ERN | EuroBloodNet

12th June 2026 - EHA Congress

EU Leadership in Clinical Trials & equitable access to innovative therapies

A strategic contribution to **HLM4RARE Working Group 4 & 7**
Clinical Trials & Early access models

Pierre Fenaux (Assistance Publique-Hôpitaux de Paris, Hôpital Saint-Louis, France)
Eduard van Beers (University Medical Center Utrecht, The Netherlands)

Funded by the European Union

SESSION 1: EU ACTION PLAN FOR RARE DISEASES

PRIORITY ACTION 4 & 7: Foster EU Leadership in Clinical Trials & equitable access to innovative therapies

EUROPEAN PRIORITY FOR RARE DISEASES

HLM4RARE WG4: Foster EU Leadership in Clinical Trials for Rare Diseases through Inclusive Collaboration between Academy, Patient Groups and Industry.

HLM4RARE WG7: Explore new business models and mechanisms to prioritize equitable access to innovative orphan therapies and diagnostics.

CHALLENGES

- Rare disease clinical trials remain fragmented across countries, with barriers in contracting, ethics, referral pathways, data interoperability and site capacity.
- Patients face unequal access to cross-border clinical trials, early access programmes and innovative orphan therapies.
- Europe lacks fast, coordinated and sustainable pathways to translate trial results into regulatory decisions, reimbursement and patient access.

ERN-EUROBLOODNET RESPONSE

Clinical Trials & Research

KEY INITIATIVES

SATISFY, LUSPARA
IMPACT-AML

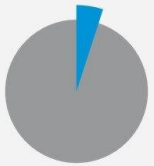
EU ACTION PLAN FOR RARE DISEASES

- WG1 Governance & Action Plan
- WG2 Workforce Development
- WG3 Diagnostics & Early treatment
- WG4 Clinical Trials
- WG5 National Infrastructure
- WG6 Real-World Evidence
- WG7 Equitable access to therapies
- WG8 Funding & Sustainability

Having a rare disease, is the most prevalent disease

7,000

Rare diseases exist and new ones are discovered each year



5% of rare diseases have FDA-approved treatments

80% of rare diseases are inherited

Rare disease affects...

