# POSITION STATEMENT ON COLLABORATION BETWEEN EUROPEAN REFERENCE NETWORKS AND INDUSTRY

## EXECUTIVE SUMMARY

For many reasons, ERNs hold major potential to alleviate challenges faced by people living with a rare disease and their families, and to put Europe at the forefront of medical innovation in the field.

To reach this potential, especially in terms of addressing the significant unmet needs of patients, ERNs must be adequately supported (financially, technically, and via sound policies and infrastructure). However, this support alone will not be enough for ERNs to fulfil their research potential: it must be accompanied by an ability to forge robust collaborations harnessing the expertise, resources, knowledge and data of all stakeholders involved in rare disease, including Industry.

To-date, overt ERN-Industry interactions have been largely limited, for a range of reasons (concerning barriers both tangible and perceived). Together4RD takes the learnings from case studies, explores frameworks for collaboration, and launches pilots for collaborative activities with the aim of establishing how best to plan and deliver multistakeholder interactions addressing real research needs in the rare disease space.

Launched in December 2021, **Together for Rare Diseases** is led by a multi stakeholder Steering Group comprising ERNs coordinators and project managers, and representatives of patients, research infrastructures, and the pharmaceutical industry. DG SANTE is an observer.

4 MEP champions have committed to spreading the vision of a collaborative rare diseases innovation landscape centred on ERNs: **Frédérique Ries** (Renew, Belgium), **Stelios Kympouropoulos** (EPP, Greece), **Ondrej Knotek** (Renew, Czechia) and **Sara Cerdas** (S&D, Portugal).

## KEY FACTS

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| There are about **30 million** (1 in 18) people suffering from a rare disease in the EU. | Only **5 to 6%** of rare diseases currently have dedicated treatment. |
| Between 2010 and 2020, **60%** of the therapies receiving orphan designation covered only 3 disease areas. | The EU is **lagging behind** other regions of the world when it comes to R&D investment. |
| European Reference Networks (ERNs) were launched in 2017 to **connect centres with expertise** in rare disease, and are organized according to broad disease/activity areas, together covering most conditions classified as rare. They have both clinical and research mandates. | Multiple stakeholders in the Rare Diseases ecosystem recognize that at present, the potential of ERNs to improve the EU's ability to care for its rare disease patients is **not being fulfilled**. |

# 1. WHY RARE DISEASE PATIENTS NEED PUBLIC-PRIVATE PARTNERSHIPS IN THE RARE DISEASE ECOSYSTEM

Small patient populations, limited natural history studies and even fewer treatment options: these are just some of the major challenges in the rare disease ecosystem. As a consequence, patients and families typically face hurdles in every stage of their journey, from seeking an accurate diagnosis to finding a specialist, participating in research studies and accessing the best available treatment and care.

To counter the sparse expertise, scattered patients, multiple diseases lacking any basic research, and tremendous inequalities between Member States in terms of access to care; **Europe has in ERNs a tool with major potential (probably unrivalled anywhere in the world) to benefit patients by connecting expertise in the best way possible.** Furthermore, the **EU's pharmaceutical Industry is dynamic, robust, and open to collaboration**, possessing expertise in clinical trial development, regulatory pathways, and data, alongside financial resources which are unattainable to ERNs on their own.

ERNs have the power to evolve to become the foundation of a future European health and research system for rare diseases, by maturing current collaborations into innovative partnerships, thus becoming powerful agents of the change which is so greatly needed for patients.

### THE ENORMOUS (UNTAPPED) POTENTIAL OF ERNS

ERNs hold a strong potential to add value to rare diseases research, for several reasons:

- They are clinical networks with patient participation fully integrated in the governance structures and activities (ePAGs).
- They have both clinical and research mandates (key for the rare diseases sector where the line between the two is inherently blurred).
- They are establishing ERN-wide registries (providing unique opportunities to share and collect interoperable data).
- They connect many centers of expertise (high potential for standardization and re-use of electronic health data).

***"ERNs are the cornerstone of clinical research on rare diseases. EURORDIS and the patient community call to establish ERN-industry collaborations under a public-private partnership framework informed by flagship pilots, to harness the research capacities of all partners, making Europe more competitive globally"***

**YANN LE CAM**
CEO OF EURORDIS

**An important barrier to ERNs fulfilling their research potential is the absence of robust and transparent collaborations with Industry: it is important to understand the historic reasons for this lack of interaction.**

# 2. CURRENT BARRIERS TO ERN-INDUSTRY COLLABORATION

## FACTORS THAT HAVE LIMITED ERN-LED RESEARCH OVER THE FIRST FIVE YEARS

- So far, of necessity most ERNs have prioritized care over research, even if ultimately activities like facilitating virtual care across borders and generating clinical guidelines have indirectly supported research.
- ERNs don't have funding schemes dedicated to direct clinical research activities
- Some ERNs have emerged from less-research-active fields – particular knowledge and support (e.g. in terms of regulatory and clinical trials expertise) are required to increase their research capacity, along with funding.

## BARRIERS TO COLLABORATION

- The Statements of the Board of Member States of ERNs (BoMS) are broadly perceived to impose significant barriers to collaboration (and certainly do not foster partnerships) - the lack of clarity on what *is* allowed is a major barrier to many ERNs engaging in substantial collaborative research activities, especially for Networks anchored in communities which have not been traditionally very research-active.
- Concerns over governance, data ownership (for collaboration involving patient data), privacy and ethics.
- Lack of institutional structures to support collaboration with Industry (as ERNs are not themselves legal entities), and – more importantly – often a lack of experience on the part of individual centres in navigating the legal and bureaucratic processes involved in working with Industry. There is no clear guidance or harmonized set of tools to facilitate these processes.

