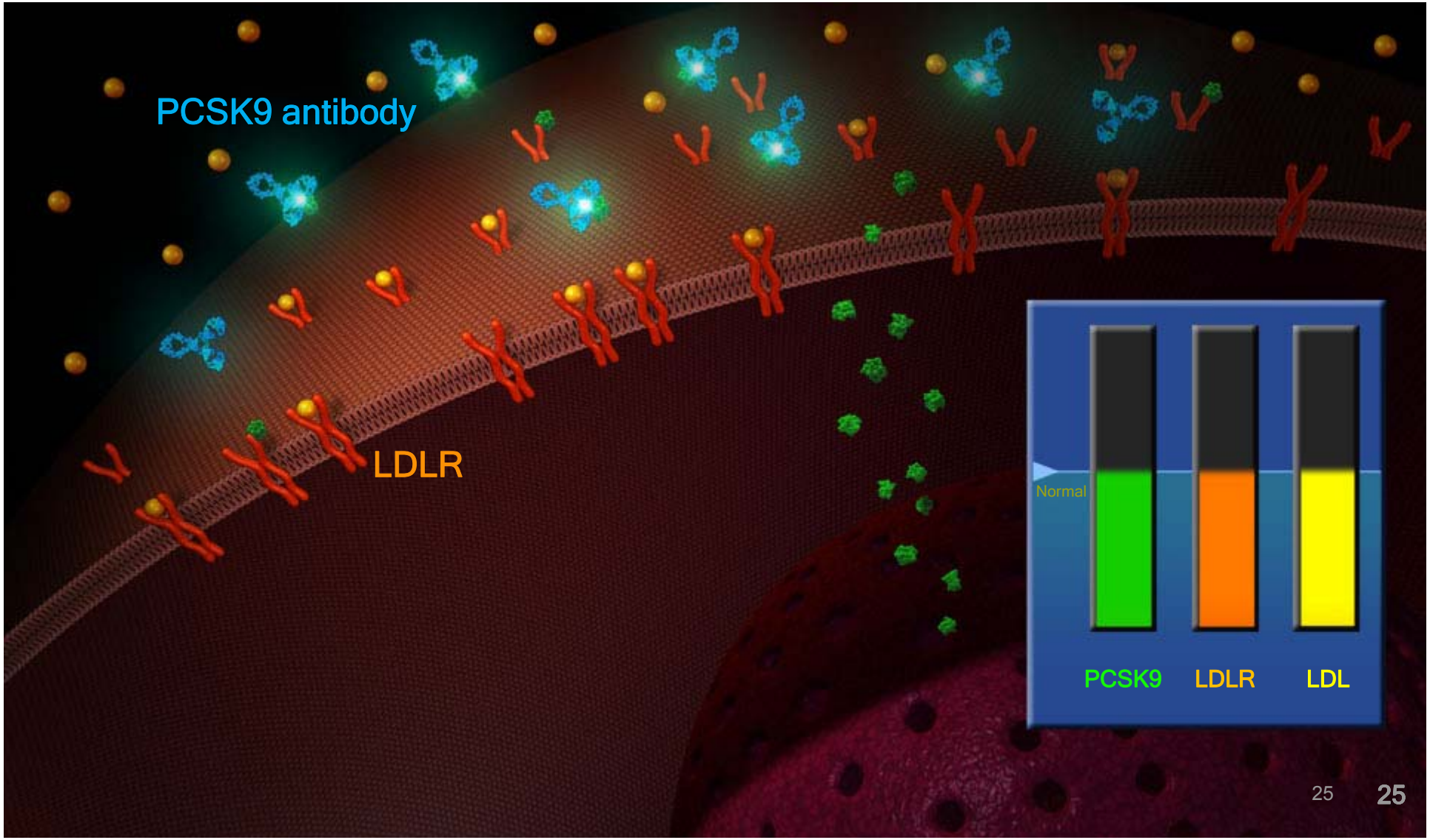
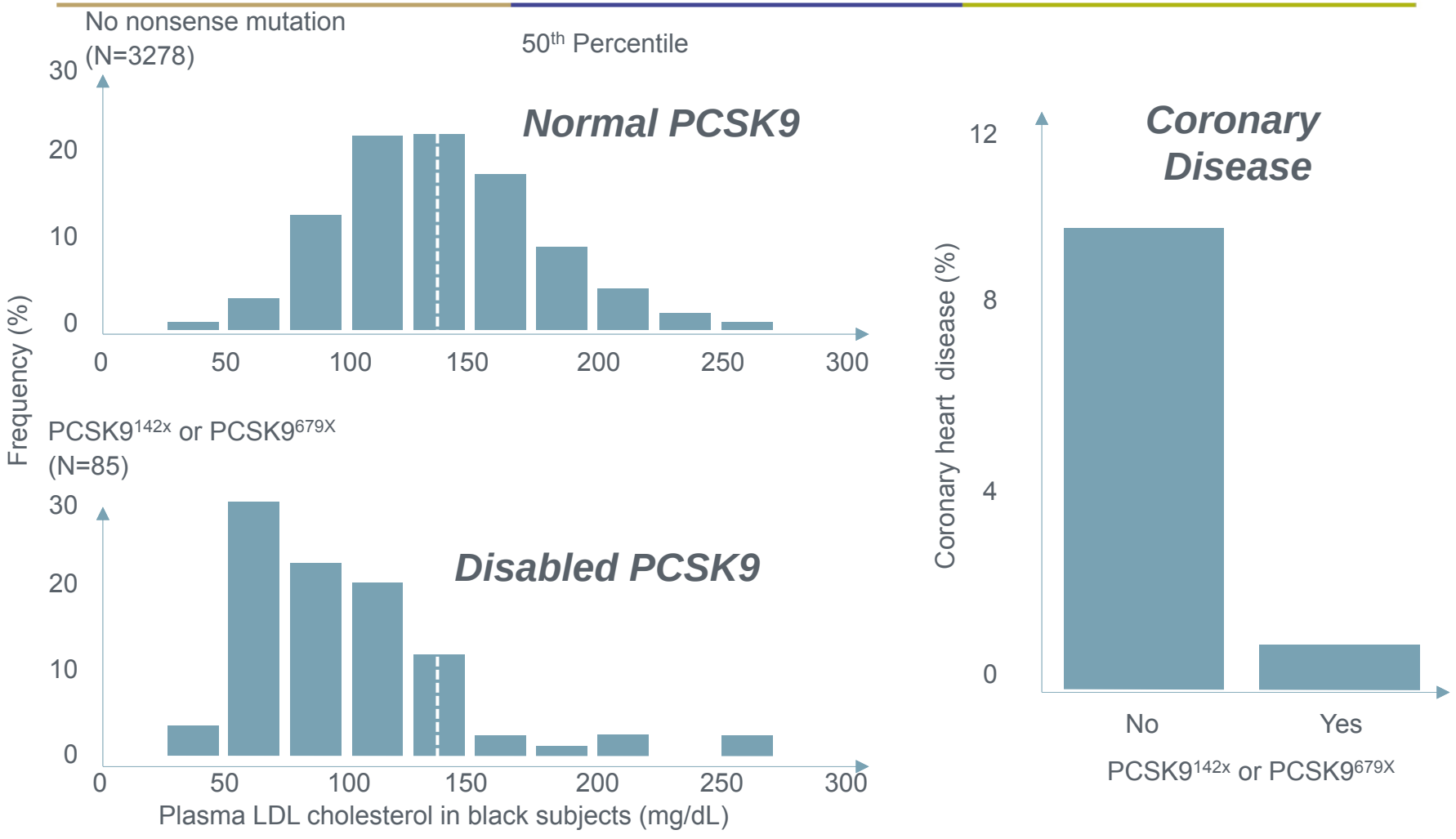
Translational medicine (2) – The PCSK-9 example

