European Reference Network
for rare or low prevalence complex diseases

Network Neuromuscular Diseases (ERN EURO-NMD)

7th ERN EURO-NMD ANNUAL MEETING

Connecting the dots in the rare diseases research ecosystem: The European Rare Diseases Research Alliance (ERDERA)

21st – 23rd February 2024

Yanis Mimouni

INSERM

Funded by the European Union

ERDERA

EUROPEAN **RARE DISEASES** RESEARCH ALLIANCE

2024 – 2034

ERDERA proposal **was approved under Horizon Europe** on 25/01/2024 for funding under the EU Research & Innovation funding programme Horizon Europe as a co-funded partnership between the European Commission, European Member States, and beyond.

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EUROPEAN RARE DISEASES RESEARCH ALLIANCE

Open until 01/03/2024

Go to: **menti.com**

Enter the Code: **3924 6281**

Or click on this link: https://www.menti.com/alp99pd71yud

Planned activities

How could they be best performed?

What should they consider?

How could your current and upcoming activities be linked (to them)?

You feedback will be processed.

The details will be exploited for preparing ERDERA launch & activities implementation.

Please provide details & links

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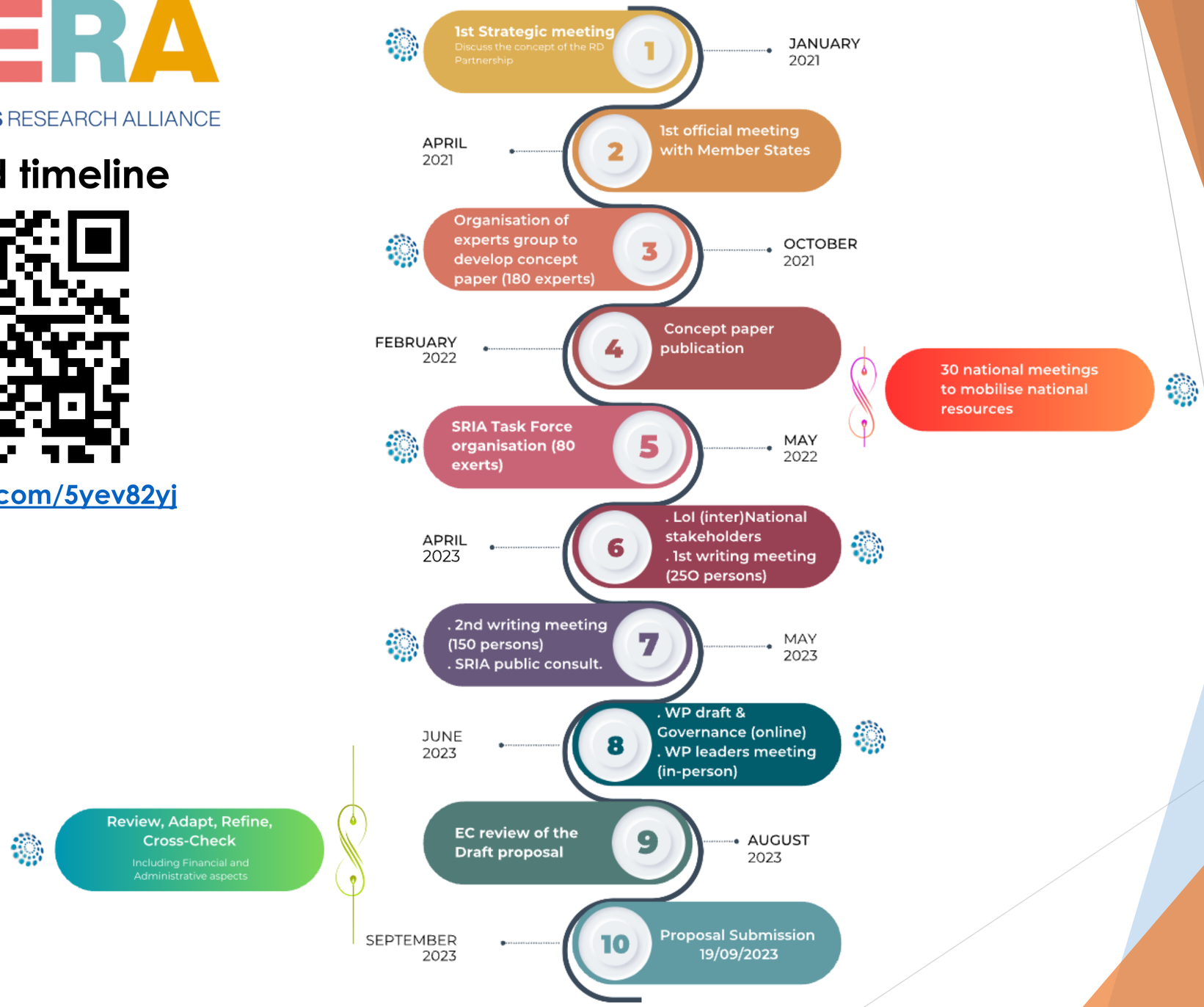
EUROPEAN **RARE DISEASES** RESEARCH ALLIANCE