# 3. BREAKING THE BARRIERS

## HOW TO MOVE THE NEEDLE?

Possible models for collaboration identified by Together for Rare Diseases:

### 3RD PARTY LEGAL ENTITY MODEL

- A "third party" legal entity that can establish agreements / contracts with other entities and oversee / manage the project(s)
- Activity is through regional and national coordinating centres and volunteer / funded contributors
- Centralised contracting functions

### CONSORTIUM MODEL

- Multiple stakeholders within an agreement / remit; each collaborator exists as its own entity but working toward branded joint effort
- Others can join the consortium as partners (not necessarily legally bound if on voluntary basis)
- Agreement on specific activities to be developed and funded with clear governance, separate to other of the Network's work

### CASE STUDIES OF PAST AND PRESENT COLLABORATIONS ERN/INDUSTRY

**Reality check:** in a small and specialist community like rare diseases, clinicians and networks have been regularly interacting with companies without issue for decades, for the benefit of many, especially the patients.

These collaborations, often predating ERNs, are responsible for the research progress observed to-date, and demonstrate that the reservations and concerns of certain countries within the Board of Member States are unfounded.

Multiple past and ongoing examples of public-private partnerships have been analysed by Together4RD, for **registries** (ERK-REG in 2019, the EBMT Registry, the TREAT-NMD registry, the Sanofi Genzyme French Pompe Registry), or for the **optimization of clinical research planning and delivery** (TREAT-NMD, ITTC consortium, ACCELERATE, ECET), and the POC Club as a collaboration forum.

# 4. THE TOGETHER FOR RARE DISEASES PILOTS (COMING 2023)

Together4RD has identified achievable pilots for ERN-Industry partnership. The lessons learned on how to manage conflicts of interest, organize governance and data ownership, or ensure transparency will be built into a possible contract template to be showcased to stakeholders, mainly the BoMS, as tangible examples of how collaboration can work and be scaled-up in future.

Together4RD will act as a neutral broker, monitoring progress to extract the key learnings and best practices, but is also interested in creating a forum for all ERNs to present their respective areas of work and expertise to companies, to build new relationships and facilitate the identification of relevant partnerships in the future.

| Barrier to ERN-Industry Collaboration | Solutions in development by Together4RD (or others, as appropriate) |
|---|---|
| Concerns of some representatives within the ERN BoMS, due to lack of knowledge on the nature of public-private partnerships and the existence of successful case studies | Development and diffusion of rare diseases case studies where networks/individual centers engage with companies effectively and responsibly, for patient benefit |
| Concerns over conflicts of interest | BoMS Working Group on Legal and Ethical issues work on conflict of interest |
| Possible lack of awareness or clarity on the *range* of activities which could take place between ERNs and Industry | Together4RD case studies, results from the working groups on registries and clinical research |
| Administrative, bureaucratic and time burden to contract with companies (amplified by absence of legal entity) | Development of standardised contracting templates based on pilot partnerships carried out within Together4RD (starting in 2023) |
| Lack of clarity for many ERNs in terms of what can openly be done with companies or how to approach activities | Lessons and good practices drawn from the Together4RD pilots<br>Proposal to revise BoMS statement (to come once first pilots are launched) |

## RECOMMENDATIONS
## POLICY ASKS (NOVEMBER 2022)

Promote transparent governance structures and open dialogue to empower and advance ERN-industry collaboration

Create a forum (or fora) for public-private exchange of pre-clinical knowledge of ERNs

Ensure ERN registries remain independent and are adequately financed via public funds, while clarifying and optimizing their potential for collaboration

Create a comprehensive European Action Plan for Rare Diseases that supports public-private partnerships

## RELEVANT STUDIES AND OTHER INITIATIVES

Together4RD connects with/takes learnings from complimentary in the Rare Disease space, again demonstrating that this ecosystem advances more effectively through collaboration and a global vision. Key projects and collaborators include the following:

- Rare2030 Foresight Study
- Rare Disease Moonshot
- ERICA
- European Joint Program on Rare Disease Research (EJP-RD)
- International Rare Diseases Research Consortium
- **The Future European RD Partnership**

**Read more here**

Together4RD
RARE DISEASES

**Together for Rare Diseases (Together4RD) is an agile multi-stakeholder initiative aimed at supporting ERNs to collaborate with stakeholders to pursue opportunities that will address unmet medical needs of people living with rare diseases.**

It is led by a Steering Group with members including ERN Coordinators, representatives from umbrella patient association EURORDIS, the European Joint Programme on Rare Diseases (EJP RD) and Orphanet. DG SANTE acts as an observer. The companies Alexion, Takeda, Sanofi, Novo Nordisk, UCB and the trade associations EFPIA & EUCOPE offer financial support to the Together4RD Secretariat, which is coordinated by FIPRA International to support the multi-stakeholder collaboration.

ERN-EYE · ERKNet The European Rare Kidney Disease Reference Network · EpiCARE · European Reference Network · MetabERN European Reference Network for Hereditary Metabolic Disorders

EURORDIS RARE DISEASES EUROPE · orphanet · EUROPEAN JOINT PROGRAMME RARE DISEASES · eatris

efpia · EUCOPE European Confederation of Pharmaceutical Entrepreneurs AISBL · ALEXION

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