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# Drug Discovery, Roche, and China: Some Personal Reflections

*Dr. Jitao David Zhang, Computational Biology and Bioinformatics*

*Roche Innovation Center Basel, Pharma Research and Early Development (pRED), Pharmaceutical Sciences*

*Insight China, FHNW, February 2019*

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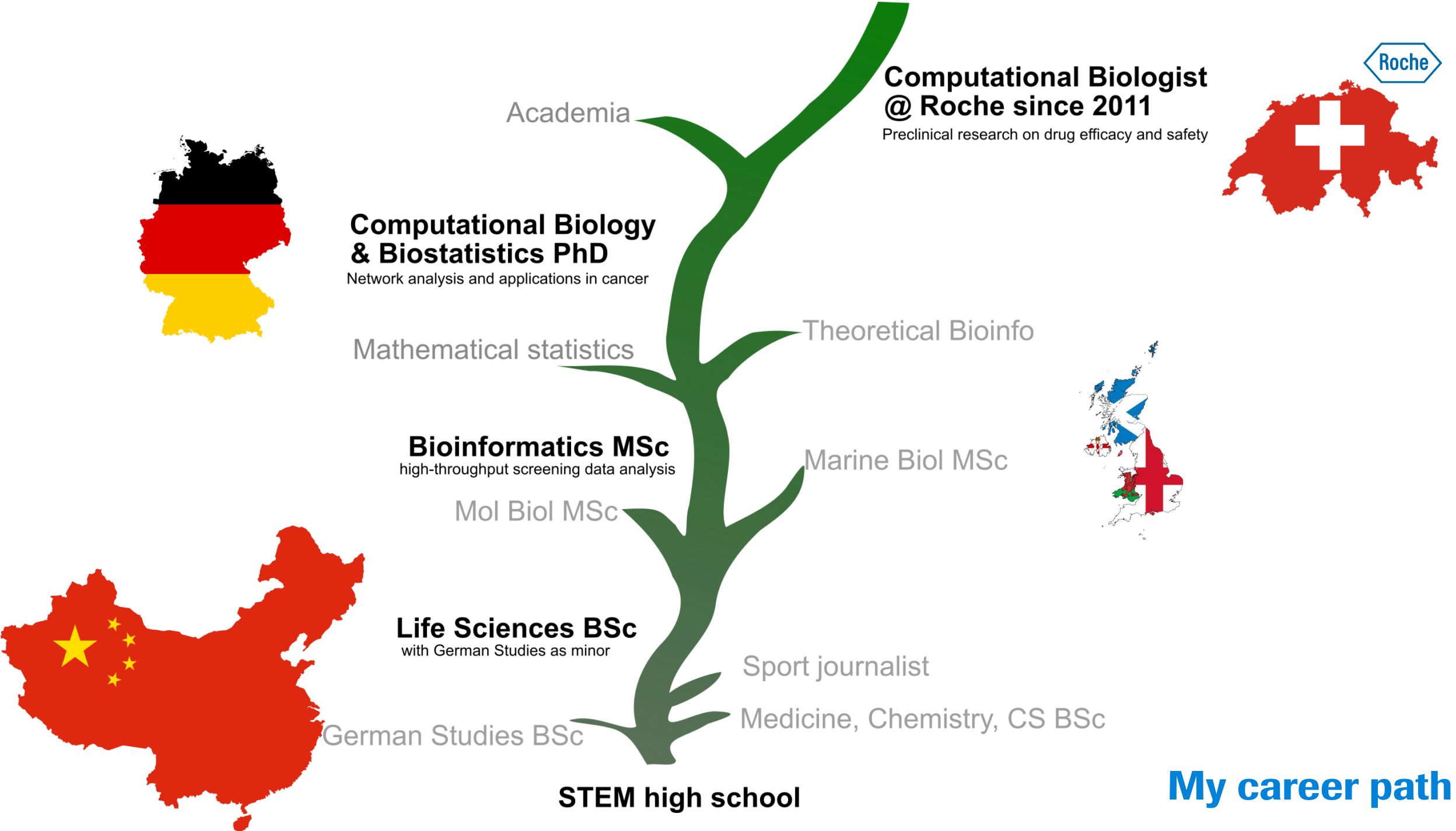
**[Contact the author](#)**

# Outline



- 1. Who am I, and what do I do at Roche?**
- 2. How does Drug Discovery work?**
- 3. Roche In China, Roche For China**

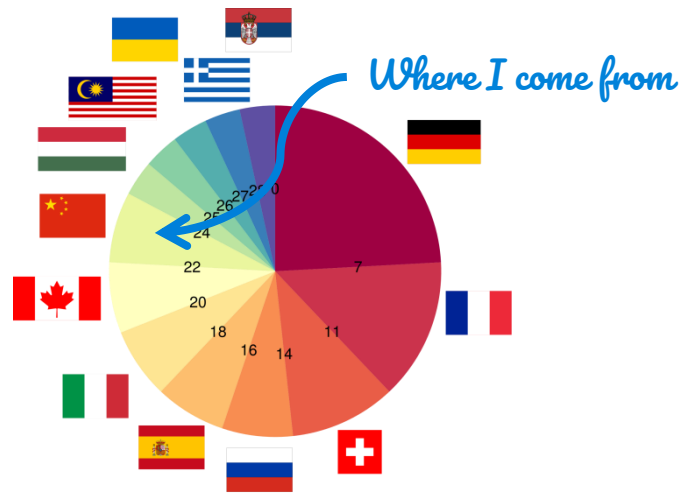
**WHO AM I?**



# pRED: International, Interdisciplinary, and Impactful

## The composition of the group I am in

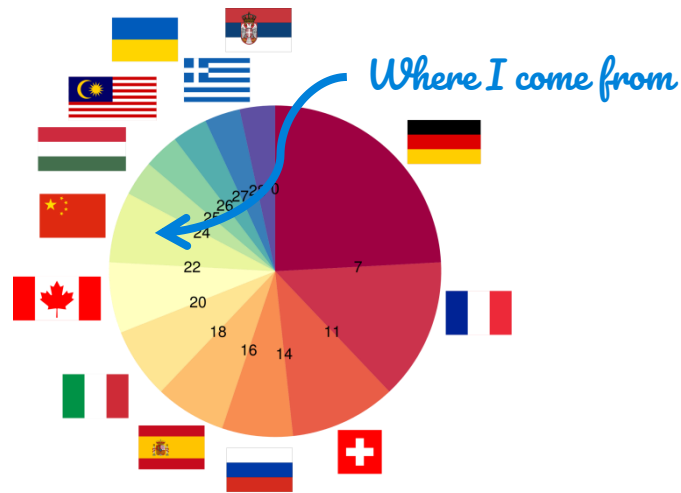
*Bioinformatics and Exploratory Data Analysis  
in Pharmaceutical Sciences, pRED (N=~30)*



