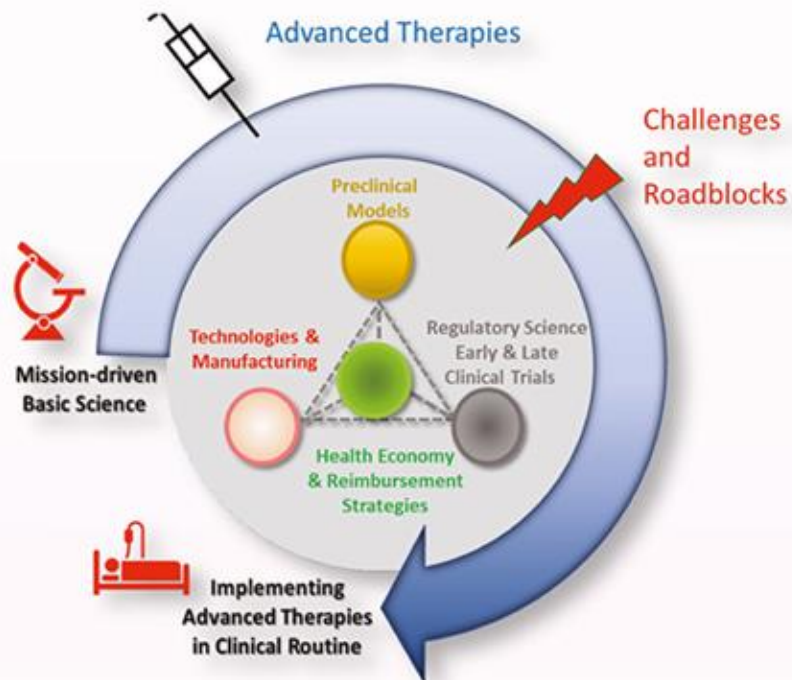




# RESTORE

## RESTORE - Health by Advanced Therapies

(Advanced Therapy Medicinal Products and Biologised Medical Devices)

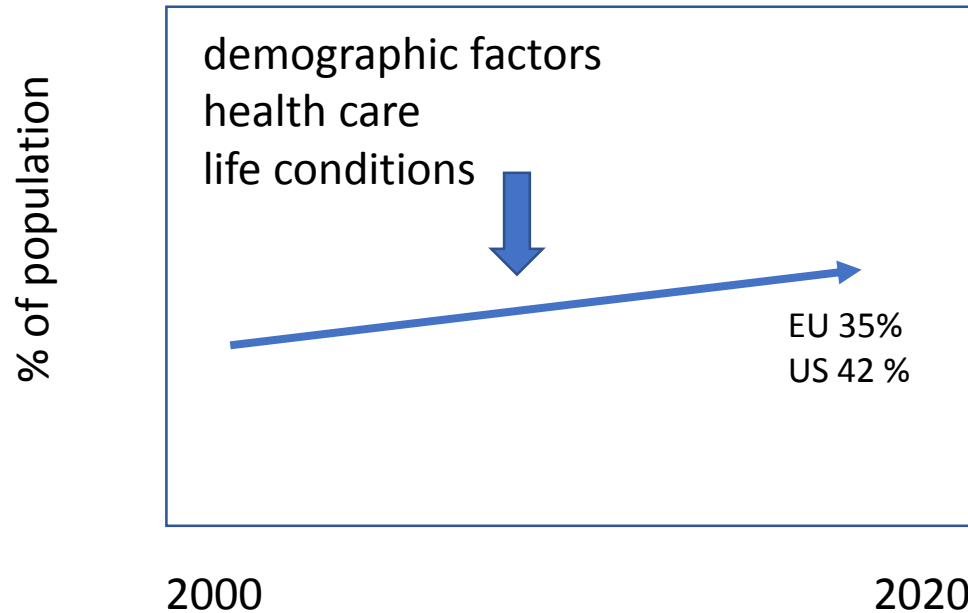


ALL for Advanced Therapies. With Passion. For Patients.

**Why** do we need **RESTORE**?

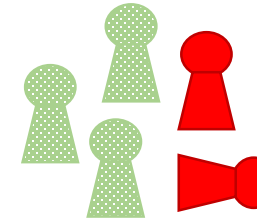
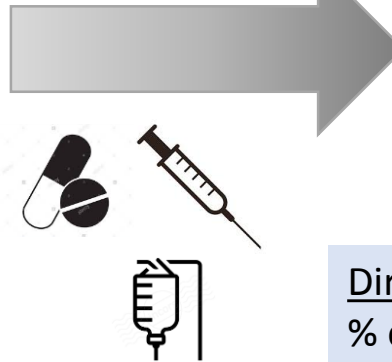
# Chronic Diseases – Burden for Patients & Society


## Increasing Prevalence of Chronic Diseases



cardiovascular, cancer, T2 diabetes,  
lung, (auto) immune, musculoskeletal,  
neurodegenerative, mental diseases ...  
=> **increase in multi-morbidity**

