

OVERVIEW

Shifting from treating symptoms to curing chronic diseases by making the transformative promise of Advanced Therapies a reality for the benefit of patients and society and making Europe a spearhead of Advanced Therapies in Science, Clinics and Biomedical Industry - that is the aspiration of the international project RESTORE, coordinated by the Charité Berlin & Berlin Institute of Health.

The initiative recently secured the support of the European Commission and receives initial funding totaling €1m for the 1-year preparatory phase of the large-scale research initiative. Having started officially on 1 March 2019, the kick off meeting of the preparatory phase will be held in Berlin on 6 and 7 May 2019.

WHY do we need RESTORE?



The increasing prevalence of chronic diseases and multi-morbidity due to demographic factors, health care, and life conditions represents a high socio-economic burden for Europe. The direct health costs increased by 50% during the last decade and reached €1.526bn in 2017, a staggering 9,6 % of Europe's GDP (EU Health at a Glance 2018). As current therapies rarely cure, but merely fight symptoms, never-ending treatment is required. This results in adverse effects, limited quality-of-life, and increasing costs for society. There is a high need to reach

sustainable improvement or even to cure of chronic diseases - in other words, to disrupt the paradigm of "treating symptoms" with "restoring health". Advanced Therapies are game changers that open up ground-breaking therapeutic Opportunities and can transform the life of patients.

What are Advanced Therapies?

Advanced Therapies, in Europe categorized as Advanced Therapy Medicinal Products (ATMP), are also often referred to as 'living drugs', and include somatic cell therapy products, ex vivo and in vivo gene therapy products and tissue engineered products, as well as the combination of these products with medical devices, such as biomaterials. (Fig. 1).

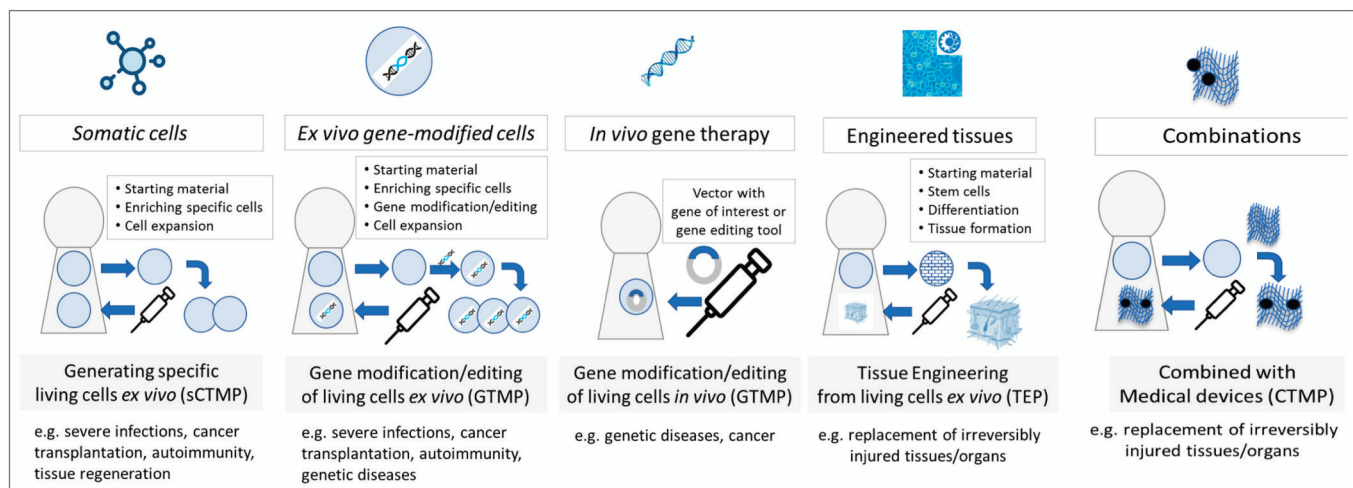


Fig. 1
Categories of
Advanced
Therapies

They are often produced specifically for individual patients (personalised therapies) but if feasible also as off-the-shelf products (one donor - many patients). In their manufacturing, clinical use, and mode-of-action they are characterized by a high degree of complexity compared with conventional drugs or antibodies.