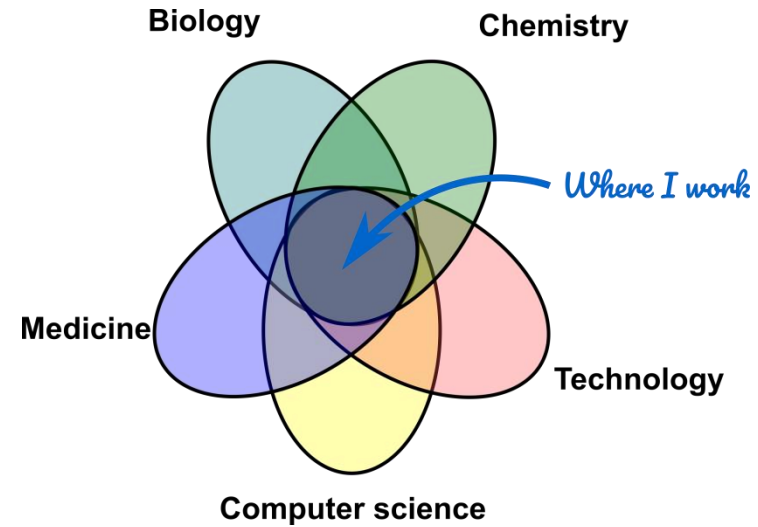
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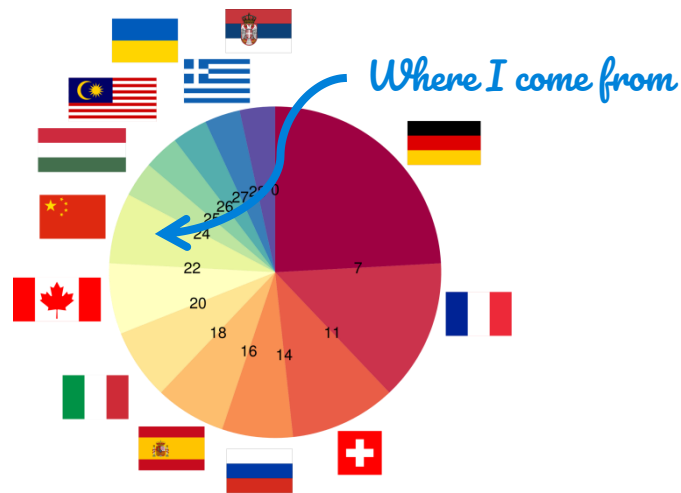
## We bring different expertise together and learn from each other



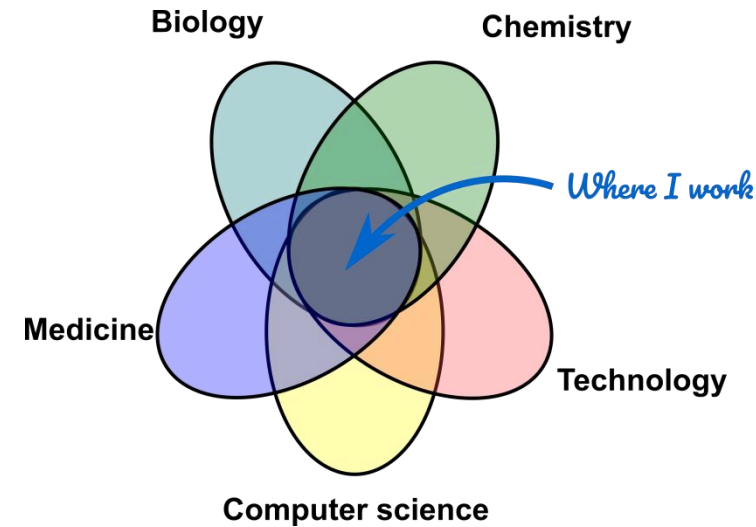
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## We bring different expertise together and learn from each other



## We support three Disease & Therapeutic Areas with a strong pipeline

**Oncology**

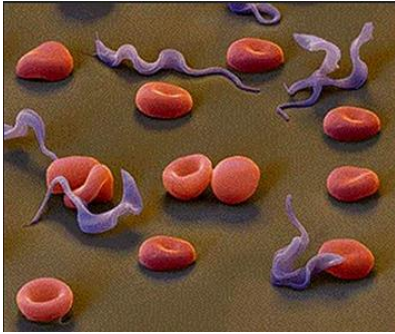
**Neuroscience and  
Rare Diseases (NSRD)**

**Immunology, Infectious  
Diseases, and  
Ophthalmology (I2O)**

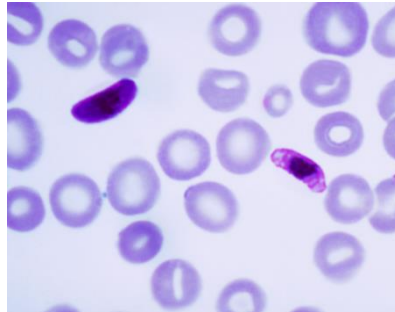


# **HOW DOES DRUG DISCOVERY WORK?**

# The history of *Homo sapiens* is a history of living with, understanding, and fighting diseases



Trypanosomes

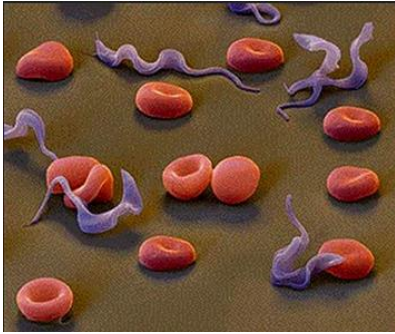


Plasmodium

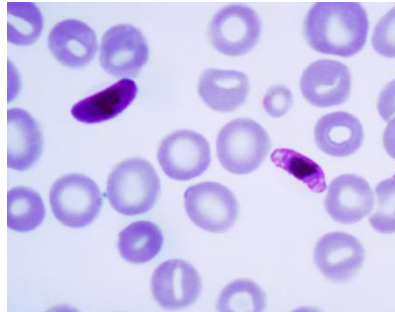
## Tropical diseases

~500,000 years ago

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Trypanosomes



Plasmodium

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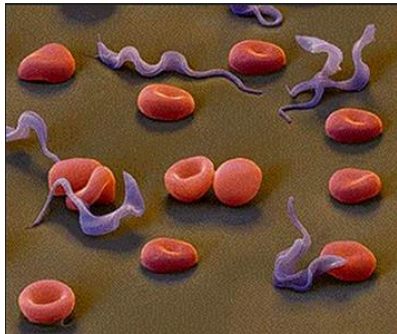


A young patient of smallpox,  
the first eradicated infectious disease

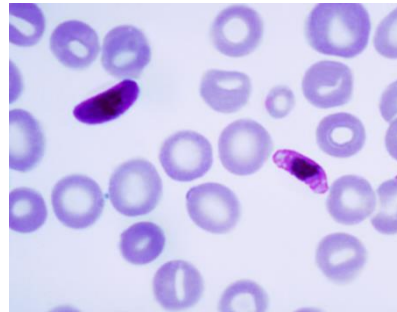
## Hygiene, vaccination, and antibiotics

~250 years ago

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Trypanosomes



Plasmodium

## Tropical diseases

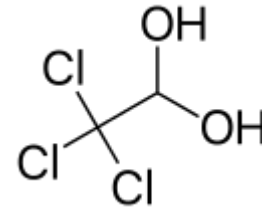
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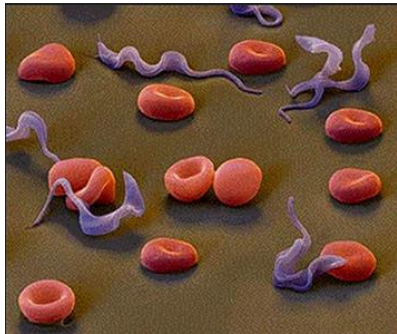


Chloral hydrate,  
the first synthesized drug

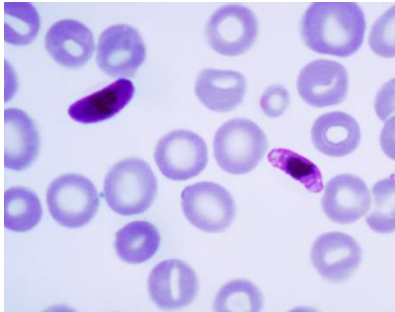
## Pharmaceutical drugs

~150 years ago

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Trypanosomes



Plasmodium

## Tropical diseases

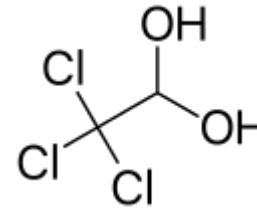
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## Hygiene, vaccination, and antibiotics

~250 years ago



Chloral hydrate,  
the first synthesized drug

## Pharmaceutical drugs

~150 years ago



Nobel prize laureates 2018,  
immune checkpoints,  
and drugs targeting the pathways

