Personalised Medicine
Rare Diseases

DG Research and Innovation

Rare diseases activities at EU level

Research and Innovation

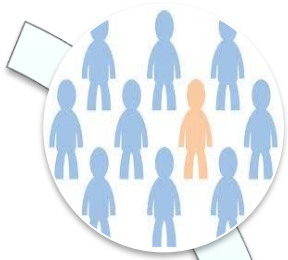
Coordination of research

National plans, information, codification, patient registries, access to best care and knowledge

EU funded rare diseases research

Research priorities

Activities



R&I funding

Over € 1 billion in more than 200 projects in FP7 and H2020 on: pathophysiology, natural history, delivered new diagnostics and therapies

Rare diseases

Linking major EU and national initiatives

E-RARE: research funders collaboration: more than € 90 million in more than 100 projects
www.erare.eu

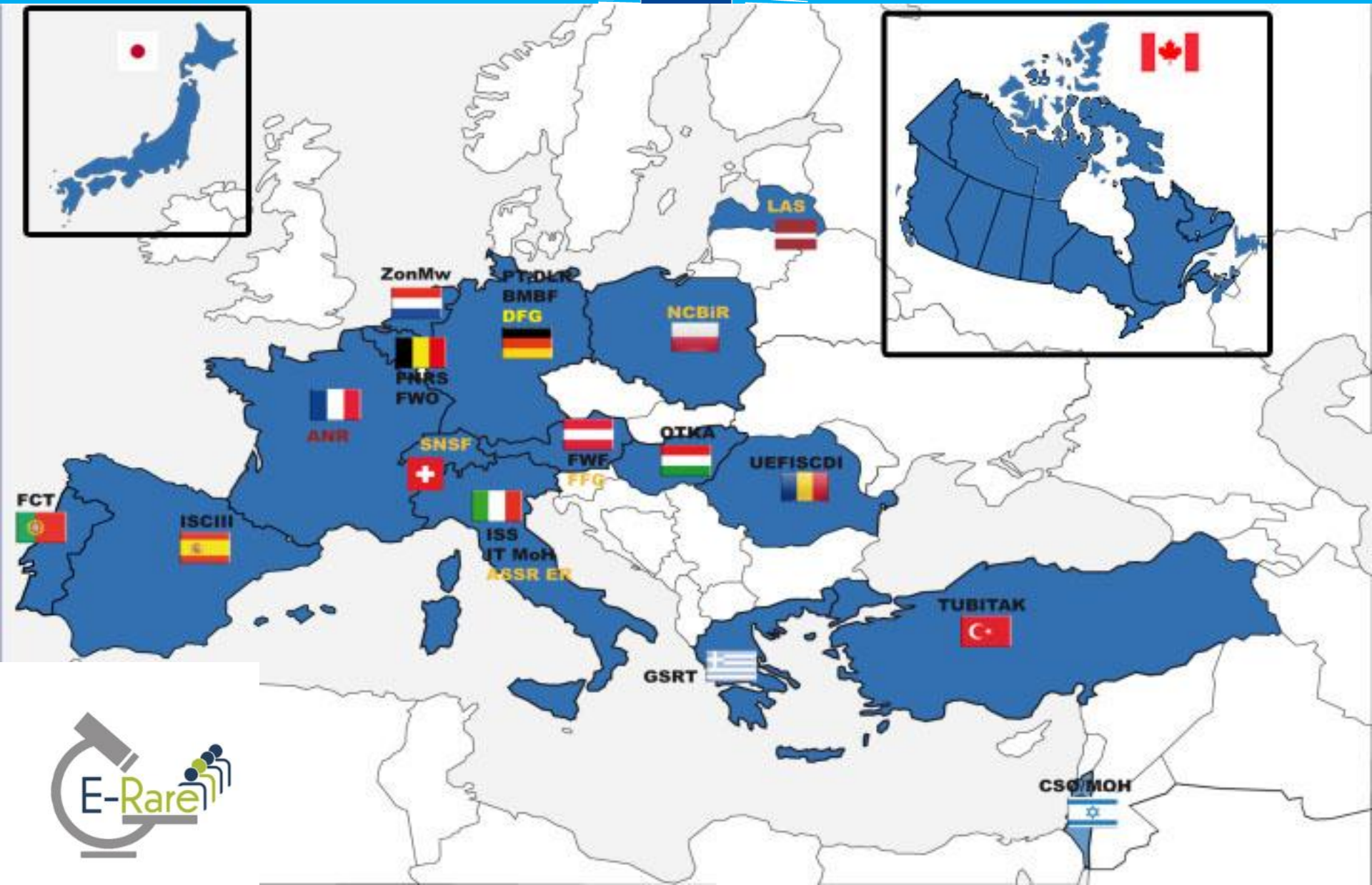
International coordination: IRDIRC

IRDIRC: Updated goals for 2027: diagnosis within 1 year, 1000 new therapies, methodologies to measure impact on patients: >50 international partners, policies and guidelines to implement goals
www.irdirc.org