Detailed timeline

https://tinyurl.com/5yev82yj



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EUROPEAN **RARE DISEASES** RESEARCH ALLIANCE

171
Organisations*

38 funders

115 research performing organisations

12 patients' organisations

3 research infrastructures

27 private for-profit partners (industry & SME)

**Some organizations belong to more than one category*

7
International Organisations

1

1

2

5
European Organisations

36 Countries

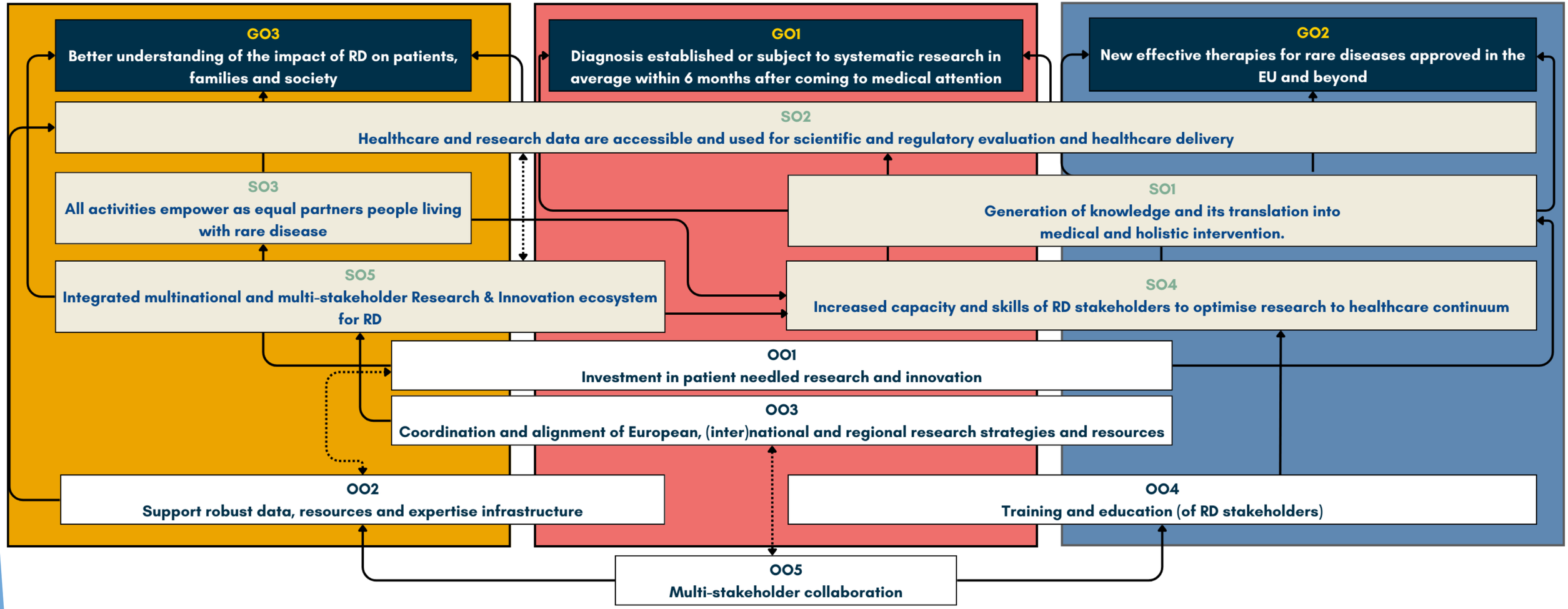
26 EU member states

7 associated countries

3 non-EU

PARTNERSHIP SPECIFIC IMPACT PATHWAYS

VISION: To improve the health and well-being of 30 million persons living with a rare disease in Europe, by making Europe a world leader in RD research and innovation, and delivering concrete health benefits to rare disease patients, through better prevention, diagnosis and treatment.