## Personalized precise healthcare

~20 years ago

# How Do You Make A Drug?

*It's simple, but...*





# How Do You Make A Drug?

*It's simple, but...*

**1,000,000,000** CHF investment  
**7,000,874** hours of work  
**6,587** experiments  
**423** researchers  
**1** drug



# Drug Discovery: From Bench To Bedside



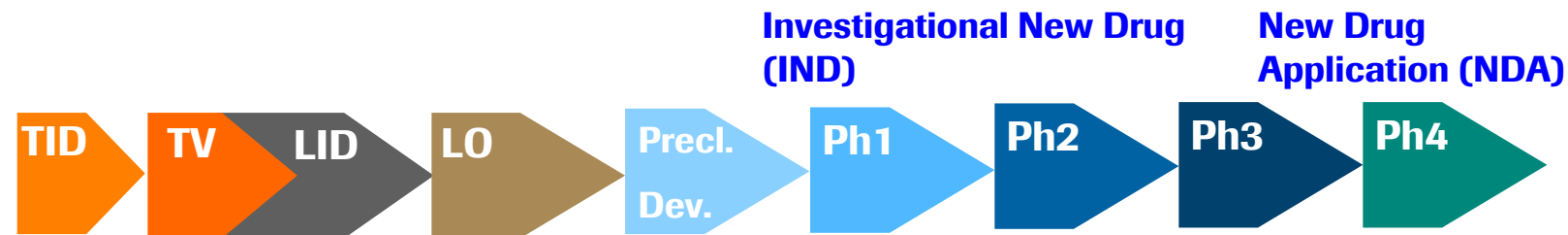
**Target Identification (TID)**

**Target Validation (TV)**

**Lead Identification (LID)**

**Lead Optimization (LO)**

**Clinical Development**





# Drug Discovery: From Bench To Bedside (and back)

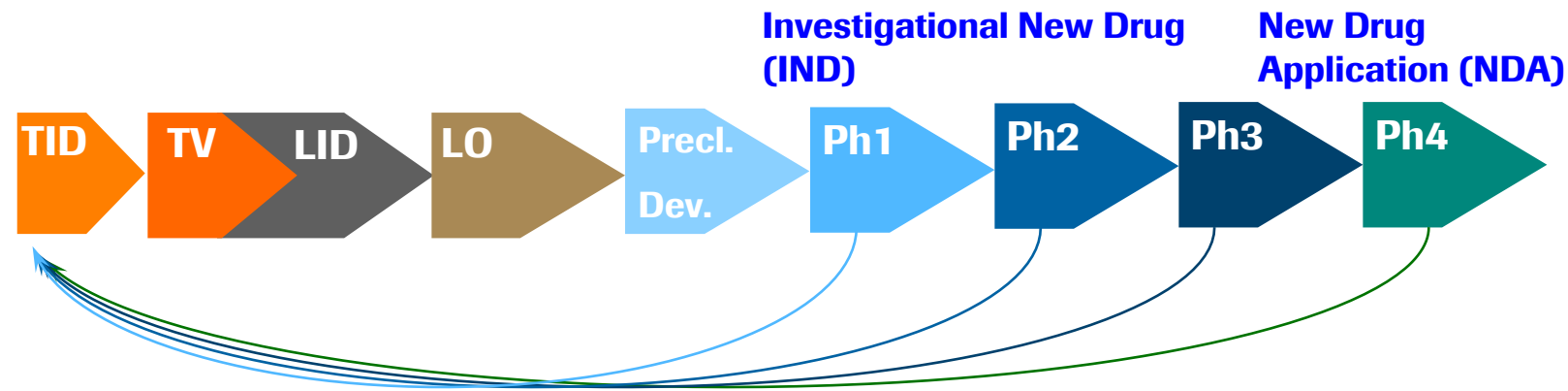
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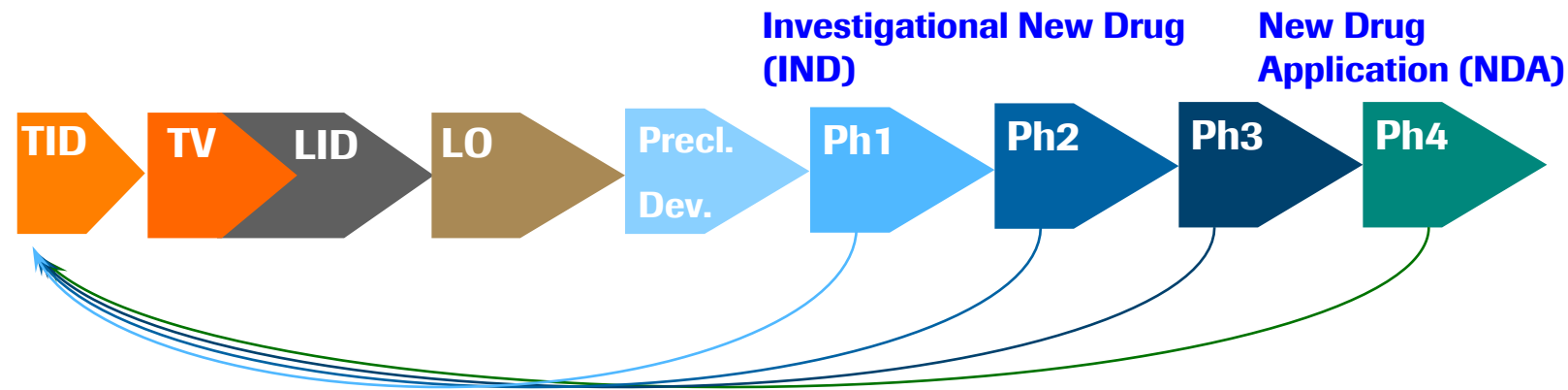
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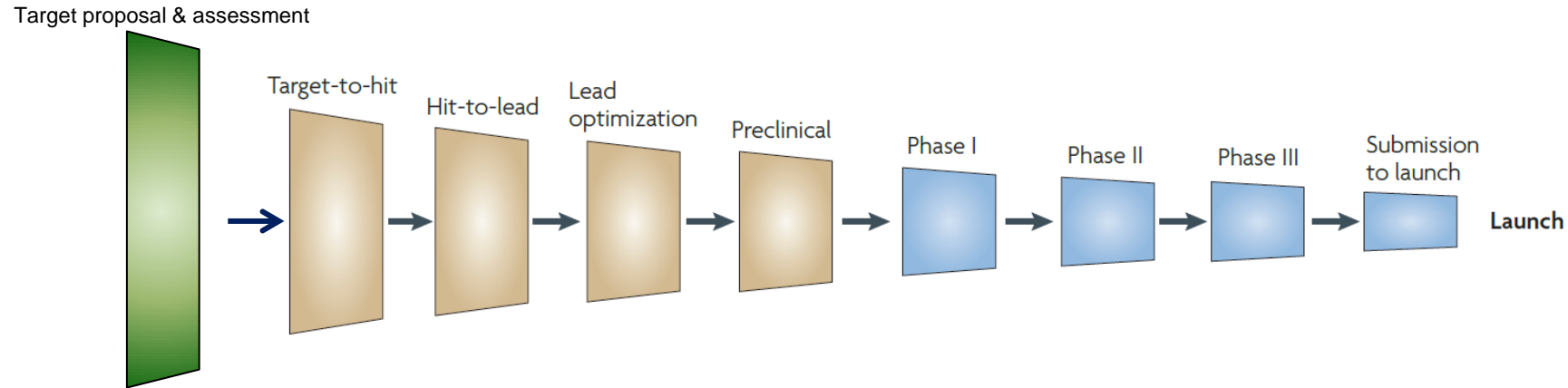
**Lead Optimization (LO)**