Research and Innovation

E-Rare-3 beyond Europe

26 partners
18 countries



Australia
- **Western Australian Department of Health**

Belgium
- **EORTC**

Canada
- **Canadian Institutes for Health Research**
- **Genome Canada**

China
- **BGI**
- **Chinese Rare Disease Research Consortium**
- **WuXi Apptec**

EU
- **European Commission**

Finland
- **Academy of Finland**

France
- **French Association against Myopathies**
- **Agence National de la Recherche**
- **Lysogene**
- **French Foundation for Rare Diseases**

Georgia
- **Children's New Hospital Management Group**

Germany
- **Federal Ministry of Education and Research**

Italy
- **Italian Higher Institute of Health**
- **Telethon Foundation**
- **Chiesi Farmaceutici**

International Consortium
- **E-RARE 3 Consortium**

Japan
- **Japan Agency for Medical Research and Development**
- **National Institutes of Biomedical Innovation, Health and Nutrition**

Republic of Korea
- **Korean National Institute of Health**

Netherlands
- **The Netherlands Organization for Health Research and Development**
- **BioMarin Nederland**

Kingdom of Saudi Arabia
- **Saudi Human Genome Project**

Spain
- **National Institute of Health Carlos III**

UK
- **National Institute for Health Research**

USA
- **Food and Drug Administration Orphan Products Grants Program**
- **Isis Pharmaceuticals**
- **National Human Genome Research Institute (NIH)**
- **National Center for Advancing Translational Sciences(NIH)**
- **National Cancer Institute (NIH)**
- **National Eye Institute (NIH)**
- **National Institute of Neurological Disorders and Stroke (NIH)**
- **National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIH)**
- **National Institute of Child Health and Human Development (NIH)**
- **NKT Therapeutics**
- **Office of Rare Diseases (NIH)**
- **PTC Therapeutics**
- **Sanford Research Institute**

International Pharma Companies
- **Genzyme (Sanofi)**
- **Shire**
- **Pfizer**
- **Roche**

Patient organisations EURORDIS, NORD, Genetic Alliance

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Projects for Policy (P4P) Report on Rare Diseases

CURRENT POLICY CHALLENGES

PORTFOLIO OF EU-FUNDED PROJECTS

IMPACT AND RESULTS OF EU FUNDING

POLICY RECOMMENDATIONS

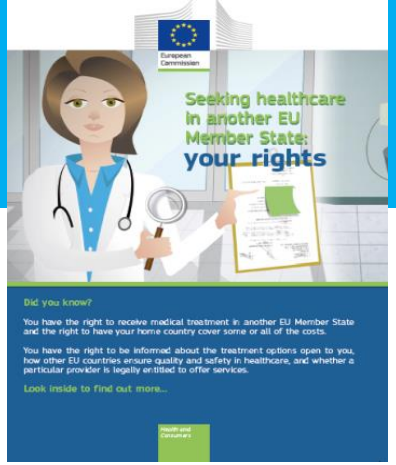
https://ec.europa.eu/info/research-and-innovation/p4p_en

Need for a coherent strategy – from research to patient to research

- More efficiently bring the results of research and innovation to the patient
- Programme to implement a research and innovation pipeline, from bench to bedside
- Integrative programme linking major EU and national initiatives – R&D, research infrastructures, registries
- Bridging to ERNs to help implementing research results and taking lessons learned from the clinic back to the bench

European Commission

European Reference Networks



Networks of healthcare providers aiming at **improving quality, and safety and access to highly specialised healthcare**

Patients affected by rare or low prevalence and complex diseases

Added value at EU level

Multidisciplinary approach (different specialities/areas of knowledge)

Need of cooperation:

- Scarcity knowledge
- Need education
- Complexity / high cost
- Effectiveness in the use of resources

"The knowledge travels, not the patient"

Research and Innovation

European Reference Networks

European Commission

BOND ERN	Bone Diseases
CRANIO	Craniofacial anomalies and ENT disorders
Endo-ERN	Endocrine Conditions
EpiCARE	Rare and Complex Epilepsies
ERKNet	Kidney Diseases
ERN GENTURIS	Genetic Tumour Risk Syndromes
ERN-EYE	Eye Diseases
ERNICA	inherited and congenital anomalies
ERN-LUNG	Respiratory Diseases
ERN-RND	Neurological Diseases
ERN-Skin	Skin Disorders
EURACAN	Solid Adult Cancers

