EURORDIS
RARE DISEASES EUROPE

A EUROPEAN BLUEPRINT FOR RARE DISEASES

Towards an EU Action Plan for Rare Diseases

Co-developed with Europe's rare disease community



October 2026

FOREWORD

For decades, rare diseases have shown what Europe can achieve when it works together. The European Reference Networks, the orphan medicines framework, Orphanet and the European Rare Disease Research Alliance (ERDERA), among other initiatives, were built on the recognition that no country can meet the needs of people living with a rare disease on its own. They are among the most tangible expressions of what the European Union can do for its citizens.

Yet for the 30 million people living with a rare disease in Europe, and for their families, the journey remains far too long and far too unequal. Diagnosis still takes nearly five years on average. Whether a person can see an expert, receive an authorised treatment, or have their disability recognised still depends largely on where they live. And for around 95% of rare diseases, there is still no approved therapy at all.

Only five years ago, a participatory foresight study co-funded by the EU (Rare2030.eu) identified a preferred scenario for rare disease policy, "innovation for social justice", and proposed a pathway to get there. Many things are on track. In an increasingly competitive world, Europe is rightly placing its bets on biotechnology, and rare disease science has long been at the forefront of that innovation. The proposed Biotech Act, welcomed by the rare disease community, is an important step: it can make Europe a better place to run clinical trials, attract investment and develop the therapies of tomorrow. But neither the Biotech Act nor other essential files, such as the pharmaceutical legislation and the Critical Medicines Act, can fully address our remaining challenges. Undiagnosed patients cannot enter trials. Fragmented data cannot generate the evidence regulators and payers need. A therapy authorised in the EU but unavailable in most Member States is a promise unfulfilled. Beyond treatments, timely diagnosis, coordinated care, social inclusion and a good quality of life are essential for our community. None of this can be achieved through a single piece of legislation, nor can it be solved by existing EU infrastructures and initiatives without further guidance and support.

This is why Europe needs an EU Action Plan on Rare Diseases. It would provide the framework to connect innovation with health systems, turn EU ambition into national delivery, make better use of data for patients, and bring existing initiatives together. In rare diseases, competitiveness and health equity reinforce one another.

Having helped shape national plans for rare diseases across Member States, patient advocates know what a well-designed plan can deliver, but also that national plans cannot succeed in isolation. National plans need a European framework to reach their full potential.

EURORDIS is far from alone in this call. Across the rare disease community, there has been a broad convergence of voices advocating for a European approach. We felt it was time to channel this momentum: to build on the work already undertaken, draw on valuable proposals put forward, and convene stakeholders to envision what a European framework could and should look like.

This Blueprint is our contribution to shaping that European framework. Co-created over ten months by patients, clinicians, researchers, public authorities, and industry representatives from across Europe, it sets out prioritised, actionable proposals alongside the building blocks that have made other EU public health plans successful. I warmly thank everyone who gave their time and expertise to it.

We are confident that the European Commission will use this contribution from the rare disease community as a basis for shaping the EU Action Plan on Rare Diseases, and that this process will lead to an ambitious Plan with people living with rare diseases at its centre. Such a Plan would help turn the Rare2030 vision into reality, ensuring that European science and innovation translate into tangible improvements in people's lives and greater social justice for everyone living with a rare disease, wherever they live.

Avril Daly, President of EURORDIS – Rare Diseases Europe

EXECUTIVE SUMMARY

WHY EUROPE NEEDS AN EU ACTION PLAN ON RARE DISEASES, AND WHY NOW

For decades, rare diseases have shown what Europe can achieve when it works together. The EU has built strong foundations, including the orphan medicinal products framework, the European Reference Networks (ERNs), Orphanet, the European Rare Disease Research Alliance (ERDERA) and the JARDIN Joint Action. These initiatives reflect a shared understanding that no Member State can meet the needs of people living with rare diseases on its own.

The challenge now is to make the most of what Europe has already built

Existing initiatives have transformed the rare disease landscape, but they have often developed through separate policies, programmes and funding cycles. Their full potential will only be realised if they are better connected, sustained and translated more consistently into national health and social systems.

An EU Action Plan would provide the framework and ambition to do this. It would bring existing efforts together around shared goals, clear responsibilities, dedicated resources and common measures of progress. Rather than creating parallel structures, it would help Europe optimise and sustain what already exists, fill remaining gaps, and turn European cooperation into better outcomes for people living with rare diseases.

The moment is now:

- **The next budget is being decided.** The 2028–2034 Multiannual Financial Framework (MFF) will determine whether Europe can sustain and build on its rare disease investments.
- **Legislation alone cannot connect the whole system.** The Biotech Act, the new pharmaceutical legislation, the Health Technology Assessment (HTA) Regulation, the European Health Data Space, and the Critical Medicines Act can strengthen innovation and access, but cannot alone address diagnosis, data, specialised care, social inclusion, research and treatment access.
- **The mandate exists.** Since the 2021 multi-stakeholder foresight study Rare2030, an Action Plan has been backed not only by patients, clinicians, researchers and industry but also by the European Parliament, the European Economic and Social Committee (EESC) and a large majority of Member States.
- **The world is moving.** The 2025 World Health Assembly Resolution requested the World Health Organization to develop a Global Action Plan, giving the EU an opportunity to lead by example.