30 million people in the United States

II

1 in 10 Americans

30 million people in the European Union

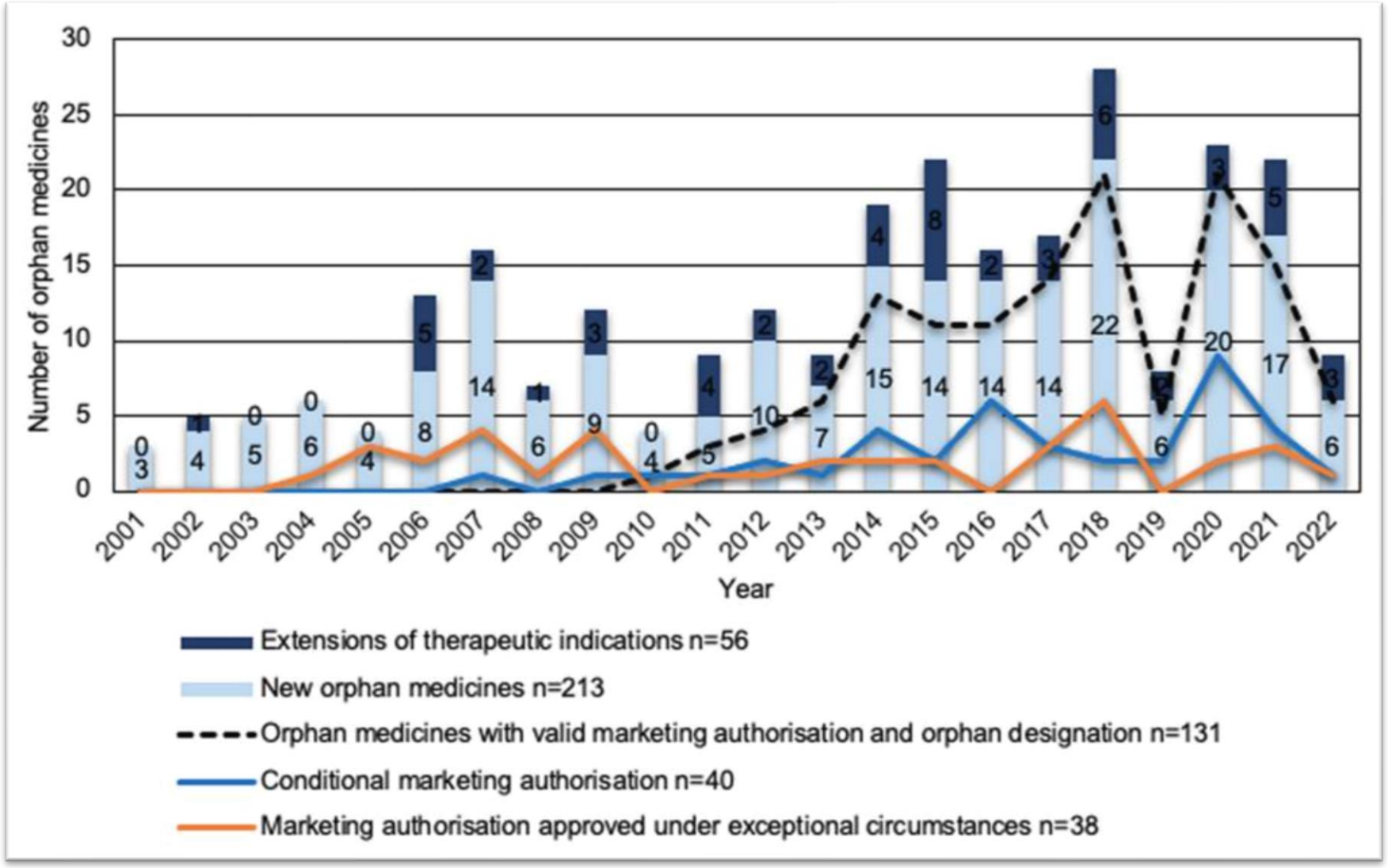
350 million people worldwide

The vast majority of rare disease patients are **CHILDREN**

From: www.chisite.org/blog/equitable-access-to-rare-disease-therapies-workshop
Center for Healthcare innovation

U-TRIAL
WE CONNECT

EMA orphan drug designation does help but, …



Orphanet J Rare Dis. 2025 Jun 2;20:266

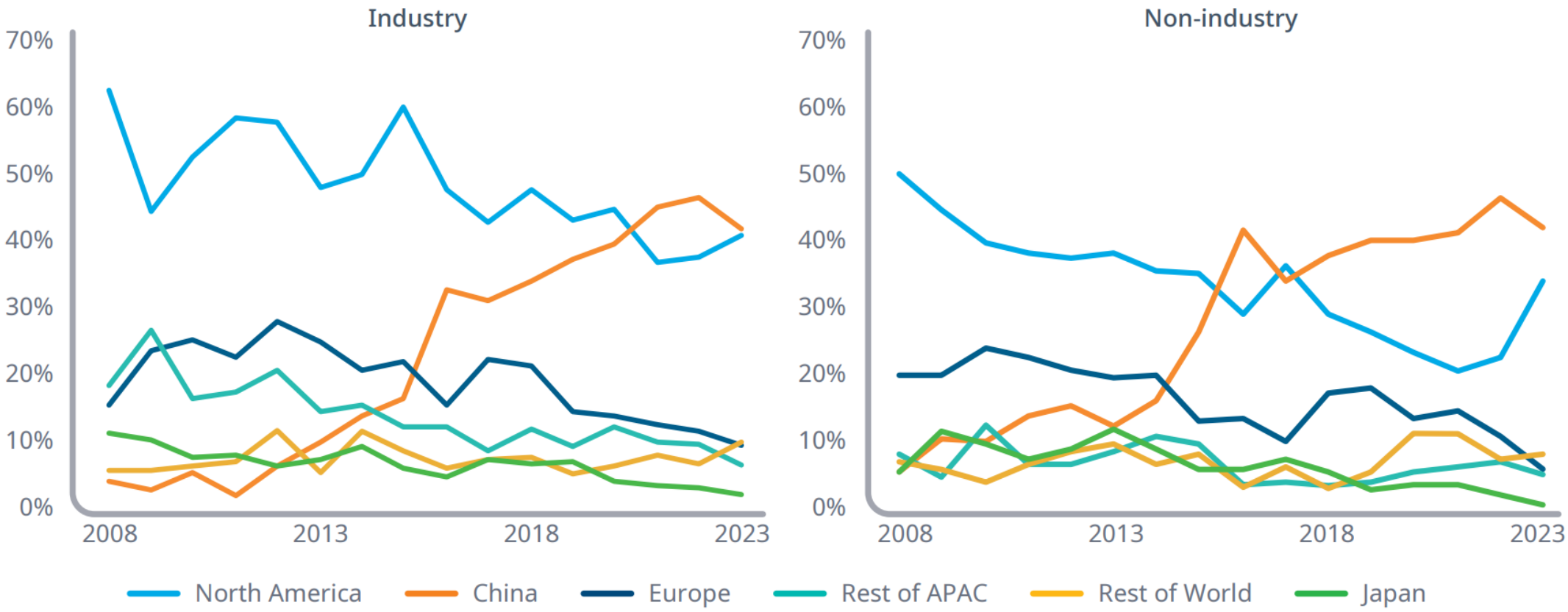
Gene and cell therapy pipeline development

