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Teaming for Excellence: CoE CREATIC

Central European Advanced Therapy and Immunotherapy Centre

Regina Demlova, LF MU a MOÚ
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Teaming for Excellence – The Idea

The Teaming action is designed to support the creation of new **centres of excellence** or **upgrading the existing ones** in low R&I performing countries, building on **partnerships** between **leading scientific institutions in Europe** and the main beneficiary institutions in low R&I performing countries that display the willingness to engage together for this purpose.

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Teaming for Excellence – The Call

- Main Goal: Improved **access to excellence** for widening countries
- Budget: up to 15 mil. EUR for 6 years
- Complementary funding: 15 mil. EUR national co-financing
- Research component: not exceeding 10 % of the HE grant

- **Two stage evaluation**
  - 5.10. 2021/ 116 projects
  - **8. 9. 2022/ 31 projects**

- **Final decision: 12.12.2022 / 12 winners**

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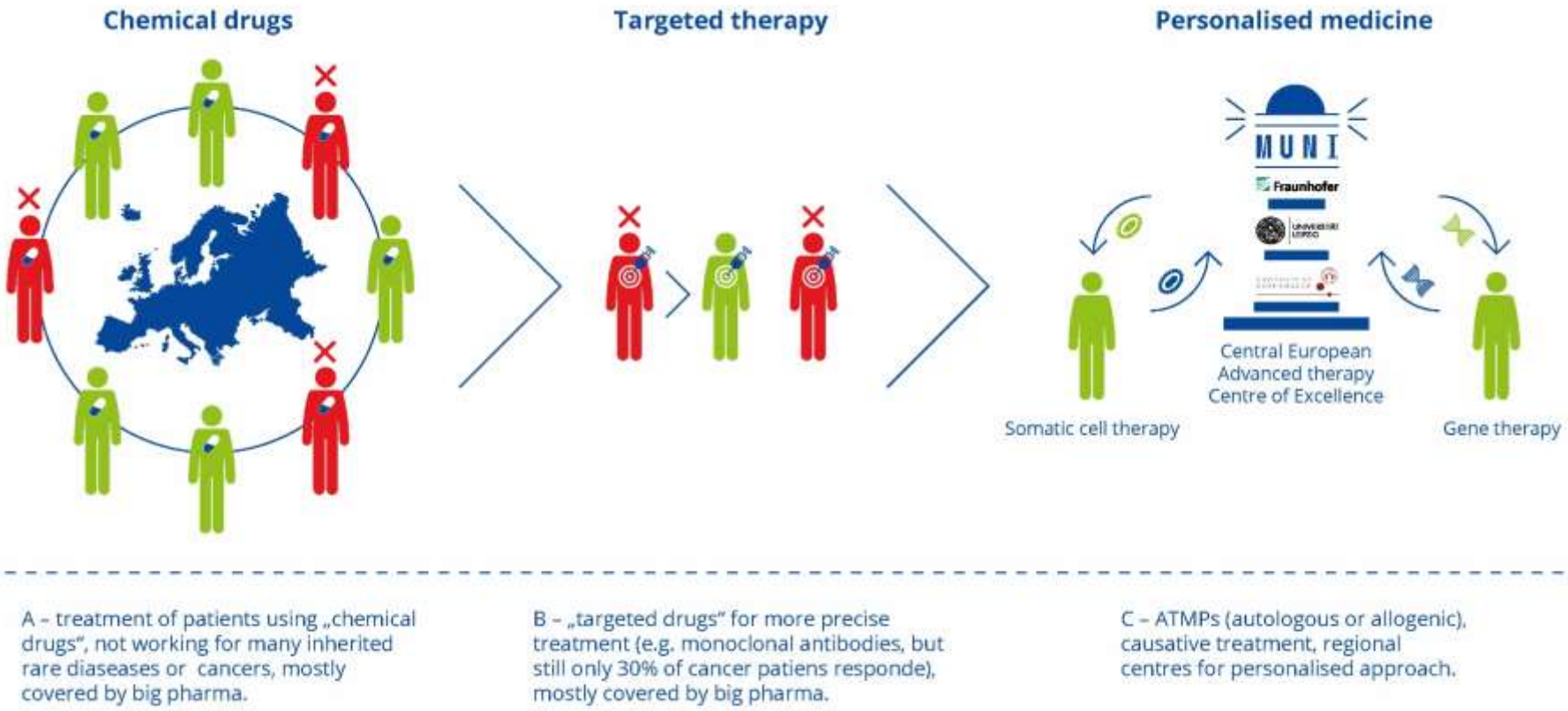
Vision of the CREATIC CoE

CREATIC: Teaming for Excellence

CREATIC: Towards Research Strategy

Central European Advanced Therapy and Immunotherapy Centre



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Background – current MU expertise

ACIU and CZECRIN

ACIU

- Advanced Cell Immunotherapy Unit
- GMP unit certified by State Institute for Drug Control
- Current stage: technological setting serves to produce cell-based investigational therapies (DC, MSCs, MSCs on nanofibre)
- 2 existing ATMP cell-based products: **MyDendrix™** (high-risk malignancies), **FlyCellix™** (Epidermolysis Bullosa)
- Both products are currently in Phase I/II clinical trials.

