Research & Development strategies in large and small companies

Doris Gabriel, Apidel SA

UNITEC course, University of Geneva, Switzerland

3rd of JUNE 2015

Contents

Part 1:General points about R&D

- *R&D in companies: definitions*
- *R&D: statistics*
- *R&D: strategy - business model- company economics*

Part 2: R&D in a start up company

- *APIDEL, Geneva*

Part 1:
General points about R&D

Definition: R&D

Research

Systematic investigative process employed to increase or revise current knowledge by discovering new facts.

Research is driven by curiosity and may lead to increased knowledge and IP

- *basic research: aimed at increasing scientific knowledge*
- *applied research: aimed at using basic research for solving problems or developing new processes, products, or techniques.*

Definition: R&D

Development

Investigative activities to develop new products or procedures or to improve existing products or procedures

Development uses existing knowledge and ideas and translates them into new products and processes

- *the systematic use of scientific and technical knowledge to meet specific objectives or requirements*
- *an extension of the theoretical or practical aspects of a concept, design, discovery, or invention*

R&D is not always the same

- *in Academic Institutions*

R&D

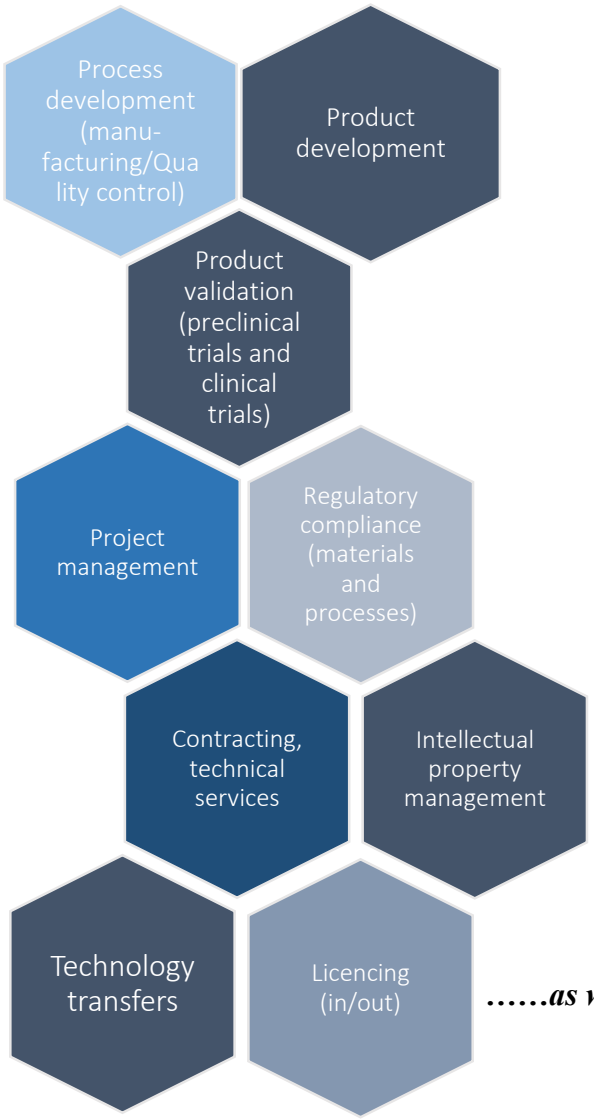
Output: Knowledge, Ideas, IP

- *in Commercial Organizations*

R&D

Output: Products, Processes

R&D activities in companies



……as well as research

R&D and business model

	Fully integrated company	Manufacturing company	Specialist component/stage developer	Service Provider
function	development, manufacturing, marketing, sales and support of own products	develops and manufactures products for marketing, distribution and sale by customer companies	development (manufacture) of components/processes for incorporation into marketed products or further development	provides scientific, engineering, software etc. development resources and services to client companies
examples	big Pharma, Chemical, Automobile	IT hardware, generic drugs, food	aerospace, biotechnology, materials	bioscience, engineering, software
organization	R&D internally owned and managed, funded from profits	internally owned and managed; generally funded from profits	internally owned and managed, and funded from profits and /or from client funding	internally owned and managed, mainly client funded, and directed primarily toward client defined goals
characteristics	innovative, confidential, IP creation responsive to company strategy and management goals	conservative, less innovative, lower creation of IP	innovative, strong IP creation, R&D function placed at centre of business	less innovative, weak IP creation, R&D function placed at centre of business. R&D revenue driven by efforts

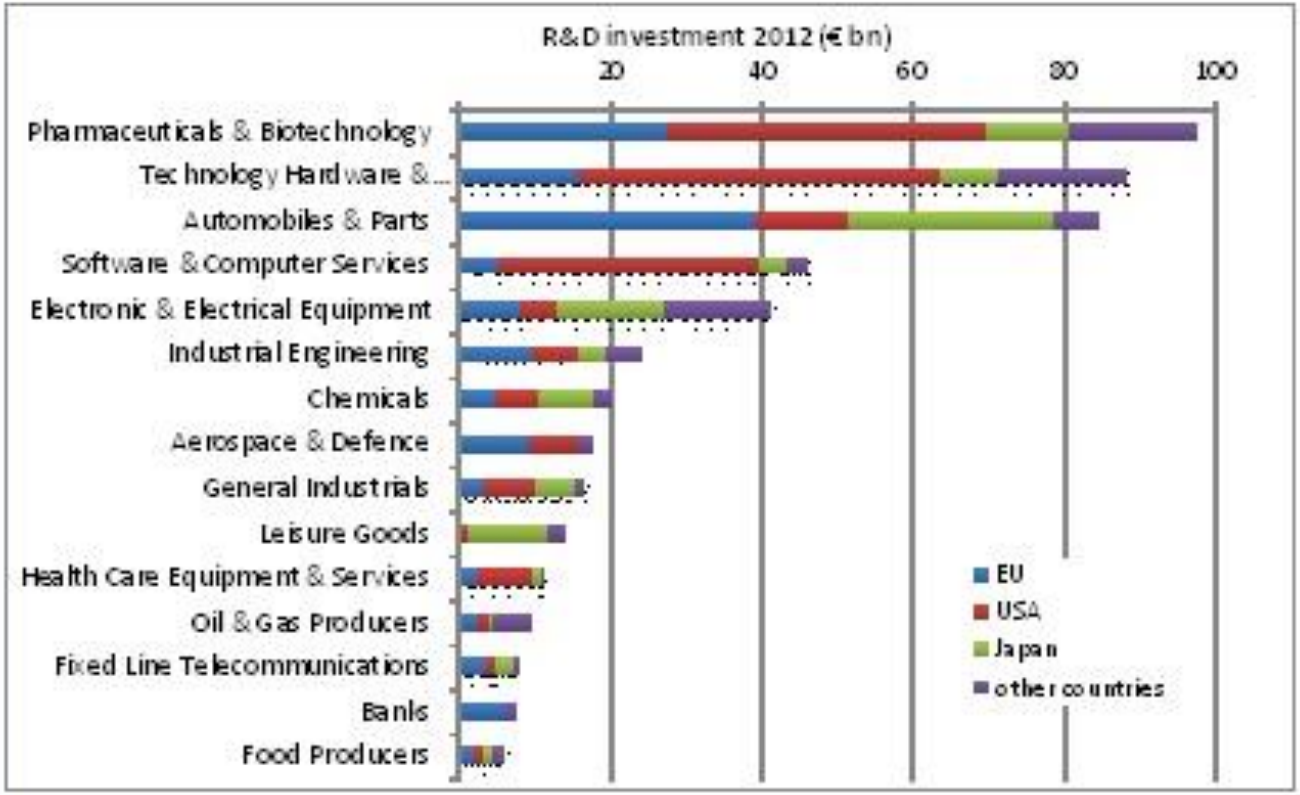
R&D management

Who / what defines the R&D strategy, objectives, goals and tactics in a company?

