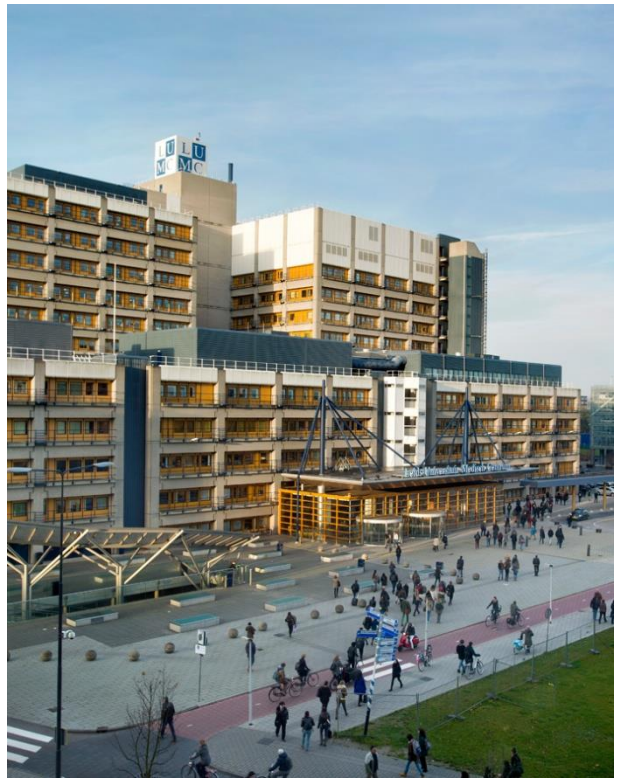
Leiden University Medical Center

Academic Pharma as a new route for drug development

Prof. Dr. T. van Gelder (Teun)
Internist – clinical pharmacologist

Clinical Pharmacy & Toxicology

Leiden University Medical Center
University Leiden



Disclosures

Name:
Teun van Gelder, MD, Leiden Univ Medical Center, Netherlands

Commercial Interests & Nature of Relationships:

- Roche, Astellas, Aurinia, CSL Behring, Chiesi, Roche Diagnostics, Thermo Fisher: Consultant/Speaker received honoraria
- Chiesi and Astellas: Research Grant Support, study on transplant related diseases
- I am an employee of LUMC

LEIDEN UNIVERSITY MEDICAL CENTER

Drug discovery and development:

Basic science:

- New targets
- New compounds

Translational research

Clinical studies:

- Phase 1
- Phase 2
- Phase 3

Registration

Translating research findings into medicinal products for clinical practice requires knowledge, skills and facilities that typically reside in pharmaceutical companies and not in public research institutes.