Current  
pharmacologic  
strategies

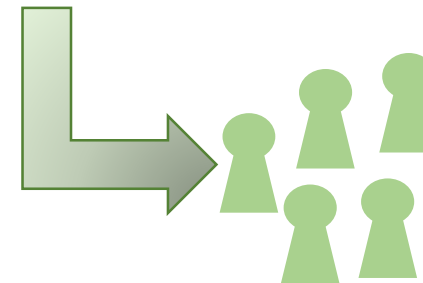


=> Many non-responders 

=> Responders: 

- No Cure, often progression
- Need for chronic treatment
- Adverse effects
- Limited quality of life
- High cost for society

Direct Health Costs EU	2008		2017
% of GDP	8.3 %	=>	9.6 %
billions €	1.070	=>	1.526

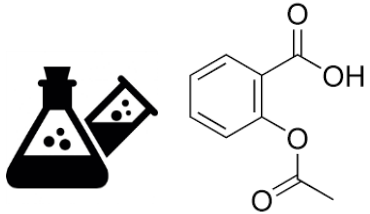


Need for sustainable  
improvement or even curing of  
chronic diseases avoiding  
conventional chronic treatment  
=> **Advanced Therapies**

Sources: Annual reports of CDC on chronic diseases, and EU Health at a Glance

# Advanced Therapies – Novel Class of „Living“ Drugs

since >120 years



Defined, chemically produced  
**Small Molecules**

since >30 years

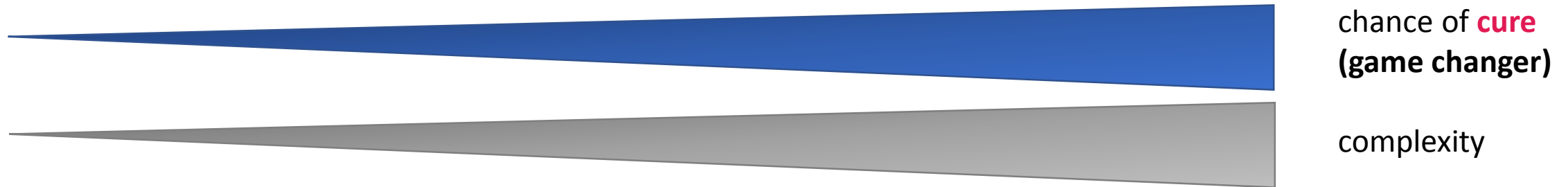


Protein-based drugs  
produced in living cells  
**Biologics**

since >10 years



**“Living” drugs**  
(gene therapies, gene modified cells, somatic cells, engineered tissues)  
**Advanced Therapies (ATMP)**

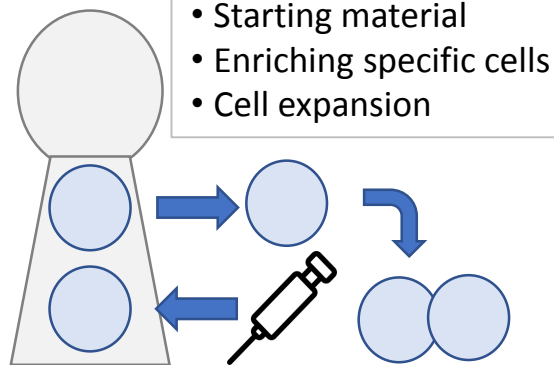


Complexity of chronic diseases requires complex therapeutic approaches

# Advanced Therapies – Novel Class of „Living“ Drugs



## Somatic cells

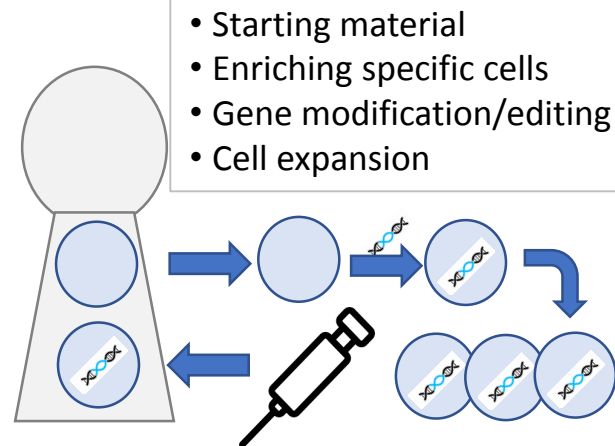


### Generating specific living cells *ex vivo* (sCTMP)

e.g. severe infections, cancer transplantation, autoimmunity, tissue regeneration