CZECRIN

- LRI – national node of European Clinical Research Infrastructure Network (ECRIN–ERIC)
- Supported by a national network of clinical sites
- Expertise in three main pillars Clinical Trials Centre (CTC), Regulatory & Pharmacoeconomy Unit (RAPHE) and GMP Units
- Senior experts in key areas as regulatory, market access, GCP, clinical trials (including 3 experts with EMA experience as members of the CHMP, PDCO and COMP committees and 2 experts with previous pharma-business senior experience).
- Education and Training in designing clinical trials: CZECRIN Academy

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ACIU current stage: technological setting serves to produce **cell-based investigational therapies** (DC, MSCs, MSCs on nanofibre)

CoE Advanced Therapies upgrade: To reflect current and future trends in therapy individualization we propose to **expand research, development and ATMP manufacturing capabilities** of the current GM unit towards

CoE Advanced Therapies

- gene therapies *(CARs…)*
- protein-engineered therapies *(stabilize FGF2 protein…)*
- cell-based therapies

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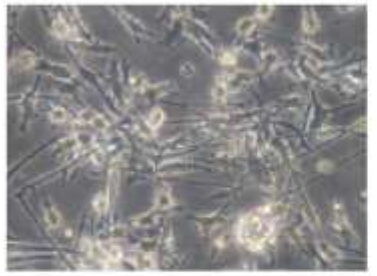

ADVANCED CELL IMMUNOTHERAPY UNIT

ACIU focuses on the development and manufacturing of advanced therapy medicinal products (ATMP) and research related to ATMP and their applications. The manufacturing of medicinal products is carried out in the Clean Rooms supported by Quality Control laboratories, analytical laboratories, and administrative rooms for ACIU staff. ACIU operates in accordance with Good Manufacturing Practice (GMP), currently applicable legislative requirements and authorization to produce, control and store specified medicinal products.

We currently investigate and manufacture a somatic cell therapy medicinal product from autologous dendritic cells, which is being tested in a clinical trial "Combined antitumor therapy with ex vivo manipulated interleukin-12 producing dendritic cells in paediatric, adolescent and young adult patients with progressive, relapsing or primarily metastatic high-risk malignancies" (EudraCT No. 2014-003388-39) at the Department of Paediatric Oncology, University Hospital Brno. We also study and somatic cell therapy with allogeneic mesenchymal cells to support wound healing in rare dermatological diseases.

The ACIU team consists of experts with experience in pharmaceutical manufacture, with expertise in cell biology and immunology, and/or in diagnostic methods.

A.1	Member State in which the submission is being made:	**Czech Republic - SUKL**
A.2	EudraCT number:	**2014-003388-39**
A.3	Full title of the trial:	
	English	**COMBINED ANTITUMOR THERAPY WITH EX VIVO MANIPULATED DENDRITIC CELLS PRODUCING INTERLEUKIN-12 IN CHILDREN, ADOLESCENTS AND YOUNG ADULTS WITH PROGRESSIVE, RECURRENT OR PRIMARILY METASTATIC HIGH-RISK TUMORS**

A.1	Member State in which the submission is being made:	**Czechia - SUKL**
A.2	EudraCT number:	**2020-002936-55**
A.3	Full title of the trial:	
	English	**Safety and Efficacy of Allogenic Adipose Tissue-derived Mesenchymal Stromal Cells in Patients with Epidermolysis Bullosa: Clinical Trial Phase I/II**

Teaming up with advanced partners

	Fraunhofer	UNIVERSITÄT LEIPZIG	UNIVERSITY OF COPENHAGEN
R&I&D	▪ excellence in research, development and training in the fields of ATMP gene and cell therapies	▪ excellence in clinical research, immuno-monitoring and biomarker research	▪ excellence in biomedical innovation law; IP, data, and technology management; and legally supported RRI framework
Research support	▪ centre management ▪ human resources ▪ data management	▪ education and training	▪ stakeholder engagement ▪ knowledge valorisation

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CREATIC Vision

„CREATIC as the flagship in CEE region, provides excellent research of gene and somatic cell therapy to deliver safe, accessible and affordable personalised treatment of life-threatening or chronically debilitating rare disease patients that are conventionally considered incurable.“

