KU LEUVEN
RESEARCH & DEVELOPMENT

Hurdles of translating basic academic research into applied clinical research

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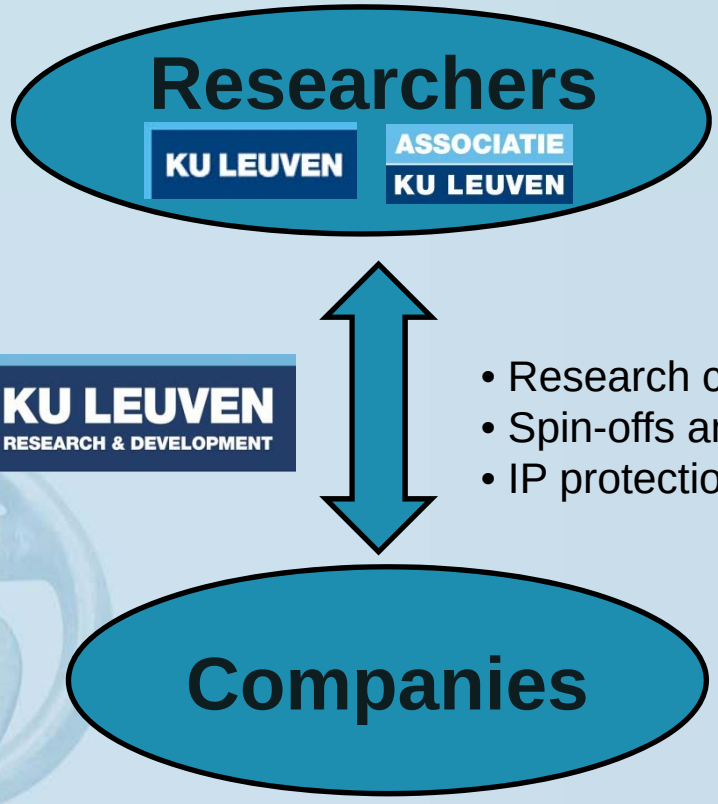
RESEARCH & DEVELOPMENT

KU Leuven Research & Development

Bridge between research and industry

Mission

“Promoting and supporting knowledge and technology transfer between university and industry”



- Research collaboration
- Spin-offs and regional development
- IP protection and licenses

LRD: what do we do?

- Manage research collaboration
- Protect and exploit intellectual property
- Set up spin-off companies
- Provide incubation instruments & seed financing
- Create high-tech ecosystem

Research collaboration

Research & services for companies or public organisations

Create awareness and transfer knowledge - Provide advice - Negotiate and follow up contracts - Manage research files financially - Offer administrative support - Prepare legal documents

Intellectual property

Create awareness and transfer knowledge - Assess the feasibility, patentability and market potential of an invention - Determine a protection strategy - Draft & file a patent application - Follow up on patent procedures and costs - Negotiate and draft NDAs, MTAs & and license agreements - Find industrial partners

Spin-off companies

ThromboGenics 1991

TiGENIX 2000

Okapi Sciences antivirals for animals 2007

icoMetrix Quantifying your Images 2011

CARTAGENIA.com 2008

reMYND 2002

Formac pharmaceuticals 2007

Instrumen Supporting your surgery 2013

DName-iT 2014

COMPLIX scaffoldtherapeutics 2008

arcarios 2010

imCyse 2011

TROD MEDICAL 2013

UGENTEC Automated PCR-analysis 2014

ADX NeuroSciences Mind your brain 2011

Promote entrepreneurship - Develop business plans - Validate business models and the market - Offer legal support - Put together a competent team - Find investors - Find infrastructure - Manage growth of spin-offs - Stimulate regional development, networks and clusters

Incubation Policy @ KU Leuven

- Extensive **AWARENESS CREATION & TRAINING**: *Doctoral school, LCIE, Leuven.Inc*

- Often **LONG** & NOT EASY **INCUBATION** within university
  - Coaching support by LRD & IOF managers: *building the key ingredients*
  - Specialized incubation instruments: *LRD, IOF, CD3, PharmAbs, CTC, LMTC, ..*
  - Identify partners & potential collaborators, experts, CROs
  - Identify & help with securing funding: EU, IWT, …

Exploitation plan: describing the structural implementation of research results into society/industry

= **multidisciplinary** teamwork

- ✓ LRD divisions
- ✓ research networks and institutes (LKI, MIRC, Rega, SCIL, BIG, LIND

Exploitation plan

= description of **what** to exploit and **how** to exploit taking into account the environment

