BNDMR
Banque Nationale de Données Maladies Rares

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Enrichir les registres des ERNs – programme ERDERA (European Rare Diseases Research Alliance)

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MINISTÈRE
DE LA SANTÉ, DES FAMILLES,
DE L'AUTONOMIE
ET DES PERSONNES HANDICAPÉES
Liberté
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Improving the health and well-being of 30 million people living with a rare disease by making Europe a world-leader in RD research and innovation.

Diagnosis established or enrolment in systematic research in average **within 6 months** after coming to medical attention

New **effective therapies approved** in Europe and beyond, the majority of which addressing diseases without approved options

Better understanding of the impact of rare diseases on patients, families and society to improve quality of life

ERDERA: Our Global Scale & Investment

Diverse Partnership Network

Our mission is powered by a broad network of nearly **180 organizations from 37 countries**, including:

- Funders
- Research Institutions
- Hospitals
- Research Infrastructures
- Patient Organizations
- Industry Partners

Extensive Global Reach

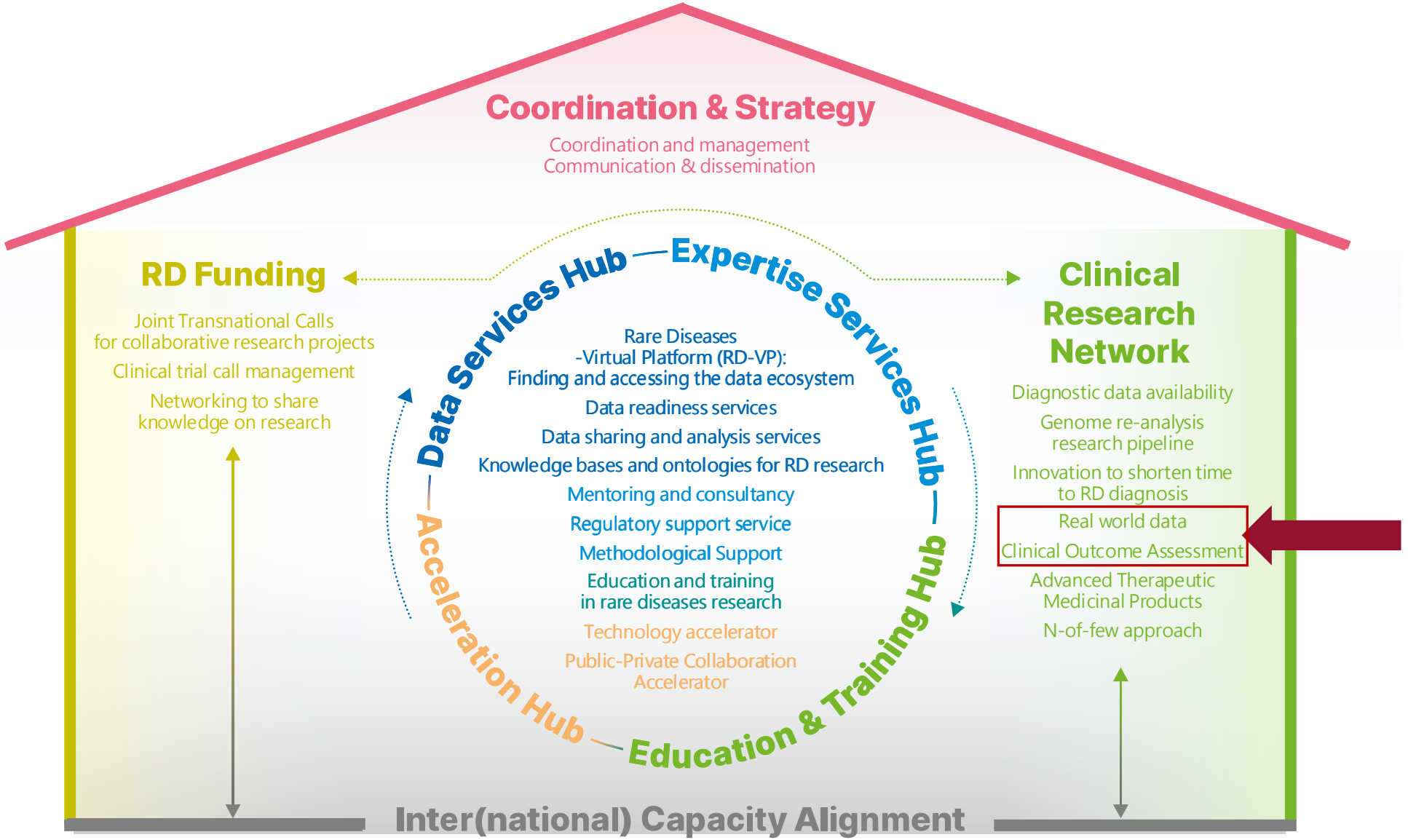
ERDERA spans **25 European Union countries** (except Croatia and Malta) and **numerous associated and non-EU countries**, fostering international cooperation (Australia, Canada, Iceland, Israel, Georgia, Morocco, New Zealand, Norway, Serbia, Switzerland, Türkiye, United Kingdom)