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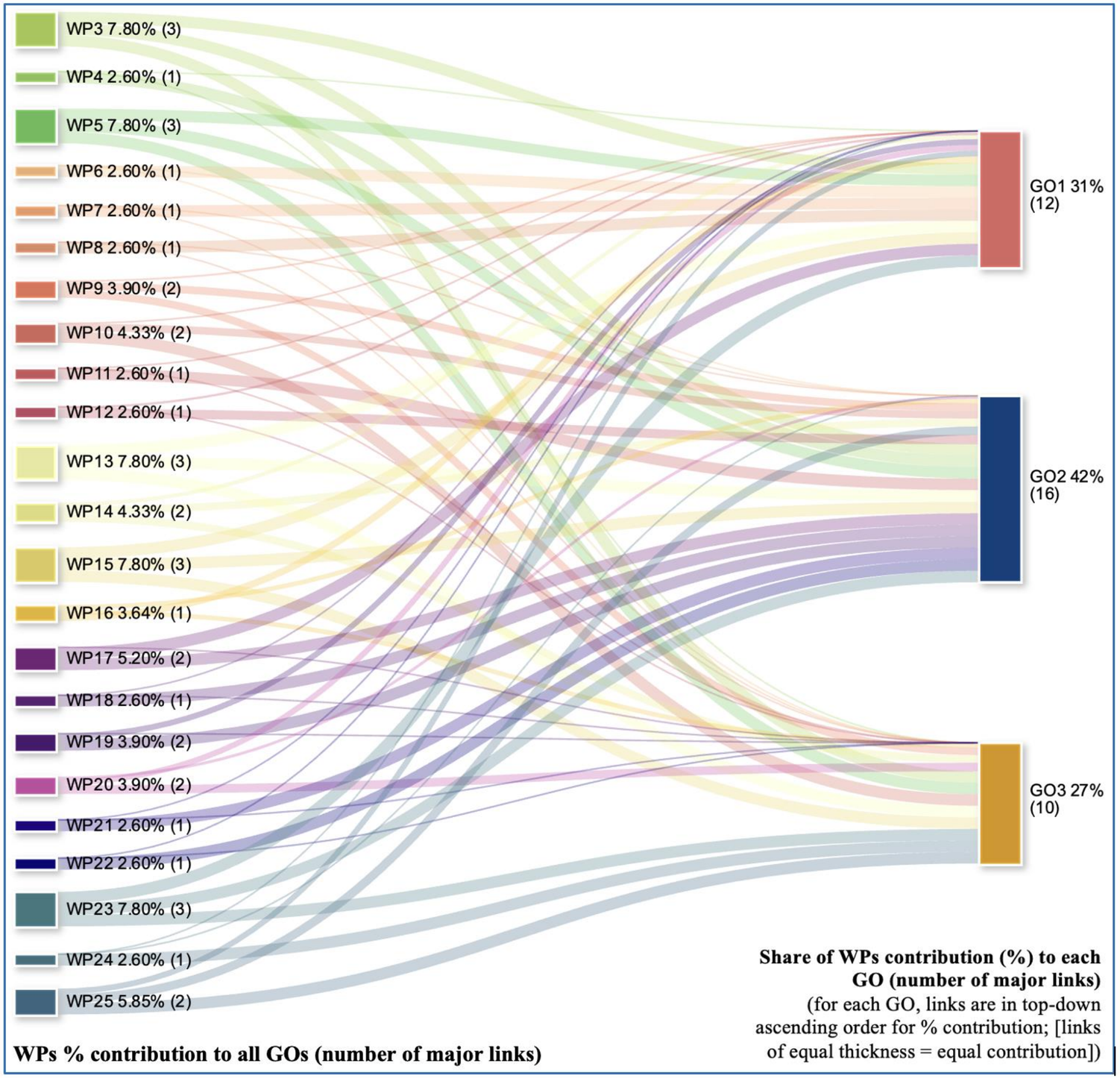

Diagnosis established or enrolment in systematic research on average within 6 months after coming to medical attention (in EU and Associated countries)

New effective therapies for rare diseases approved in the EU and beyond

Better understanding of RD impact on patients, families and society

Work Package relative contribution to the General Objectives based on the number of tasks involved