- ***Strategy:*** *Market, competition, shareholders, board*
- ***Objectives:*** *Board*
- ***Goals:*** *Marketing*
- ***Tactics:*** *Scientists / engineers (+ accountants)*

R&D spending by industry sector

Figure 1. R&D ranking of industrial sectors and share of main world regions for the world's top 2000 companies.

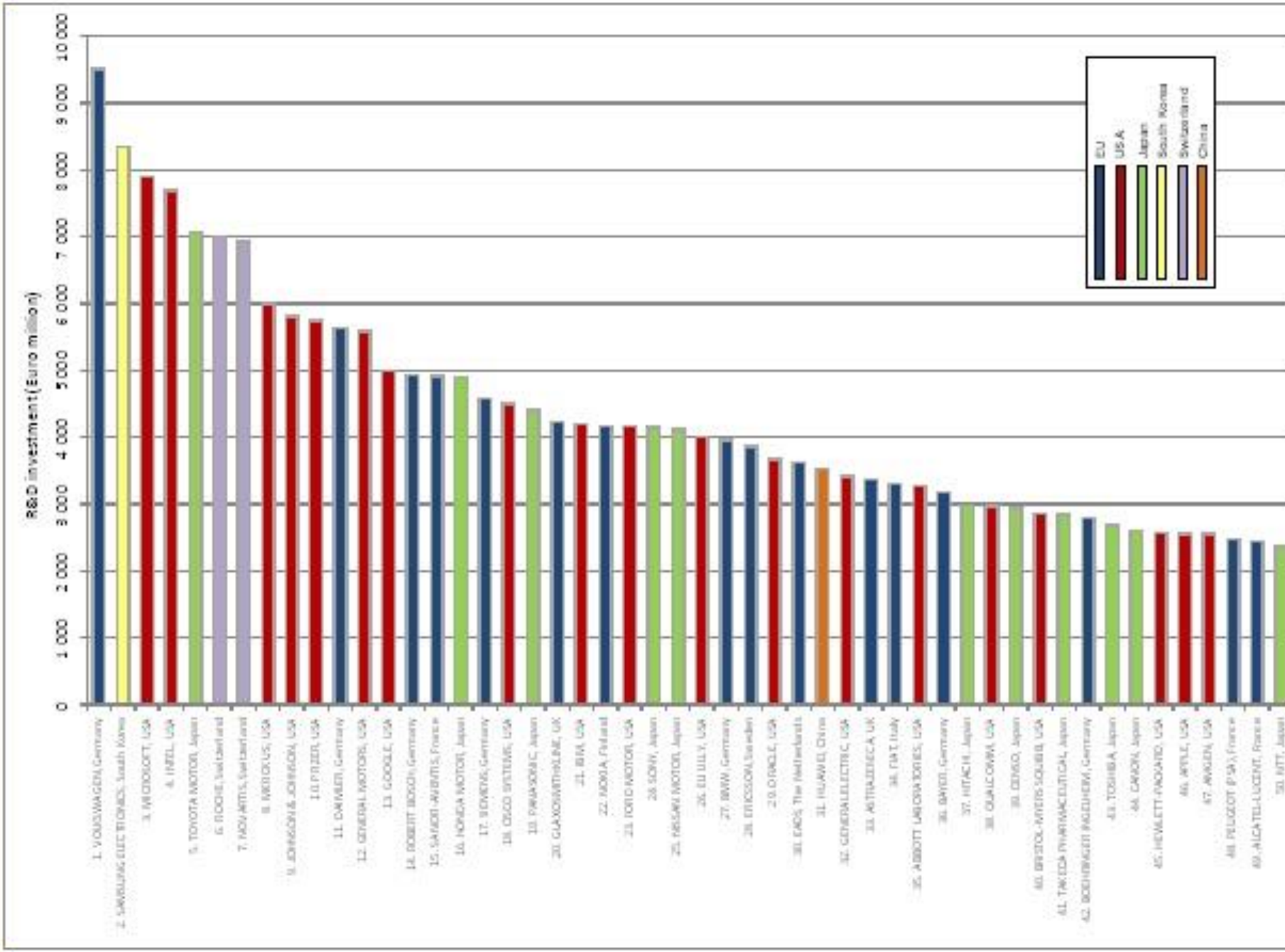


Source: The 2013 EU Industrial R&D Investment Scoreboard

European Commission, JRC/DG RTD.

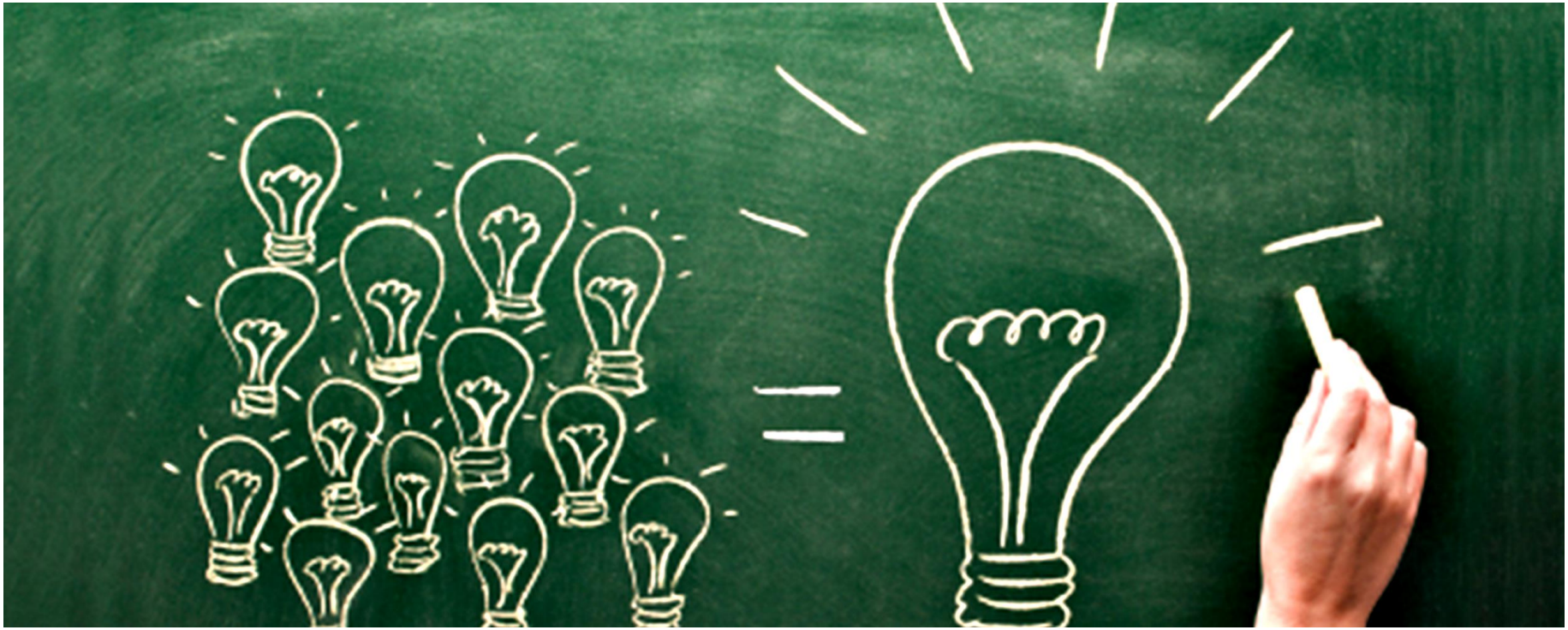
2013 EU Industrial R&D Investment Scoreboard. European Commission, JRC/DG RTD.