There are potential cures for genetic diseases, immune diseases, cancer, tissue injury by Advanced Therapies – it is not fiction but reality. Some products are already on the market, mostly for rare diseases (Fig. 2). This means that only a few thousand patients worldwide have benefitted from Advanced Therapies until today.



Fig. 2
Advanced Therapy Products approved in Europe for treatment of cancer, genetic diseases, immune diseases, tissue injury.

Why are only few Advanced Therapies implemented in clinical routine so far?

“Living” drugs are a disruptive innovation that challenges the “tried and tested” paradigm of drug development at almost all Technology Readiness Levels (Fig. 3).

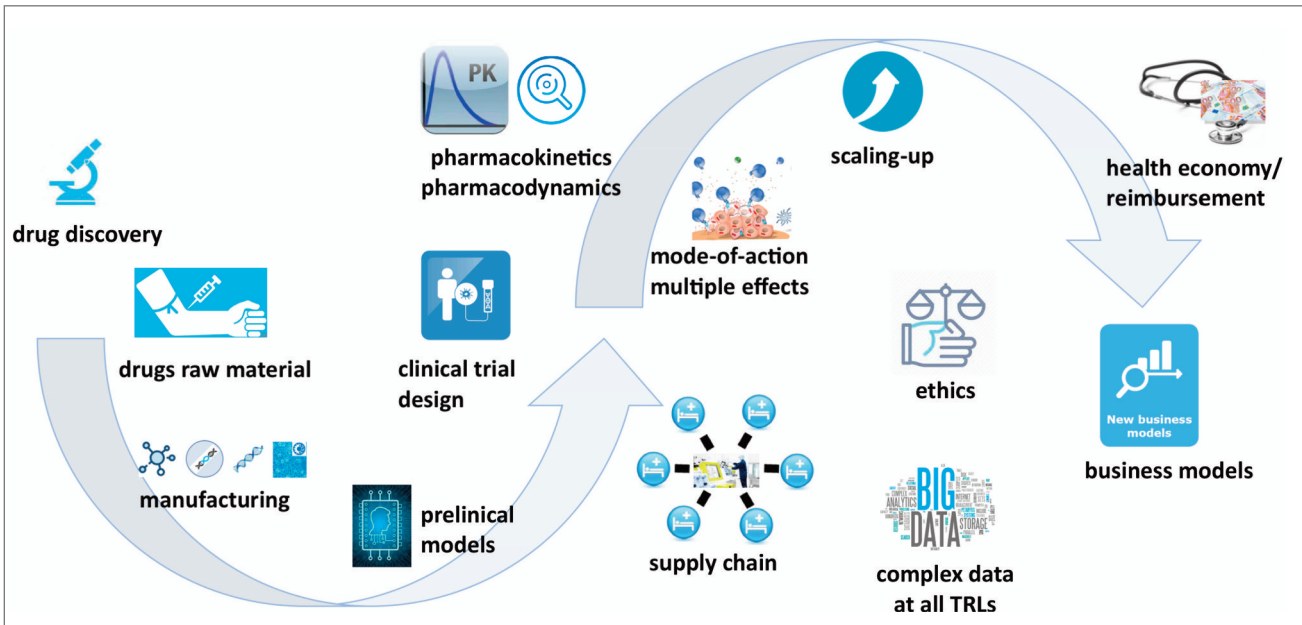


Fig. 3
„Living“ Drugs - a disruptive innovation shatters current paradigms but generates new high-value developments

At the advent of such a trailblazing change, obstacles and roadblocks abound. The recently approved Advanced Therapy Products required a long and costly added-value chain (>20 years) and the complex manufacturing, development and clinical benefit results in high product prices.