PCSK9 Antibodies bind to PCSK9, LDL-Receptors increase, LDL decrease



Translational medicine (3) – The PCSK-9 example

The "translational" aspect: Disabled PCSK-9 results in significantly lowered LDL

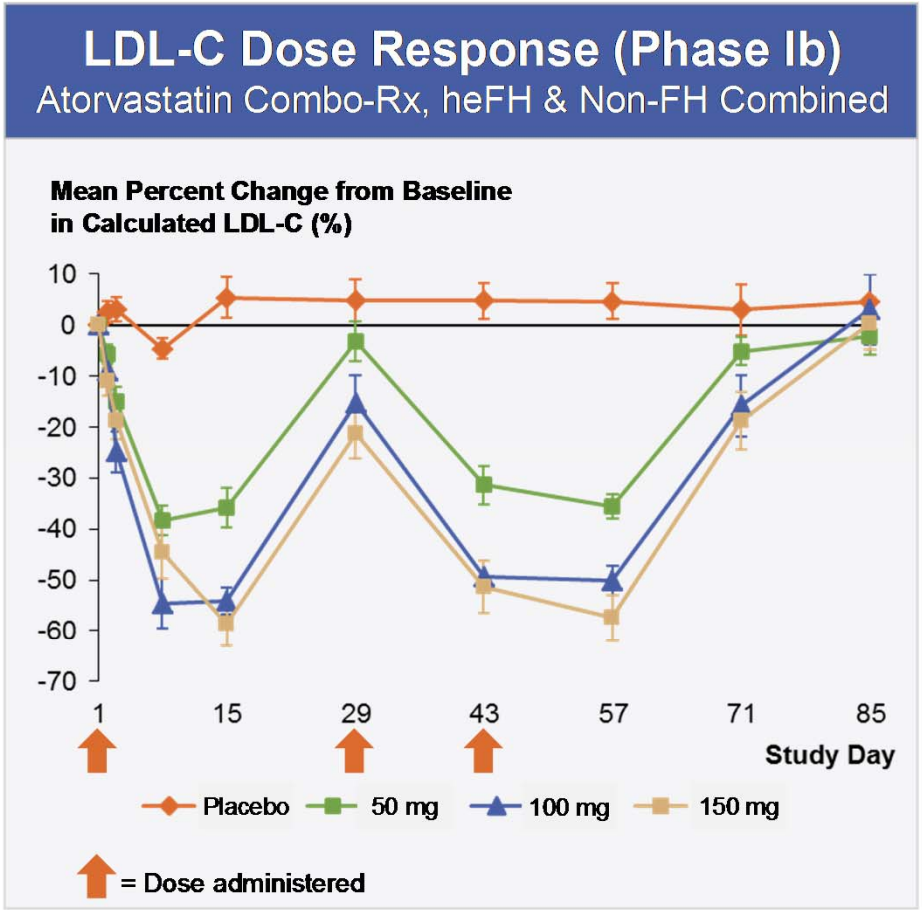


Cohen JC. *N Engl J Med* 2006;354(12):1264-72

Translational medicine (4) – The PCSK-9 example

… and it works

- Landmark study demonstrated that when PCSK9 is disabled, cholesterol and risk of CHD are greatly lowered(1)
- Preliminary Phase II data
  - >65% LDL-C reduction in FH and primary hypercholesterolemia on top of baseline statin use
  - Generally safe and well tolerated
- Phase III targeted to start Q2 2012



G. Swergold et al. Circulation 2011; 124: A16265

CHD – Coronary Heart Disease, heFH – Heterozygous familial hypercholesterolemia , ACC – American College of Cardiology