Substantial Financial Commitment

A significant financial commitment underpins our ambitious goals, with a total budget of approximately **€380 million**:

- **€150 million** investment from the European Commission
- Over €230 million contributed by participating countries and institutions
- **Every partner contributes** to our collective actions

ERDERA brings together diverse expertise and significant resources to advance its mission, demonstrating a strong commitment to global collaboration.



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WP9 – Real-World Data Integration and Trial Readiness for Rare Diseases

WP9 operationalises the pathway from real-world data to trial-ready evidence through integration, modelling and regulatory alignment — supporting clinical trial design, external comparators and regulatory decision-making for rare diseases.

ERDERA WORK PACKAGE 9

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WP9 Overview

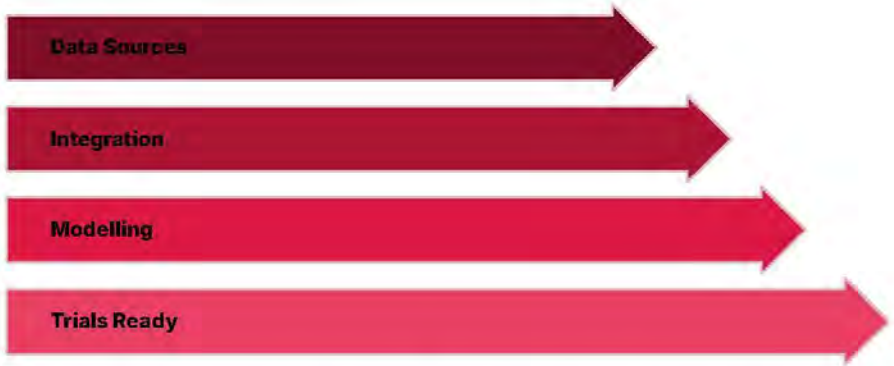
Overall Objectives

- Augment trial readiness of real-world data (RWD) available to ERDERA partners
- Enable generation of robust, integrated, regulatory-grade evidence for rare diseases
- Support clinical trial design, external comparators and regulatory decision-making

Expected Impact

- Improved availability and quality of trial-ready RWD
- Integrated reference cohorts suitable for external comparator use
- Increased regulatory acceptability of registry-based evidence (EMA, PASS/PAES)
- More efficient clinical trial design for rare diseases

The WP9 Logic Line



This logic is implemented across Tasks 9.1–9.6, drawing on ERN registries, national databases, hospital EHRs, the ERDERA Data Services Hub and RDCA-DAP® for trial simulation.

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Task 9.1 – Use of Primary Healthcare Data for RD Outcome Research

Objectives

- Enable reuse of structured and unstructured EHR data for rare disease outcome research
- Improve trial readiness of real-world data
- Establish legal, ethical and technical prerequisites for EHR data extraction

Core Activities

- Extraction and preparation of structured and unstructured EHR data
- Application of Natural Language Processing (NLP) to unstructured records
- Inventory of consent conditions, GDPR and national legal constraints
- Mapping of data elements to ontologies and semantic models
- Validation of extracted EHR data against registry data

Progress

Extraction Approach

Stepwise automated EHR data extraction methodology refined

ERN Engagement

Multiple meetings held with ERN representatives; research questions defined for several HCP duos

Legal & Validation

Legal basis and patient consent verified; validation strategies against registry data defined for selected use cases

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Task 9.2 – Use of Population-Based Data for RD Outcome Research

Demonstrating the use of population-based healthcare and social security data for rare disease outcome research, linked to disease registries for cross-country analyses of care pathways and outcomes.