## Ex vivo gene-modified cells

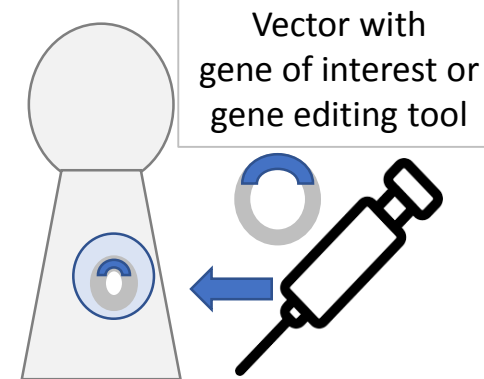


### Gene modification/editing of living cells *ex vivo* (GTMP)

e.g. severe infections, cancer transplantation, autoimmunity, genetic diseases

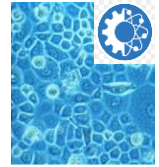


## In vivo gene therapy

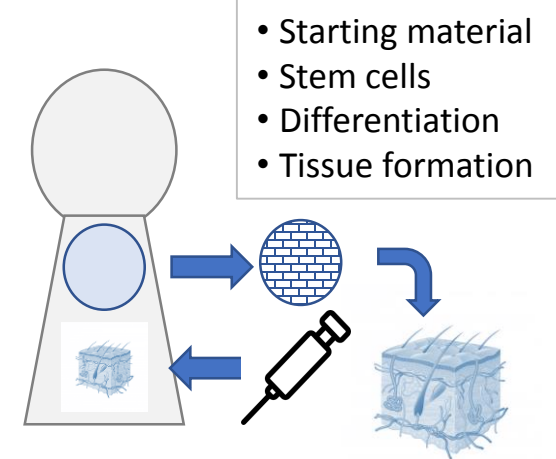


### Gene modification/editing of living cells *in vivo* (GTMP)

e.g. genetic diseases, cancer



## Engineered tissues



### Tissue Engineering from living cells *ex vivo* (TEP)

e.g. replacement of irreversibly injured tissues/organs

# Advanced Therapies – Novel Class of „Living“ Drugs



*Somatic cells*



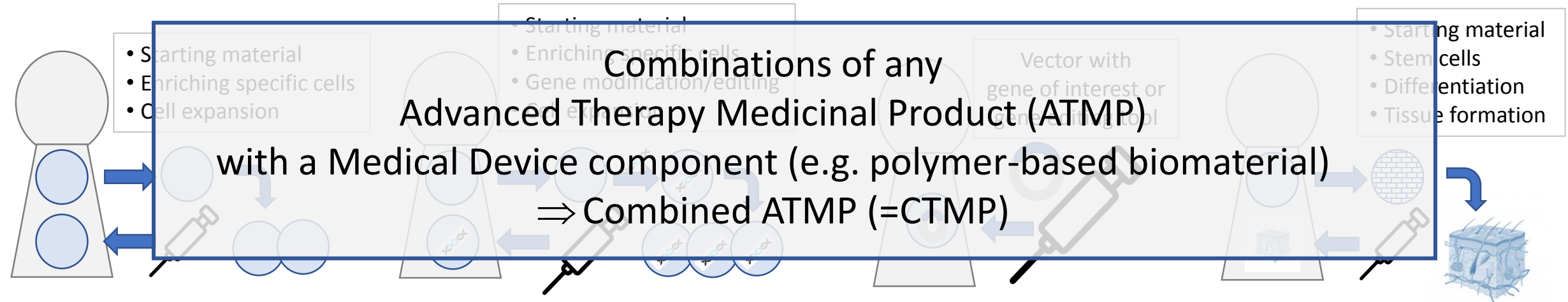
*Ex vivo gene-modified cells*



*In vivo gene therapy*



*Engineered tissues*



Generating specific  
living cells *ex vivo* (sCTMP)

e.g. severe infections, cancer  
transplantation, autoimmunity,  
tissue regeneration

Gene modification/editing  
of living cells *ex vivo* (GTMP)

e.g. severe infections, cancer  
transplantation, autoimmunity,  
genetic diseases

Gene modification/editing  
of living cells *in vivo* (GTMP)

e.g. genetic diseases, cancer

Tissue Engineering  
from living cells *ex vivo* (TEP)

e.g. replacement of irreversibly  
injured tissues/organs

# Curing by Advanced Therapies – not just a dream, it is **reality**

## Cell Therapy

=> Immune Disease (chronic GvHD)



### Regulatory T cells

=> isolation from 50 ml blood => expansion  
=> single shot therapy => long-lasting benefit



Landwehr-Kenzel S ... Reinke P, submitted

## Cell & Gene Therapy

=> Genetic Disease (skin)



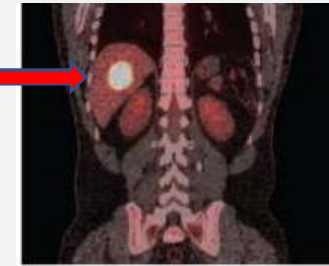
skin biopsy => gene repair in  
skin stem cells => expansion