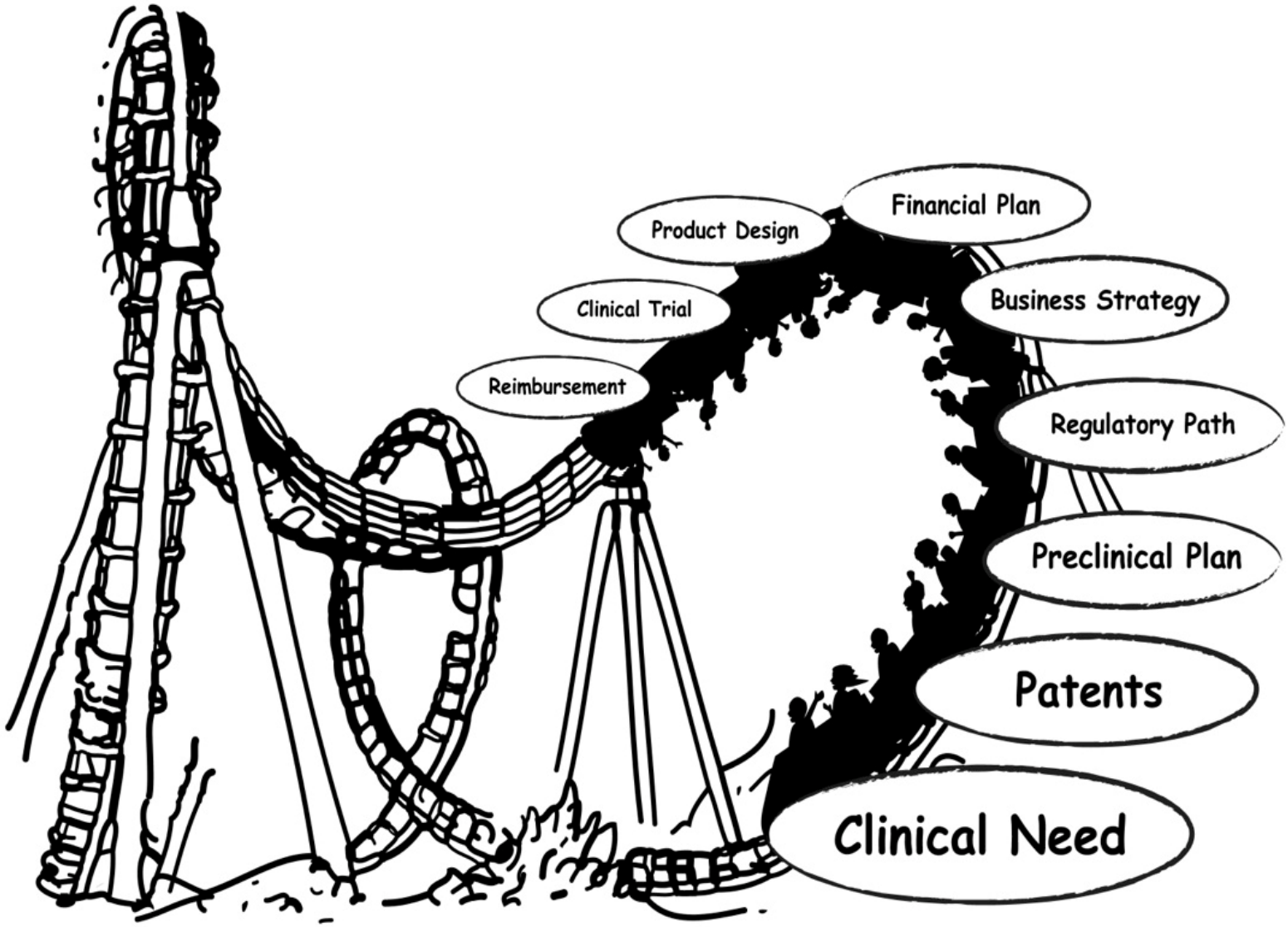
= structured way of thinking / assessment of which results to exploit and which **exploitation route** is the most appropriate

= a multi-facetted

- **Technology due dil.: OK?** Can the product be developed within an acceptable timing & with acceptable resources?
- **Market assessment: OK?** What is the product-market combination? Are potential customers ready to buy it & to pay sufficient ?
- **IPR & legal due diligence: OK?** Can the huge investments be protected against copying by competitors? Sufficient freedom-to-operate?
- **Financial review: OK?** Costs? Income? Multiplication?
- **Team assessment: OK?** Balanced team?