**Clinical Development**



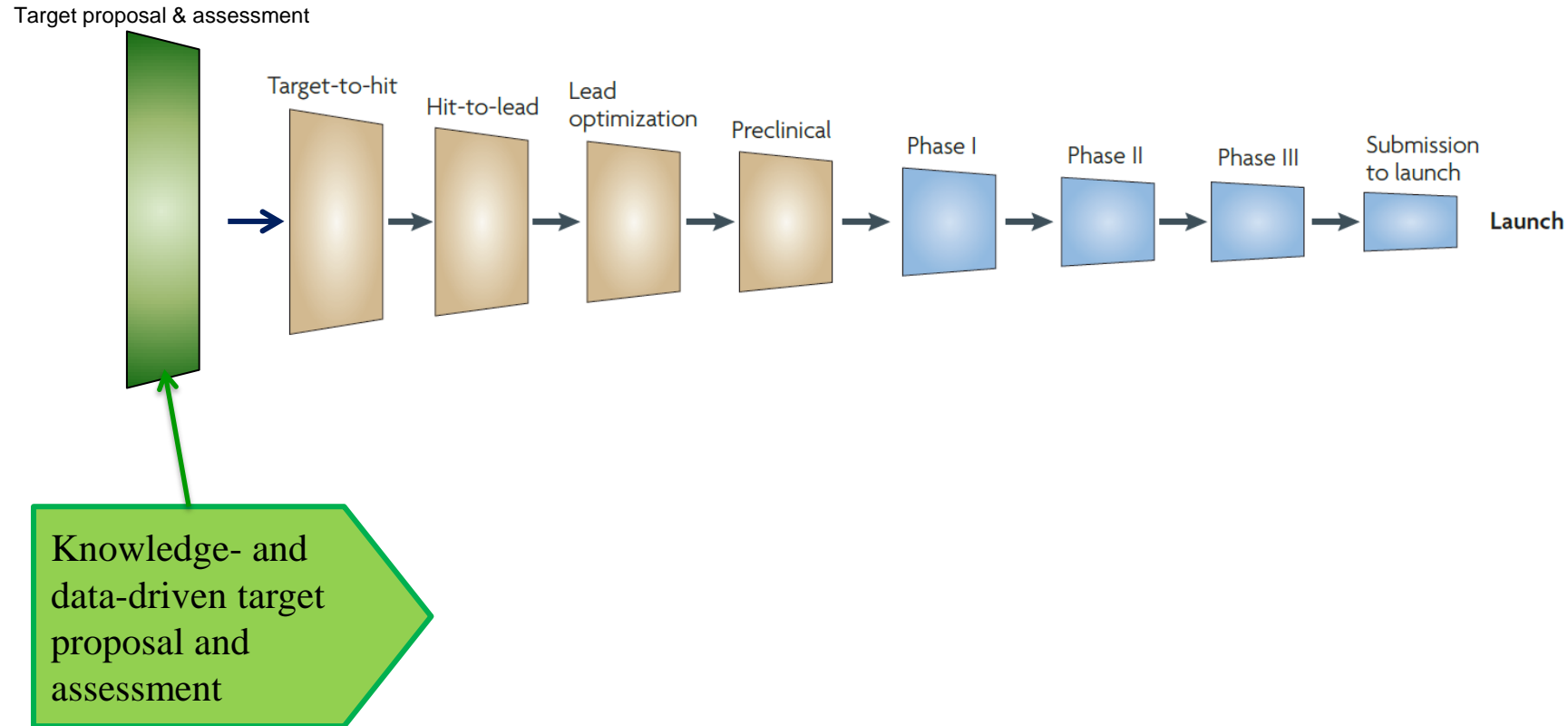
Drug discovery is a long process (~10 years) , involving both forward and reverse translation

# Bioinformatics and computational biology, a branch of applied mathematics, are indispensable for modern drug discovery



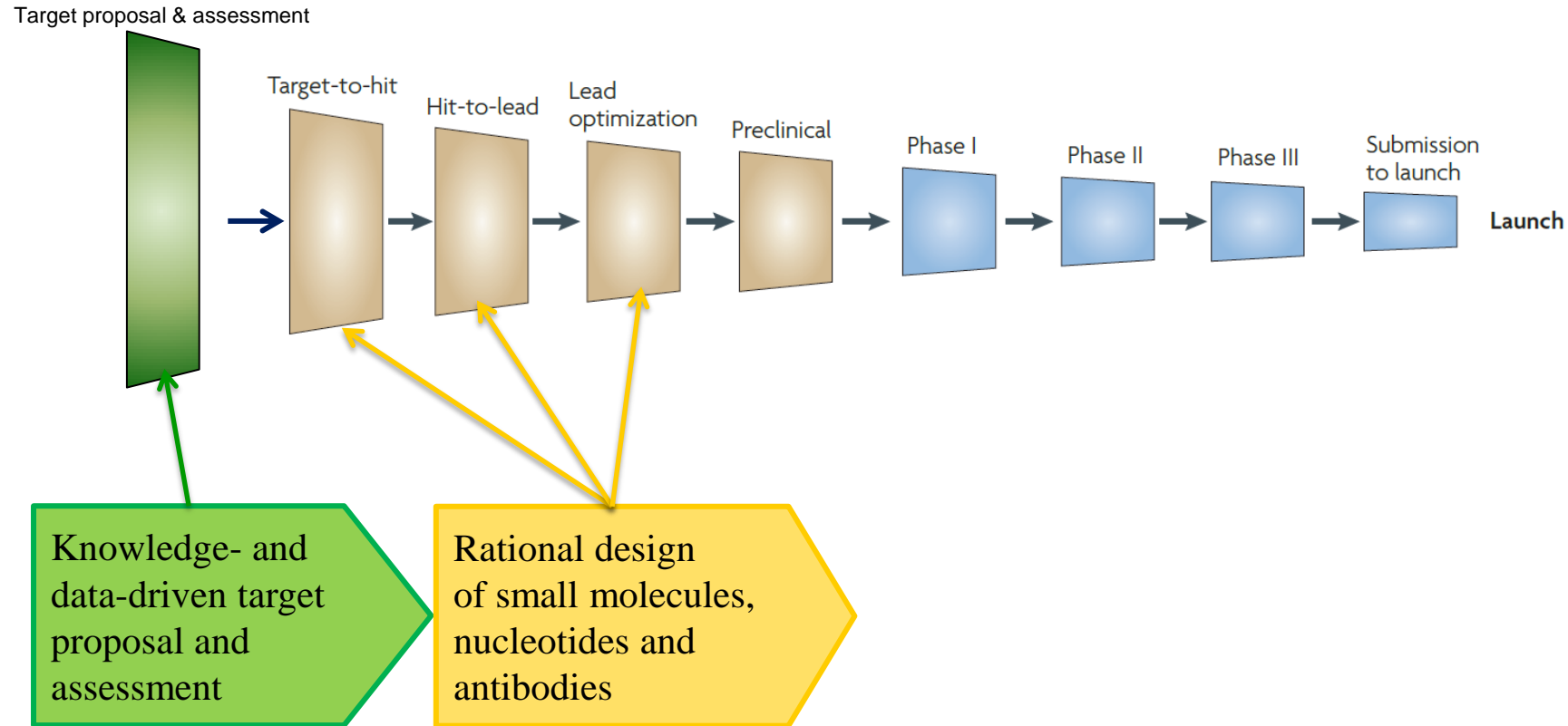
Modified from Paul *et al.* "How to Improve R&D Productivity: The Pharmaceutical Industry's Grand Challenge." *Nature Reviews Drug Discovery*, 2010