Fraunhofer

UNIVERSITÄT LEIPZIG

UNIVERSITY OF COPENHAGEN

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What lies ahead

CREATIC: Teaming for Excellence

CREATIC: Strategic and Specific Goals

SG A Strengthen and widen comprehensive ATMPs R&I expertise

SO 1: Create a cell and gene therapy development pipeline (from bench to bedside)
SO 2: Extend high-end precision medicine platform for therapy individualization, monitoring of patients and for ATMPs clinical research (from bedside to patient)
SO 3: Develop a research platform to explore socioeconomic aspects of ATMPs and technology transfer

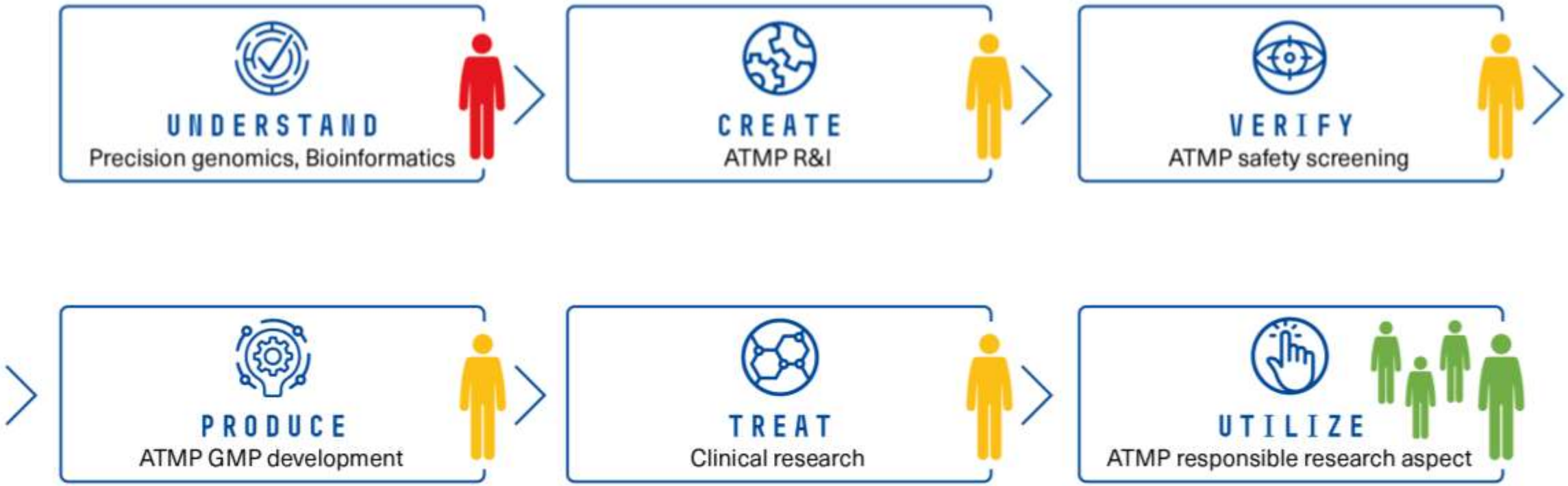
SG B Build a role model institution

SO 4: Establish decision-making autonomy, research management and capacity building for long term sustainability
SO 5: Invest in research and GMP infrastructure facilitating the R&I (to be financed from Jan Amos Komensky Operational Programme)
SO 6: Improve R&I culture by implementing progressive standards of management

Strategic Goal C: Establish environment and tools for multidimensional knowledge transfer

SO 7: Wide and consolidate centre's ecosystem as a knowledge base for systemic reforms and policymaking
SO 8: Set up industry - research collaboration as a base for knowledge transfer across Europe
SO 9: Develop education and training to make health professionals ready to exploit the full potential of ATMPs