Translational Drug Discovery & Development

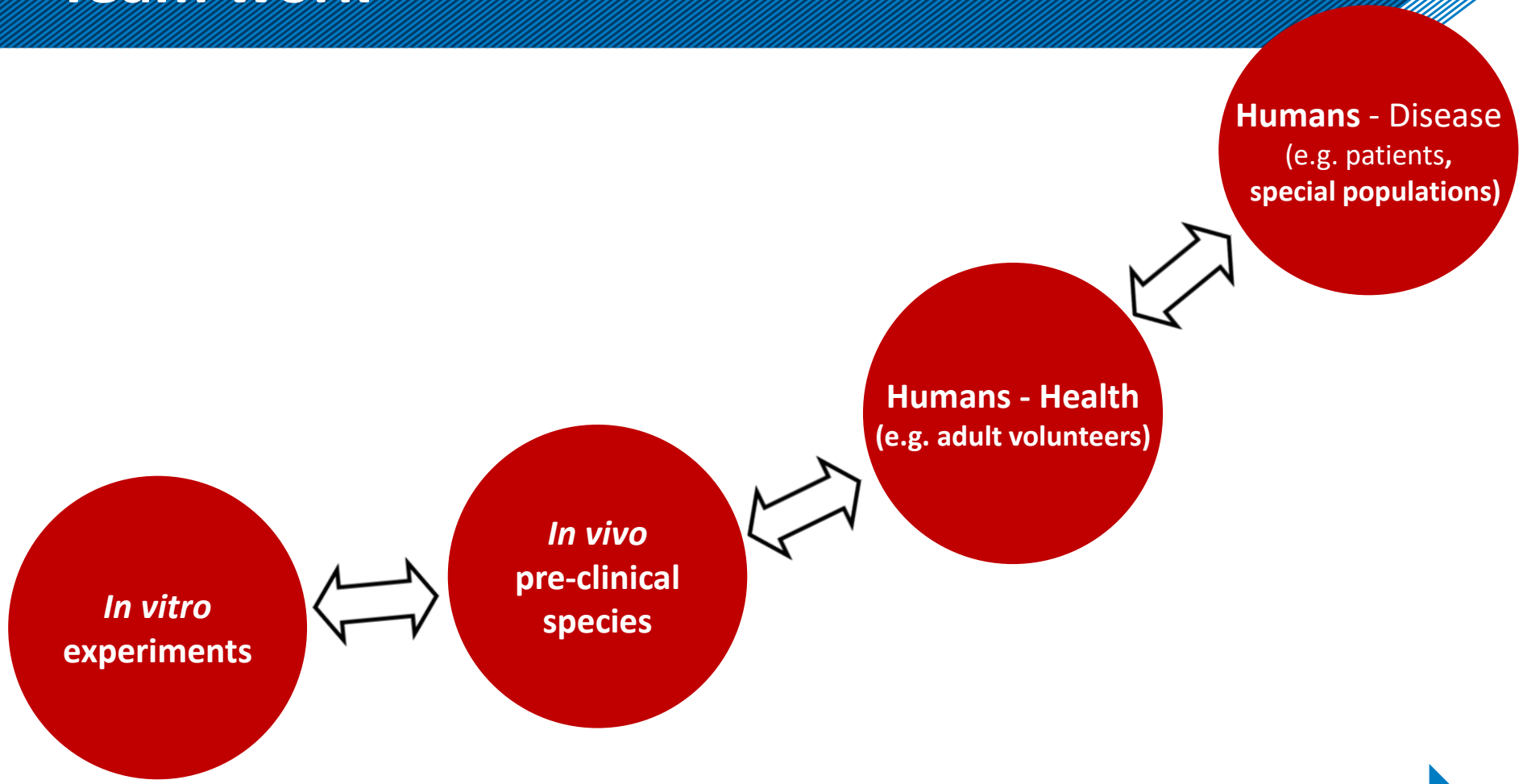
University Leiden Faculty of Science Research Program
'Translational Drug Discovery & Development'

Matched funding from strategic fund Leiden Univ Medical Center:
Academic Pharma 2.0: Innovative drugs from bench to bed-side.

The Leiden Landscape

Landscape for drug development:
Leiden Institute for Chemistry, Leiden Academic Centre Drug Research, CHDR, LUMC, Leiden BioScience Park, TNO

Team work



Target finding
Drug lead synthesis
Proof of pharmacology

Preclinical toxicity
Metabolism & PK
Effectiveness

GMP manufacturing
First in man Phase I
Safety, PK

Proof of effectivity
Safety, biomarkers
Comp. efficacy

What is the link with VNVN??

Lots of pharmacokinetics/pharmacodynamics and pharmacogenetics:

- Phase 1 (single/multiple ascending dose studies, tox, dose proportionality)
- Phase 2 (PK/PD modeling, finding best dose for phase 3, therapeutic window)
- Phase 2 (concentration-effect relationship for efficacy and/or toxicity)
- Phase 3 (TDM? PGx?)
- Phase 4 (populations of special interest, drug-drug interactions)

Aiming high

Complex.

For academia the same rules apply.

No “light” version for academia.

Proceed in “value chain”

Ultimate: registration

Challenges in academic pharma:

Drug development is a long process (10 yrs) with involvement of a variety of disciplines.

Start with the end goal and define what is needed to reach that goal.