= **tool to convince all the stakeholders / involved parties of translation value!**

Translating basic academic research into applied clinical research



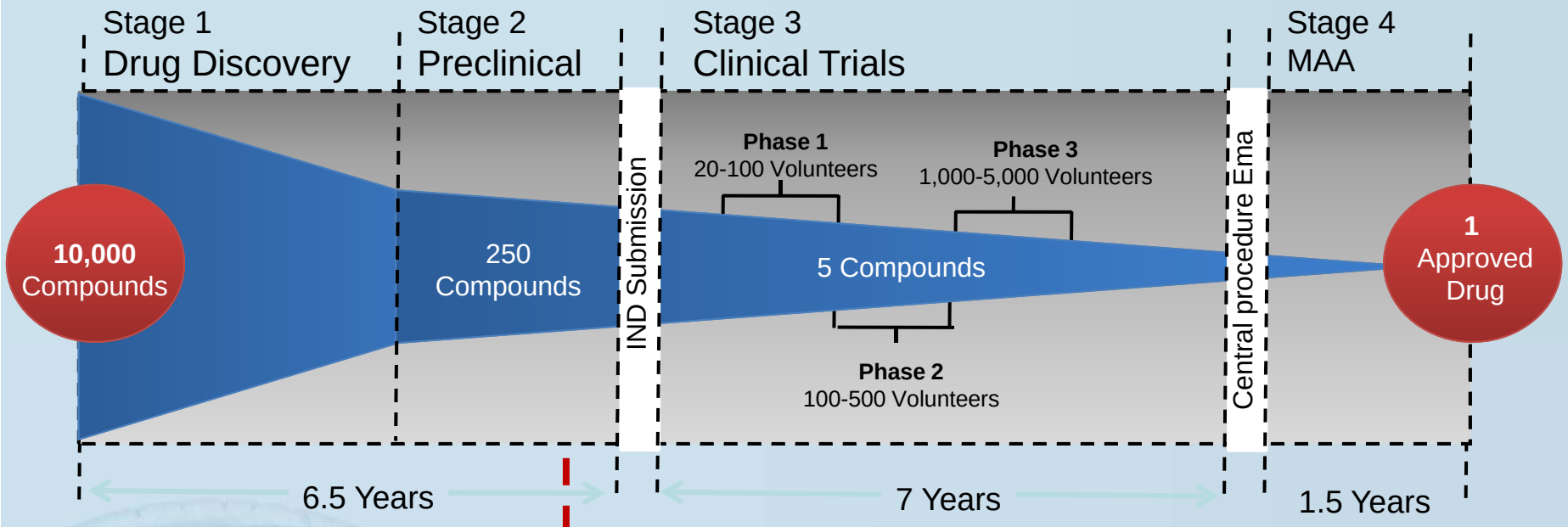
Ref. Translational Medicine Symposium 2014: The Roller Coaster Ride to the Clinic

Successful Translation

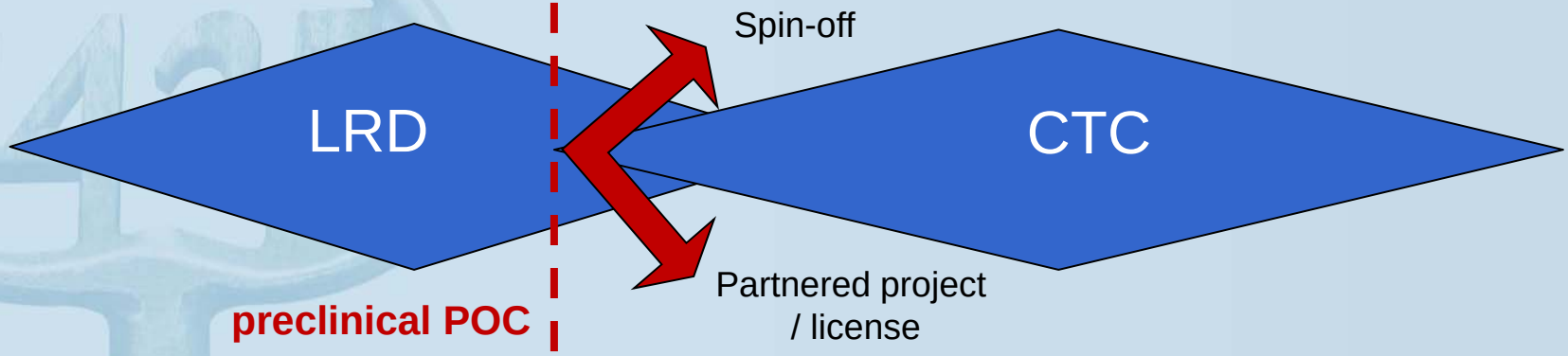
- effective and swift transfer of promising research results into medical practice
- challenge basic research findings in clinical settings
- all relevant stakeholders need to work together and share experiences as well as identify common challenges:

  - **Diseases, Mechanisms, Signaling Pathways & Targets**
  - **Drug Discovery toward Preclinical Candidate Selection**
  - **IND enabling Studies toward IND Filing & Clinic**