(1) Cohen JC. N Engl J Med 2006;354(12):1264-72

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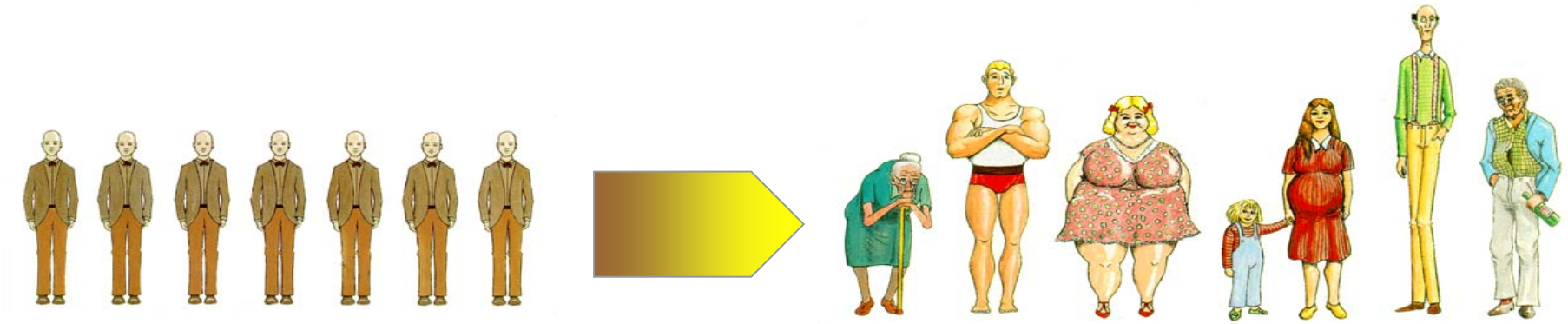
Personalized Medicine (1) – what is it?



Personalized medicine is a medical model emphasizing in general the customization of healthcare, with all decisions and practices being tailored to individualized patients in whatever ways possible. Recently, this has mainly involved the systematic use of genetic or other information about an individual patient to select or optimize that patient's preventative and therapeutic care[1]

- … to improve the **efficacy** of a medication
- … to improve the **safety** of a medication
- … to improve the **dose regimen** of a medication

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Personalized Medicine (2) – more actual than ever

The New York Times
May 14th, 2013

My Medical Choice

By Angelina Jolie

LOS ANGELES

MY MOTHER fought cancer for almost a decade and died at 59. She held out long enough to meet the first of her grandchildren and to hold them in her arms. But my other children will never have the chance to know her and experience how loving and gracious she was.

We often speak of "Mommy's mommy," and I find myself trying to explain the illness that took her away from us. They have asked if the same could happen to me. I have always told them not to worry, but the truth is I carry a "faulty" gene, BRCA1, which sharply increases my risk of developing breast cancer and ovarian cancer.

My doctors estimated that I had an 87 percent risk of breast cancer and a 50 percent risk of ovarian cancer, although the risk is different in the case of each woman.

Only a fraction of breast cancers result from an inherited gene mutation. Those with a defect in BRCA1 have a 65 percent risk of getting it, on average.

Angelina Jolie is an actress and director.

Once I knew that this was my reality, I decided to be proactive and to minimize the risk as much I could. I made a decision to have a preventive double mastectomy. I started with the breasts, as my risk of breast cancer is higher than my risk of ovarian cancer, and the surgery is more complex.

On April 27, I finished the three months of medical procedures that the mastectomies involved. During that time I have been able to keep this private and to carry on with my work.

But I am writing about it now because I hope that other women can benefit from my experience. Cancer is still a word that strikes fear into people's hearts, producing a deep sense of powerlessness. But today it is possible to find out through a blood test whether you are highly susceptible to breast and ovarian cancer, and then take action.

My own process began on Feb. 2 with a procedure known as a "nipple delay," which rules out disease in the breast ducts behind the nipple and draws extra blood flow to the area. This causes some pain and a lot of bruising, but it increases the chance of saving the nipple.