Global Status	Q3 2023	Q4 2023	Q1 2024	Q2 2024	Q3 2024
Preclinical	1,522	1,528	1,471	1,436	1,393
Phase I	256	270	301	314	318
Phase II	267	274	282	279	289
Phase III	30	33	35	34	35
Pre-registration	7	6	4	5	6
Total	**2,082**	**2,111**	**2,093**	**2,068**	**2,041**

Gene, Cell, + RNA Therapy Landscape Report, American Society of Gene & Cell Therapy and Citeline, 2024 Q3 Original report source at https://asgct.org/publications/landscape-report

U-TRIAL
WE CONNECT

Cell and gene therapy clinical trials by region

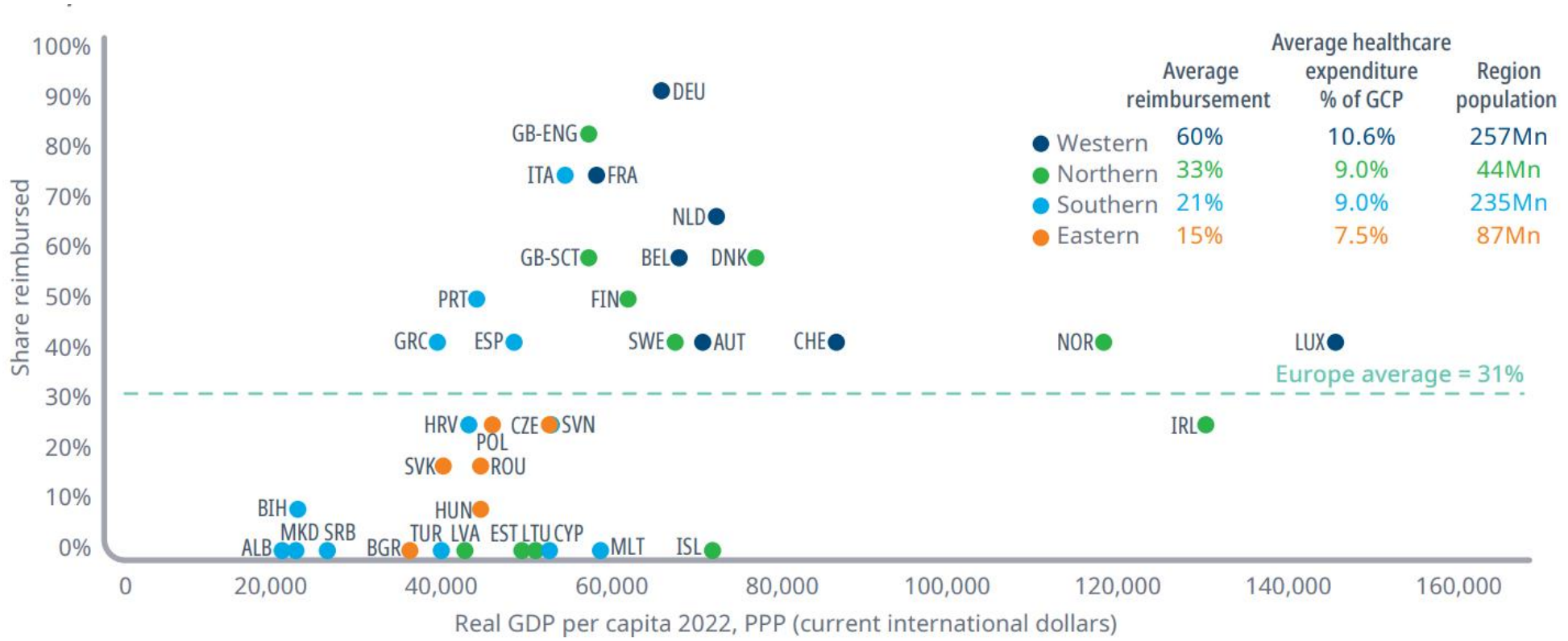


Source: Citeline Trialtrove, Dec 2023; IQVIA Institute, Jan 2024.