Figure 3. The world's top 50 companies by their total R&D investment (€m) in the 2013 Scoreboard.

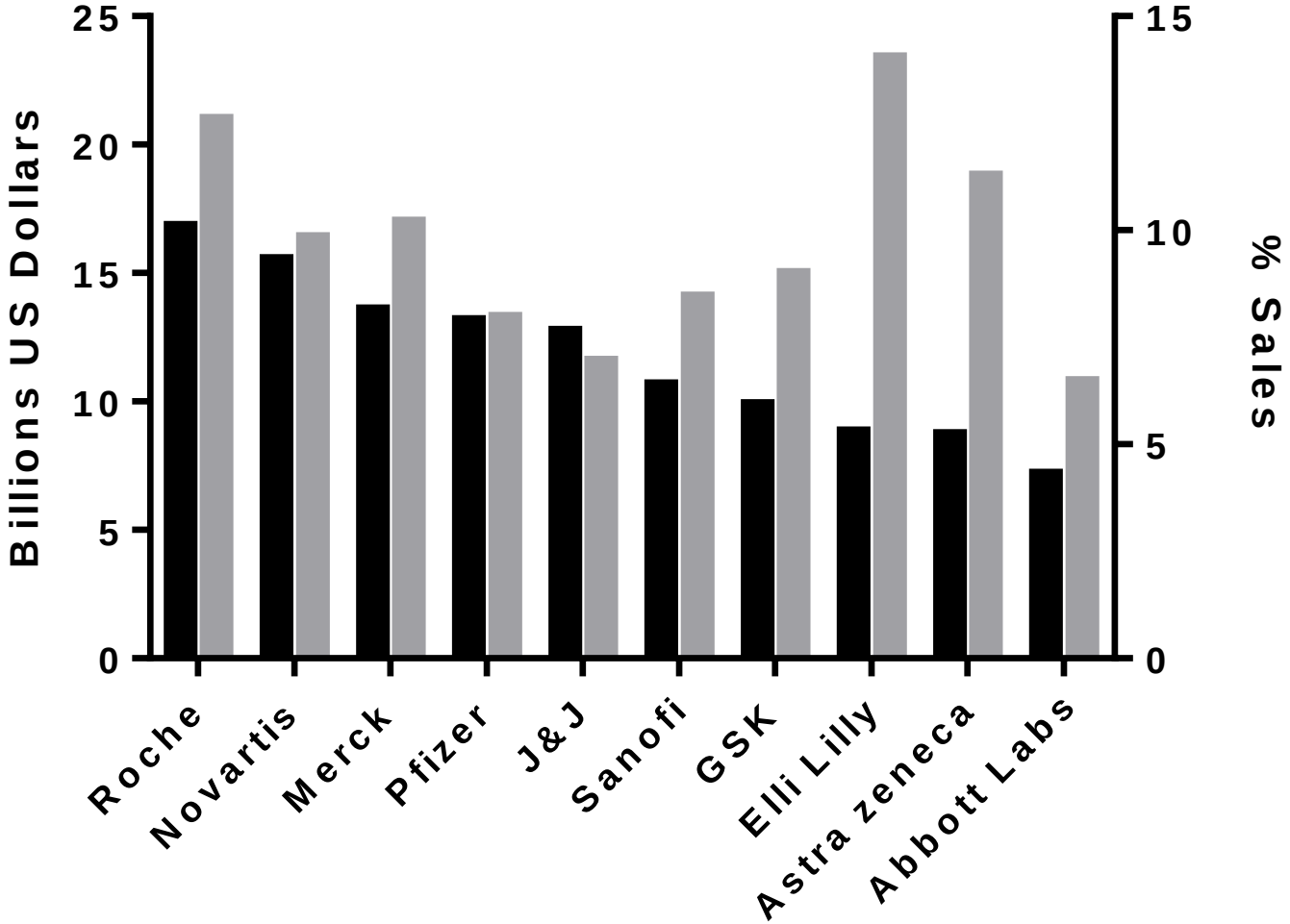


2013 EU Industrial R&D Investment Scoreboard. European Commission, JRC/DG RTD.

Innovation and R&D spending

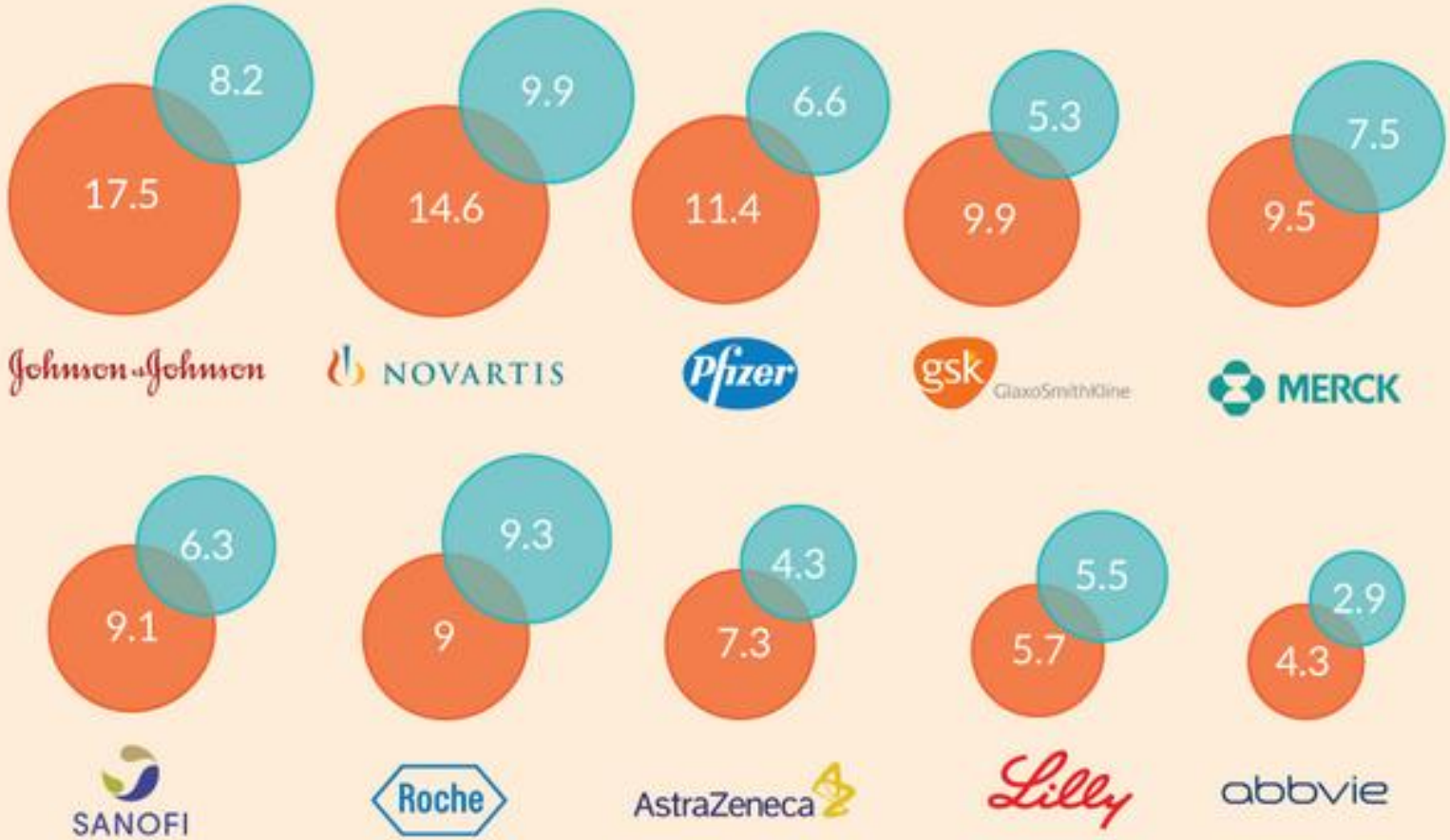