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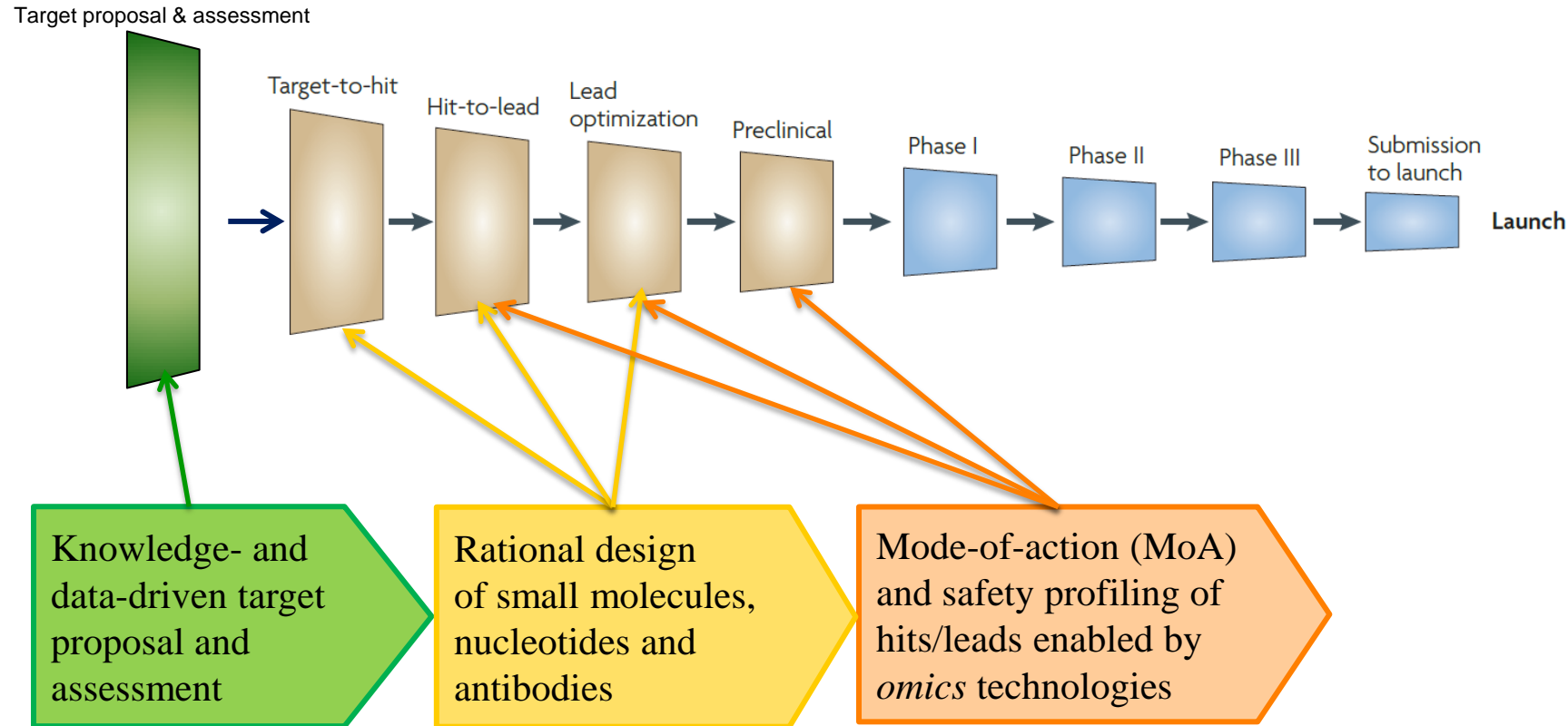
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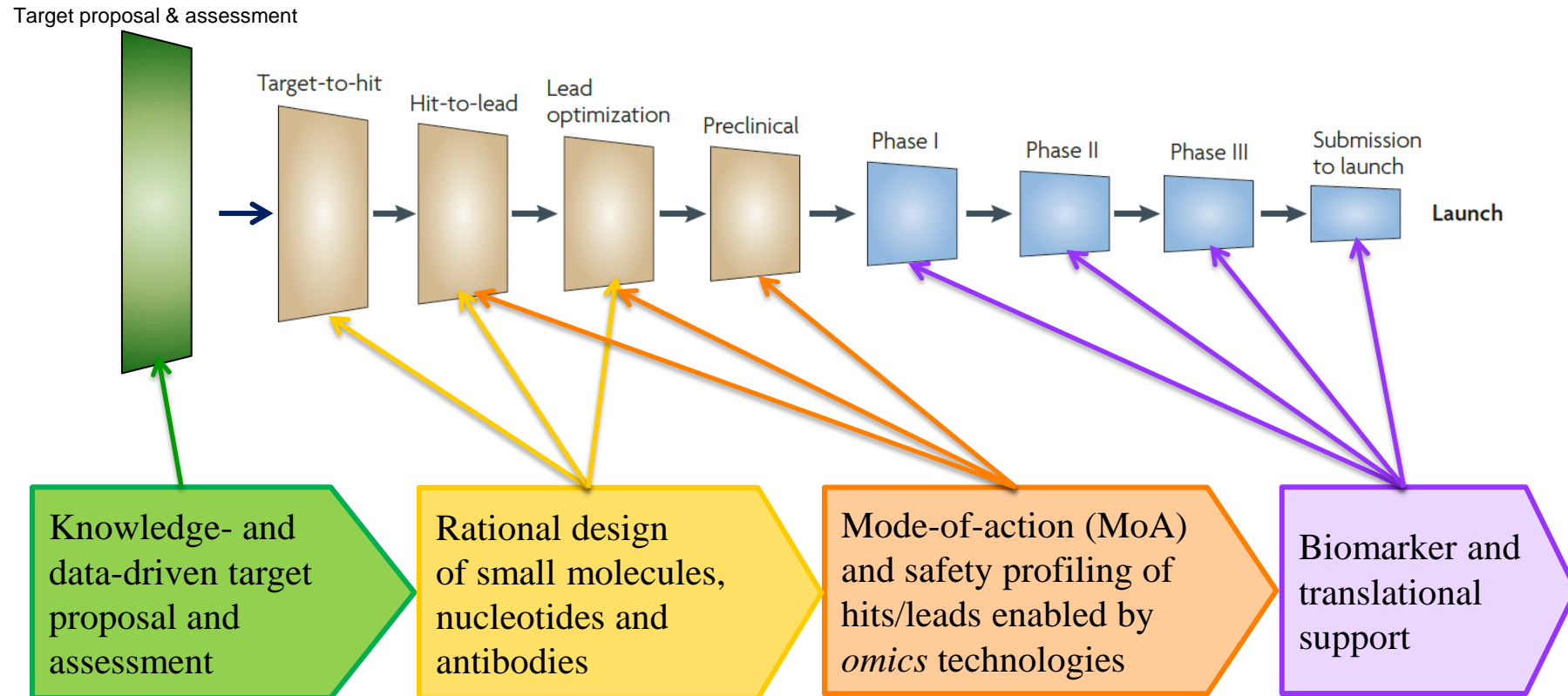
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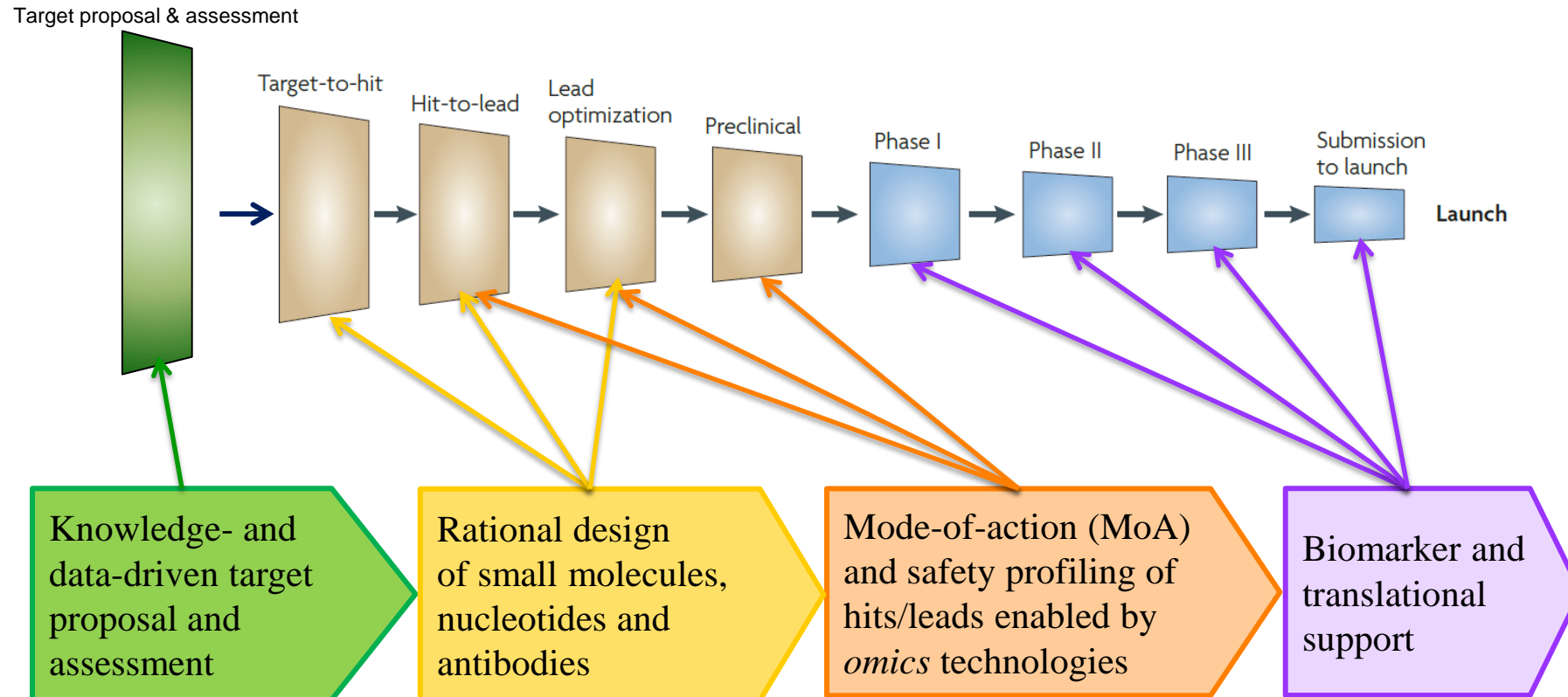
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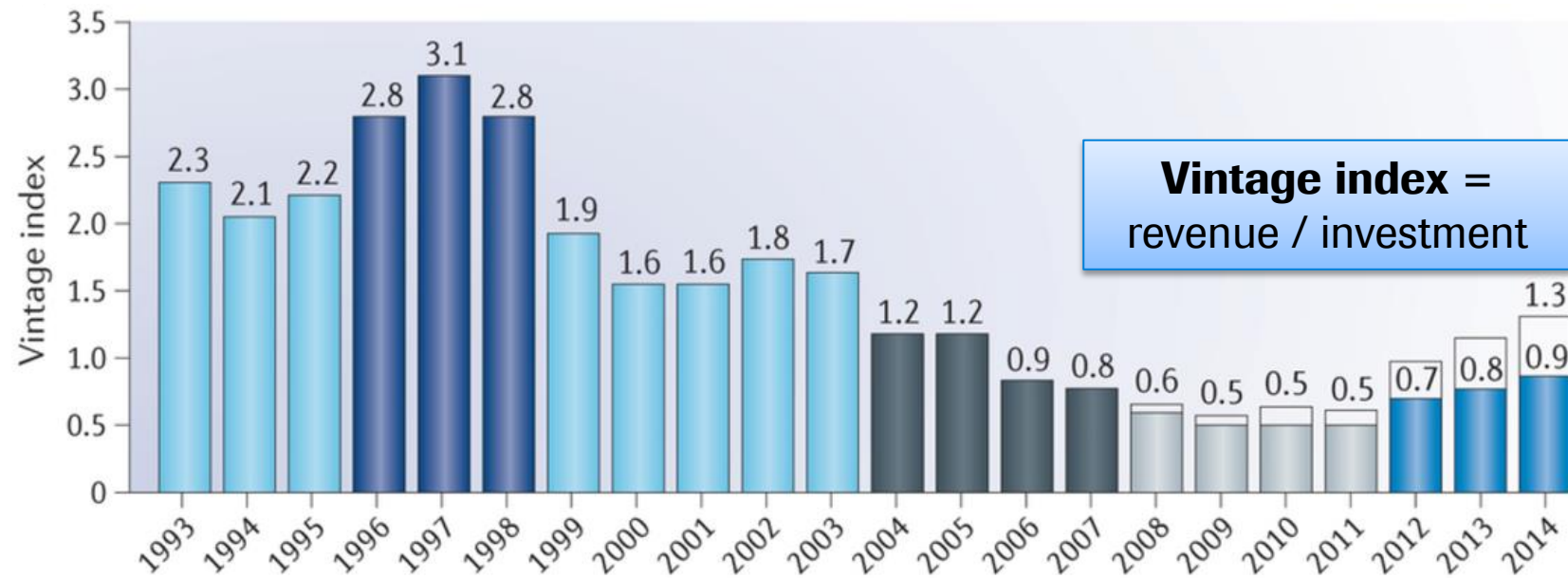