EuroBloodNet	Onco-Hematological Diseases
EUROGEN **EURO-NMD**	Urogenital Diseases Neuromuscular Diseases
GUARD-HEART	Diseases of the Heart
ITHACA	Congenital Malformations and Intellectual Disability
MetabERN	Hereditary metabolic diseases
PaedCan-ERN	Paediatric Cancer
RARE-LIVER	Hepatological Diseases
ReCONNET	Connective Tissue and Musculoskeletal Diseases
RITA	Immunodeficiency, AutoInflammatory and Auto Immune Diseases
TRANSPLANT-CHILD	Transplantation in Children
VASCERN	Multisystemic Vascular Diseases

Research and Innovation

Rare Disease European Joint Programme Cofund

Create research and innovation pipeline "from bench to bedside" ensuring rapid translation of research results into clinical applications and uptake in healthcare for the benefit of patients.

Implement joint programme of activities including research, coordination, networking, training, demonstration and dissemination:

1. Research and innovation programme to be funded through transnational calls
2. Virtual platform for RD information, research data, samples, tools and standards; pilots to ensure usefulness to be followed by upscaling in progressive manner
3. Capacity building include training and support activities to improve R&I potential
4. Strategic coordination and management through annual programming

Establish connections across RD community in particular with ERNs and patient organisations. Follow the policies and contribute to objectives of IRDiRC.

Indicative budget and deadline:
€ 50-55 M, 18 April 2018

Information is indicative. Check full topic text against published Work Programme.

European Commission

Key action 1

Transnational calls for proposals to fund rare diseases research.

Joint funding by EC and national funding agencies.

Key action 2

Virtual platform for coordinated access, data exchange and repository facilities building on existing resources.

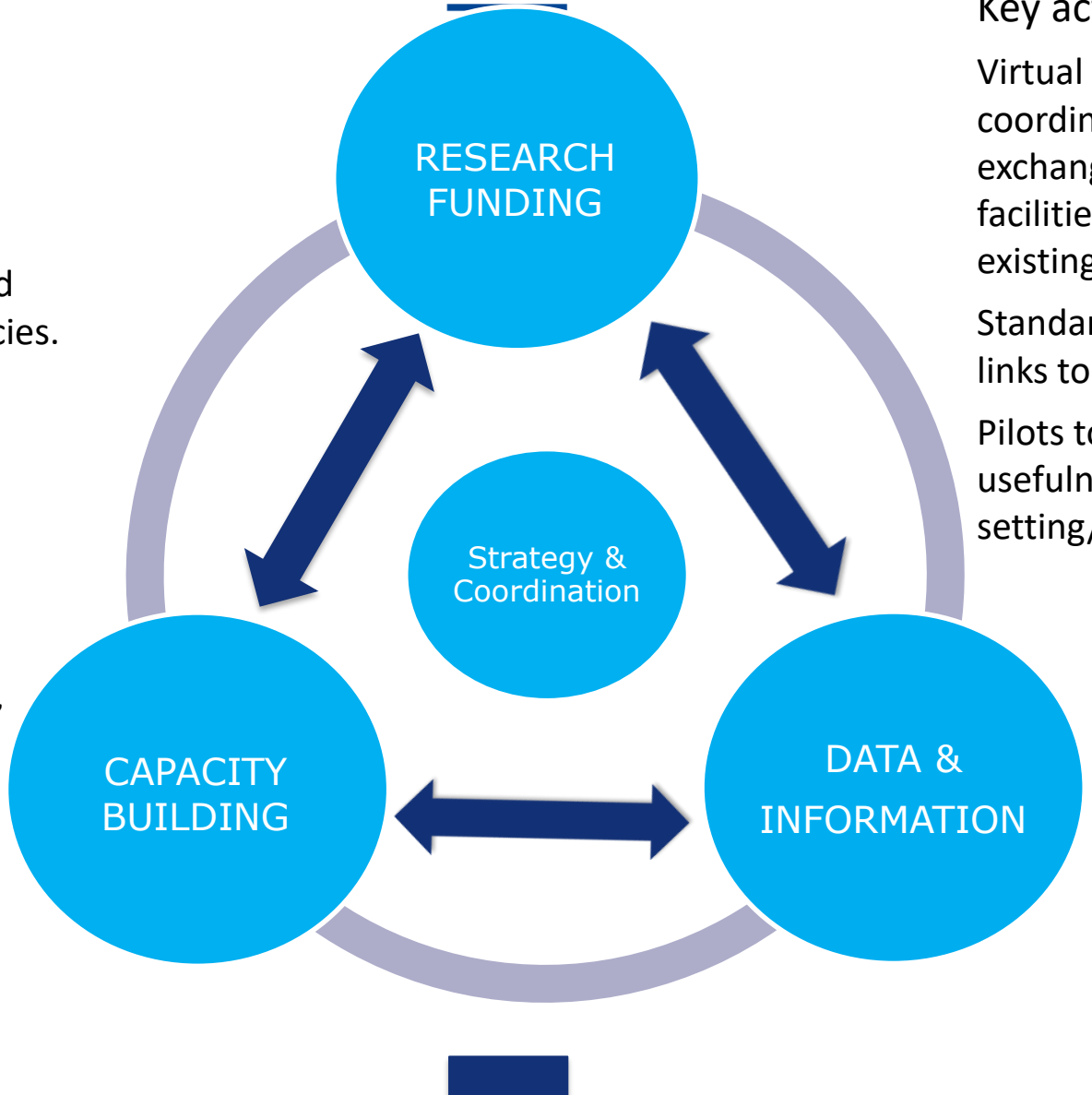
Standards, analysis tools, links to care data.