R&D expenses



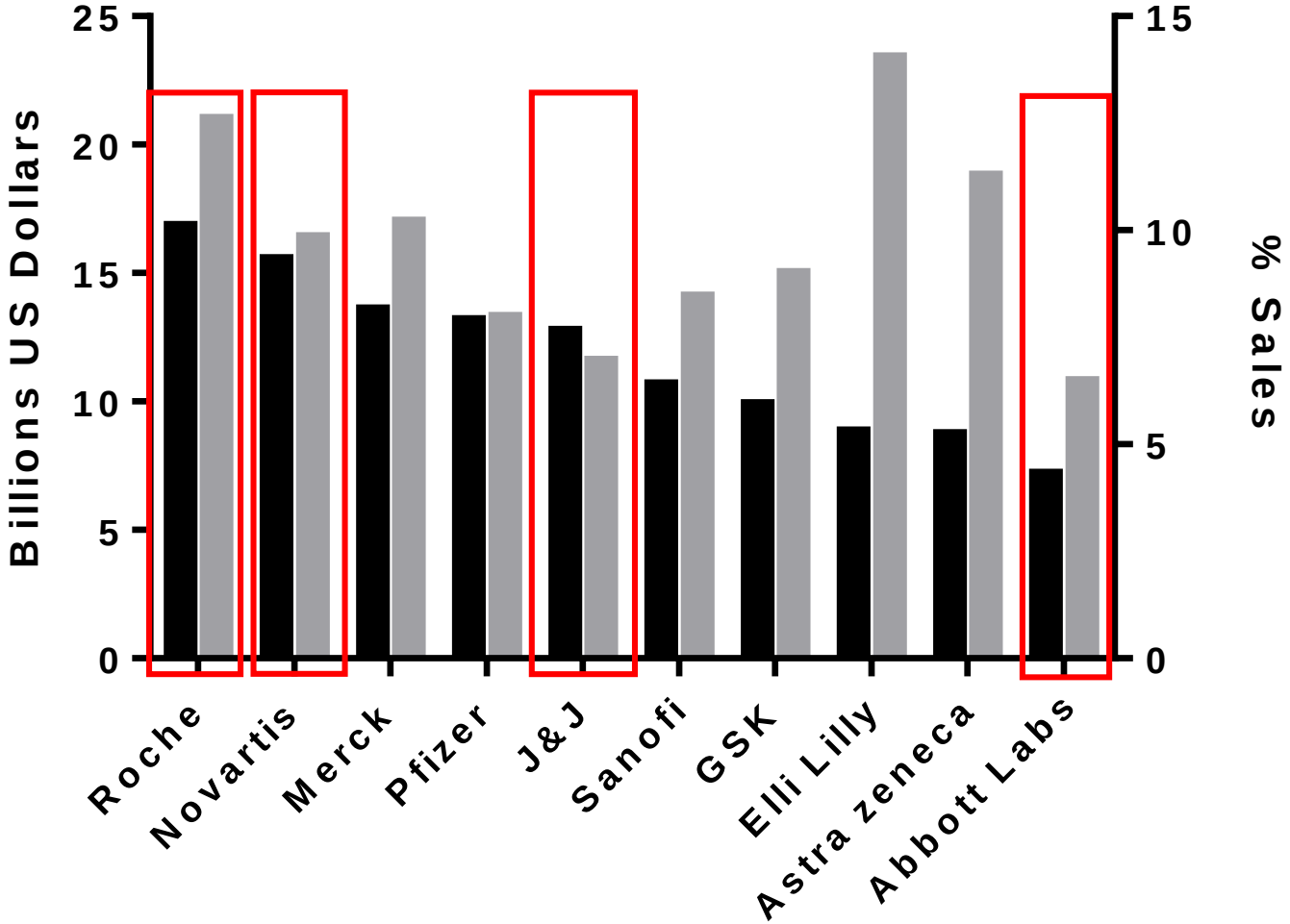
Source: Fierce Pharma, 2012

HOW MUCH DOES BIG PHARMA SPEND ON: SALES & MARKETING VS. RESEARCH & DEVELOPMENT



IN US $ BILLION, FOR 2013

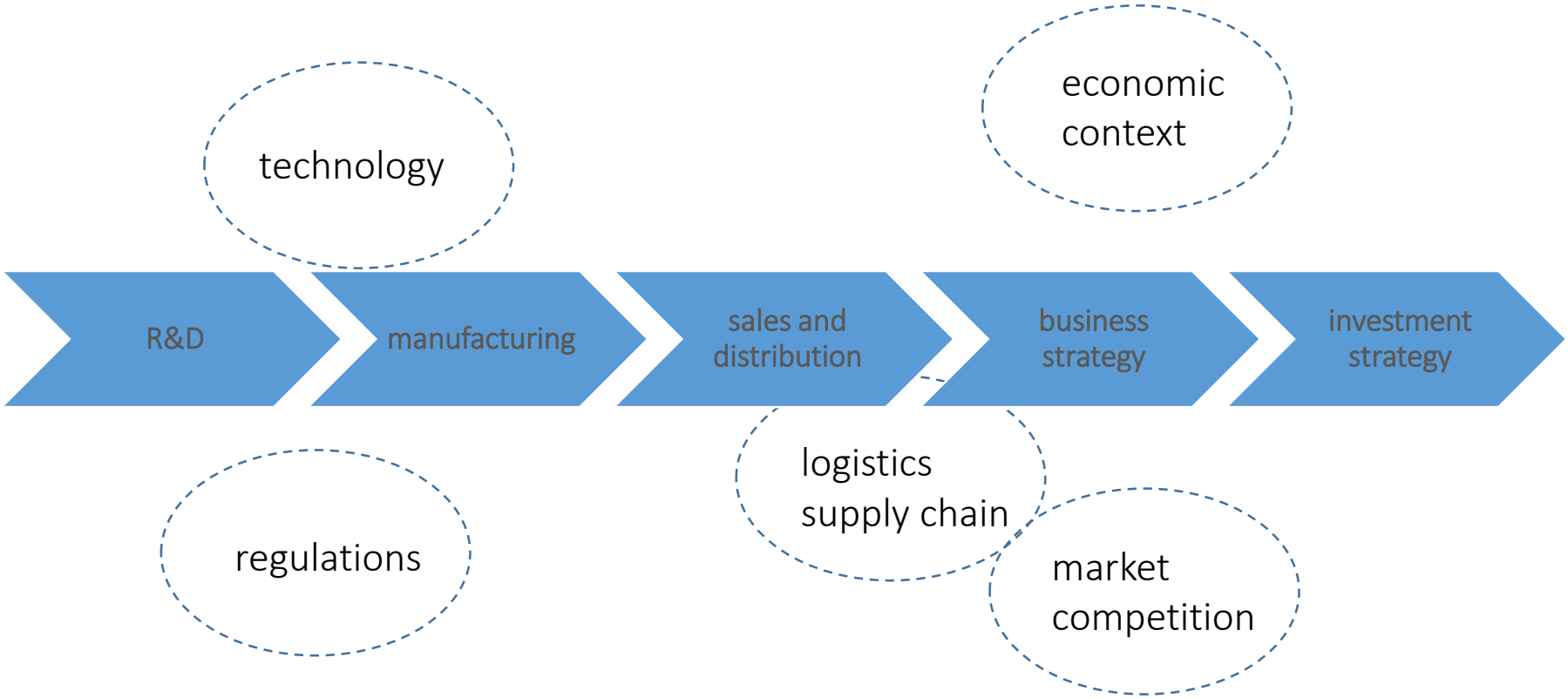
R&D expenses



* TOP 100 innovators (Thomson Reuters 2014)