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**Bioinformatics and computational biology have become indispensable for modern drug discovery**

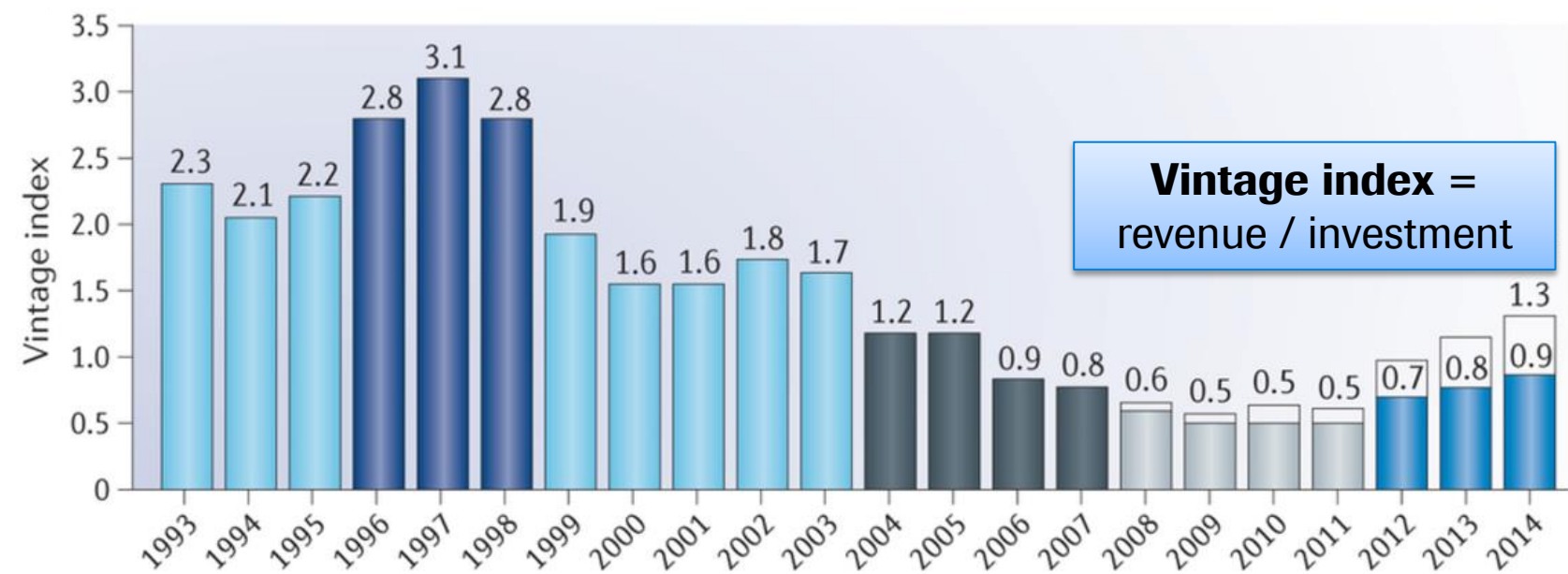


# Increasing Cost and Decreasing Return Of Investment in Drug Discovery



Modified from Smietana *et al.* "Improving R&D Productivity."  
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# Increasing Cost and Decreasing Return Of Investment in Drug Discovery