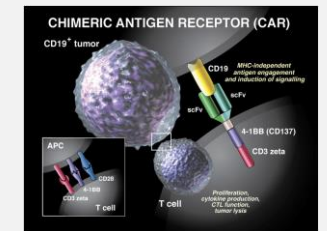
Hirsch T ... De Luca M, Nature 2017

## Cell & Gene Therapy

=> Cancer (non-Hodgkin lymphoma)



Before first  
CAR-T cell infusion



T cell isolation from blood  
=> generation of anti-cancer CAR-T cells  
=> expansion => 2 infusions



After first  
CAR-T cell infusion



After second  
CAR-T cell infusion

Turtle CJ et al., Sci Transl Med 2016

# Curing by Advanced Therapies – not just a dream, it is reality

## Current Clinical Trials on Advanced Therapies (Q2 2018)

**977**  
**Clinical Trials**  
underway worldwide  
by end of Q2 2018

**Phase I: 324**  
**Phase II: 560**  
**Phase III: 93**



Gene Therapy

317



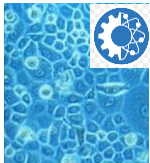
Gene-modified  
Cell Therapy

314



Somatic Cell  
Therapy

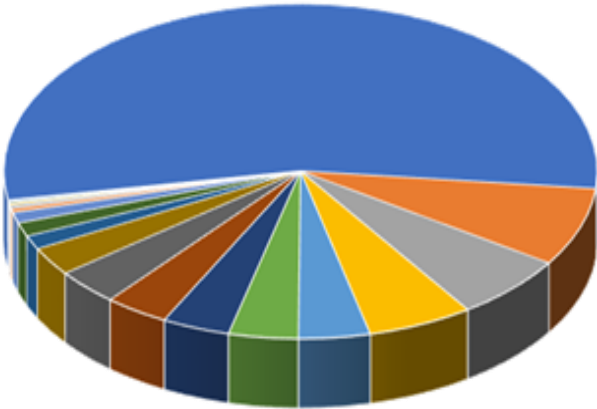
322



Tissue Engineering

24

## Clinical Trials by Indication: Q2 2018

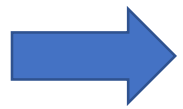


- |  |                               |
|--|-------------------------------|
| ■ 1 Oncology                                 | ■ 2 Cardiovascular            |
| ■ 3 Musculoskeletal                          | ■ 4 Central Nervous System    |
| ■ 5 Endocrine, Metabolic & Genetic Disorders | ■ 6 Dermatology               |
| ■ 7 Hematology                               | ■ 8 Immunology & Inflammation |
| ■ 9 Ophthalmology                            | ■ 10 Infectious Diseases      |
| ■ 11 Genitourinary Disorders                 | ■ 12 Gastroenterology         |
| ■ 13 Respiratory Diseases                    | ■ 14 Surgery                  |
| ■ 15 Lymphatic Diseases                      | ■ 16 Ear Diseases             |
| ■ 17 Geriatric Diseases                      | ■ 18 Radiation Diseases       |

Alliance for Regenerative Medicine Report 2018

# The Pain

- Society became accustomed to being treated for chronic diseases but rarely healed by conventional drugs resulting in high burden for patients and society
- Advanced Therapies might be transformative by their sustainable efficacy
- Unfortunately, **only a few** Advanced Therapy products that cure from chronic disease have reached the market so far because of **several major challenges**  
⇒ selecting and manipulating the right cells, manufacturing, preclinical models, mode-of-action, scaling-up/scaling-out, regulatory sciences, reimbursement...
- Progress is happening quickly in the US and Asia – Europe lags behind despite its high innovation potential



The need for strategic positioning in Europe through  
a well-coordinated large-scale research initiative



What is  aiming at?

# The Vision

- Making the transforming promise of Advanced Therapies a reality for the benefit of patients and society
- Making Europe a spearhead in R&D and application of Advanced Therapies