LRD: mainly involved in pre-IND phase



Source: Adjusted from Pharmaceutical Research and Manufacturers of America



Clinical Trial Center - CTC

- Established in 2008
- Central contact point for all in vivo patient related studies
  - Investigator driven trials
  - Commercial trials
- Helpdesk for
  - administration:
  - registration (FAMHP, EudtraCT, FDA,…)
    - public register (clinicalTrials.gov, …)
    - registration @ UZ Leuven
  - financial support & follow-up
  - legal support & follow-up
  - contact person FAMHP, EudraCT
  - training
  - IT projects (electronic CRF)
  - …

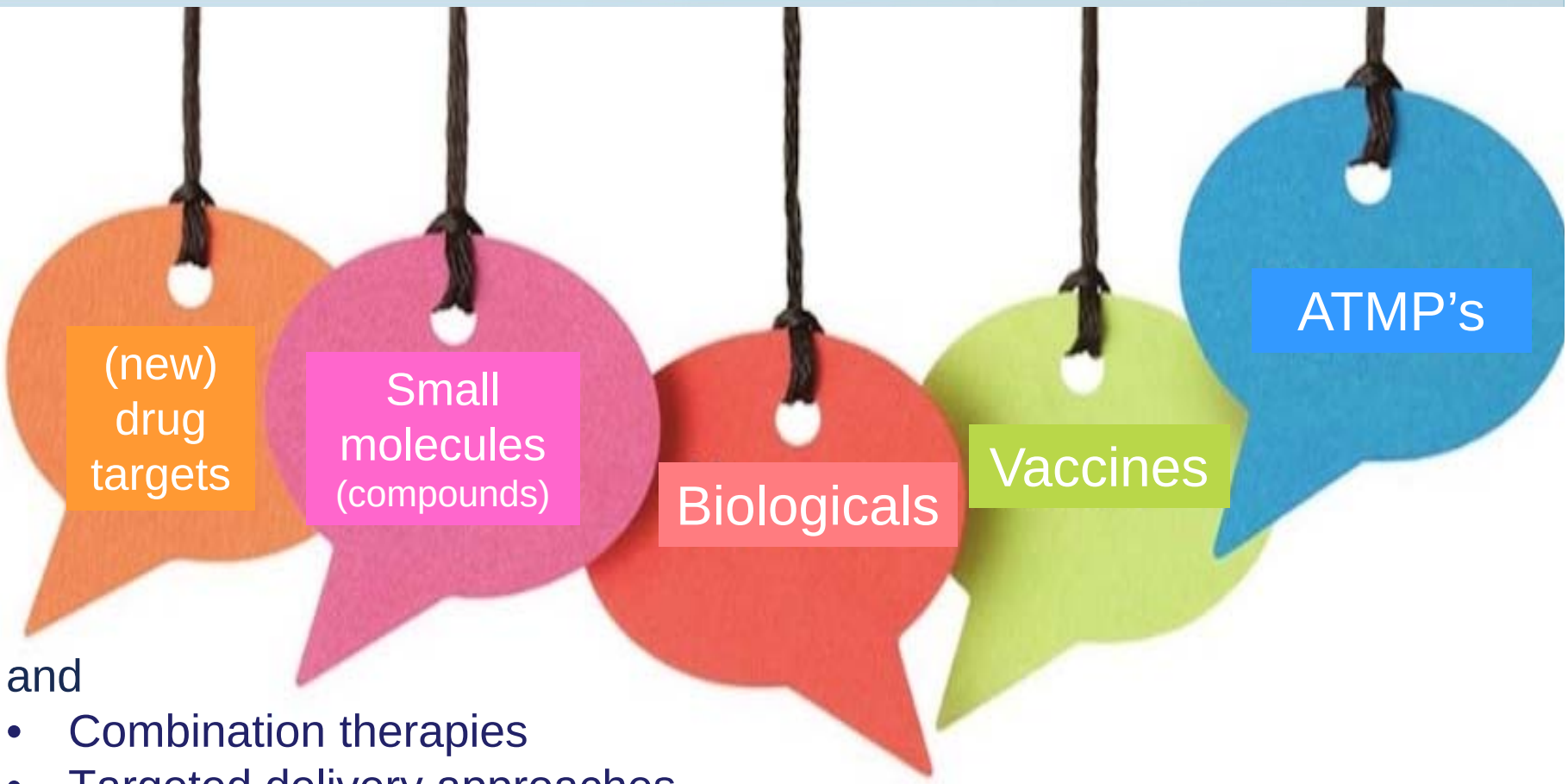
http://www.uzleuven.be/clinical-trial-center/clinical-trial-center