U-TRIAL
WE CONNECT

Reimbursement of rare disease drugs in Europe

(Apr 2023)



Source: European Medicines Agency, IQVIA EFPIA Patients W.A.I.T. Indicator 2022 Survey, Apr 2023; International Monetary Fund, Oct 2023; IQVIA Institute, Jan 2024.

U-TRIAL
WE CONNECT

THE CHALLENGE: OPERATIONAL MODEL IS STILL SUBOPTIMAL, ESPECIALLY FOR MULTINATIONAL CLINICAL TRIALS

ERNs are still not systematically financed, governed or recognised as Europe's default rare disease clinical trial networks.

Contracting, budgeting, indemnity, site activation and institutional negotiations still differ widely between Member States and institutions

Rare disease registries and study datasets are still uneven in quality and interoperability

Differences in ethical review practice remain a practical source of delay and inconsistency for cross-border studies

Patient recruitment remains difficult, depending on reliable cross-border referral, registry use, and trial-ready disease networks

Academic or other non-commercial sponsors frequently lack the regulatory, methodological and operational support needed to run multinational trials

Lenghty timelines for approval of rare disease clinical trials in the EU (110 days)

Patients still face practical barriers in referral, information, reimbursement, and travel support that prevent access to cross boarder clinical trials

Potentially viable clinical trials are delayed, reduced in ambition, or never launched at all, with the EU losing competitiveness against the U.S. and Asia

Clinical trials: global map of timelines and regulatory

Executive view 2026. Indicative time to decision / possible start; real start-up may take longer.

Key message: the EU remains slower in multinational trials

Indicative comparison; regulatory clocks do not always reflect the total activation time.

EU
113 days

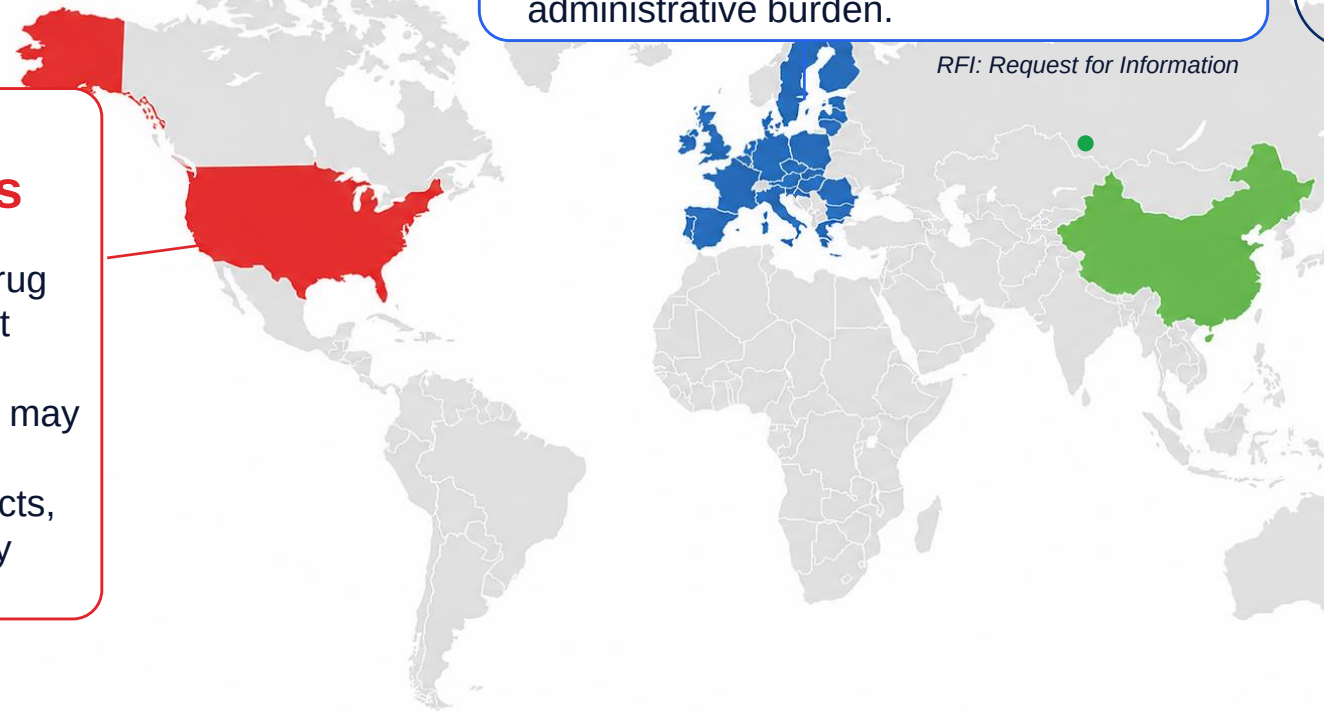
Current average for multinational trials.
Problems: fragmentation across Member States,ethics review + Part II, RFIs, and administrative burden.