Pilots to ensure usefulness in clinical setting/ERNs.

Key action 3

Training and support on data management, product development, translational research etc for stakeholders including patient organisations. Sharing best practices.

Tech transfer facility towards industry.



"-Omics" for rare diseases

EUReNOmics

www.eurenomics.eu

Coordinator: Franz Schäfer
Heidelberg University MC

NeuromOmics

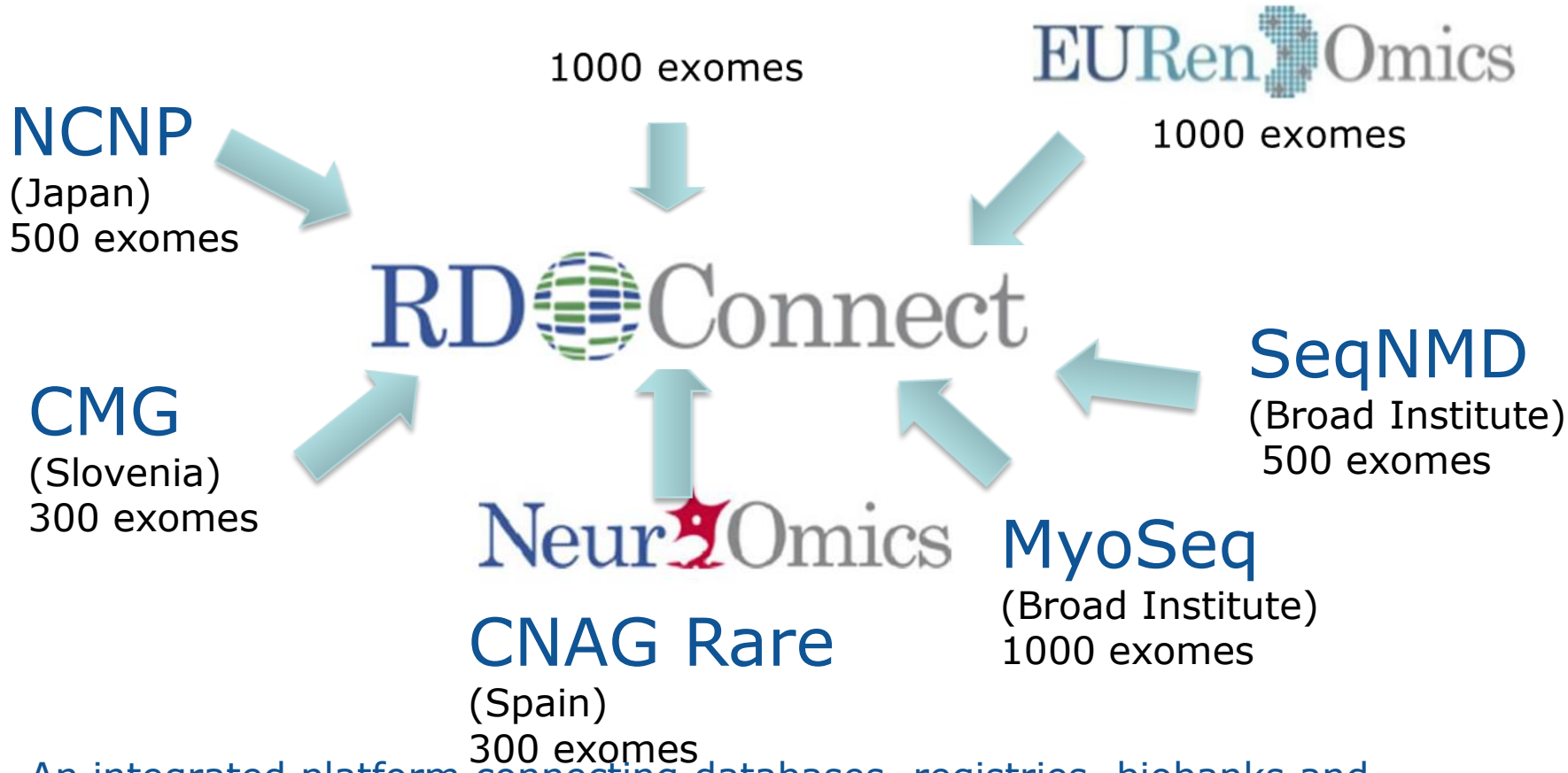
www.rd-neuromics.eu

Coordinator: Olaf Riess
University of Tübingen

- **Molecular characterisation of a large groups of rare diseases using –omics technologies**
- **Focus on rare neurodegenerative, neuromuscular and kidney diseases**
- **Ontologies, reference –omics profiles, diseases models, development of technologies**
- **Identification of over 120 new disease genes**
- **Targeted NGS panels that have been used for diagnosis of over 4700 patients**
- **Novel biomarkers for disease onset and progression**
- **Initiation of therapeutic trials**

SEVENTH FRAMEWORK PROGRAMME

European Commission
Research and Innovation