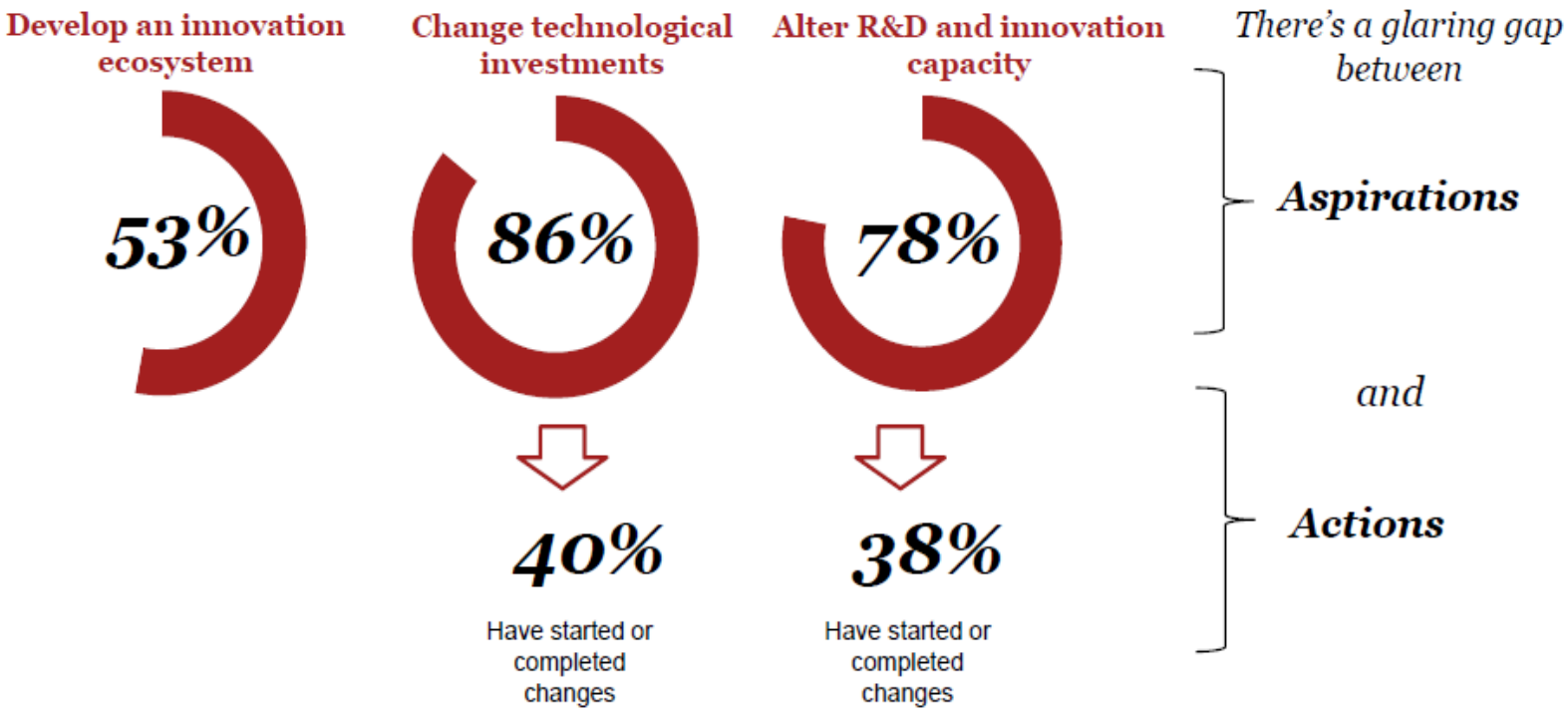
Innovation and the role of R&D

- Innovation: the process of translating an idea or invention into a good or service that creates value or for which customers will pay
- Innovation includes the entire value chain



Innovation is critical….

Most pharmaceutical & life sciences CEOs want to improve their company's ability to innovate



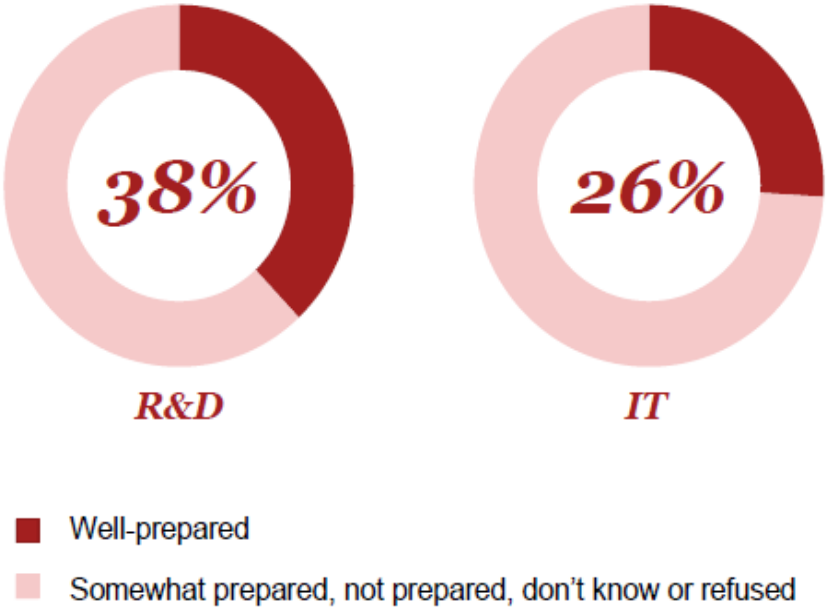
Q: Which, if any, of these national outcomes is your organisation focusing on as a priority over the next three years?
Q: To what extent are you currently making changes, if any, in the following areas?
Base: All respondents (Total sample, 1,344; Pharmaceuticals & life sciences, 119) Aspirations responses include: recognise need to change, developing strategy to change, concrete plans to implement change programmes, and change programme underway or completed.

Source: 17th CEO survey 2014, PwC

Innovation and the role of R&D

While nearly four in ten pharmaceuticals and life sciences CEOs told us that their R&D functions are well-prepared for change, just over a quarter show the same confidence in their organisation's IT department.

Q: Thinking about the changes you are making to capitalise on transformative global trends, to what degree are the following areas of your organisation prepared to make these changes?



Source: 17th CEO survey 2014, PwC

R&D funding: Where is the money coming from?