Dravet Syndrome

National cohorts shared with ERN EpiCARE; regulatory procedures initiated. Data sources: RESIDRAS (Italy), BNDMR & SNDS (France).

Hirschsprung Disease

Variable alignment with ERNICA registry ongoing. Cross-country harmonisation of care pathway data progressing.

Newborn Screening

Generic NBS module implemented in MetabERN's U-IMD registry; governance approvals obtained.

Data integration between BNDMR and SNDS progressed; data access secured via the Dromos project. Regular coordination meetings established.

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Task 9.3 – Integration of Patient Cohorts for Natural History / Standard-of-Care Reference Studies

Objectives & Activities

- Create large, high-quality reference cohorts for future clinical trials
- Integrate national, regional and international patient registries
- Harmonise data dictionaries, variables and consent frameworks
- Establish governance structures and data-sharing agreements
- Technical interoperability via ERDERA data hub services

Progress

Data harmonisation and technical interoperability advanced across registry clusters. Multiple data dictionaries finalised. Governance frameworks and consent alignment actively progressing.

Registry Integration Examples

RASopathies

National registries integrated via ERN ITHACA (ILIAD registry)

Nephrotic Syndrome

PodoNet integrated with ERKReg (ERN ERKNet)

Endocrine & Bone

ENDO-ERN / BOND registries pooled with national datasets (EuRRECa, EuRR-Bone)

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Task 9.4 – Blueprint and Inventory of Regulatory-Grade Natural History Cohort Data

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Objectives

- Establish procedures for academic registries to achieve EMA qualification
- Develop blueprints for regulatory-grade natural history registries
- Create an inventory of registries by regulatory readiness

Core Activities

- Review of existing registries against EMA requirements
- Gap analysis covering governance, data quality, coverage and core datasets
- Blueprint development for selected registries
- Continuous interaction with EMA (CHMP, SAWP)

Blueprint Registries

→ **International Mitochondrial Registry**

→ **International Hereditary Spastic Paraparesis Registry**

→ **CompCure C3 Glomerulopathy Registry (sub-registry of ERKReg)**

→ **Inherited Retinal Dystrophies Registry (REDgistry)**

Inventory of previously EMA-assessed registries established. Gap analysis initiated for all four blueprint registries. Direct dialogue with EMA representatives ongoing.

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Task 9.5 – Disease Progression Modelling and Prognostic Biomarker Research

Objectives & Activities

- Predict individual disease trajectories using real-world data
- Support trial-ready outcome modelling for rare and ultra-rare diseases
- Integrate multimodal clinical and biomarker data
- Develop statistical toolboxes for n-of-1 and n-of-few studies
- Collaborate with WP19 on advanced modelling methodologies

Data Types Used

Clinical Outcomes (ClinROs)

Digital Motor Outcomes

Imaging Data

Genomic & Molecular Biomarkers

Key Registries & Progress

Sickle Cell Disease

RADeep registry (ERN EuroBloodNet) — multimodal datasets aggregated and curated

Spinal Muscular Atrophy

SMArtCARE registry (EURO-NMD) — disease progression models developed and validated