- An integrated platform connecting databases, registries, biobanks and clinical bioinformatics for rare disease research
- The RD-Connect platform will accept data from IRDiRC research projects worldwide
- http://rd-connect.eu

RD Connect

Infrastructure for data sharing in rare disease research

Flagship IRDiRC project implementing IRDiRC policies and guidelines on data sharing

EU 7th Framework Programme, 12M EUR, 6 years

Genomic analysis and gene discovery

Standardized phenotypic data collection

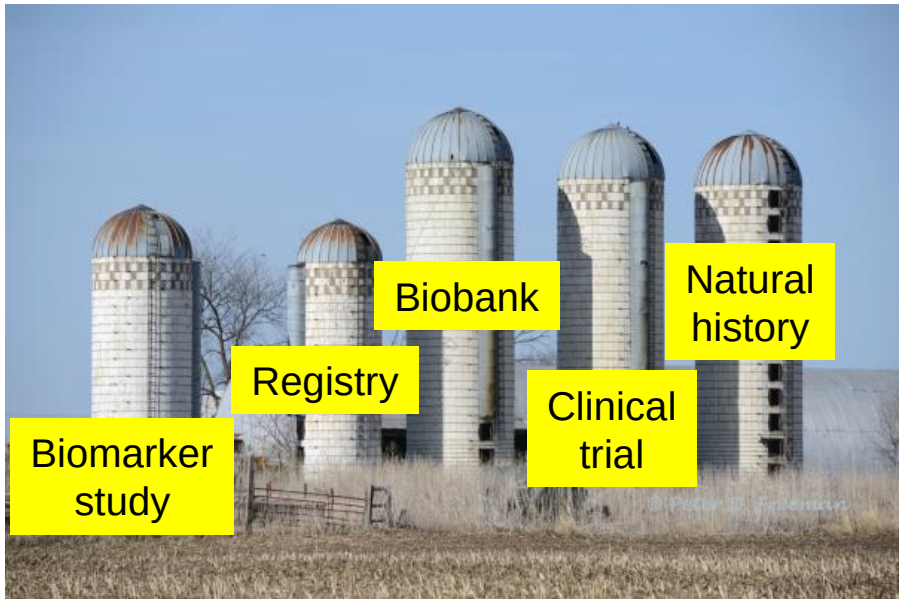
Searchable catalogue of biosamples

Data linkage across resources

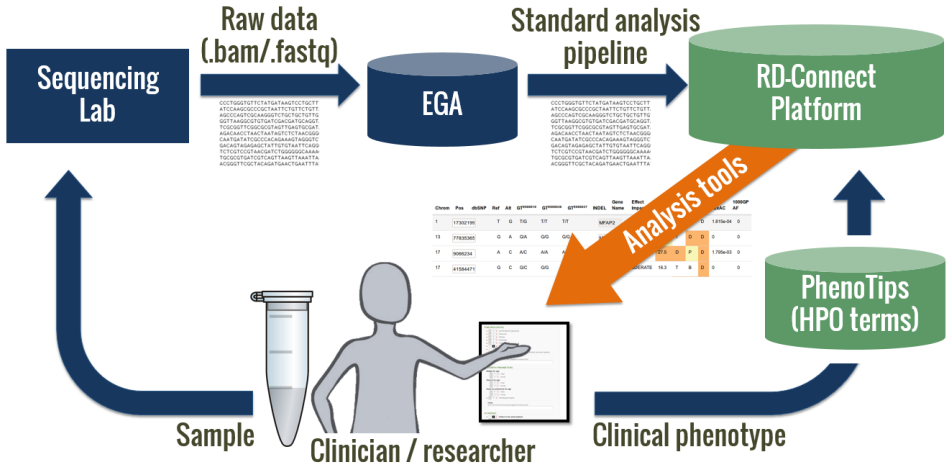
Overcoming Silos

Data sharing for research and better data analysis

rd-connect.eu



Omics data, clinical data and biosamples from individual with RD



Disease-causing variant can be identified using the genomics analysis platform

Sample is findable in the Sample Catalogue

Registry data in the ID-Cards directory of registries and biobanks

European Commission

SolveRD

"Solving the unsolved rare diseases"