- *on average, major companies fund about 65% of R&D spending from internal funds (i.e. from profits)*
- *about 35% is sourced from outside e.g. governments, not for profits, etc.*

Part 2

R&D in a start up company: Apidel, Geneva

APIDEL – the beginnings

2007 → 2010 → 2011

University of Geneva licences two early-stage polymeric compounds to a US company

Company does not develop technologies

University of Geneva recovers rights and decides to create a spin-off

Apidel is created

APIDEL – the people

Founders:

- Alan Cookson, CEO
- Robert Gurny, CSO
- Michael Moeller, Technical Director

Employees:

- Victoria Sarraf, Alliance Manager
- Vitalia Bakhtina, Funding Coordinator
- Thibault Mugnier, Development Scientist
- Herve Courthion, Development Scientist
- Emilie Belisse, Pharmaceutical Intern
- Naoual Dahmana, PhD student at UNIGE
- Doris Gabriel, R&D Manager

Eclosion – a first home for Apidel

Eclosion – Geneva Life Science Incubator

- *Eclosion: life science incubator financed by the State of Geneva*

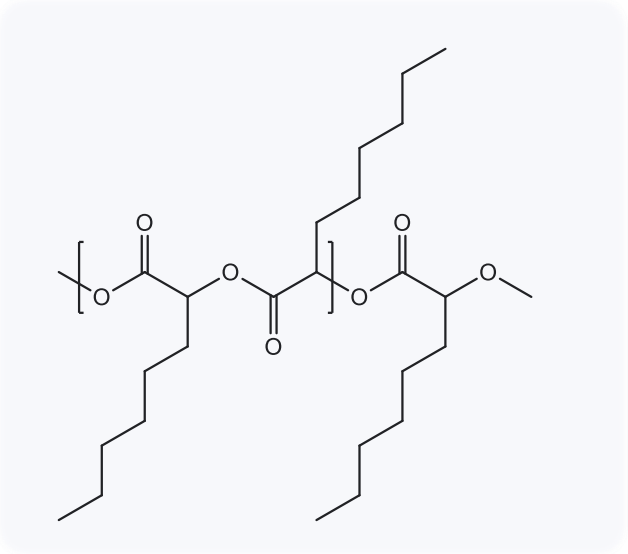
- *Eclosion provides office/lab space and access to state of the art equipment to Apidel*

- *Special equipment (microscopes, rheometers, particle sizers etc.) which is not available in the incubator is accessed through* ***UNIGE***

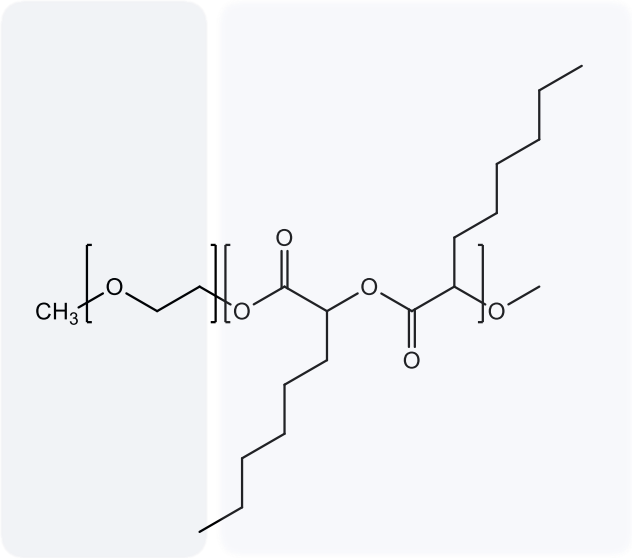
- *Further services include:*

- *clinical, manufacturing, business and financial support required to assess the discovery's scientific and business potential*
- *the production resources, infrastructure and high-level expertise required to validate it experimentally*
- *access to finance for the creation and development of a new company*

APIDEL: the technology



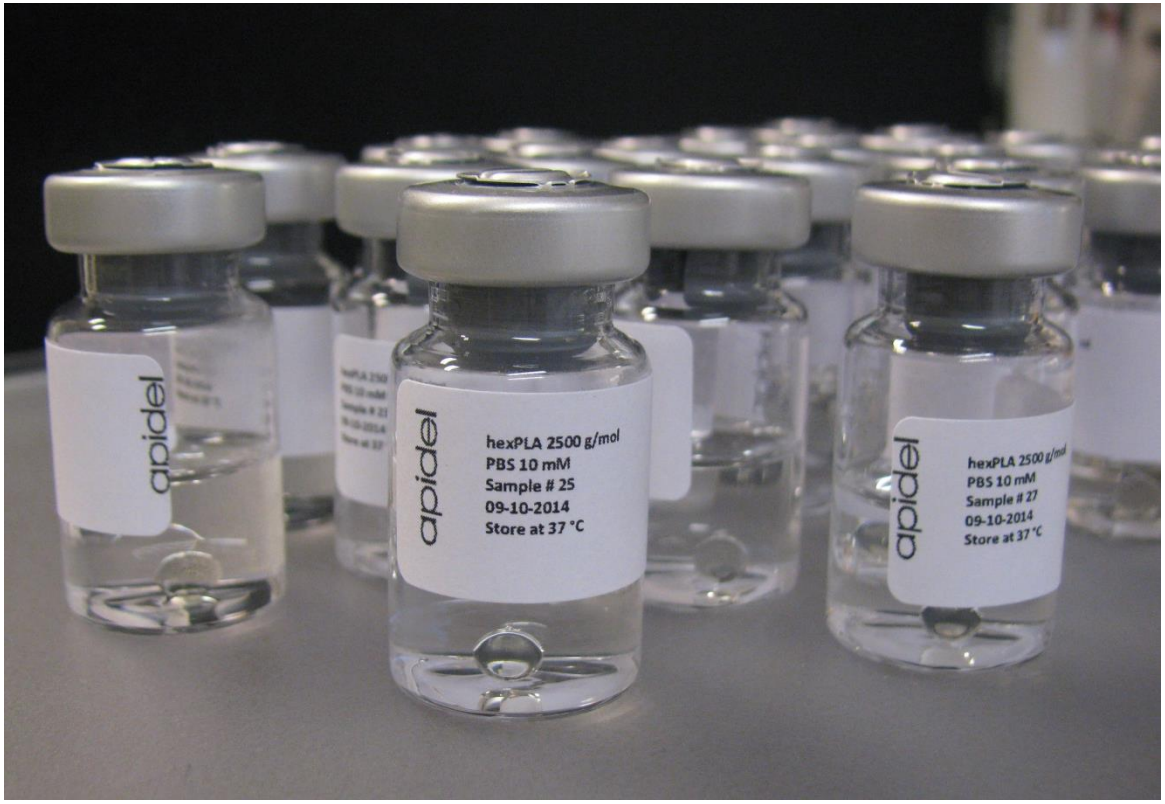
ApidCOR: hexPLA
injectable, liquid polymer for extended release formulations



ApidSOL: mPEGhexPLA
micellar nanocarriers for drug solubilization and transport across biological barriers (skin, mucosa or cornea)

ApidCOR platform

- Liquid, injectable polymer for sustained release



How is ApidCOR different?

Versatile delivery platform	• for proteins, peptides and small molecule APIs; multiple administration routes
Improved release profiles	• steady release up to 6 months, low burst effect and inter-individual variability
Improved biocompatibility	• no signs of foreign body reaction or chronic inflammation; safe degradation products
«Mix and use» manufacturing	• no organic solvents, simple dispersion or dissolution of drug in ApidCOR
Patient-friendly	• small needle injection; ready-to-use syringe