# The Mission

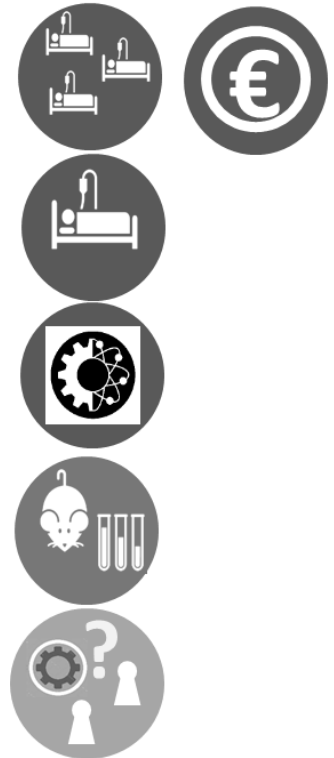
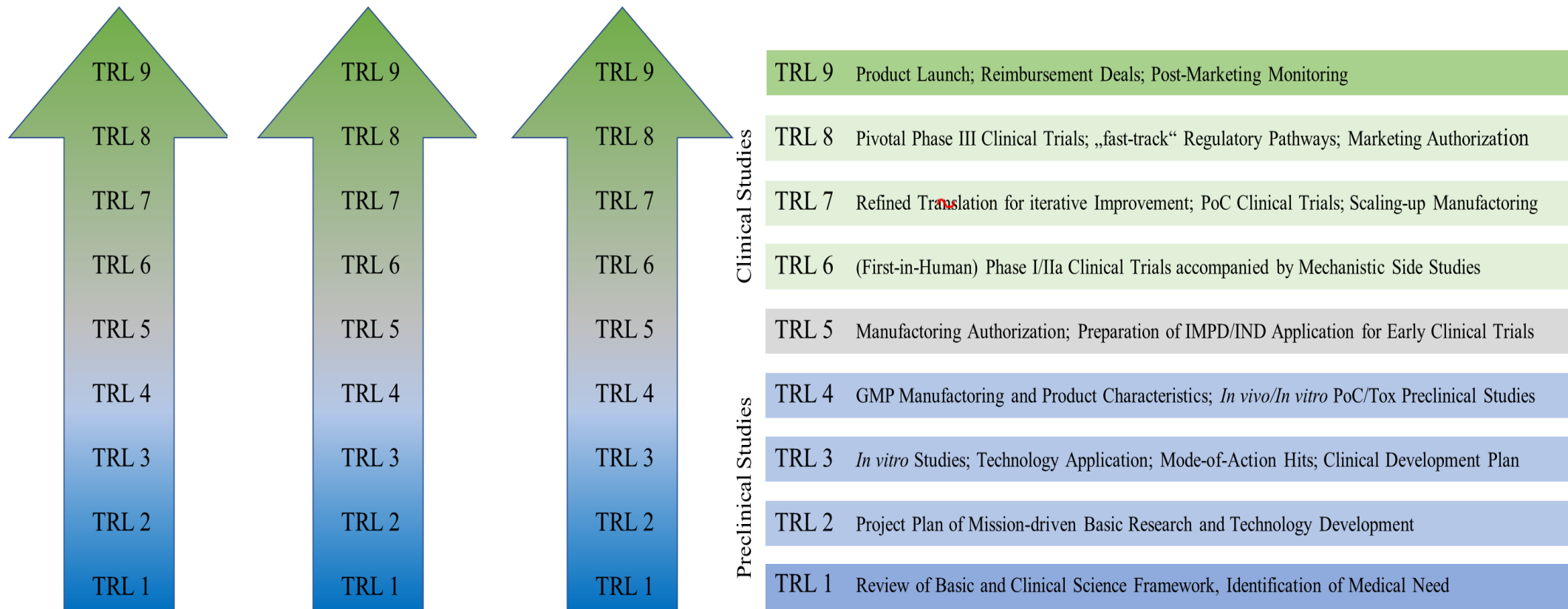
- Creating a pipeline of dozens of Advanced Therapy products developed and made in Europe by 2030 by addressing roadblocks
- Driving innovation and patient-centered clinical research, adhering to high quality and ethical standards
- Establishing a European ecosystem that will carry the effort further into the future

# Long way along the Technology Readiness Levels

*Strimvelis*<sup>®</sup> (Genetic Disease)    *Yescarta*<sup>®</sup> (Cancer)    *Kymriah*<sup>®</sup> (Cancer)