- *To solve large numbers of rare diseases by sophisticated combined omics- approaches*
- *Pooling and re-analysis of 19.000 cases, WGS for 2000, multi-omics, matchmaking and functional analyses, clinical utility and cost-effectiveness aspects*
- *Coordinator Eberhard Karls Universitaet Tuebingen + 20 partners*
- *ERN-RND, ERN-ITHACA, ERN-Euro-NMD and ERN-GENTURIS form core ERNs, will reach out to all ERNs*

www.solve-rd.eu

Diagnostic characterisation of rare diseases (SC1-PM-03–2017)

Research and Innovation

ALPHA-MAN: Building on successes from FP5 and FP6 in FP7

From biochemical characterisation of mutations in the alpha-Mannosidase gene to "First in Man" clinical trials in patients

- Genetic and biochemical characterisation of mutations in the alpha-Mannosidase gene
- Pre-clinical Enzyme Replacement Therapy protocol
- Large-scale production of the recombinant enzyme
- Defined clinical endpoints for the future clinical trials in a European wide natural history study
- "First in Man" clinical trials in alpha-Mannosidosis patients of recombinant human lysosomal acid alpha-mannosidase (designation 2005)
- Chiesi Group received Marketing Authorisation for Lamzede® in April 2018

FP5 EURAMAN

FP6 HUE-MAN

FP7 ALPHA-MAN

Clinical trial methodologies for small populations

- Innovative statistical design methodologies for clinical trials in small populations focussing on rare diseases
- 3 projects bringing together international experts in innovative clinical trial design methodology along with key stakeholders
- ASTERIX, IDEAL, INSPIRE
- IRDiRC-EMA joint workshop March 2016, report available on IRDiRC website, EMA workshop March 2017, publication submitted

IRDiRC
INTERNATIONAL RARE DISEASES RESEARCH CONSORTIUM

Research and Innovation

ALPHA MAN: Building on successes from FP5 and FP6 to FP7 and beyond

FP5 EURAMAN

Enzyme replacement therapy for mouse model for alpha-mannosidosis

FP6 HUE-MAN

Pre-clinical and clinical therapy protocols
Conditions for large-scale enzyme production

FP7 ALPHA MAN

First in Man clinical trials for the therapy
Demonstration of safety and efficacy

Research and Innovation

Personalised medicine at EU level

- Personalised medicine drives innovation and contributes to sustainable healthcare by better prevention, prediction and disease management strategies

- EC was an early mover in Personalised medicine with workshops 2010 and a first conference 2011.

- Personalised Medicine Conference June 2016 launched IC PerMed – now established with elected Chair and Vice Chairs and dedicated secretariat

Research and Innovation

Definition of personalised medicine

Council Conclusions on personalised medicine for patients (2015/C 421/03)

"Personalised medicine refers to a medical model using characterisation of individuals' phenotypes and genotypes (e.g. molecular profiling, medical imaging, lifestyle data) for tailoring the right therapeutic strategy for the right person at the right time, and/or to determine the predisposition to disease and/or to deliver timely and targeted prevention"

Definition developed by the Advisory group for the H2020 Health, demographic change and well-being challenge

European Commission

Personalised medicine at activities at EU level

2010: Preparatory workshops
2011: European Perspectives conference
2013: Commission Staff Working Document on "use of '-omics' technologies in the development of personalised medicine"
2015: Council conclusions on Personalised Medicine
2015: Strategic Research and Innovation Agenda of PerMed
2016: Personalised Medicine Conference
2016: Launch of International Consortium of Personalised Medicine

Research areas

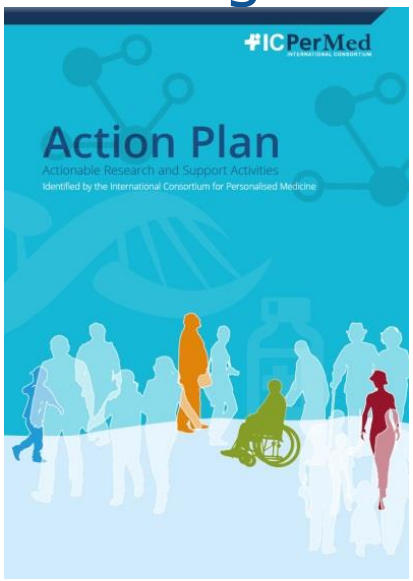
- Large scale data gathering and "-omics"
- Technology development
- Statistics
- Diagnostics
- Biomarkers
- Clinical trial methodologies
- Pre-clinical and clinical research
- Rare diseases: small patient populations
- Omics for health promotion and disease prevention
- Piloting personalised medicine in healthcare