Academia versus Industry

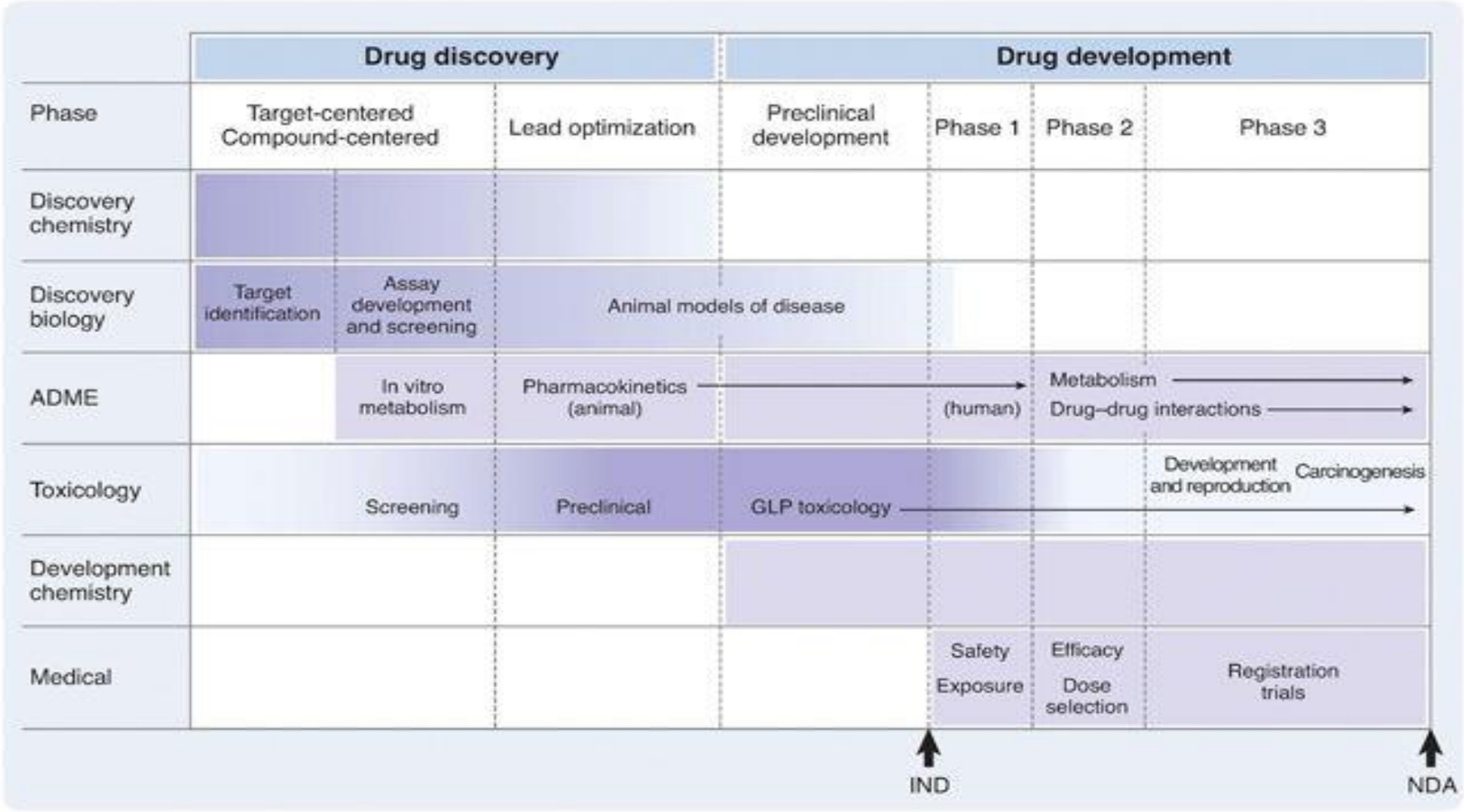


FIGURE 51-1. **Sequence and phases of drug discovery and development.** The important points to note are the general sequence of activities and the considerable overlap of functions with time. The process is highly interactive among multiple disciplines in an attempt to obtain the drug molecule with the greatest efficacy, least serious adverse effects, and greatest safety. The clinical trials and regulatory approval phases are described in Chapter 52. The entire process from hit to drug approval can take 8–12 years and cost more than $1 billion. IND, investigational new drug application; NDA, new drug application; ADME, absorption, distribution, metabolism, excretion; GLP, good laboratory practices.

Perspective of “the” academic researcher:

- Focus on science, innovation, top-publications.
- Focus on own domain, not on development plan or pipeline.
- After finishing project: risk that finding ends up on a shelf.
- Missed opportunities.
- Less awareness for intellectual property or valorisation.