*<= examples for approved „living“ drugs*

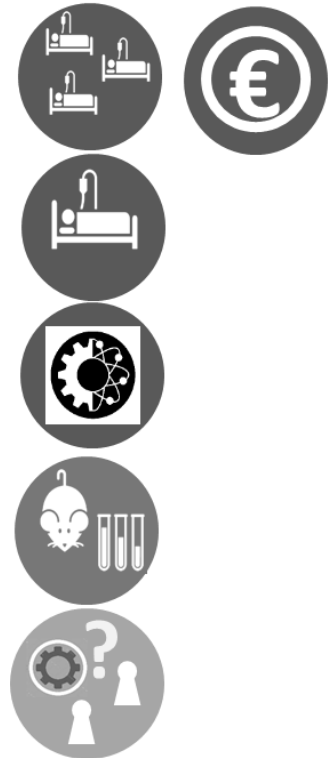
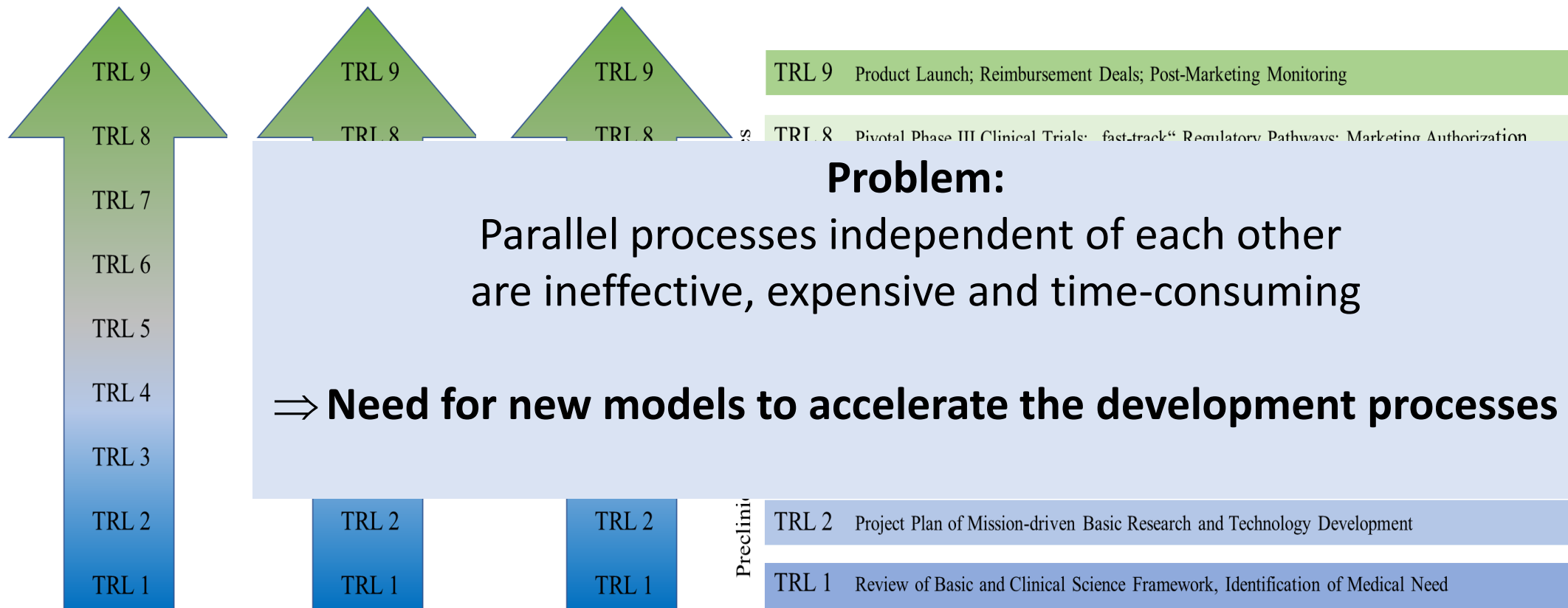
development time each ~20 yrs



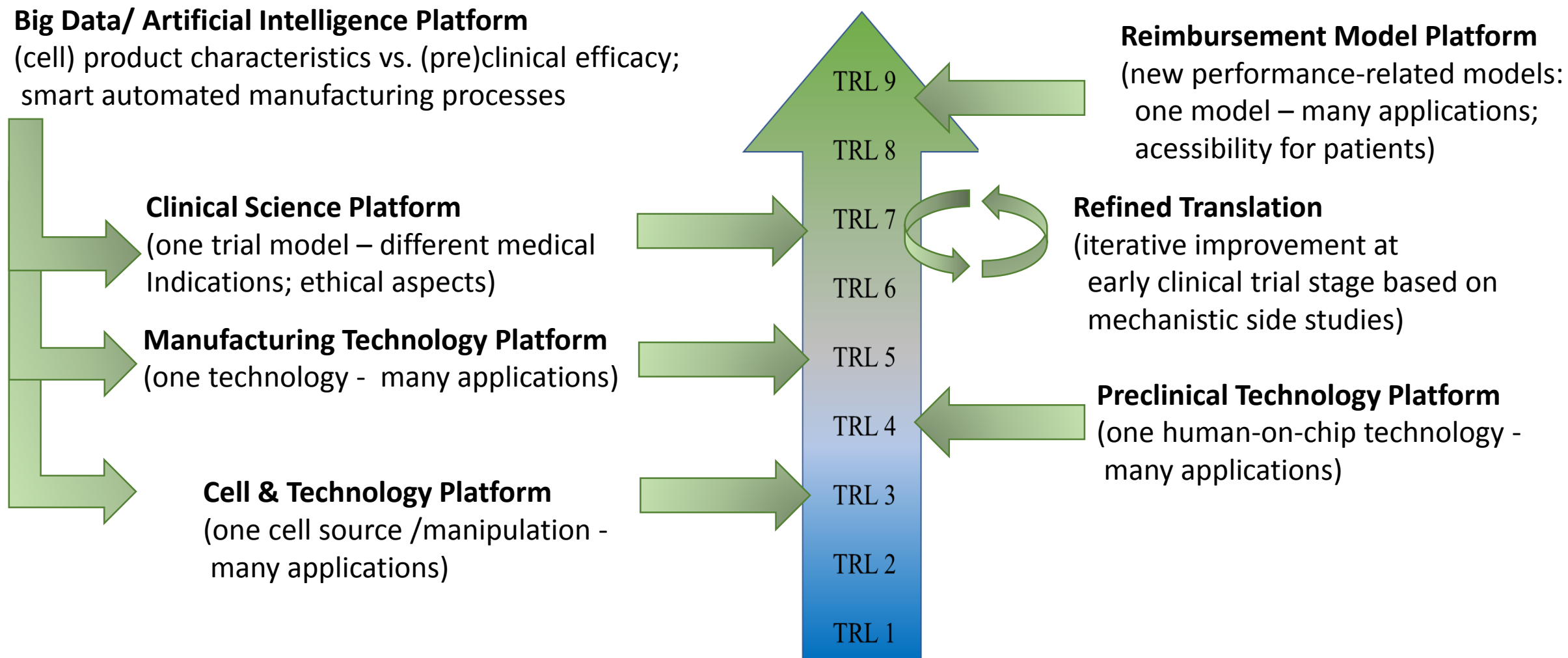
# Long way along the **T**echnology **R**eadiness **L**evels