Research and Innovation

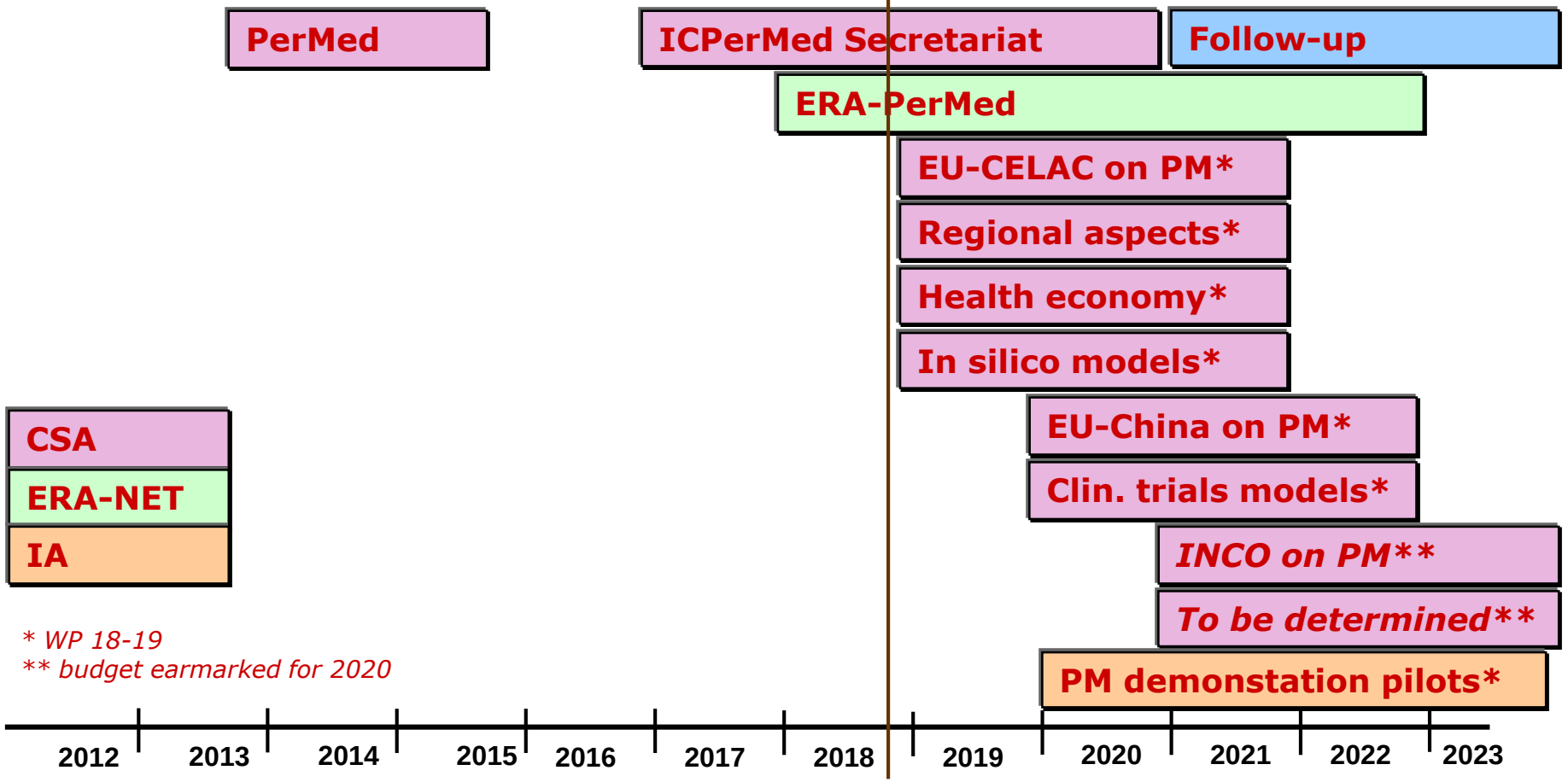
International Consortium for Personalised Medicine

41 members - ministries and funders - including:

- Eleven Health Ministries
- Six Science and Education Ministries
- Five regional authorities
- 22 EU MS, including 9 of EU13
- 5 Associated Countries (to H2020)
- 2 Canadian partners and 1 Brazilian



Projects supporting ICPerMed



ERAPerMed

- ERA-Net for Personalised Medicine
- To implement parts of the Action Plan
- Started on 1st December 2017, runs 5 years
- Over 30 million Euros total investment
- 32 partners from 23 countries (all in ICPerMed)
- First co-funded call launched 9 February 2018