RFI: Request for Information

UK
~41 days

Combined MHRA + HRA/REC review benchmark
Problems: NHS contracting, capacity, local set-ip and site activation may delay real start-up

MHRA: Medicines and Healthcare products Regulatory Agency
HRA: Health Research Authority
REC:Research Ethics Committee
NHS: NAtional Health Service



USA
60-47 days

Investigational New Drug (IND): if FDA does not impose
a clinical hold, the trial may start.
Problems: IRB, contracts, and site activation may delay start-up.

IRB: Insitutional Review Board

China
~60* days

Implicit approval CTA pathway; 30-working-day route for selected innovative drugs.
Problems: NMPA/CDE requirements, local coordination and region-specific implementation.

NMPA: National Medical Products Administration
CDE: Center of Drug Evaluation

Sources: COM(2025) 1022 — European Biotech Act proposal; FDA IND framework. USA/China values are indicative regulatory benchmarks; operational start-up may take longer.
EFPIA (European Federation of Pharmaceutical Industries and Associations) de 2024; NMPA Announcement No. 86/2025; NIH ClinRegs China.
Launch of clinical trial reforms - GOV.UK

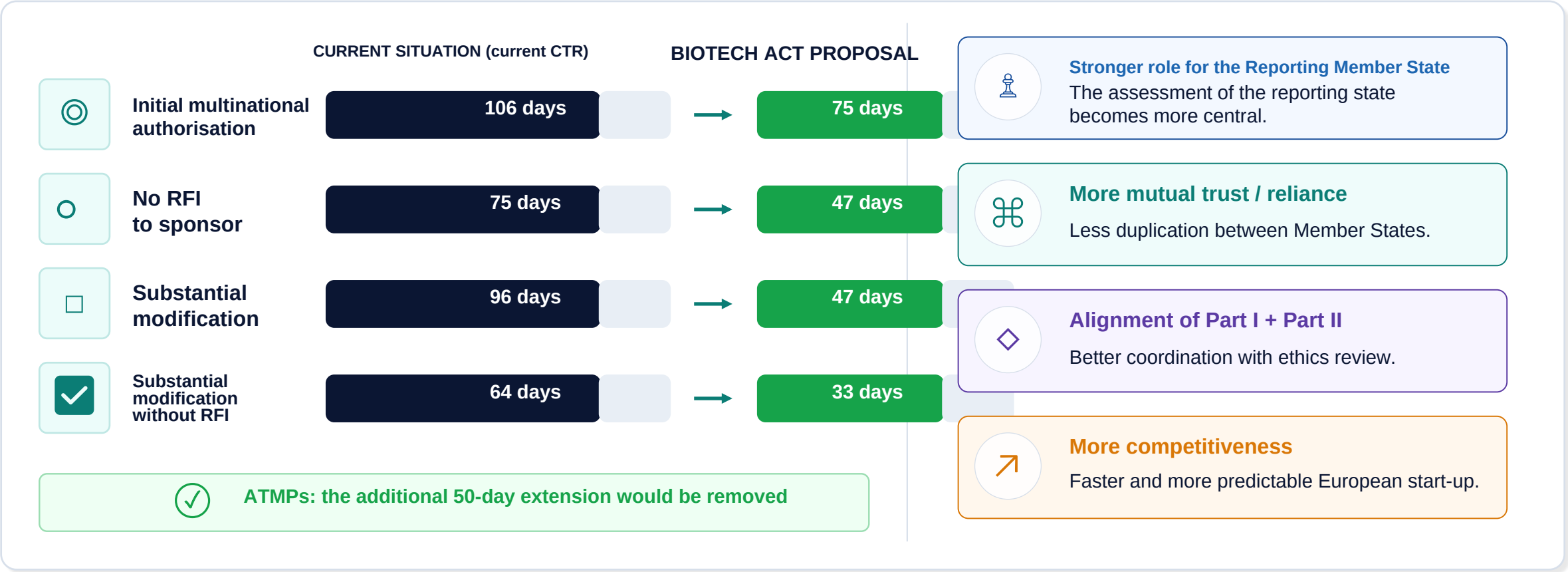
THE OPPORTUNITY: EUROPE NOW HAS THE RIGHT INGREDIENTS

Clinical Trials Regulation	Clinical Trials Information System	Accelerating clinical trials in the EU (ACT EU) initiative	European Reference Networks
Biotech Act and the life sciences agenda	Clinical Research Investment Plan	HTA and early access frameworks	ERDERA
RealiseD	Conect4children	ECRIN's rare diseases clinical trials toolbox	ERDERA/ECRIN multinational trial training programme