Clinical trials @ UZ / KU Leuven (2014)

	Non-comm	Comm	Art.21	TOTAL
Phase 1	6	26		**32**
Phase 2	19	63		**82**
Phase 3	22	107		**129**
Phase 4	24	32		**56**
NA	737	38	72	**847**
TOTAL	**808**	**266**	**72**	**1146**

Drug related	Device related	Drug& Device	Others
284	51	4	807

Very diverse starting points



and

- Combination therapies
- Targeted delivery approaches
- Use of approved medicines in new therapeutic indications
- Medical devices > investigator driven clinical trial (non-CE marked)
- Biomarkers
- Technology platforms

Common hurdles

Need early on input & expertise from:

clinicians (KOL), biology, genetics, medicinal chemistry, pharmacology, toxicology, process chemistry, computational design & regulatory

+ selection of translational projects
+ secure sufficient incubation funding – valley of death
+ GMP manufacturing
+ insight in regulatory path & options (pre-regulatory support)
+ insight in reimbursement context

- **Realistic timelines & budget**
- **Clear roadmap including requirements & priorities**
- **ROI for licensing or VC partners**

Selecting translational projects is challenging

Knowhow on:

- Technological feasibility
- Probability of success
- Intellectual property strategy, strength & value + FTO
- Reasonable development cost & timelines: from preclinical POC to clinical POC
- Importance of the unmet medical need
- Competitive landscape (in development & marketed)
- Adoptability by the end users [buyers, physicians, patients,…]
- Clear regulatory requirements

Incubation instruments

LRD has set up specialized incubation instruments to facilitate & finance projects at an early stage of development.

- **LRD research divisions**
  - Researcher-controlled finances
  - Multidisciplinary collaboration
  - Incentives & rewards

- **KU Leuven Patent Fund**
  - Financial support for researchers who apply for a patent

Incubation instruments

- **Centre for Drug Design and Discovery**
  - Founded in 2006 by LRD and the EIF
  - Provides academic research groups and small companies with:
    - Small molecule drug discovery expertise
    - Scientific & financial support

- **PharmAbs**
  - Founded in 2007 by LRD
  - support academic research aimed at therapeutic antibody lead /immunoassay development
  - Brings projects to a stage at which they can be adopted by an industrial partner or lead to spin-off creation

Quality preclinical PoC studies

Translating *innovative academic research* into new drugs

Centre for Drug Design and Discovery

Mission: closing the innovation gap by translating early-stage academic insights into new valuable assets

Focus: Innovative small molecule drug discovery and development

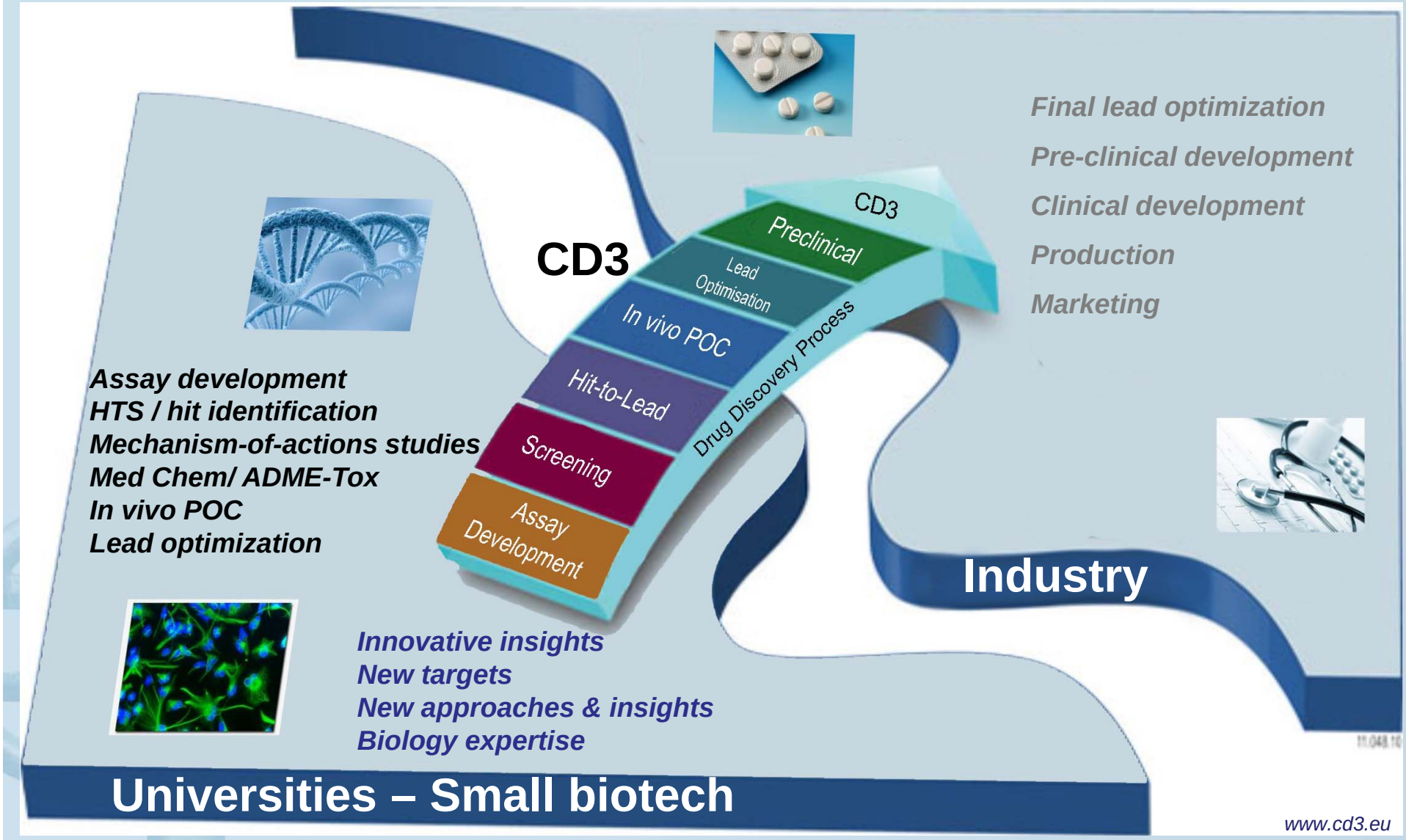
Hand-in-hand partnerships with university research groups and biotechs