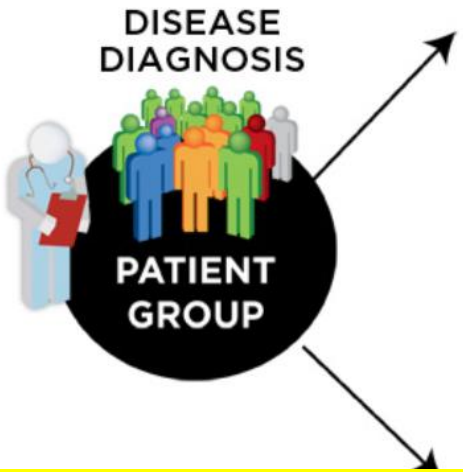
  "Smart combination of pre-clinical and clinical research with data and ICT solutions"
- http://www.erapermed.eu/

- First ICPerMed Conference
  20-21 November 2018
  DBB forum in Berlin, Germany
- Key note lectures on personalised medicine related topics
- Best practise examples of successful translation of personalised medicine research
- Whole research and implementation chain

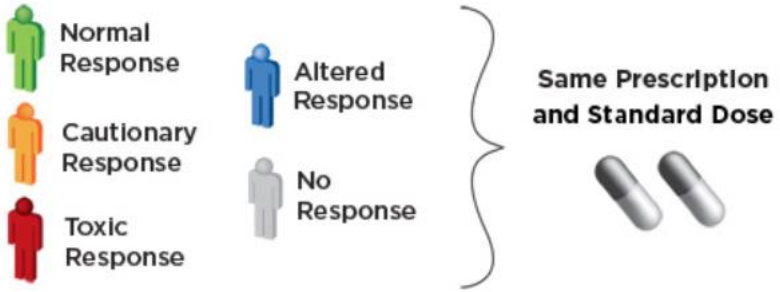
U-PGx: Ubiquitous Pharmacogenomics

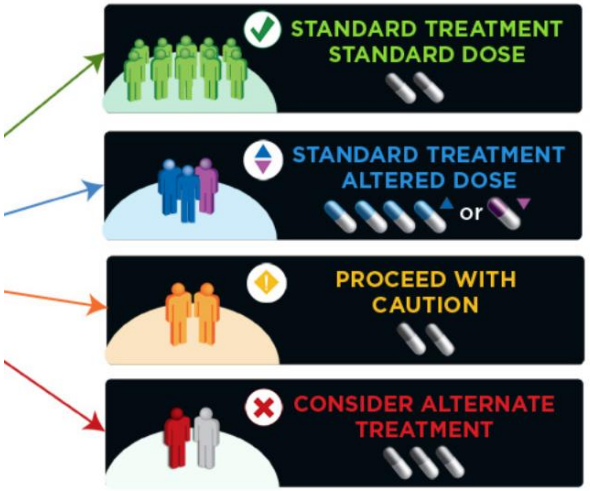
Adverse Drug Reactions cost ~EUR 100 billion per year

Traditional approach: same drug, same dose for everyone



Personalised approach: right drug and right dose for the right patient





Research and Innovation

Adapted from: admerahealth.com, genesisgenome.com

U-PGx

Ubiquitous Pharmacogenomics: Making actionable pharmacogenomic data and effective treatment optimisation accessible to every European citizen

- Pre-emptive genotyping of multiple important pharmacogenes
- Data collected prospectively and embedded into the electronic records of patients in NL, ES, UK, IT, AT, GR and SL
- Prescribers and pharmacists alerted through electronic clinical decision support systems when a drug is ordered or dispensed for a patient with an at-risk genotype
- Analysis of cost-effectiveness and health outcomes

European Commission

Interruptive, active CDS inside the EHR / e-prescription system

The system alerts the physician when a potentially harmful or ineffective drug would be prescribed *(gold standard but hard to achieve)*

Interpretive, passive CDS ***inside*** the EHR system

E.g. in PDF format

Interpretive, passive CDS ***outside*** the EHR system

At sites with no health-IT infrastrcuture: printout or safety-card

U-PGx

European Commission

Makes PGx data available everywhere

Independent of existing IT infrastructures

http://safety-code.org/

Research and Innovation

RTD articles and videos on PM

- Perspective for the Journal Personalised Medicine: ***'Enabling personalised medicine in Europe by the European Commission's funding activities'*** www.futuremedicine.com/doi/full/10.2217/pme-2017-0003

- Clinical and Translational Sciences: ***'Personalised Medicine in Europe'*** http://onlinelibrary.wiley.com/doi/10.1111/cts.12446/full

Personalising healthcare: Focusing on citizens' health - European Commission

WebsEdgeHealth • 567 views • 4 months ago

How co-operation paves the way for **personalised** medicine. Innovative and **Personalised** Medicine Unit Directorate E - Health