Two weeks later I had the major surgery, where the breast tissue is removed and temporary fillers are put in place. The operation can take eight hours. You wake up with drain tubes and expanders

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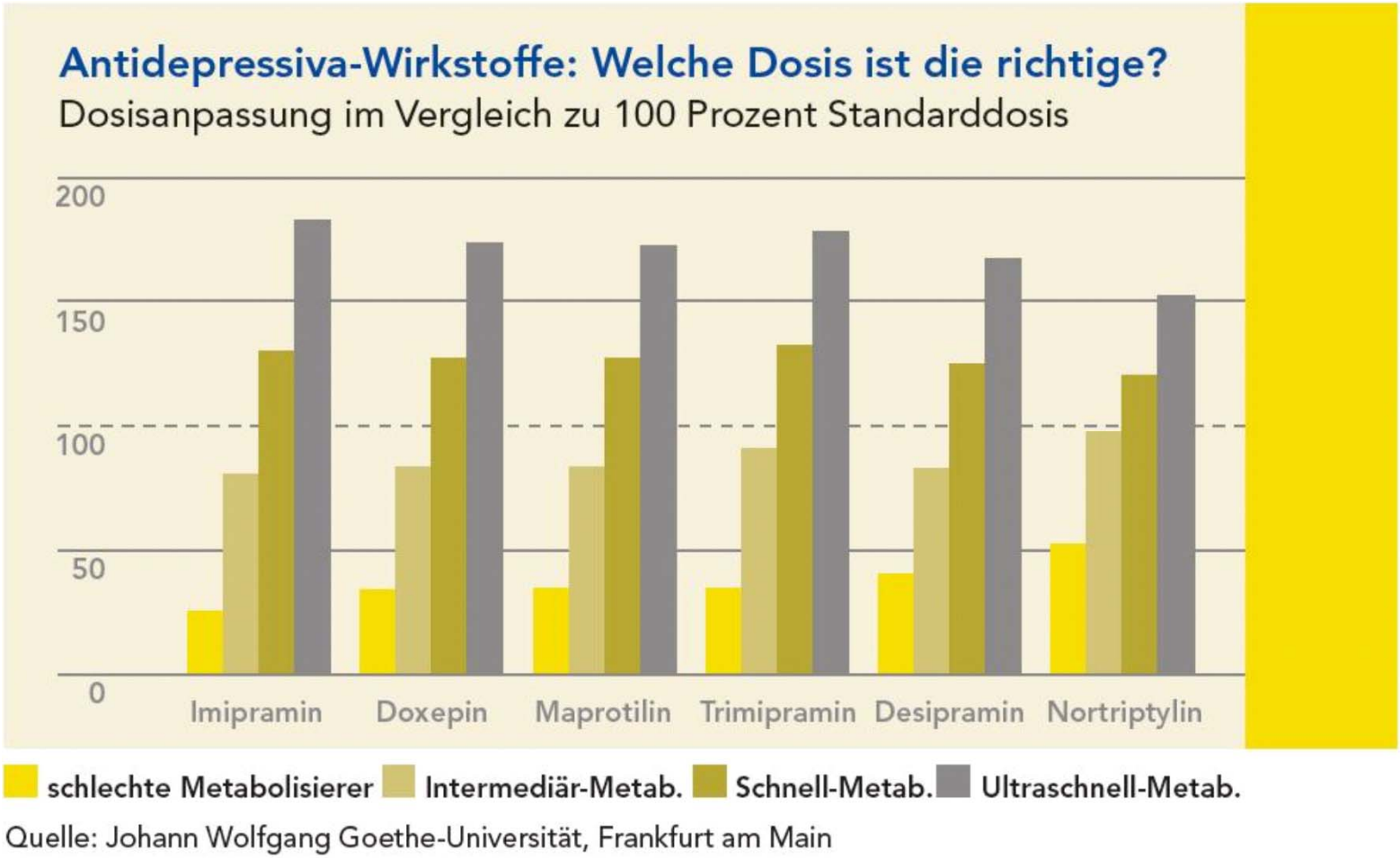
Personalized Medicine (3) – Is it already implemented?