Access to ~30 mill. € and an interdisciplinary expert team with strong industry pedigree

www.cd3.eu

Transforming early-stage projects into valuable assets

KATHOLIEKE UNIVERSITEIT LEUVEN



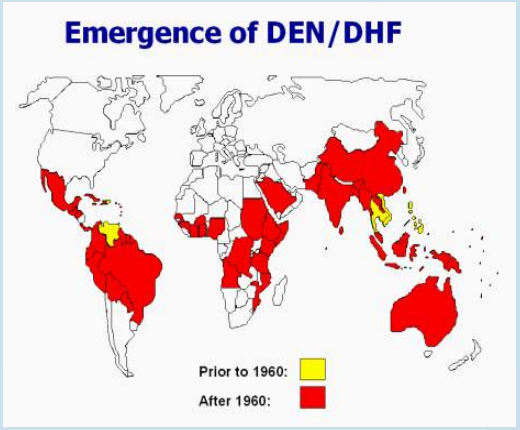
Partnered CD3 projects

Target	Disease	Partner
LEDGF – Integrase inhibitors	HIV infections	ViiV Healthcare, Pfizer
Tau induced toxicity inhibitors	Alzheimer's disease	reMYND
NS4B inhibitors	Dengue virus infections	janssen
Malt 1 inhibitors	Auto-immune, cancer	AstraZeneca
BMP modulators	Osteoarthritis	arcarios
FCV antivirals	Cat FCV infections	ARATANA THERAPEUTICS
2C inhibitors	COPD / Asthma: Human rhino virus	NOVARTIS

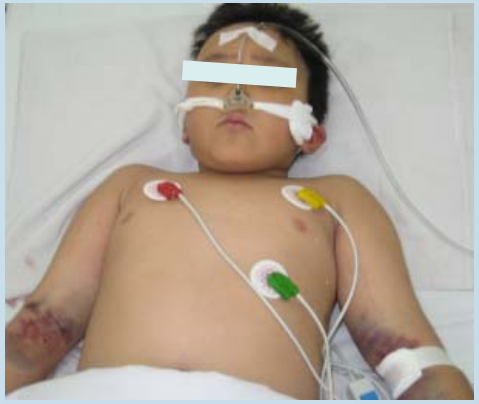
www.cd3.eu

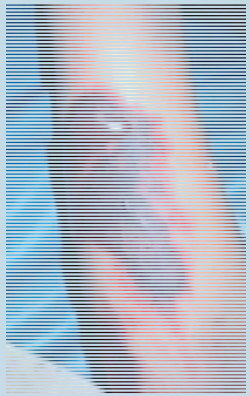
Case example: Discovery and development of Dengue anti-viral drugs

High unmet clinical need for a dengue antiviral



Adapted from http://www.who.int/csr/disease/dengue/impact/en/index.html





Courtesy of Dr. Trung Dinh The (Ho Chi Mingh City, Vietnam)