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**Finding new drugs has become more challenging and expensive**

# 危机

*n.* crisis

# 危机

~~*n.* crisis~~

Danger + Opportunity

# Three Challenges in Drug Discovery

**Biology:** Incomplete understanding of etiology and development of diseases

- **Integration and interpretation of public and internal data by advanced mathematics and informatics tools**

**Efficacy:** Variable translatability from preclinical models to patients

- **Data-driven evaluation of *in vitro* and *in vivo* models with integrated prior knowledge**

**Safety:** Suboptimal predictivity of human safety profiles by existing assays

- **New predictive tools using novel assays and computational-biology analysis**

**We do research in computational biology, bioinformatics and biostatistics and collaborate to address these challenges**

# **ROCHE IN CHINA, ROCHE FOR CHINA**

Swallowing bitter pills

# China is sprucing up its pharma sector

*The changes are helping multinational drugmakers. In time they may boost the domestic industry*



Brett Ryder

The Economist, August 2018

Swallowing bitter pills

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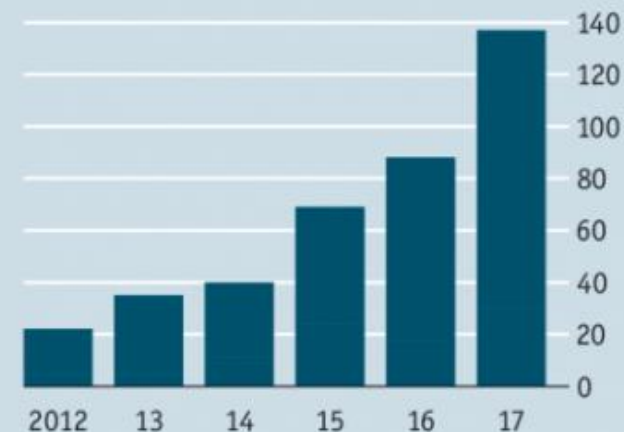


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## Macro-dosing

China, number of new molecules approved for clinical trials



Source: McKinsey

The Economist



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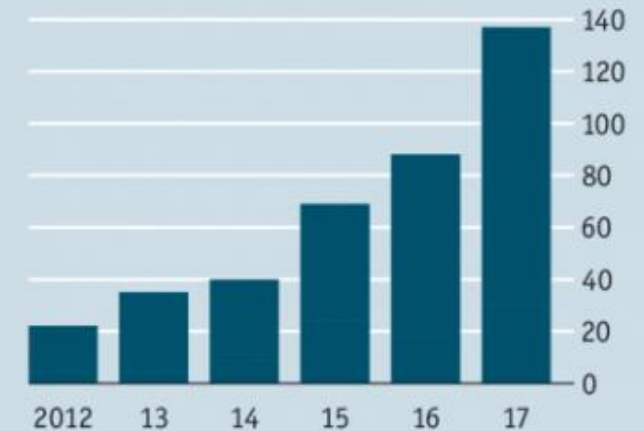


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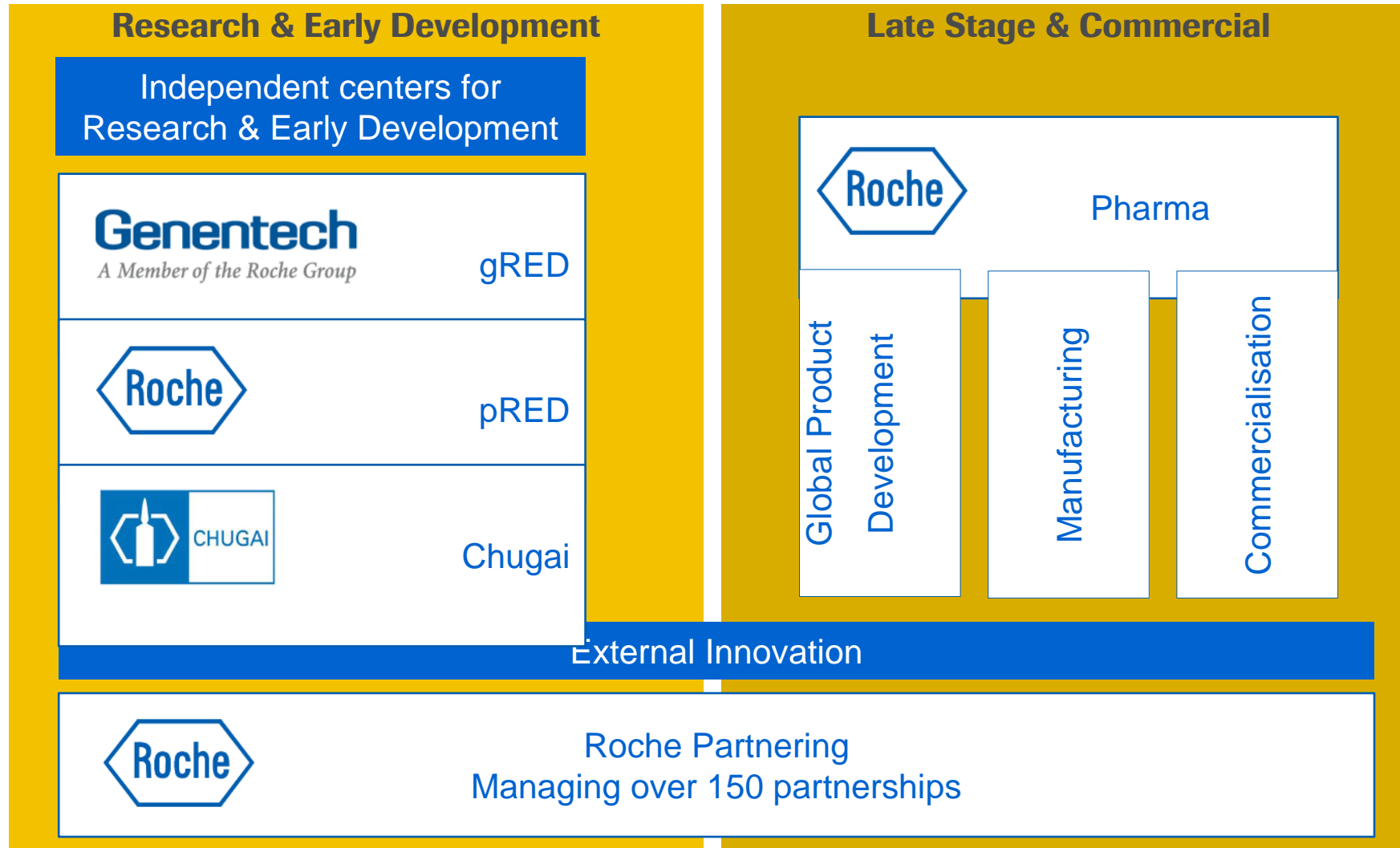


Source: McKinsey

The Economist

**A revolution in regulation and drug discovery is happening in China**

# R&D structure of Roche



# pRED Innovation Centers



# Roche's Long Heritage in China



Pharmacy with Roche products, 1921



1<sup>st</sup> Roche office in Shanghai, 1926

## Roche In China

- 2007 Establishment of the Roche Pharma Development Center in China (PDCC)
- 2005 Zhimin manufacturing centre built in Shanghai's Zhangjiang High-Tech Park to produce CellCept and Xeloda
- 2004 Establishment of the Roche Research & Development Center China in Shanghai Zhangjiang
- 1995 Foundation of Roche China Limited (Holding Group)
- 1994 Second joint venture in China, Roche Shanghai, with Chinese partner Sunve Pharmaceuticals
- 1984 First joint venture, with Beijing General Pharmaceutical Corporation
- 1981 Roche starts marketing pharmaceutical products
- 1975 Roche re-enters the Chinese market (with vitamins)
- 1961 Roche sets up branch operations in Hong Kong
- 1952 Liquidation of Roche Shanghai
- 1935 Roche opens subsidiary (Hoffmann-La Roche Limited Company Shanghai)
- 1926 Roche starts export business to China