Drug Development Board

Leiden Institute for Chemistry

Institute of Biology Leiden

LACDR

CHDR

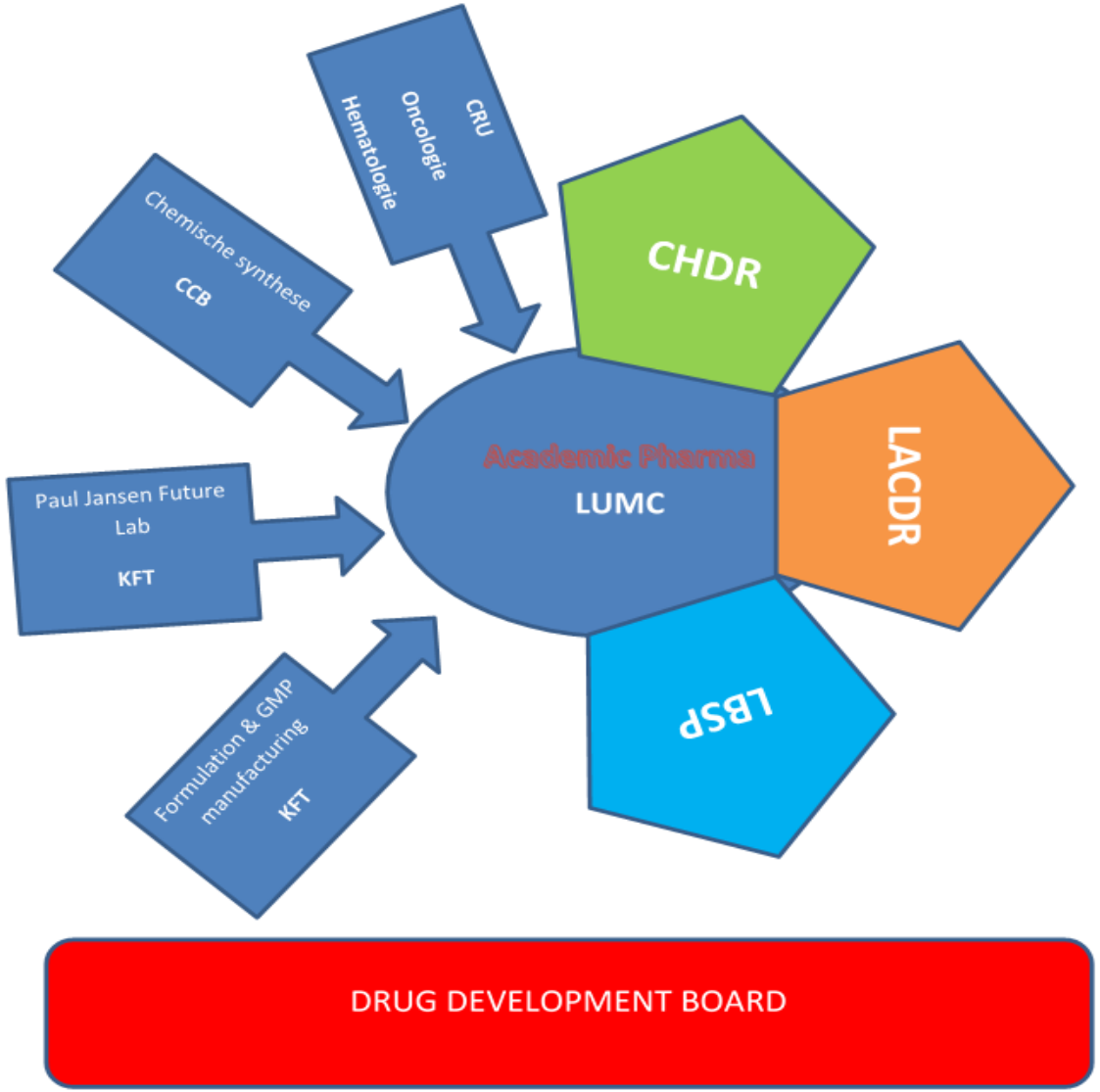
LUMC

TNO

Review and evaluate scientific, clinical and technical issues related to the discovery and development of drug products for the treatment of a broad spectrum of human diseases.

Provide recommendations to investigators who submitted requests or proposals for new compounds/targets.