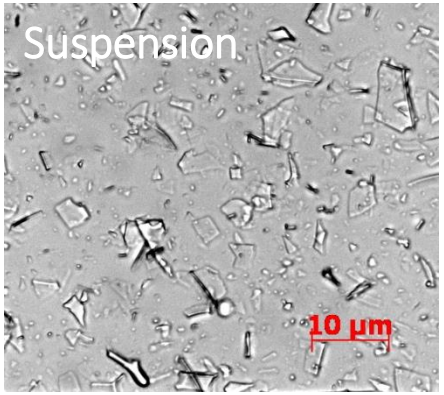
ApidCOR: formulation process

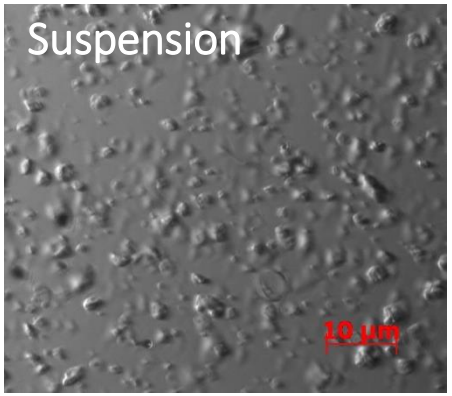
- "Mix and use" formulation process

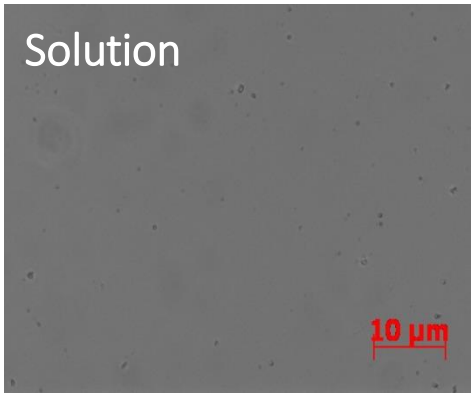
API + hexPLA → API-hexPLA formulation

Suspension

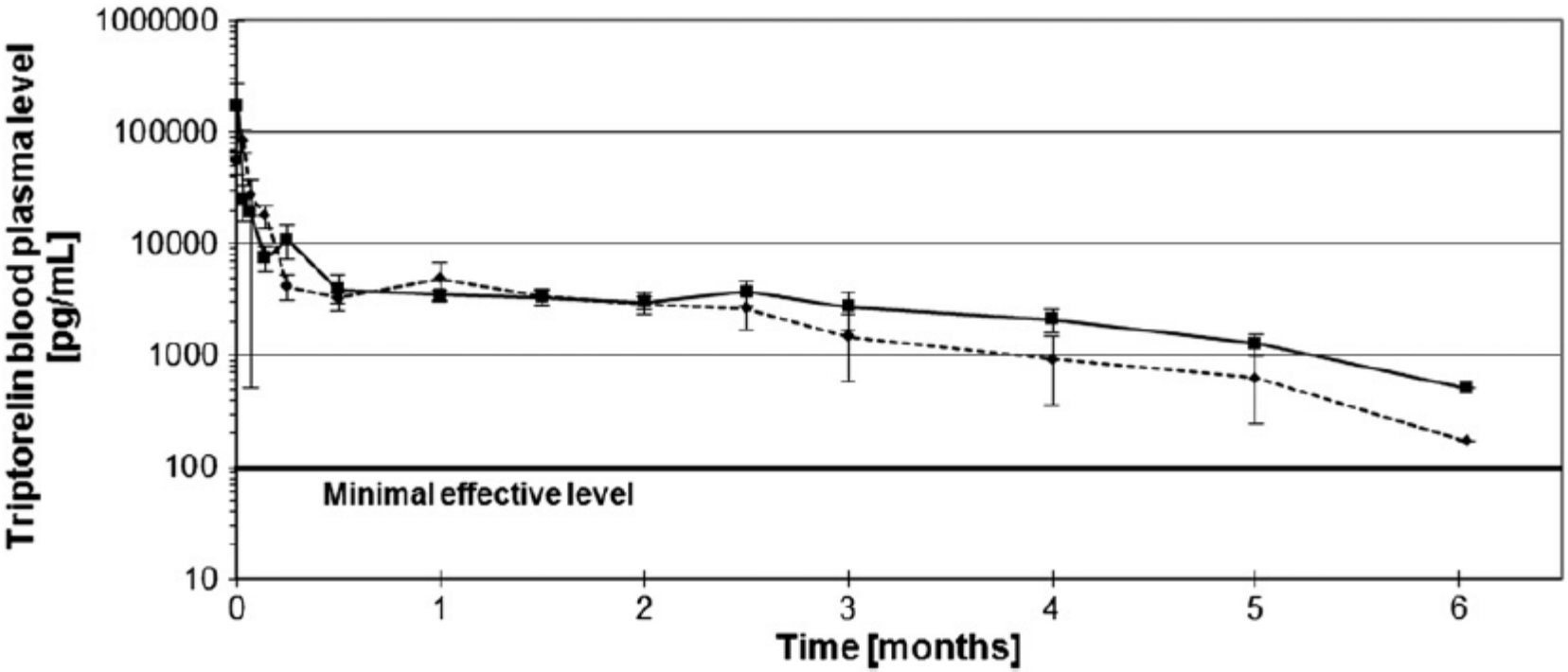
Solution







ApidCOR: improved efficiency



Solid line: 10% triptorelin; dashed line: 5% triptorelin

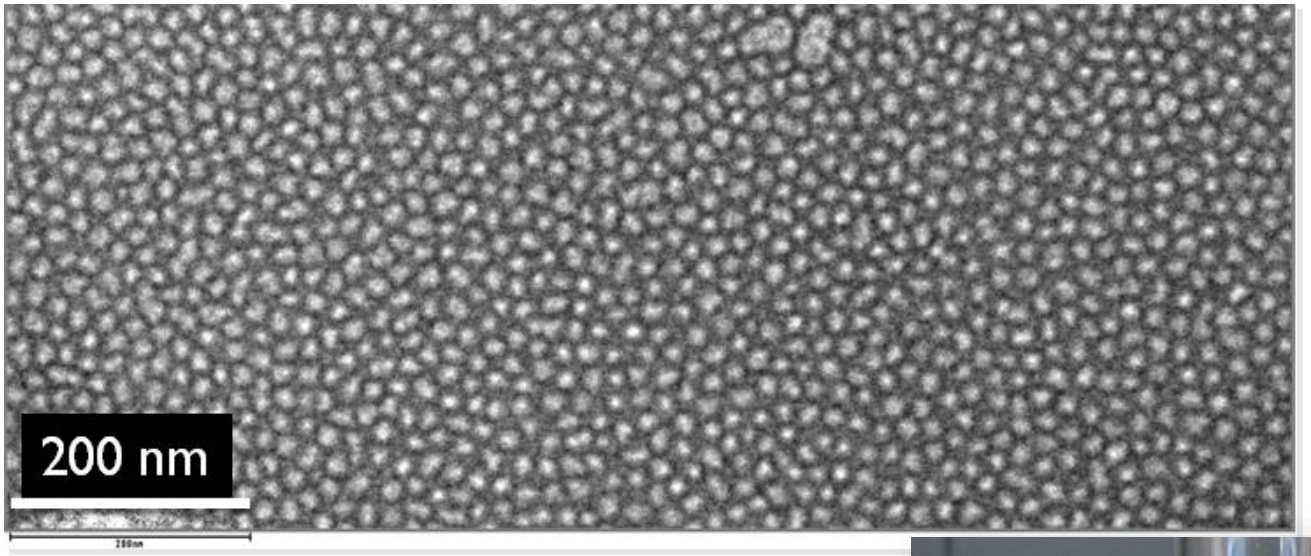
Asmus Lutz et al, Journal of Controlled Release 2012

ApidSOL platform

- *Nanocarrier for drug solubilization and local delivery*

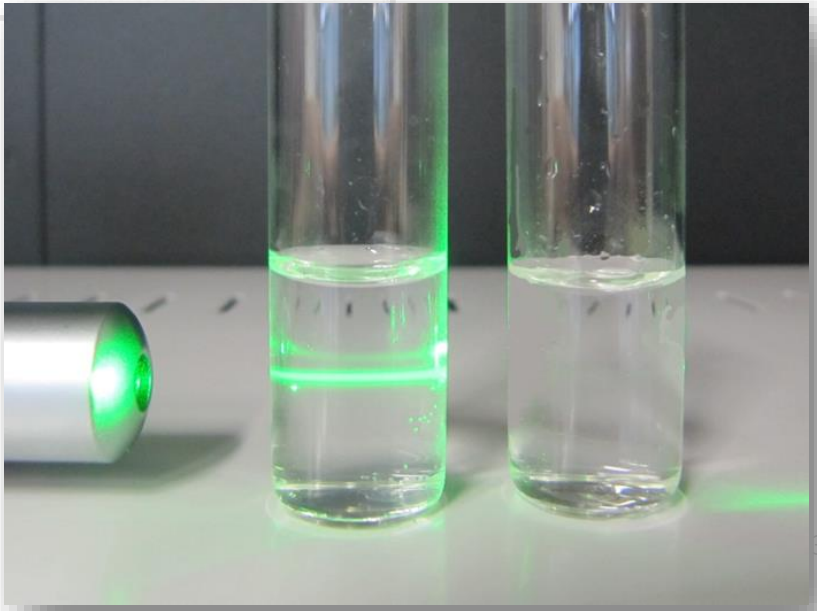
ApidSOL platform

- *Nanocarrier for drug solubilization and local delivery*



Small & uniform size (TEM)