How the Biotech Act proposal changes it

Proposed changes to the Clinical Trials Regulation (CTR) to reduce timelines and harmonise the EU

Goal: fewer days, less duplication, more predictability



Base: COM(2025) 1022 — European Biotech Act proposal, p. 27 and CTR recitals. Note: legislative proposal pending approval and implementation.

European Reference Network Hematological Diseases (ERN EuroBloodNet)
Funded by the European Union

WORKING GROUP 4 (WG4) ASPIRATION

Creating an environment that is favourable to attract clinical trials in the EU as well as accelerate translation of trial results to clinical practice, fostering EU leadership in this area

- Incentivise Public-Private partnerships to bring innovative therapies from bench to bedside
- Close collaboration between ERNs and regulatory agencies
- Establish funding mechanisms that reward clinical development in areas of high unmet need as well as implementation of positive trial results
- Harmonise ethical reviews across Member States
- Increase involvement of patient representatives in research strategies design and implementation
- Adopt a risk-based regulatory approach, that includes a fast track approval pathway for rare disease clinical trials

CLINICAL TRIALS: STRATEGIC PRIORITIES UNDER DISCUSSION

4 areas prioritised by the working group

1. Formal recognition and financing of ERNs as clinical trial networks

2. Integration of existing resources (ERNs, ERDERA, RealiseD, conect4children and related infrastructures)

3. Incentives for public-private partnerships dedicated to innovative diagnostics and therapies

4. A risk-based regulatory approach and a faster evidence pathway for rare disease trials

5. Practical challenges of multi-country clinical trials

6. Innovative strategies for improving rare disease clinical trial methodologies

7. Standardisation of collaboration between ERNs and regulatory agencies

8. Access to cross-border clinical trials

EuroBloodNet sponsored clinical trials

- Academic trials differing from industry sponsored trials and large institution sponsored trials
- Often in a field not largely explored by pharma companies
- Close cooperation with a pharma company which provides
  - The study drug
  - research funding
- International (at least 2 EU countries)
- Centralized submission (CTIS)

Funded by the European Union

Eurobloodnet sponsored clinical trials

- EuroBloodNet performs all trial sponsor requirements
  - Submission
  - Drug shipping
  - Data monitoring
  - Pharmacovigilance
  - Publication…
- Currently 2 trials (both in inherited anemias)
  - Satisfy (E Van Beers, A Glenthoj)
  - Luspara (T Leblanc)

Funded by the European Union

SATISFY Phase II trial (NCT05935202) - Mitapivat in hereditary anemias

Funded by Agios | 2 Centers: Rigshospitalet (DK) & UMC Utrecht (NL) | Start date: Dec 2023 | End date: Dec 2026

- Patient Population
  - 29 screened → 24 enrolled: 16 HS, 4 HX, 4 CDAII
  - 96% completed the 32-week core treatment period (23/24)
- Efficacy
  - Hb response (>1 g/dL increase) achieved in 54% of participants
    - 12/16 HS · 1/4 CDAII
  - Mean Hb increase: 1.1 g/dL during the 24-week fixed dose period
- Safety
  - 96% of SAEs were Grade 1–2
  - Most common: headache (54%) and upper respiratory infection (47%)
- Extension & Next Steps
  - 24-month fixed dose extension approved (9 DK + 7 NL patients; up to 212 weeks total)
  - Goals: assess long-term safety/efficacy; maintain patient access to study drug
  - Dissemination:
    - Abstract submission planned for EHA 2026
    - Target publication in a high-impact journal

ERN-EuroBloodNet: **sponsored Clinical Trials**

LUSPARA Phase II trial (NCT07331818) - Luspatercept in rare inherited anemias

Funded by Bristol-Myers Squibb | 6 Centers (France & Italy) | Start date: Jan 2026 | End date: Sept 2029