# Roche's Long Heritage in China



Pharmacy with Roche products, 1921



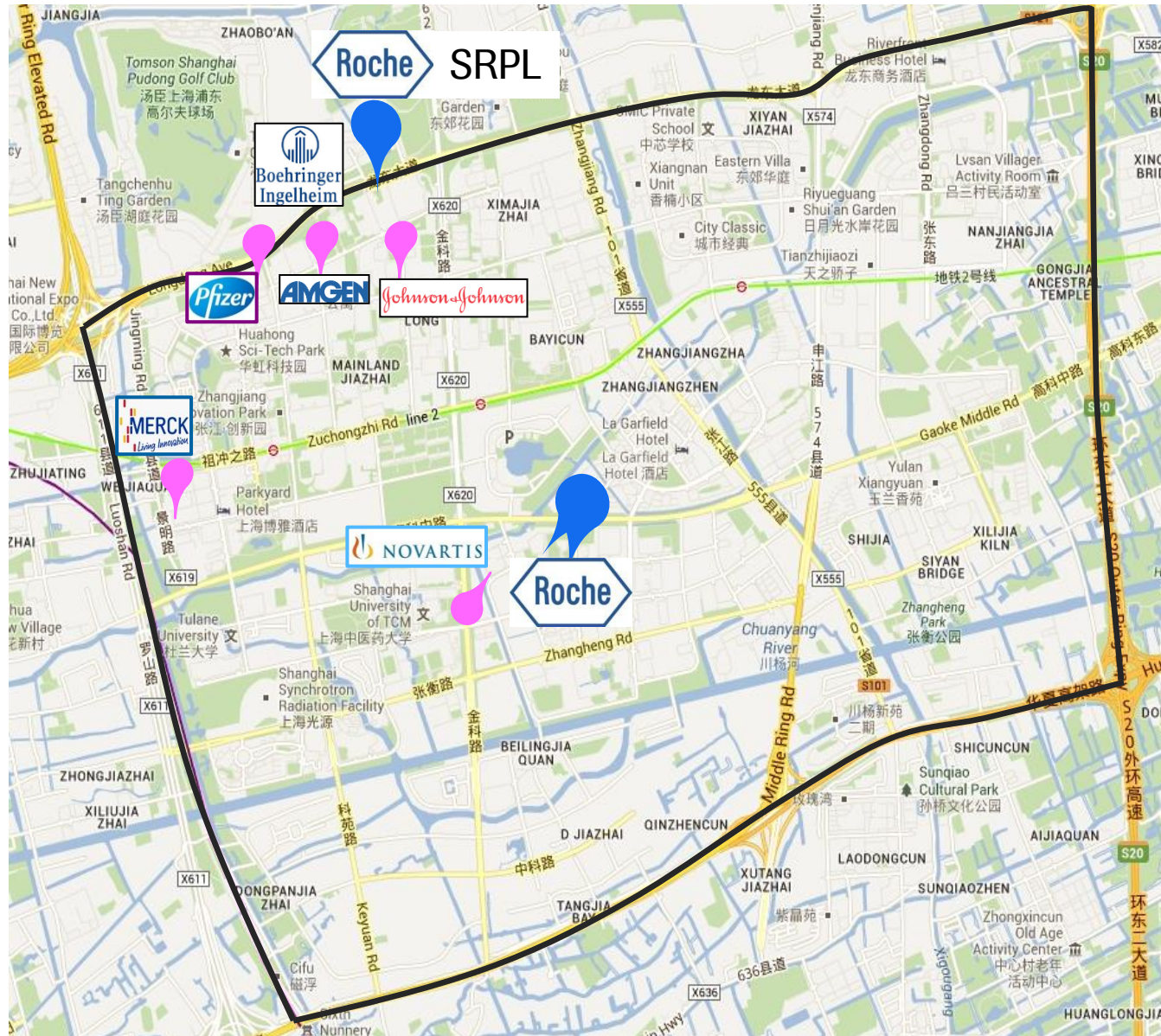
1<sup>st</sup> Roche office in Shanghai, 1926

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# RICS Location



- **Zhangjiang Hitech Park: Pharma valley of China**
  - ~600 companies in life science
  - MNC, biotech, pharma, medical device, CRO
  - 40 k scientists in life science

# RICS Evolves into a Highly Productive Innovation Engine for pRED



## *Our 15-year journey*



**MedChem Hub**

**2004-2010**

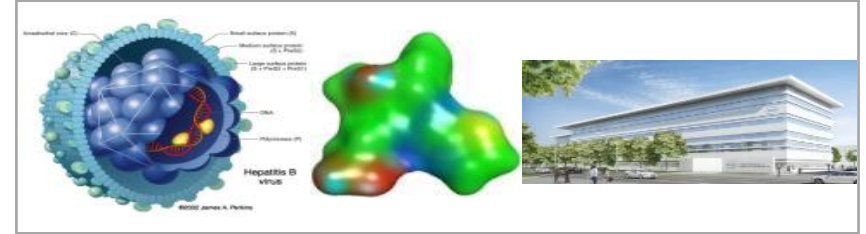
- 1st MNC research center in Shanghai
- Started chemistry support to global



**pRED China**

**2010-1H2012**

- ~150 scientists
- Full discovery functions + Early development
- Virology/Oncology/CVM
- Support PD SH/SRPL



**DTA Integration → RICS**

**2H2012-current**

- First focused on ID, and then expanded to I3
- Successful built up HBV discovery platform and pipeline
- Partner with PD SH/SRPL for synergy
- CHF 136 mio for new research building
- ~140 Scientists (~40% PhD, ~25% overseas experience)

First clinical compound  
(joint with US)

First home-grown compound  
in GLP tox

Multiple clinical projects, multiple EIH  
Full pre-clinical pipeline



# RICS – Our Focus and Future

*Delivering long term value to Roche and China*

## I2O Focus



- Launch early development studies in HBV
- Continue HBV and anti-biotic discovery; build and strengthen I2 group and projects; capture scientific synergies in oncology programs
- Center of Excellence for Small Molecule Research

## pRED Impact



- Continue to increase contribution to pRED portfolio
- Provide flexible functional and outsourcing support to global
- **Explore agile R&D and external collaboration models**

## China Impact



- Long term commitment in China and in Innovation
  - Advance pipeline with parallel global/China development
  - Serve unmet needs of Chinese & global patients
  - Bring in cutting edge technologies and assets
  - Develop local R&D talents
  - **Collaborate with local partners and HA**





**Future Home of Roche China and Welcome Your Visit**

# Conclusions

- 1. I am Jitao David Zhang, a computational biologist working at Roche.**
- 2. Drug Discovery is a long process involving both forward and reverse translation**
- 3. Roche In China, Roche For China**

# Conclusions

1. **I am Jitao David Zhang, a computational biologist working at Roche.**
2. **Drug Discovery is a long process involving both forward and reverse translation**
3. **Roche In China, Roche For China**

**Questions? Ask Me Anything!**

# *Doing now what patients need next*





# Acknowledgements



F. Hoffmann-La Roche Ltd	
<b>Clemens Broger<sup>†</sup></b>	<b>Faye Drawnel</b>
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Klas Hatje	Iakov Davydov
Laura Badi	<b>Ulrich Certa</b>
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Thomas Singer	Shen Hong



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Wolfgang Huber
<b>Ozgür Sahin</b>
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Alexandros Stamatakis
Michael Prummer
Mark D. Robinson
Michael Hennig
<b>Florian Haller</b>
Jung Kyu Canci
<b>Verdon Taylor</b>
Maria Anisimova
Lorenzo Gatti
Erhard van der Vries
Ab Osterhaus
Nevan Krogan
Oliv Eidam



*Doing now what patients need next*