Yes in specific PK-populations



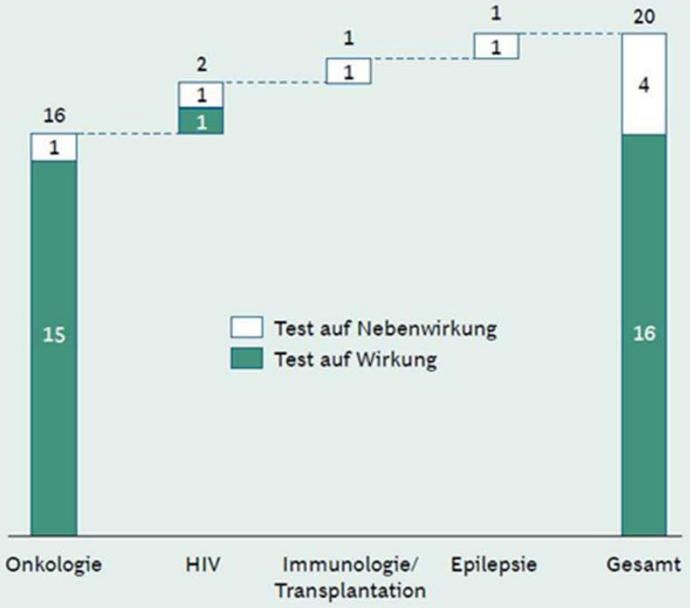
Personalized Medicine (4) – Is it already implemented?

Yes in specific PD-populations

Clear focus on Oncology

Wirkstoff	Indikation	Test
Abacavir	HIV	P
Anastrozol	Brustkrebs	P
Arsentrioxid	Leukämie	P
Azathioprin	Transplantation	E
Carbamazepin	Epilepsie	E
Cetuximab	Darmkrebs	P
Dasatinib	ALL	P
Exemestan	Brustkrebs	P
Fulvestrant	Brustkrebs	P
Gefitinib	Lungenkrebs	P
Imatinib	ALL/CLL	P
Lapatinib	Brustkrebs	P
Letrozol	Brustkrebs	P
Maraviroc	HIV	P
Mercaptopurin	Leukämien	E
Nilotinib	CML	P
Panitumumab	Darmkrebs	P
Tamoxifen	Brustkrebs	E
Toremifen	Brustkrebs	P
Trastuzumab	Brustkrebs	P

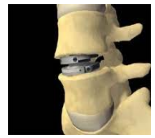
Anzahl der in Deutschland aktuell zugelassenen Arzneimittel mit verpflichtender oder empfohlener Personalisierung

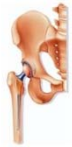


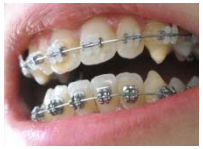
P Pflichttest E Test empfohlen Wirkung Nebenwirkung

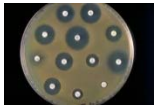
Quelle: www.vfa.de/personalisiert

And there are several other areas to be considered….









Personalized Medicine (4) – Is it already implemented?

No in most of the common diseases

Nevertheless, expectations are high….

„ In 10 years we would see half of our portfolio to be targeted therapies. And if anything, I would assume in 20 years this percentage is going to increase „

Severin Schwan, CEO Roche

… but there are still open questions….