Advanced Therapy development is driven by academia and small biotech (a new phenomenon in drug development), although Big Pharma steps in now. The pace of progress has accelerated over the last few years, notably in US and Asia. Europe lags behind despite its high innovation potential and demonstrable success in the past. Therefore, there is a need for focused, determined and well-funded large-scale research initiative in Europe - that's the motivation to found RESTORE.

WHAT is RESTORE aiming at?

The Vision



„Living drugs“ will RESTORE health to chronic diseases

- Make the disruptive promise of Advanced Therapies a reality to **cure** chronic diseases
- Make Advanced Therapies accessible as **“standard-of-care”** for every European patient in need
- Make Europe a **spearhead** of Advanced Therapies in **Science, Clinics and Biomedical Industry**
- Make use of the enormous **socio-economic potential** of novel breakthrough-therapies also in Europe

The Mission



- Overcome the **technological and regulatory roadblocks** for Advanced Therapies in Europe
- Deliver a pipeline of **dozens of revolutionary AT products** “developed and made in Europe” by 2030
- Establish a **sustainable pan-European ecosystem** integrating research, clinics, industry and patients

The overarching goal of Advanced Therapies/Regenerative Medicine is to restore the function of impaired cells, tissues, or organs by addressing two basic principles that depend on the kind of injury and tissue involved:

- Stimulating endogenous regeneration and tissue repair mechanisms (angiogenesis, stem cell activation, immune balance, immune restitution) for combating many chronic diseases, such as cancer, tissue injury, immune, cardiovascular, musculoskeletal, and neurological diseases etc.
- Providing biological replacement strategies if the targeted cells/tissues/organs are irreversibly injured or do not possess regenerative capacity. Biological replacement strategy approaches require also additional support of engraftment and sustained function of those products after delivery to the patient for combating genetic diseases and end-stage tissue/organ injury.

HOW to get there?

- Establish a well-funded consortium with long-term perspective that is backed-up by the transdisciplinary scientific community, relevant stakeholders, patient advocates and the public and that is embedded into international networks (Fig.4)
- Devise the strategic roadmap 2021-30 to overcome roadblocks in order to make our vision come true
- Accelerate and de-risk the development of Advanced Therapies by implementing the Research & Technology Innovation Platforms and Refined Translation Tool (Fig 4+5)
- Form the RESTORE consortium as the docking point for biotech/medtech/pharma industry and special interest venture funds
- Implement a governance that allows flexibility
 - to respond to new trends and to achieve defined key performance indicators
 - to engage at any time more scientists and further stakeholders who can contribute significantly to the success of Advanced Therapies