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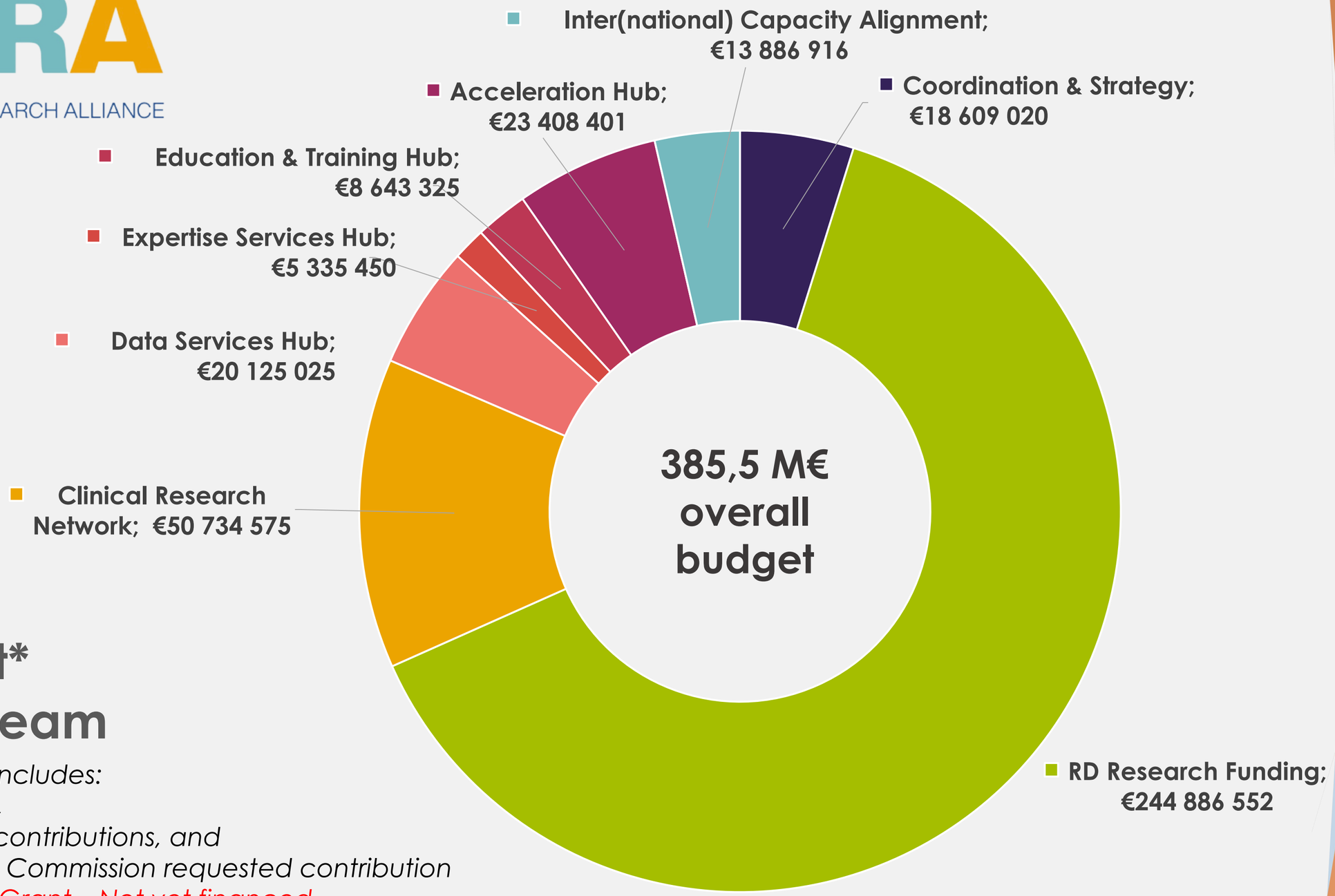

Total Budget* per Work Stream

**estimated for 7 years, includes:*
(1) associated partners,
(2) in-kind and in-cash contributions, and
(3) 160 M€ of European Commission requested contribution

Submitted Grant – Not yet financed

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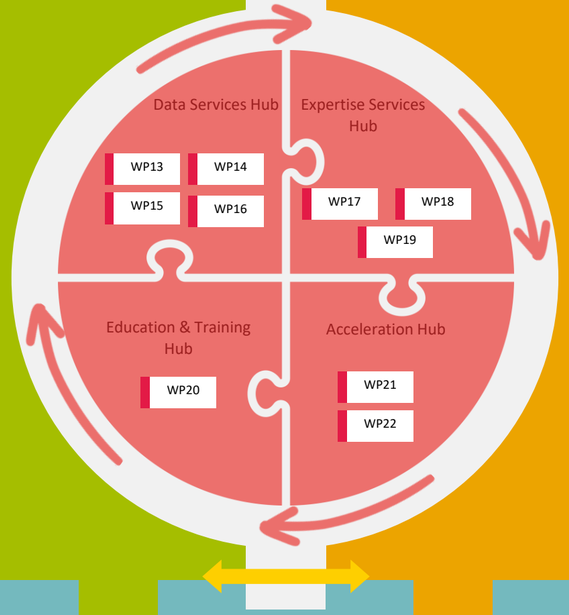