2009

2013

KATHOLIEKE UNIVERSITEIT LEUVEN
Rega Instituut

Prof. Johan Neyts

wellcome trust

+

Janssen

www.cd3.eu

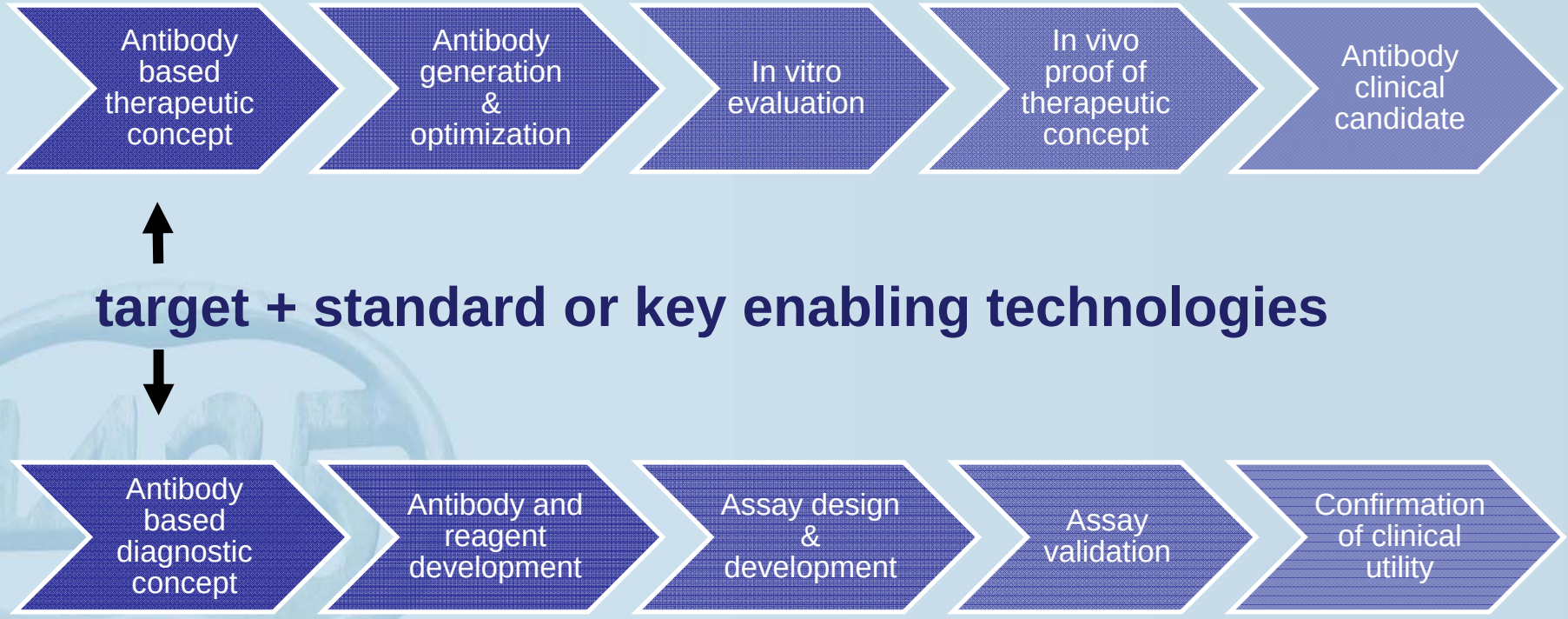
PharmAbs

PharmAbs
The K.U.Leuven Antibody Center

KATHOLIEKE UNIVERSITEIT LEUVEN

Mission: bridge discovery and valorization with antibodies

Focus: support projects aiming at innovative monoclonal therapeutics, antibody-based diagnostics, imaging tools and immunosensors



Project assessment

Non-financial

Technical

- Validation of the target
- Suitability of a mAb
- Immunogenicity of the antigen
- Assay format

Market

- Market size and growth rate
- Current state-of-the-use
- Competition
- Time to market

Regulatory

- Freedom-to-operate
- Patentability

Corporate

- Skills & tools needed
- Strategic fit
- Track record of the submitter
- Expertise of The submitter

Financial

- Level of investment
- Funding possibilities

PharmAbs R&D programs

PharmAbs
The KU Leuven Antibody Center

INNOVATIVE ANTIBODY TECHNOLOGIES

- Monoclonal antibodies — EU H2020 ND4ID
- (Multi)functional nanoparticles — IWT SBO NANOCOMIT
- Antibody gene transfer — IWT IM SO

ANTIBODY THERAPEUTICS

- *Clostridium difficile* infection – tcdA/B mAbs
- Submassive pulmonary embolism – PAI-1/TAFI diabody — CETROMED Ltd