Drug Development Board



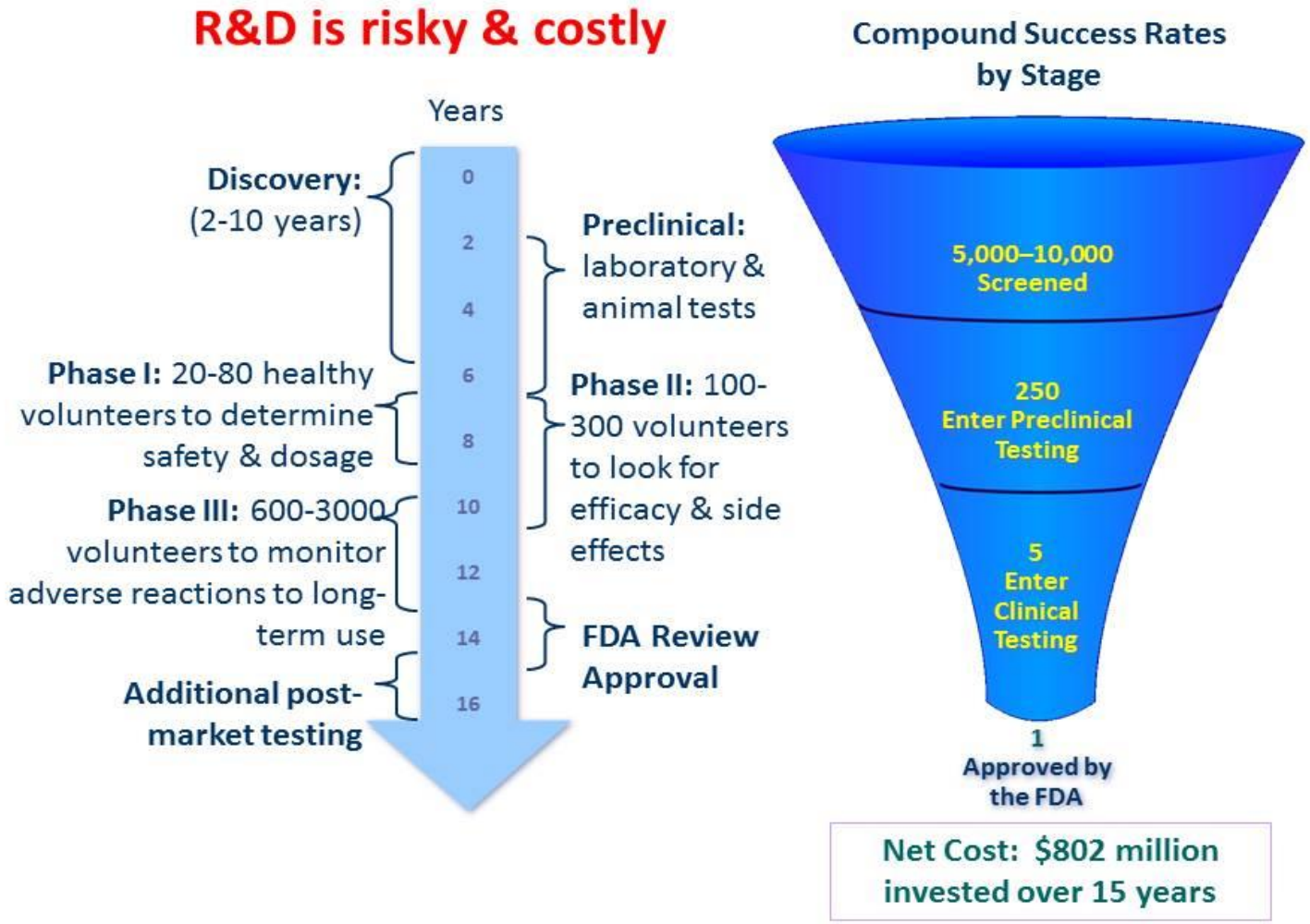
Challenges in academic pharma:

Drug development is a long process (10 yrs) with involvement of a variety of disciplines.

Start with the end goal and define what is needed to reach that goal.

Money.

Risky investment, return on investment takes forever:



Niche for academia

Rare diseases:

- Unmet clinical need
- Pharma not interested for commercial reasons
- Clinical studies in limited number of subjects

Repurposing existing drugs:

- Risk of failure much smaller as tox already known
- Patent issues, reimbursement issues

Money and drug development in academia

“In kind” contribution from academia.

Funding : government based, charity funds (up to 5-10 Million Euro)

BIG money: investors (1-100 Million Euro)

Spin-out companies (University may hold equity in exchange for IP)

Background Hybridize Therapeutics & the rich ecosystem in Leiden

Our background

Hybridize Therapeutics is a spin-off from the Leiden University Medical Center (LUMC). The LUMC has been a frontrunner in both Nephrology & RNA-based medicine since 1943. Prof. Dr. Willem Kolff, inventor of the kidney dialysis machine (1943), studied Medicine at the LUMC, while Prof. Dr. Jacques van Boom played a pivotal pioneering role in oligonucleotide chemistry (LUMC, 1975). Dr. Eric van der Veer (Founder Hybridize) joined the Nephrology Department of the LUMC as a post doc fellow in 2007. During his extensive research period (2007-2015) he focused mainly on RNA-based therapies for kidney diseases. His first breakthrough project focused on a very specific protein that regulates tissue injury through inflammation & fibrosis. His second breakthrough project focused on the kidney virus (BK-virus) that leads to devastating clinical complications in kidney transplant and hematopoietic stem cell transplant patients. In september 2019, Hybridize Therapeutics spun out from the LUMC.