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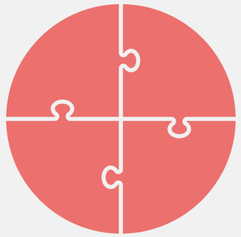

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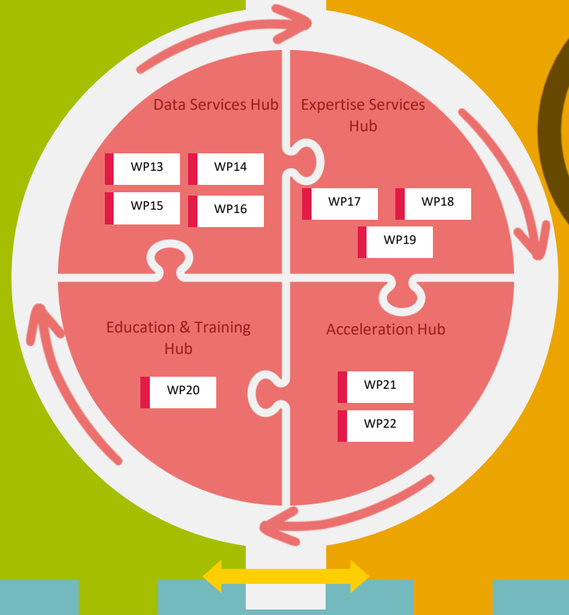

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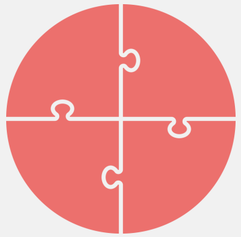

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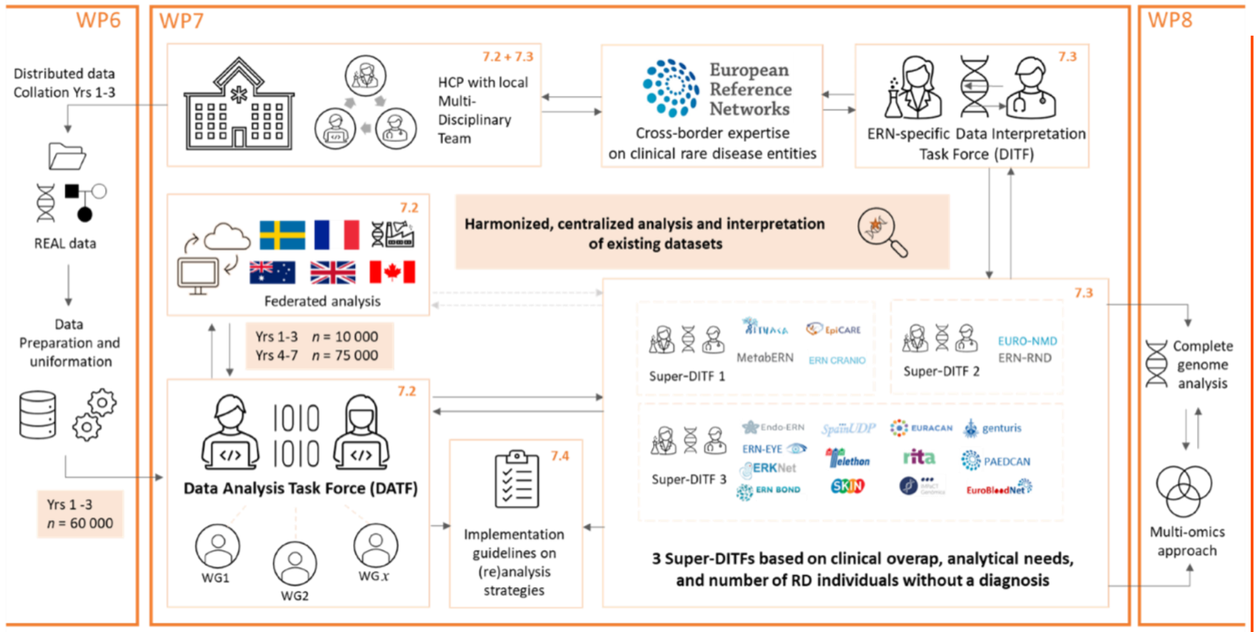
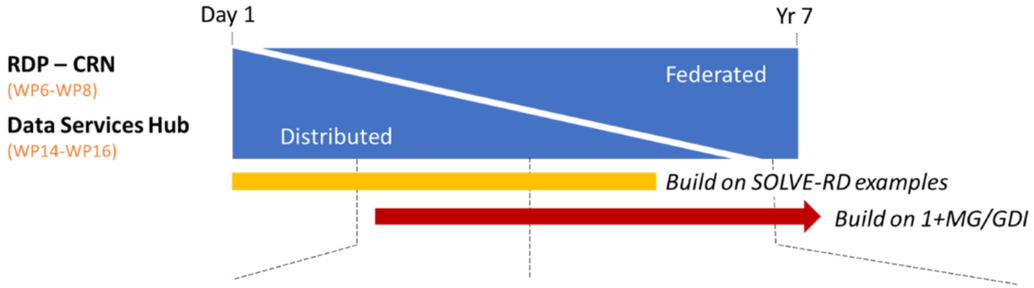
CRN: Diagnostic Research workstream