ATMP treatment lifecycle – 6 pillars



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Research Part: WP2

Developing GD2-targeted CAR-modified healthy effector immune cells

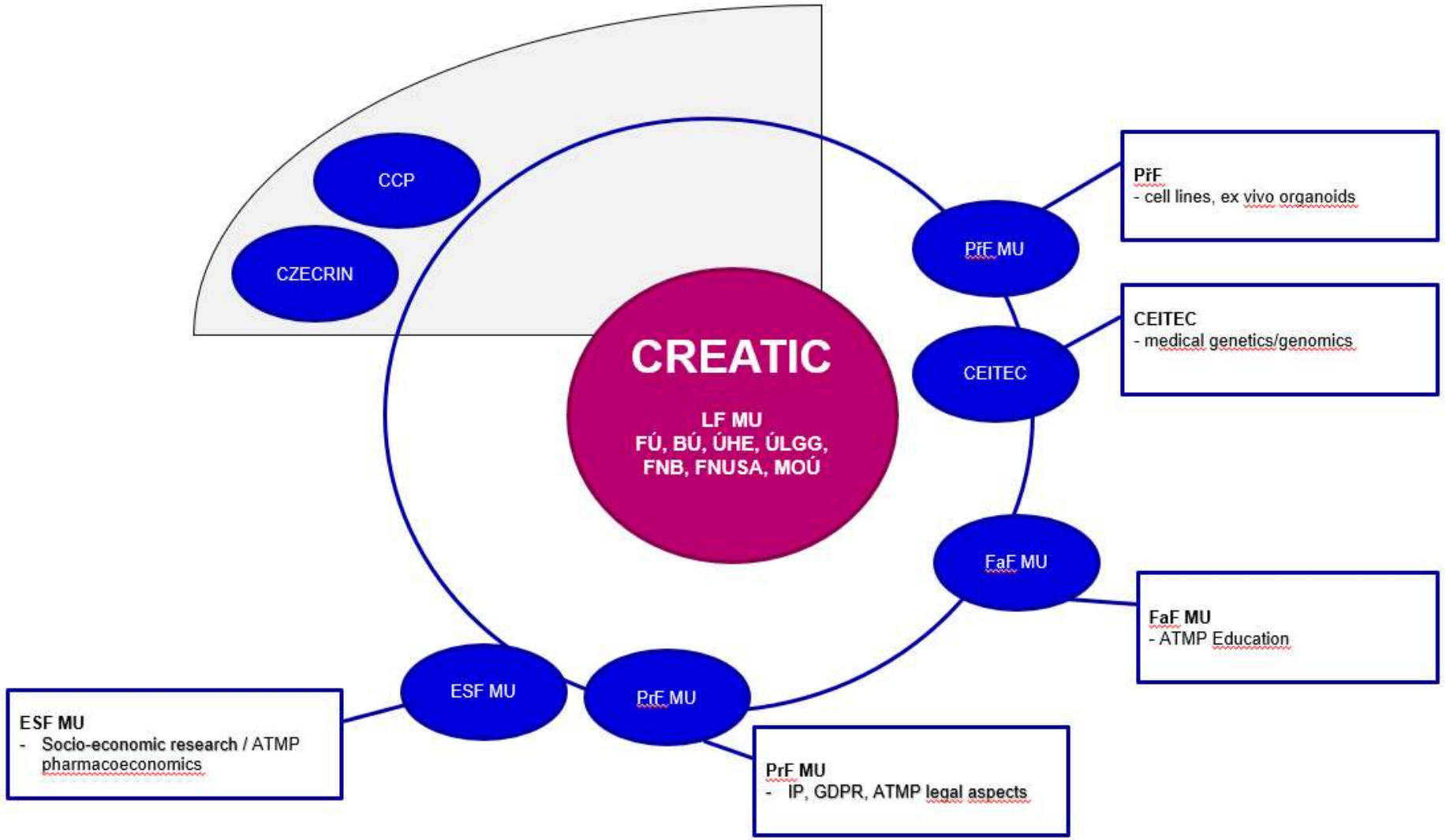
T2.1 Research design and development of GD2 CAR-NK and GD2 CAR-Mφ (Fraunhofer IZI, MU, ULEI)

– ATMP development, targeting research aspects of ▪ source of effector immune cells, i.e. allogeneic donor iPSC (induced pluripotent stem cells), cell line, monocyte for differentiation to Mφ including protocols for manipulation, e.g. isolation, expansion, differentiation ▪ vector (i.e. viral: lentivirus, adenovirus) vs non-viral transposon approach (piggyBac, Sleeping Beauty) ▪ functional studies including cancer-derived *in vitro* organoid testing ▪ the manufacturing process (incl. storage conditions and stability testing) and quality control protocol (incl. QC assay validation) ▪ immuno-monitoring protocol development including single cell NGS

T2.2 GD2 CAR intellectual property rights (IP) research landscape (UCPH, MU, Fraunhofer IZI, ULEI, M1-M60)

– description of the landscape of existing IP and proprietary rights associated with GD2 technologies ▪ mapping of relevant IP, data, and regulatory landscape applicable to the development of GD2 ▪ developing IP, data, and regulatory strategy

MU collaboration



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Platform for Advanced Therapies Implementation

- Engage key stakeholders: patient representatives, regulators, payers, government institutions, research infrastructures,…
- Ensure exploitation of the CREATIC results and co-creation of the specifications for the research activities
- Obtain real-world data to help better understand real and perceived challenges and opportunities for the effective implementation of ATMP innovations.
- Provide systematic identification of actual and perceived obstacles and inconsistencies in applicable laws and policies and national regulatory, pricing and reimbursement systems for ATMPs and orphan diseases

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Cultivating the CREATIC Ecosystem

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Thank you for attention

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