- Therapeutic drug monitoring — r-biopharm, MSD, apDia, Pfizer

IMMUNODIAGNOSTICS

- RCC exosome quantification/profiling for improved diagnosis/prognosis — VLK
- Early detection and prognosis of Alzheimer's disease — ADx
- Prognostic test for acquired TTP — EU H2020 PROFILE
- p53 diagnostic assay to stratify patients for p53 targeted therapies — IWT SBO P53
- Test to stratify IBS patients for ebastine treatment

pharmabs.org

Case example:

Drug repositioning – orphan designation
Sildenafil for severe CDH (congenital diaphragmatic hernia)

Sildenafil approved for use in PHT in adults and is effective & well tolerated in children > 1 year

In vivo data in rabbit model (CDH-fetuses) show efficacy

Aim: move towards RCT on maternal sildenafil for severe CDH

Next steps?

- Determine the needed preclinical data set (in vivo, ex-vivo)
- CDH meets criteria for orphan designation: drug regulatory process?
- Identify funding & collaboration opportunities
- RCT design
- ….

Ref: Russo FM et al., Deprest J. Transplacental sildenafil rescues vascular and airway morphometry in the rabbit model of congenital diaphragmatic hernia. Am J Obstet Gynecol 2015; 212:S44-S45

Case example

Drug repositioning – orphan designation

New therapeutic strategy for skin cancers in transplant patients: combination of a local AKT inhibitor with a local (approved) chemotherapeutic

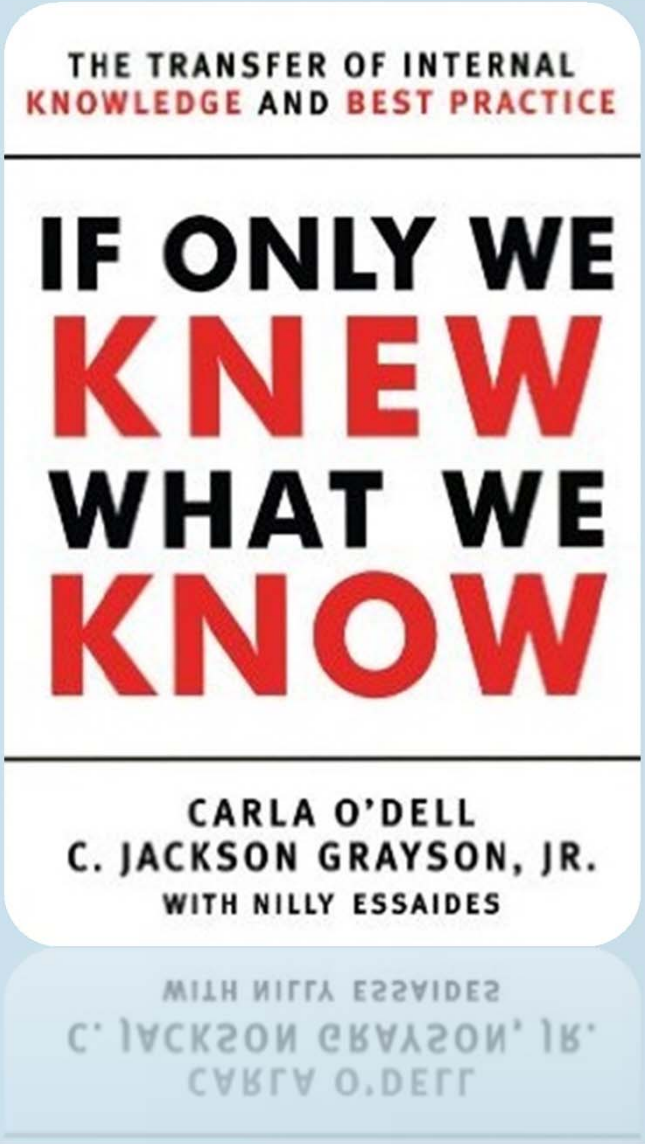
Aim: develop this novel combination therapy and bring it to the clinic

Next steps given that the AKT inhibitor is currently still under development (phase II):

- topical formulation of AKT inhibitor under GMP
- further establish preclinical data set
- local tolerance/toxicity studies of both active drugs
- orphan designation: drug regulatory process?

Ref: Barrette K et al, Garmyn M. Epithelial-mesenchymal transition during invasion of cutaneous squamous cell carcinoma is paralleled by AKT activation Br J Dermatol.2014,171(5):1014-21

Thank you


THE TRANSFER OF INTERNAL
KNOWLEDGE AND BEST PRACTICE
IF ONLY WE
KNEW
WHAT WE
KNOW
CARLA O'DELL
C. JACKSON GRAYSON, JR.
WITH NILLY ESSAIDES

Contact

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