SPAX Diseases

TreatHSP, ARCA, PROSPAX registries — advanced modelling results produced

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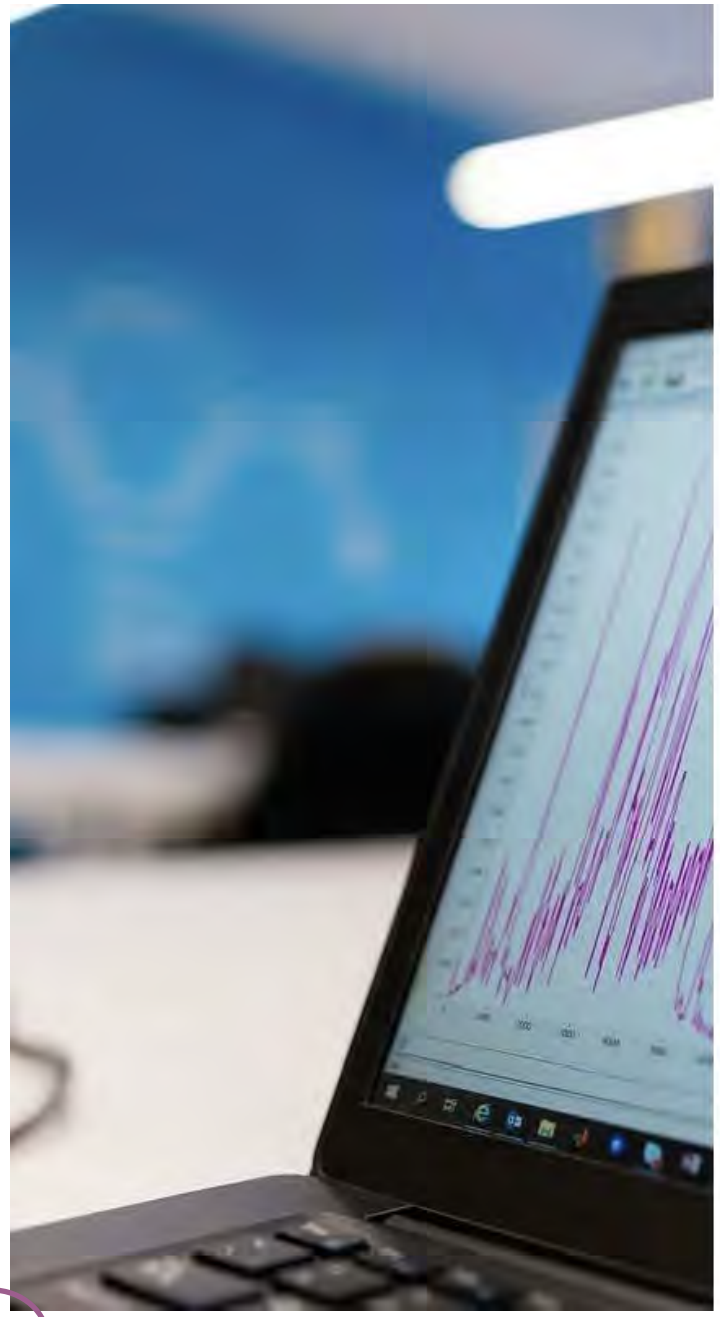

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Task 9.6 – Model-Based Clinical Trial Simulation Platform for Rare Diseases

Objectives

- Develop model-based clinical trial simulation tools for rare diseases
- Improve prediction of treatment effects and trial design optimisation

Core Activities

- Ingestion, mapping and curation of cohort and clinical trial datasets
- Development of Drug Development Tools (DDTs)
- Trial simulation modelling using RDCA-DAP® platform

Progress

1 Legal & Access

Legal frameworks and data access procedures initiated for industry-led and academic trial datasets (ADPKD, DMD)

2 ADPKD Modelling

ERKReg (ERN ERKNet) leveraged for ADPKD cohort modelling and data expansion

3 DMD Interoperability

Semantic interoperability and data mapping advanced; trial simulation models under active development via C-Path RDCA-DAP®

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ERN Registries Maturity Evaluation: Services

17 / 24 ERNs responded

15 / 17 responding ERNs consider themselves ready to provide registry-based services

Services span the research and trial lifecycle, from feasibility to recruitment

Service Portfolio Offered by Mature ERN Registries

Data Collection & Enhancement

- Prospective collection of project-specific data
- Targeted quality improvement and missing data completion

Study & Trial Feasibility

- Aggregated registry data for patient counts and key data availability
- Supports study design for rare populations

Descriptive & Analytical Services

- Retrospective analyses using core data elements
- Extended datasets for longitudinal and outcome modelling

Site & Patient Engagement

- Outreach to clinical centres for trial interest
- Aggregated identification of eligible patients

Key Maturity Characteristics Across ERNs

Structured access committees and approval processes

Consent-based data use and contact mechanisms

Registries positioned as service providers, not just repositories

Mature ERN registries are increasingly able to deliver end-to-end, governance-ready services supporting feasibility, analysis, and trial execution.