Diagnostics workflow



Moving towards federation



Accelerate diagnosis through Distributed approach (Phase I)
- → Upload phenotype + data
- → Coordinated analysis
- → Coordinated interpretation together with submitters for feedback to patients

For: local HCPs without infrastructure or bioinformatic support

Accelerate diagnosis through Distributed approach (Phase II)
- → Provide analytical tools & interpretation guidelines
- → Local analysis
- → Local interpretation
- → Share results with ERDERA

For: local HCPs without infrastructure or bioinformatic support

Accelerate diagnosis through Federated approach
- → Access to data in other centres
- → Local & federated interpretation
- → Share results with ERDERA

For: National programs and industry from the start, and allowing for scalability to local HCPs later in project

CRN: Analysis + interpretation incl. tool development
Data Hub: compute services and data platforms

CRN: Analytical + interpretation support incl. tool development
Data Hub: Operational/Deployment aspects
Intrastructure for Data Access: 1+MG / GDI

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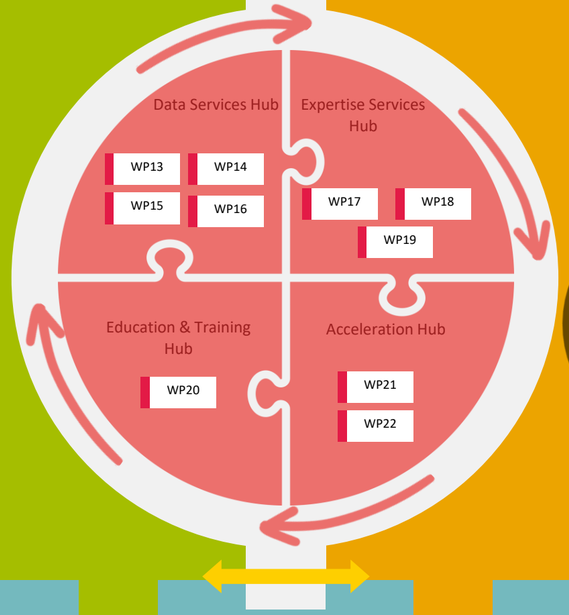

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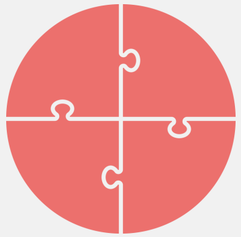

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CRN: Outcome Research workstream _ Involvement of ERNs

	9.1	9.2	9.3	9.4	9.5	9.6	10.1	10.2
BOND			x					
CRANIO	x						x	
ENDO			x					
EpiCare	x	x					x*	x
ERKNet			x	x		x		x
ERNICA		x						
EURO-NMD / DDF	**x**				**x**	**x**	**x***	**x**
RND				x	x		x*	x
EuroBloodNet	x			x	x		x	x
eUROGEN	x							
EYE				x			x*	
ITHACA			x				x	
MetabERN		x					x*	

*** Mito-InterERN workgroup**

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EUROPEAN RARE DISEASES RESEARCH ALLIANCE

CRN: Outcome Research workstream

Real World Data

- **Task 9.1 –** Use of primary healthcare data (EHRs) for RD outcome research
- **Task 9.2 –** Use of population-based data for RD outcome research
- **Task 9.3 –** Integration of patient cohorts for natural history / standard-of-care reference studies
- **Task 9.4 –** Blueprint and inventory of regulatory-grade natural history cohort data
- **Task 9.5 –** Disease progression modelling and prognostic biomarker research
- **Task 9.6 –** Development of a regulatory grade clinical trial simulation platform for rare diseases