February 9, 2022

AiCuris and Hybridize Therapeutics enter worldwide license agreement of up to €100M for a direct-acting RNA-based therapy against BK Virus

- **AiCuris acquires exclusive rights to develop and commercialize Hybridize's program to prevent severe disease from BK virus (BKV) infections in immunocompromised patients**
- **Both companies to collaborate in further development until start of clinical studies expected to start within two years**
- **BKV reactivation poses a significant unmet medical need in patients undergoing kidney transplantation**
- **BKV-associated nephropathy is one of the leading causes of allograft loss in kidney transplant recipients**
- **BKV is difficult to treat, RNA antisense oligonucleotides are a promising novel approach to block BKV replication**
- **With the licensed program, AiCuris is building on its strong track record in the field of transplant infections**

Wuppertal, Germany and Leiden, The Netherlands, February 9, 2022 – AiCuris Anti-infective Cures AG (AiCuris), a leading company in the discovery and development of drugs against infectious diseases, and Hybridize Therapeutics (Hybridize), focused on the development of RNA-based therapies for patients with acute and chronic kidney diseases, today announced that they have entered into a worldwide licensing agreement for Hybridize's BK virus (BKV) program. The licensed program is based on a novel RNA-based therapeutic approach developed by Hybridize.

Under the terms of the agreement, AiCuris will gain exclusive rights to develop and commercialize Hybridize's BKV program, with focus on the treatment of BK virus-mediated nephropathy in renal transplant patients. Hybridize will receive an upfront payment and further milestone payments of up to €100 million in total based on successful achievement of development, regulatory and commercialization goals. In addition, Hybridize will receive tiered royalties on net sales. Hybridize and AiCuris will collaborate in the further development of the BKV-targeting therapy until the start of clinical studies, which is expected within two years.

"We are excited to gain the rights to this exciting RNA-based antisense approach against BKV infections, further strengthening our anti-infective pipeline and building on our strong track record in the field of infectious diseases in transplant patients," **said Dr. Holger Zimmermann, CEO of AiCuris.** "With PREVYMIS® approved and licensed to MSD for use in bone marrow transplants for the prevention of

Challenges in academic pharma:

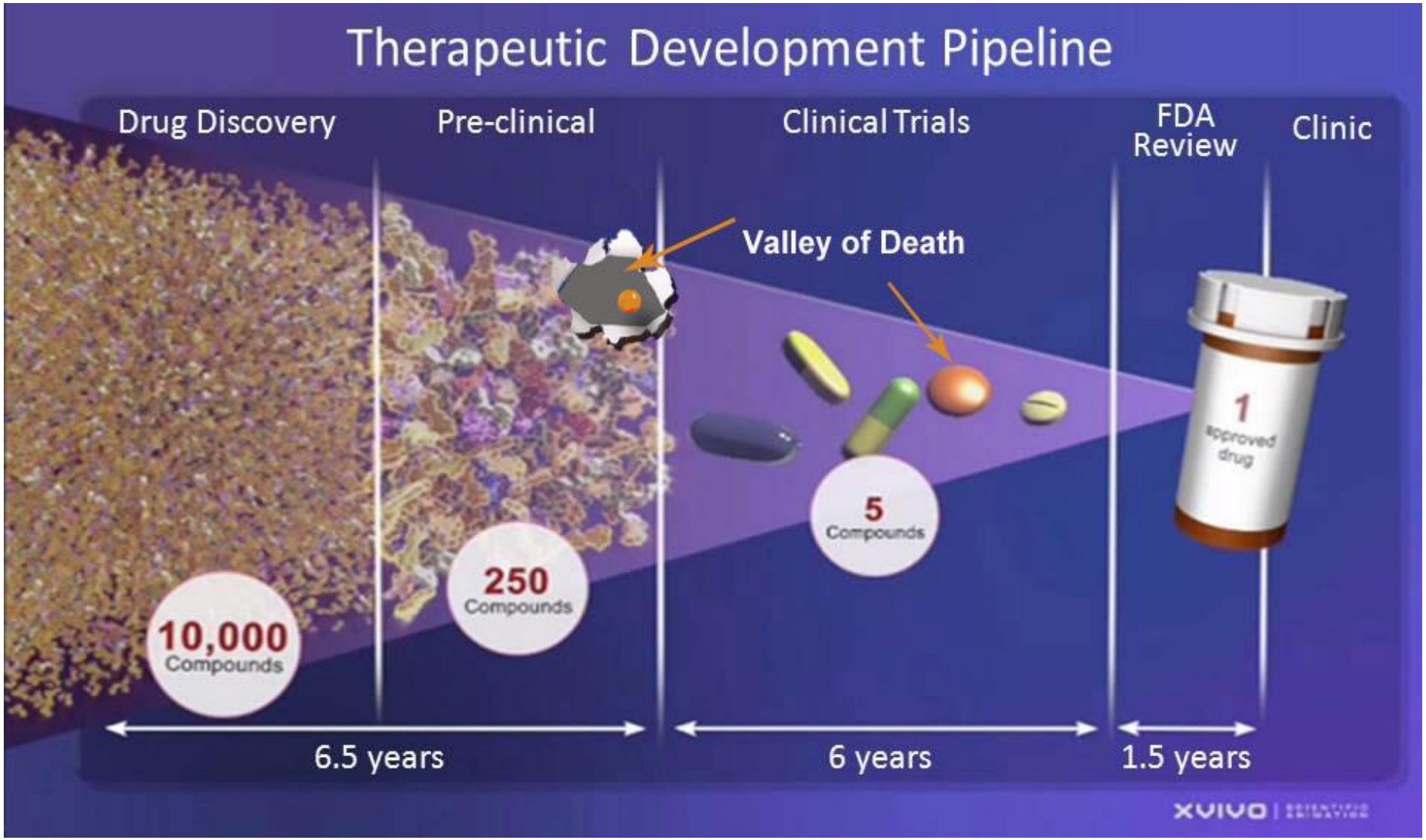
Drug development is a long process (10 yrs) with involvement of a variety of disciplines.