- Study Design
  - Target enrollment: 45 patients (15 per cohort)
  - Total duration: 42 months
    - Inclusion period: 24 months
    - Treatment period: 52 weeks
    - Follow-up: 6 months
  - Luspatercept administered every 3 weeks
- Participating Centers
  - France (5): Saint-Louis, Robert Debré, CHU Bordeaux, CHU Montpellier, Saint-Vincent de Paul
  - Italy (1): IRCCS Ca' Granda – Ospedale Maggiore Policlinico, Milan
- Current Progress
  - ☑ Regulatory approval received
  - ☑ Most centers open for patient inclusión
  - ☑ First patients recruited and included (2 receiving the treatment, 1 screened).
  - 🔄 Amendment pending to add 2 additional French centers
  - 🔄 Spanish center ready to activate — expansion incoming

ERN | EuroBloodNet

12th June 2026 - EHA Congress

Optimizing Treatment and Assessing Quality of Life for Patients

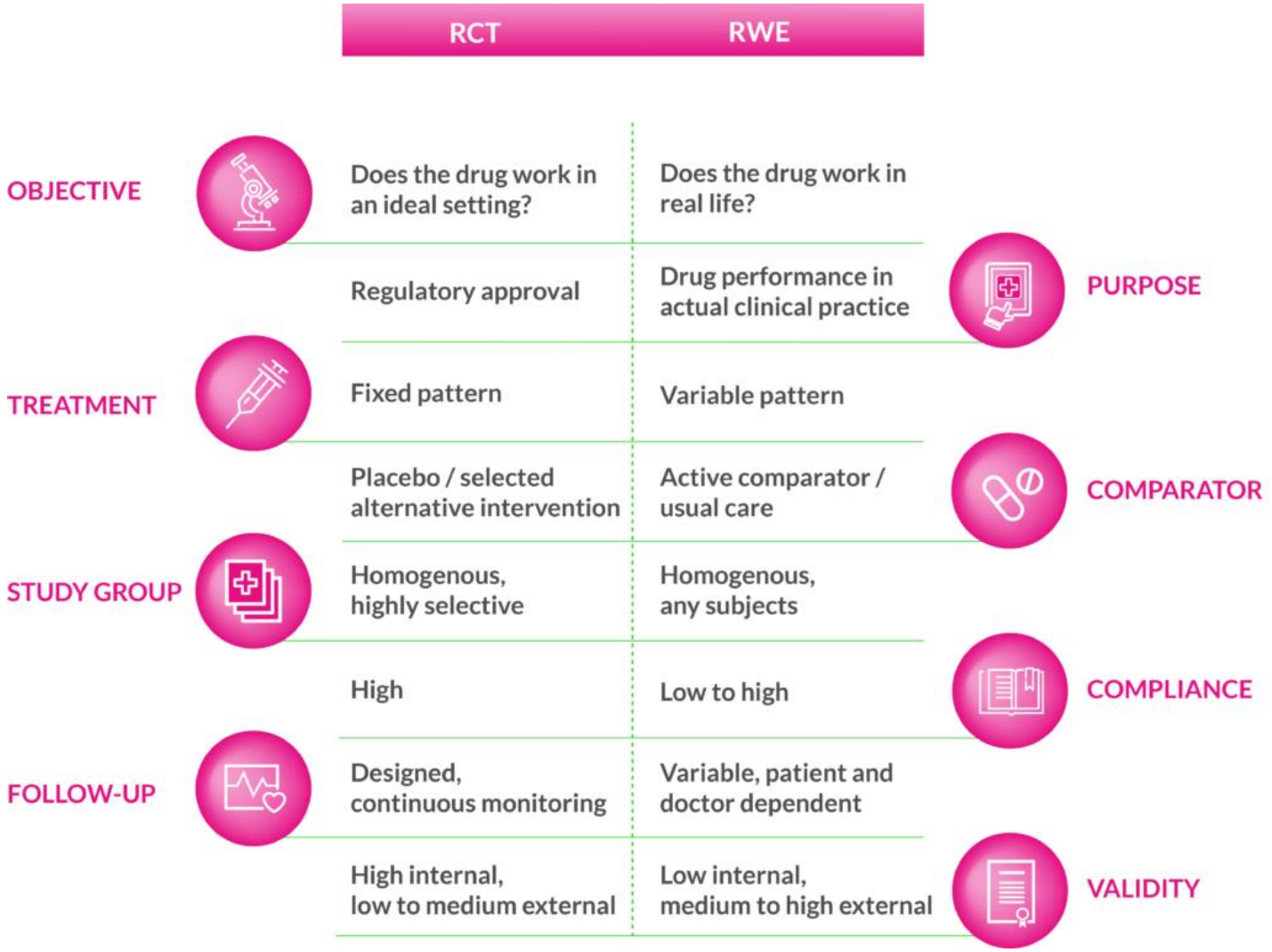
A strategic contribution to **HLM4RARE Working Group 4 & 7**