CRN: Outcome Research workstream _ Real World Data

T9.1: Use of primary healthcare data (EHRs) for RD outcome research

Extraction of structured and unstructured data from electronic health records (EHRs) for registry/research re-use

- **Studied Disease Groups:**
  - Urogenital and craniofacial anomalies, neuromuscular disorders, encephalopathic epilepsies, mitochondrial diseases, rare anaemias
- **Multi-Site Process:**
  - Involvement of EHRs from multiple **HCPs**, with various data **platforms** (commercial and internal) and different **languages**
- **Benchmarking:**
  - **Comparison of different solutions** on a common set of manually annotated EHRs in different languages
- **Automated Extraction:**
  - Demonstration of **automated EHR extraction** for each site.

CRN: Outcome Research workstream _ Real World Data

T9.1: Use of primary healthcare data (EHRs) for RD outcome research

Workflow:

Obtaining Institutional Approvals:

- Institutional approval and data use conditions for EHR data extraction

Data Pseudonymization:

- Data pseudonymization and determination of the level of anonymity

Data Compilation:

- Compilation of structured and/or unstructured data elements to be extracted

Ontological Mapping:

- Implementation of mappings to existing ontologies and semantic models, starting with "Common Data Elements"

Using NLP:

- Creation of structured output forms from unstructured texts using natural language processing (NLP) methods
  and **evaluation of their usefulness by clinical domain experts**

CRN: Outcome Research workstream _ Real World Data

T9.5: Disease progression modelling and prognostic biomarker research

Aim: To develop and apply innovative methodologies for disease progression modelling in RDs

Spastic Ataxias (SPAX):

- Use of longitudinal multimodal datasets established in task 9.3
- Innovative Statistical Toolkit for predicting individual/group disease progression based on clinical profiles and biomarkers
- Simulation of treatment-induced variations to set stage for innovative n-of-1 and n-of-few therapeutic trials (WP12)

Sickle Cell Disease:

- Risk modelling to improve disease characterization and health status monitoring, personalize therapeutic approaches, optimize health outcomes
- Multimodal Data Analysis: metabolomic, genomic, and radiomic data

Spinal Muscular Atrophy:

- **SMArtCARE registry: longitudinal data from patients treated with one of the three approved drugs**
- **Model SMA disease trajectories and test reproducibility of clinical trial outcomes in real-world context**

Methodological Support:

- ERDERA's modelling expert group (WP19)
- **Extension of EJP RD work on individual disease prediction**, uncertainty quantification, **simulation of treatment-induced variations**

CRN: Outcome Research workstream _ Real World Data

T9.6: Development of a model-based clinical trial simulation platform for RDs

Aim: Demonstrate development of **Drug Development Tools (DDTs)** that will improve understanding of RD progression patterns
and help predict more rapidly, with greater certainty and at lower cost, the efficacy and safety of new drugs

Prediction Models:

- **Combine natural history data and data from previous clinical trials to develop prediction models that can simulate the effects of therapeutic interventions on clinical endpoints** and **estimate required number of subjects**, **using conventional trial methodologies and small population approaches**

Data Modelling: on C-Path RDCA-DAP platform

Formal Review and Regulatory Endorsement:

- Develop strategy for formal review and potential regulatory approval of disease progression models based on quantitative methods and/or artificial intelligence as DDTs

Therapeutic Areas (selected based on their advanced stage for regulatory qualification and initial modelling experience):

- **Duchenne Muscular Dystrophy (DMD)**
- Autosomal Dominant Polycystic Kidney Disease (ADPKD)

CRN: Outcome Research workstream _ Real World Data

T9.6: Development of a model-based clinical trial simulation platform for RDs

Transcontinental Collaboration:

- For ADPKD: ERKNet registry cohort of over 3,000 patients, C-Path, and US-based PKD Outcome Consortium will undertake transcontinental collaboration to develop a globally applicable PKD progression model towards regulatory maturity as a DDT.

Modelling Expertise:

- The **experience of the Duchenne Data Foundation in innovative machine learning methods** and **C-Path's expertise in developing quantitative solutions** will be **combined** to generate an **enhanced Clinical Trial Simulation (CTS) tool for DMD**.

Extension to other Diseases:

- Modelling expertise generated in ADPKD project for modelling loss of glomerular function (eGFR) will also be considered for other progressive rare kidney diseases with a therapeutic perspective for which high-quality Real-World Data is available.