*Strimvelis*<sup>®</sup> (Genetic Disease)    *Yescarta*<sup>®</sup> (Cancer)    *Kymriah*<sup>®</sup> (Cancer)    <= examples for approved „living“ drugs

development time each ~20 yrs

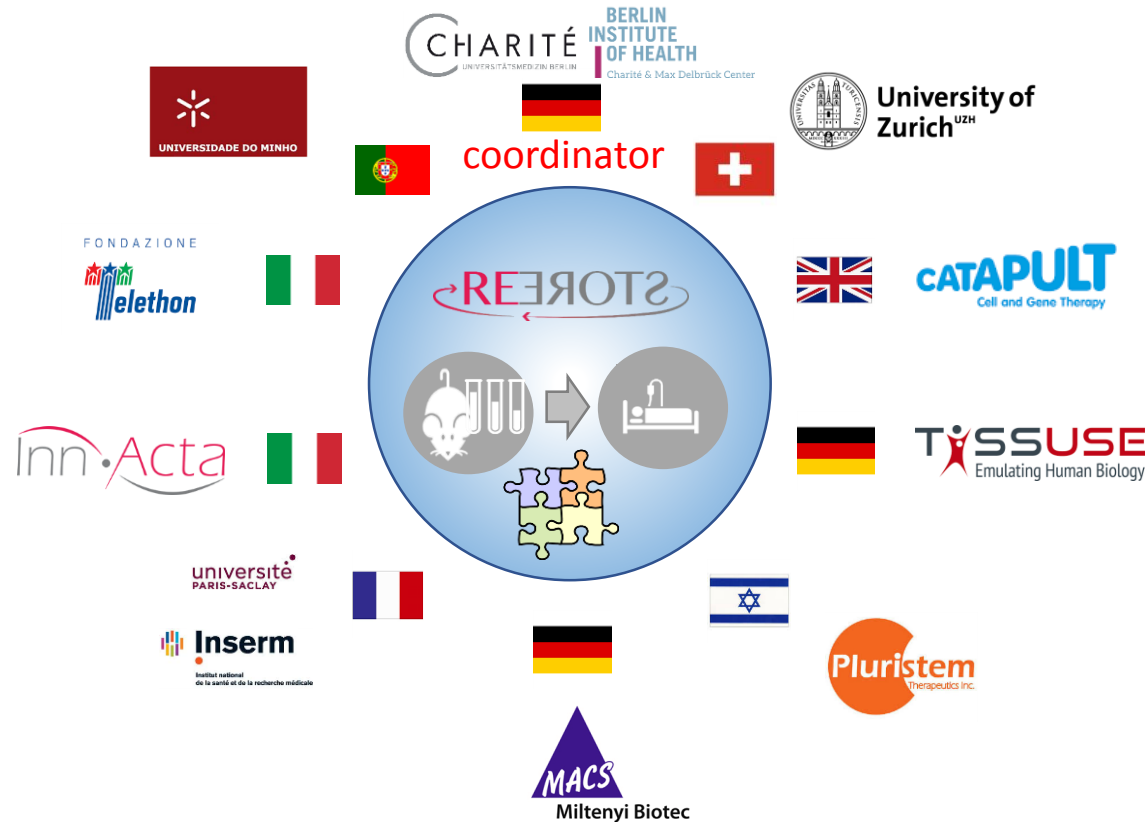


# Accelerating and De-Risking by non-linear TRL Development Model (roadmap)



# Who we are – RESTORE community

## Core Team (Academic Centers & Biotech)



## Supporters



from 26 countries (EU-MS, EU-AC, USA, Singapur)

[March 13th, 2019]