Clinical Trials & Early access models

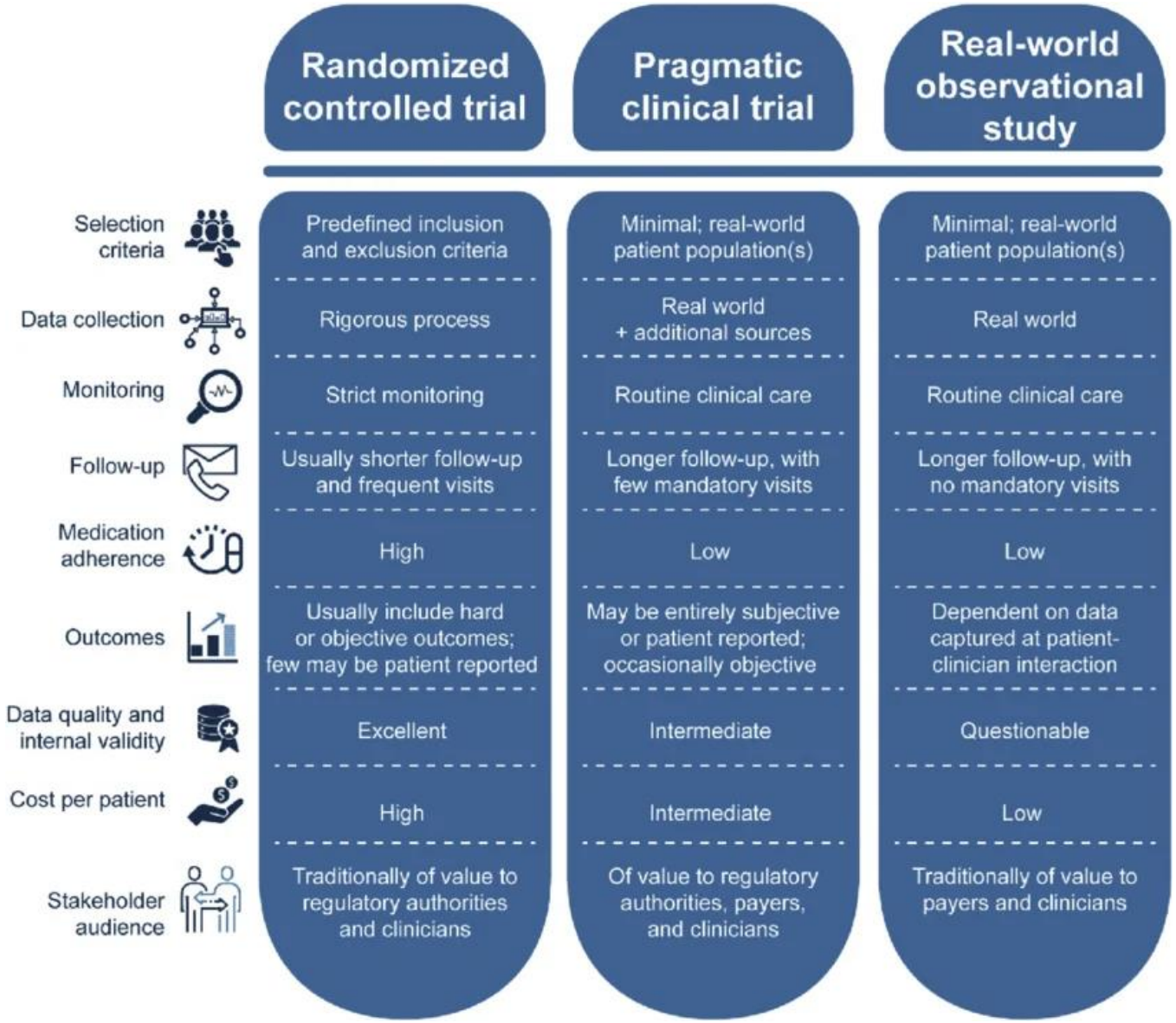
Giovanni Martinelli (University of Bologna Dipartimento di Scienze Mediche e Chirurgiche (DIMEC), Italy)

Funded by the European Union

Randomized Controlled Trials (RCT) Vs. Real World Evidence (RWE)



Reimbursement of rare disease drugs in Europe



THANK YOU!

European Reference Network | Hematological Diseases (ERN EuroBloodNet)

Funded by the European Union