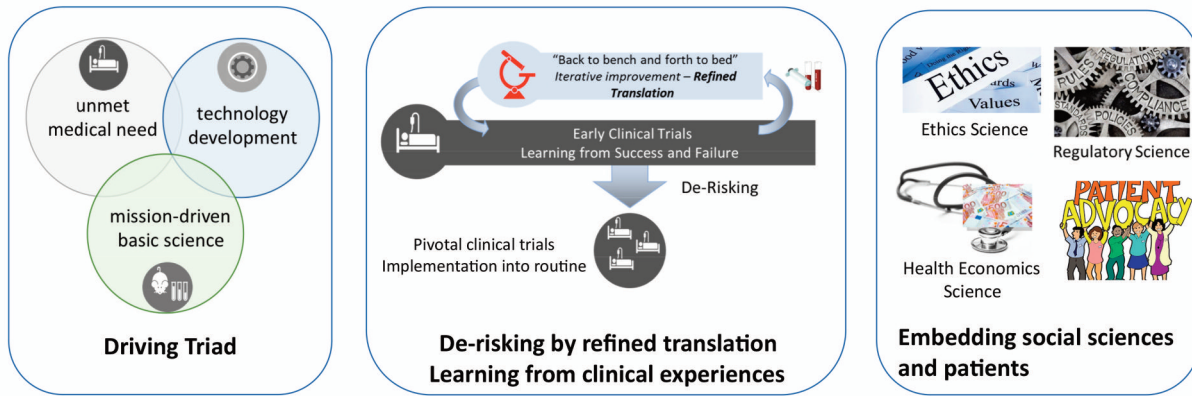


Fig. 4
Building on the 3T's:
T Transdisciplinarity,
T Technology,
T Translation

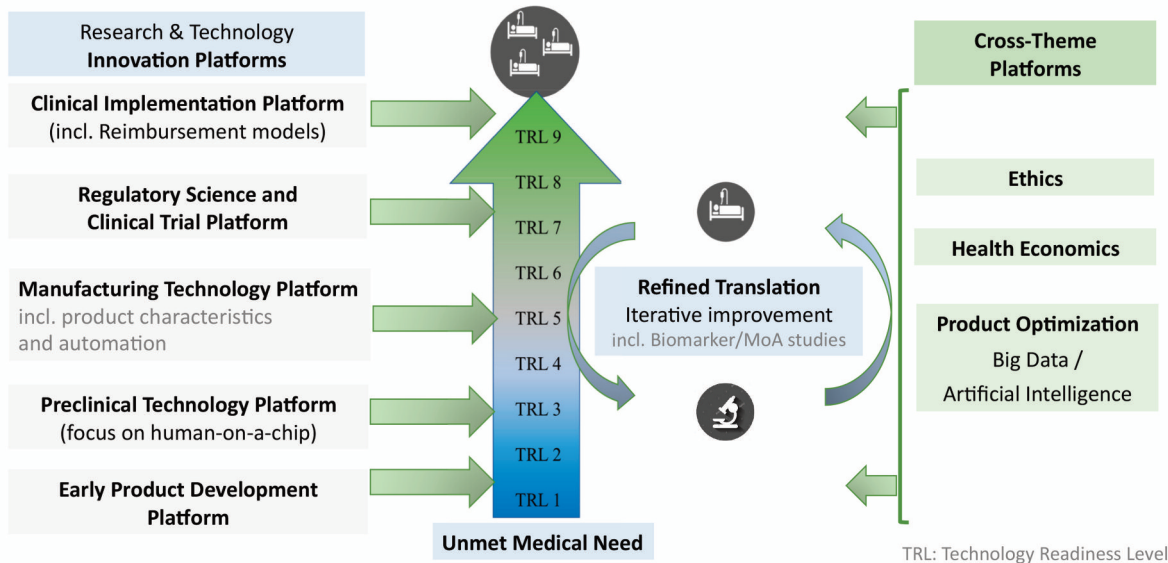


Fig. 5
Accelerating and
De-Risking by
Research & Technology
Innovation Platforms

One solution
⇒ Many applications

IMPACT of RESTORE

by Disruptive Innovations and Technologies on:



Science and Technology

- ⇒ infrastructure and **translational centers of excellence**
- ⇒ boosting Europe's competitiveness in the groundbreaking area of **"living" drugs**
- ⇒ fundamental knowledge and technology **breakthroughs** relevant for many areas
- ⇒ next generation of **translational scientists** with new mindset



Societal Benefits for European's Society and Economy

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

Fig. 6
Scientific and societal
Impact of RESTORE

The RESTORE Core Team is a formidable group of 10 partners from academic centers and biotechs with excellent international reputation and a strong track record (Fig. 7)

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Logos of various patient and non-profit organizations:

- achse: Adult Cholesterol Solute Exchanger
- ATBS: www.atbs.org
- Fondazione Paracelso: "la medicina diventa arte"
- ANTHONY NOLAN: saving the lives of people with blood cancer
- IPOPI: INTERNATIONAL PEDIATRIC ORGANIZATION
- A.T.S.K.
- F.I.R.M.
- ring14 INTERNATIONAL ONLINE
- UNIPILAN
- Associazione Persone Williams Italia
- dsai
- Mitocon: malattie mitocondriali e malattie mitocondriali
- PTEN RESEARCH FOUNDATION
- spinal research

Patient- and other non-profit organisations



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