Start with the end goal and define what is needed to reach that goal.

Money.

The valley of death

The valley of death



Learning from previous failures:

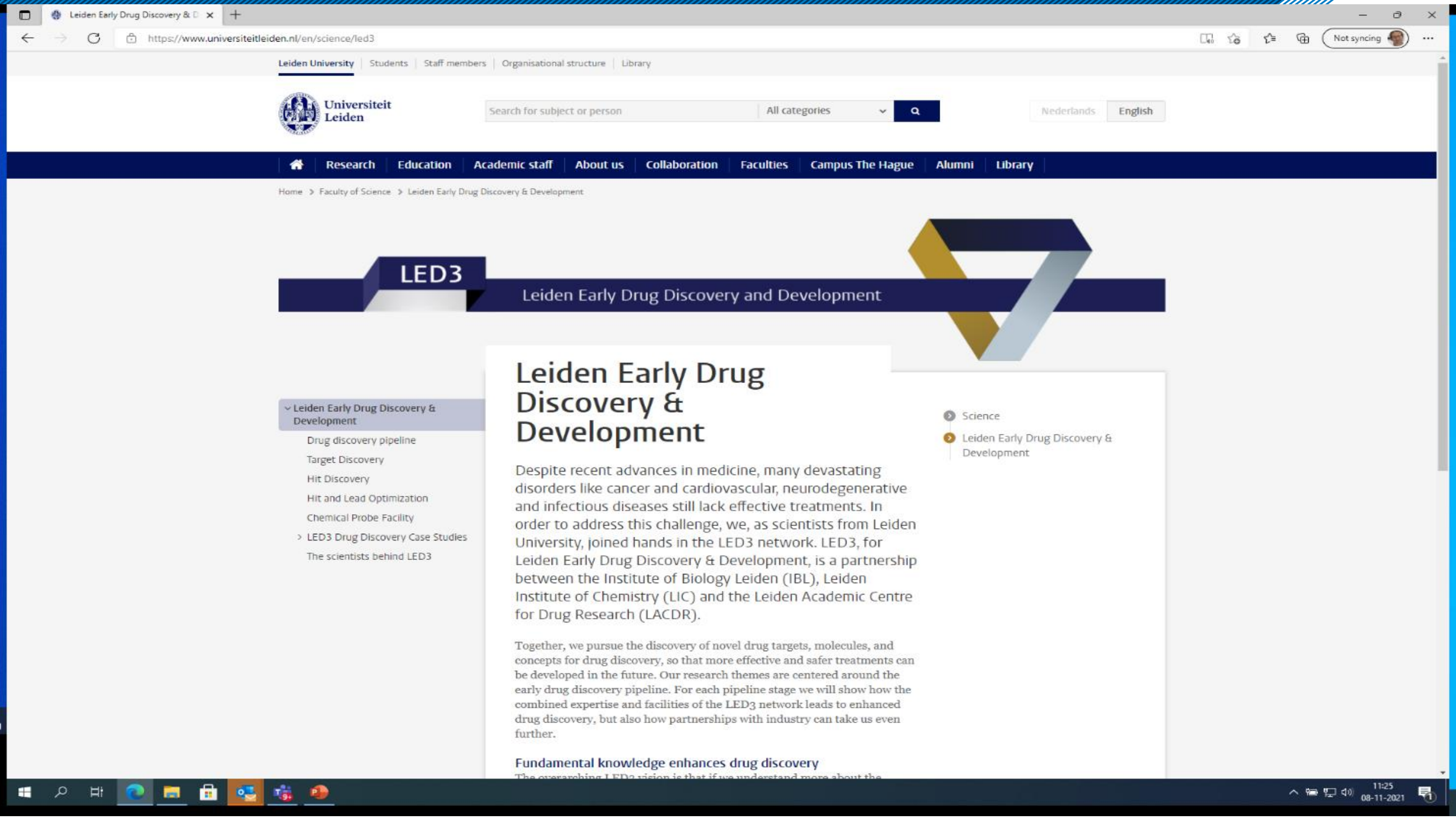
Drug Discovery Today • Volume 13, Numbers 21/22 • November 2008