Micelles detected by light scattering only



How is ApidSOL different

Versatile delivery platform	• applicable to most poorly water-soluble small molecule APIs
Improved solubility	• leads to a significant solublity enhancement (up to several 1000 x)
Improved delivery	• improved delivery into cornea, skin and mucosal surfaces
Improved biocompatibility	• safe in preclinical studies
«Mix and dispense» manufacturing	• single operation manufacturing, self assembly of nanocarrier

EYE delivery: improved efficiency

Restasis ® formulation

- Anionic microemulsion (castor oil-water, stabilized by polysorbate 80)
- 0. 5 mg/mL (cyclosporine A)

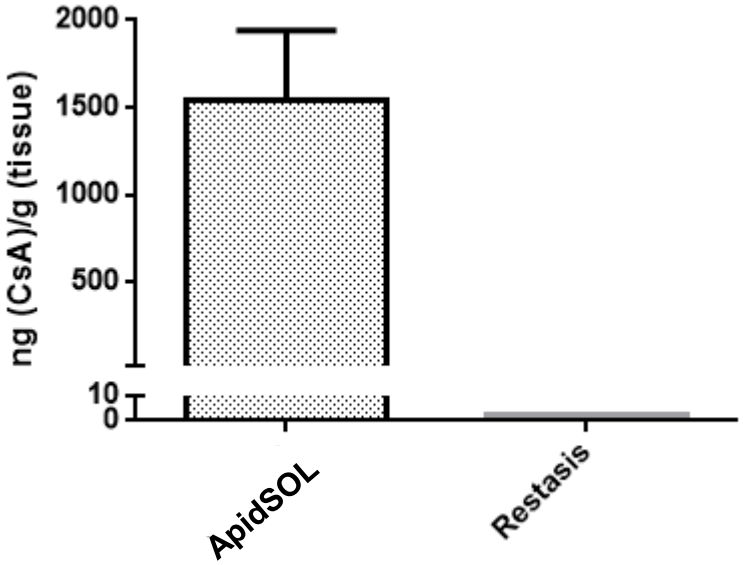
ApidSOL formulation

- Micelle formulation
  - Size (Z_{av}) < 50 nm
- 0.5 mg/mL (cyclosporine A)

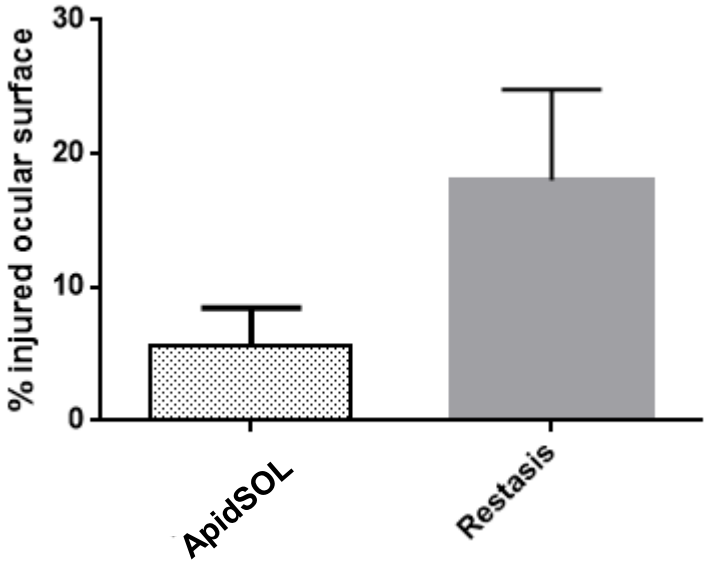
Di Tommaso C et al, IOVIS 2012

EYE delivery: improved efficiency

Corneal drug delivery



Corneal surface damage



Di Tommaso C., Miller F. et al, IOVIS 2012

APIDEL: business model

ApidSOL/ApidCOR technology

3 ways revenue generation:

- Licence fees granting rights to parters to exploit Apidel technology (including milestone payments and royalties)
- Supply of drug delivery technology raw materials
- Development and consulting fees linked to Apidel expertise and participation in product development and formulation

APIDEL: R&D strategy

PARTNER PROJECTS

ApidCOR/ApidSOL formulations for improved delivery of partner's proprietary molecules

- *Formulation feasibility studies*
- *Preclinical proof of concept studies at CRO (or at partner site)*
- *Clinical development (at CRO or partner site)*

INTERNAL PROJECTS

ApidSOL/ApidCOR formulations for improved delivery of non-proprietary molecules

- *Formulation feasibility studies*
- *Preclinical proof of concept studies at CRO*
- *Clinical development (at CRO)*

R&D: collaborative projects

Partners: *big-, mid- and small-sized pharmaceutical companies*

Funding: *research fees to be paid by Pharma partner*

Active pharmaceutical ingredients: *small molecules, proteins, peptides*

Applications: *topical, ophtalmic, parenteral, intravitreal*

Typical project steps:

1. *Establishment of a workplan, budget and timelines*
2. *Formulation work: feasibility and optimization*
3. *Formulation work: stability and optimization*
4. *Selection of formulation candidate*
5. *Preclinical studies: sample shipment*
6. *Further formulation optimization and long term stability*

FEASIBILITY

PRECLINICAL PROOF OF CONCEPT

FORMULATION DEVELOPMENT

R&D: preclinical toxicology

Toxicology studies according to development program

Dermatology topical

Opthalmology topical

Opthalmology ivt

GIT rectal

Otology it

Selection of formulation candidate

Estabilishing of formulation specifications (sterility, endotoxins etc.)

Transfer process/analytics to GMP qualified manufacturing site

Sample shipment logistics/project management

R&D: internal projects

Partners:
Universities, Hospitals,

Funding:
federal or european funding (CTI etc), company funds

Fields:

- *Delivery to the anterior and posterior segement of the eye*

- *Delivery of the GIT tract*

- *Delivery to the ear*

- *Dermal delivery (inflammatory, oncology)*

R&D: polymer manufacturing

- *Upscale: from g to kg scale*
- *select robust synthetic strategy*
- *establish purification tools*

- *Polymer specifications and analytical methods*
- *identify, develop and transfer analytical methods*
- *establish effect of dispersity/impurities/residuals on functional performance*
- *establish effect of dispersity/impurities/residuals on toxicological profile*

- *GMP production*

R&D: formulation upscale/transfer

- Upscale: from mL to L
- *select process which is allows handling of several liters (heat generation, wear, generation of bubbles etc)*
- *optimize process time*

- GMP: selection of compliant processes
- *testing of equipment which is compliant for use in pharmaceutical production*

- Aseptic/sterile manufacturing
- *testing of equipment which can be sterilized*
- *Filter and pressure systems for handling large volumes*

- Documentation and transferability to CMO

Summary

- R&D is dual: collaborative reserch & internal development programs
- R&D is «multi-task»
- R&D is flexible/responsive
- R&D stage will change with company development
- R&D is part of management