- *Are the patients sufficiently prepared for an individualization of treatments ?*
- *Are the physicians sufficiently prepared for an individualization of treatments ?*
- *Are the payors sufficiently prepared for an individualization of treatments ?*
- *Is the society sufficiently prepared for an individualization of treatments ?*
  - *Insurances, patents?*
- *Is the pharmaceutical industry sufficiently prepared for an individualization of treatments ?*

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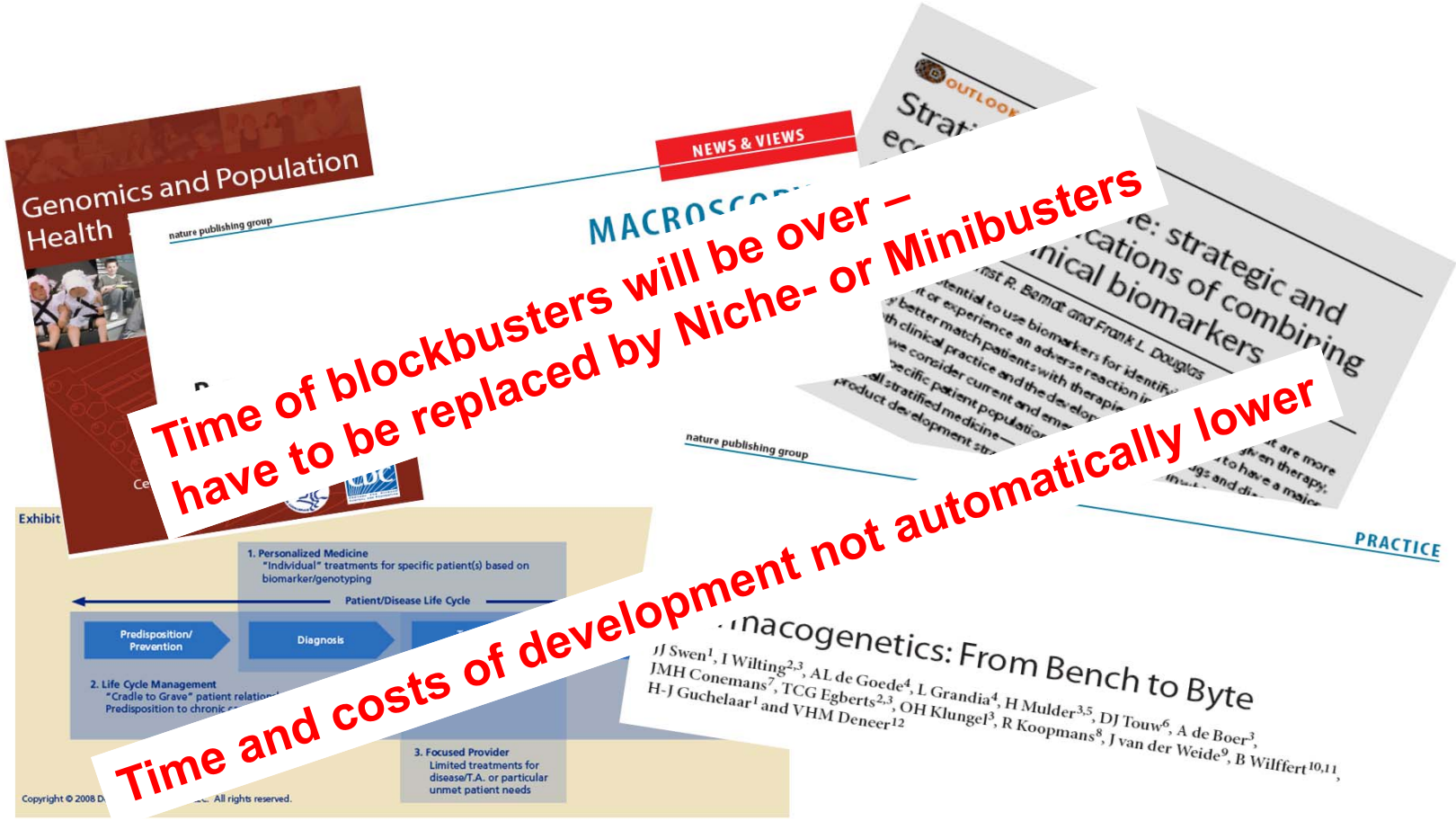
Personalized Medicine (5) – Impact on Pharma Industry



Overall conclusion

Presence

Future