Failure is an option: learning from unsuccessful proof-of-concept trials

Stefan Schäfer, Stefan.schaefer@bayerhealthcare.com **and Peter Kolkhof**

Enter clinical development based on preclinical experiments

- using the wrong compound
- using the wrong experimental model
- using the wrong endpoint


Leiden Early Drug Discovery & D
https://www.universiteitleiden.nl/en/science/led3
Not syncing
Leiden University | Students | Staff members | Organisational structure | Library
Universiteit Leiden
Search for subject or person
All categories
Nederlands
English
Research | Education | Academic staff | About us | Collaboration | Faculties | Campus The Hague | Alumni | Library
Home > Faculty of Science > Leiden Early Drug Discovery & Development
LED3
Leiden Early Drug Discovery and Development
Leiden Early Drug Discovery & Development
Drug discovery pipeline
Target Discovery
Hit Discovery
Hit and Lead Optimization
Chemical Probe Facility
LED3 Drug Discovery Case Studies
The scientists behind LED3
Leiden Early Drug Discovery & Development
Despite recent advances in medicine, many devastating disorders like cancer and cardiovascular, neurodegenerative and infectious diseases still lack effective treatments. In order to address this challenge, we, as scientists from Leiden University, joined hands in the LED3 network. LED3, for Leiden Early Drug Discovery & Development, is a partnership between the Institute of Biology Leiden (IBL), Leiden Institute of Chemistry (LIC) and the Leiden Academic Centre for Drug Research (LACDR).
Together, we pursue the discovery of novel drug targets, molecules, and concepts for drug discovery, so that more effective and safer treatments can be developed in the future. Our research themes are centered around the early drug discovery pipeline. For each pipeline stage we will show how the combined expertise and facilities of the LED3 network leads to enhanced drug discovery, but also how partnerships with industry can take us even further.
Fundamental knowledge enhances drug discovery
Science
Leiden Early Drug Discovery & Development
11:25
08-11-2021

Challenges in academic pharma:

Drug development is a long process (10 yrs) with involvement of a variety of disciplines.

Start with the end goal and define what is needed to reach that goal.

Money.

The valley of death.

Complex rules and regulations (FDA, EMA, national regulators)

Strengthening regulatory science in academia: STARS, an EU initiative to bridge the translational gap

Viktoriia Starokozhko[1,2], Marko Kallio[3], Åsa Kumlin Howell[4], Anna Mäkinen Salmi[4], Gunilla Andrew-Nielsen[4], M. Goldammer[5], Manja Burggraf[6], Wiebke Löbker[7], Anne Böhmer[7], Eleonora Agricola[8], Corinne S. de Vries[9], Anna M.G. Pasmooij[1] and Peter G.M. Mol[1,2]
, p.mol@cbg-meb.nl, p.g.m.mol@umcg.nl on behalf of the STARS consortium

Academic Pharma:

- No “me too” drugs
- No generic production
- Unmet clinical need
- Rare diseases, compounds without patent are welcome
- New Chemical Entities, as well as repurposing
- Protect magisterial preparations against price hikes

Academic Pharma

What if we are “marketing authorization holder” ??

Not our ambition to be a big drug factory

Licencing agreements

Portfolio:

Non cardiotoxic anthracyclines (aclarubicine, dimethyldoxorubicine).

Repurposing penfluridol (bladder cancer)

Repurposing mifepristone (anticonceptive drug)

Protecting 3,4 diaminepyridine

Conclusions & Discussions

- Academic Pharma has been put on the map.
- Complementary to (big) pharma.
- Crossing the valley of death.
- Develop expertise, bundle forces, go national.