RESTORE - Health by Advanced Therapies



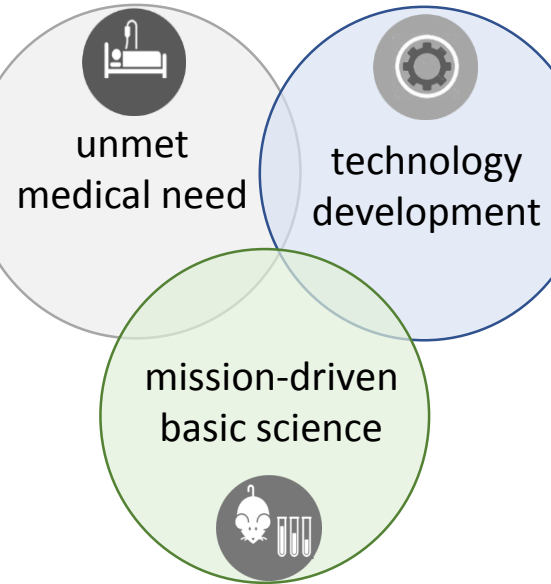
# How to get there

- Establishing a well-funded consortium with **long-term perspective** that is backed-up by the interdisciplinary scientific **community**, relevant **stakeholders, patient advocates** and **the public** and embedded into international **networks**
- Devising the **strategic roadmap** for the allocation of funds in order to make our vision come true
- RESTORE consortium as the docking point for biotech/medtech/pharma **industry** and **special interest funds**
- Implementing a governance that allows **flexibility**
  - ⇒ to respond to new **trends** and define **key performance indicators** and
  - ⇒ to engage at any time further **scientists and stakeholders** who can contribute significantly to the success of the mission

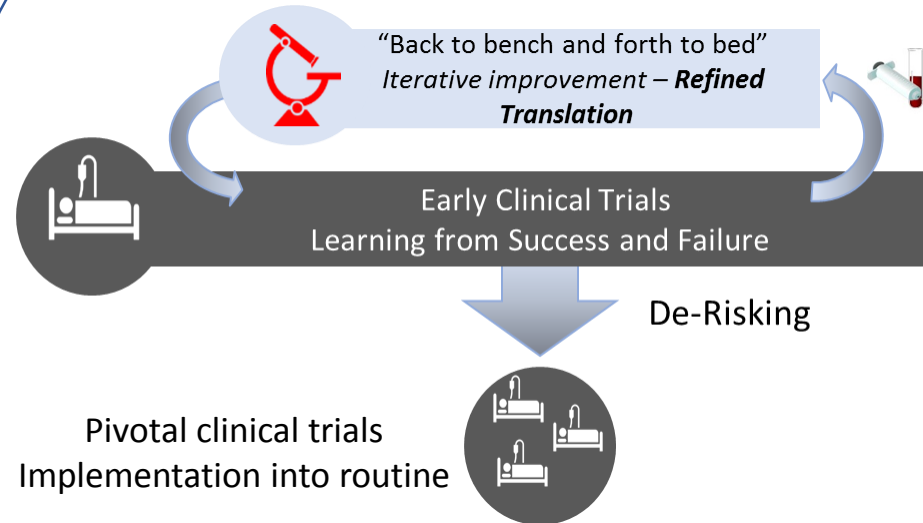
EU „Large-Scale Research Initiative“ (formerly: FET-Flagship)  
(€1m for 12-months preparatory phase, up to €1bn afterwards)



# Strengths of



**Driving Triad**



**De-risking by refined translation  
based on clinical experience**



Ethics Science



Regulatory Science



Health Economics  
Science



**Embedding social sciences  
and patients**



### Science and Technology

- ⇒ infrastructure and translational centers of excellence
- ⇒ boosting European competitiveness in the groundbreaking area of “living” drugs
- ⇒ fundamental knowledge and technology breakthroughs relevant for many areas
- ⇒ new generation of translational scientists with new mindset

### Societal Benefits for European's Society and Economy

- ⇒ improved survival and quality-of-life of patients suffering from chronic diseases
- ⇒ decreasing financial burden of the society by chronic diseases
- ⇒ developing an innovative product pipeline for medtech/biotech/pharma industry
- ⇒ generation and retention of highly specialized workforces and expertise in Europe
- ⇒ setting the ethical and quality standards for these new therapies



# FET Flagship call 10/2017 => now under the new name „Large-Scale Research Initiative“ (LSRI):

- Areas:**
- Information and Communication Technology and Connected Society (ICT/AI)
  - Health and Life Sciences (Life Sciences)
  - Energy, Environment and Climate Change (Energy)



# Thank **you**

## **Join** us!

<https://www.restore-h2020.eu/>

[info@restore-h2020.eu](mailto:info@restore-h2020.eu)

This preparatory phase CSA project has received funding from the European Union's Horizon 2020 research and innovation programme under grant agreement No 820292