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EUROPEAN RARE DISEASES RESEARCH ALLIANCE

CRN: Outcome Research workstream

Clinical Outcome Assessment

- **Task 10.1** – Platform for development and validation of regulatory-grade patient-centred COA
- **Task 10.2** – Development and Implementation of Clinical Outcome Assessment Tools
- **Task 10.3** – Unveiling the Hidden Burden: Estimating the Socioeconomic Impact of Rare Diseases for Informed Decision Making and Resource Allocation

T10.1: Platform for development and validation of regulatory-grade patient-centred COA

Patient-centred multi-stakeholder process to develop patient-reported outcome (PRO) assessment tools and evaluate patient relevance of top-ranked clinical outcome assessment (COA) tools for five rare disease groups: HSP/ataxia [RND], RASopathies [Ithaca], rare anaemia disorders [EuroBloodNet], craniofacial anomalies [CRANIO], mitochondrial diseases [5 ERNs]

- **Establishing Reference Data Sets Coded According to International Classification of Functioning (ICF)**

- **Matching with Existing PROMs**
  Match ICF-coded functional impacts with appropriate existing patient-reported outcome measures (PROMs)
  (Collaboration with ERICA)

- **Validation of PROMs in at least three European languages**
  Establish sensitivity to change, meaningful change to the patient, and equivalence between languages

- **Anchoring Studies for COA Candidates:**
  Establish relevance of top-ranked COA candidates to patients

T10.2: Development and Implementation of Clinical Outcome Assessment Tools

Development of methodologies to collect and implement data from Patient-Centred Outcome Measures (PCOMs) related to patient registries, considering legal, technological, and regulatory requirements, and validation in 4 case studies using mobile health solutions and devices for rare neurological, neuromuscular, renal, and haematological disorders.

- **Study Protocol Development:** Collect clinical and technical requirements from end-users and standardize data (Collaboration with WP13)
- **Identification of Mobile Apps and Devices** and assessment of their research readiness (Collaboration with WP14)
- **Clarification of Regulatory Aspects,** including privacy and security protections in mobile health (Collaboration with WP18)
- **Development/Adaptation of Mobile Health Solutions** for use with patient registries (Collaboration with ERN Registries)
- **Execution of Clinical Studies**
- **Validation of Patient-Generated Data**
- **Development of a Data Visualization Framework**

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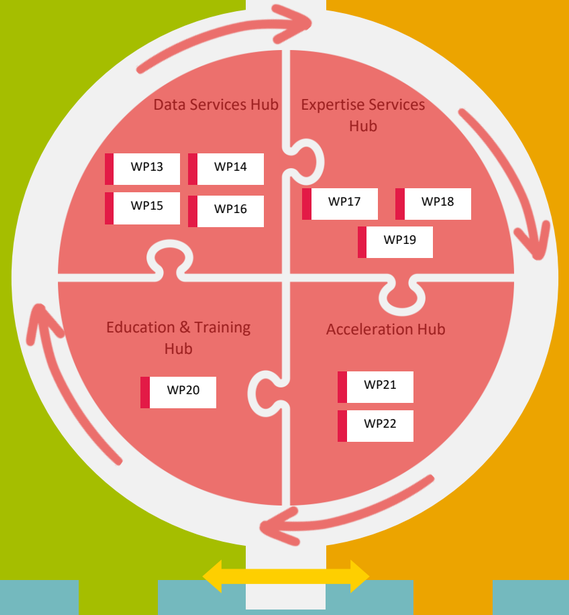

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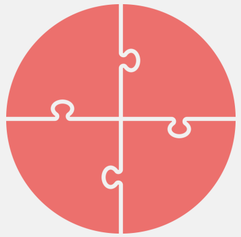

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FUNDING

ERA4Health Partnership

PerMed

European Directory of Registries (ERDRI.dor)

Central Metadata Repository (ERDRI.mdr)

ERDRI

Search Broker (ERDRI.sebro)

SPIDER

EOSC

The European Open Science Cloud

EOSC-Life

DATA SERVICE HUB

Global Alliance for Genomics & Health

Collaborate. Innovate. Accelerate.

DARWIN EU

ACCELERATION HUB

INNOVATIVE SME

innovative health initiative

EHDS

HealthData@EU Pilot

JARDIN

European Genomic Data Infrastructure

RARE DISEASE MOONSHOT

SCALING UP PUBLIC-PRIVATE PARTNERSHIPS TO ACCELERATE RESEARCH IN RARE DISEASES

eit Health

THCS

TRANSFORMING HEALTH AND CARE SYSTEMS

SCREEN 4CARE

EDUCATION & TRAINING

CLINICAL RESEARCH NETWORK

Thank you

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