THE PROBLEM: 30 MILLION PEOPLE STILL FACE UNEQUAL, FRAGMENTED CARE

For the 30 million people living with a rare disease in Europe, two thirds of whom experience onset in childhood, the journey remains too long and depends on where they live. Gaps persist at every step, for example:

Along the patient journey	What people face today
Diagnosis	Nearly **5 years** on average from first symptom to diagnosis; **60%** are first misdiagnosed; **40%** are never referred to a Centre of Expertise
Data	Rare diseases remain insufficiently visible in health systems, with ORPHAcode use below **20%** in some countries
Treatment	Around **95%** of rare diseases have no approved therapy; fewer than half of innovative medicines reach patients across Europe
Access delays	**578 days** on average from EU authorisation to reimbursement decision, rising to more than 900 days in some Member States
Daily life	Eight in **10** live with a disability; **53%** struggle to obtain public support; seven in **10** patients and carers reduce or stop work
Economic burden	Unemployment is **23%** compared with an EU average of **6.1%**; estimated costs might reach **€121,900** per person per year

WHAT THE BLUEPRINT PROPOSES

The Blueprint was co-created over ten months by patients, clinicians, researchers, public authorities, and industry, through engagement and consultations with a Core Group of 36 experts, a survey shared with the European Regional Taskforce that received 236 responses from 33 countries, and a workshop of more than 150 participants in Prague at the European Conference on Rare Diseases and Orphan Products (ECRD) in June 2026.

It proposes the core building blocks of an effective Action Plan:

- **Vision and goals:** a shared vision of "better lives for people living with rare diseases in Europe", supported by three strategic goals: health and quality of life; equality and inclusion; resilient systems, innovation and competitiveness, alongside SMART targets.
- **Governance:** an Advisory Board bringing together the European Commission, Member States, patient representatives and other stakeholders from the rare disease community.
- **Funding:** better alignment of existing EU and national funding, complemented by adequate dedicated resources and visible rare disease objectives in future EU programmes.
- **Monitoring:** shared indicators, public reporting and independent evaluation.
- **Patient partnership:** embedded throughout governance, implementation and evaluation.

18 PRIORITY ACTIONS FOR EU-LEVEL IMPACT

The Blueprint identifies 18 priority actions across six areas where EU coordination can make the greatest difference.

Thematic area	Priority actions
Earlier, faster and more accurate diagnosis	• Structured diagnosis and referral pathways • Coordinated European guidance on newborn screening • Improved access to genetic testing and genomic sequencing
Specialised and highly specialised healthcare	• Updated national rare disease plans • A sustainable and better integrated ERN framework • Improved cross-border access to ultra-rare and highly specialised care
Integrated care and social inclusion	• Person-centred integrated care pathways • Better access to social services and protection • Formal mechanisms for patient and family co-design
Optimising the data ecosystem	• Systematic use of ORPHAcodes • Stronger registries and data linkage • Better integration of rare disease data into the European Health Data Space
Innovative and needs-led research	• Better aligned EU investment • Meaningful patient partnership in research • Connected and sustainable research infrastructures
Available, accessible and affordable medicines and medical devices	• Better aligned evidence generation and assessment • Stronger compassionate-use frameworks • EU solidarity and coordinated access mechanisms

WHY IT MUST BE DONE AT EU LEVEL

Around 85% of rare diseases affect fewer than 500 people in the EU, so no single country can create the scale needed for shared data, research infrastructure, cross-border care or highly specialised expertise. EU action can strengthen national plans through common objectives and indicators, while respecting national responsibilities. It can also help connect Europe's existing rare disease assets more effectively. In doing so, equity and competitiveness can reinforce each other: better-connected data, trial-ready networks and pooled expertise can improve access and research efficiency while making Europe more attractive for life-science investment.

OUR ASK

We call on the European Commission to propose an EU Action Plan on Rare Diseases, using this Blueprint as the community's contribution to its design. The Plan should include:

- A shared vision, common goals and SMART targets linking EU and national action.
- Dedicated resources under the EU's Multiannual Financial Framework (MFF) 2028–2034.
- Patient partnership embedded in governance through a multi-stakeholder Advisory Board.
- A common monitoring framework with public reporting and independent evaluation.
- Delivery of the Blueprint's 18 priority actions.

We call on the Council and Member States to support this proposal, including through a renewed Council Recommendation on rare diseases by the end of 2027. Building on Europe's existing foundations, an EU Action Plan would close gaps across the patient journey, strengthen innovation and help translate European science and expertise into better outcomes for people living with rare diseases across all health systems.



"At the Centre of the Circle" - Turkey

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INTRODUCTION

Why an EU Action Plan?

Rare diseases are an area of high EU added value: no Member State can meet the challenges alone. People living with rare diseases face long and difficult diagnostic journeys, very small patient populations, fragmented data and knowledge, limited access to specialised care, and the absence of approved treatments for most conditions. These challenges are compounded by inequalities in access to diagnosis, care and support across countries and regions. People living with rare diseases and their organisations have been central to, and often at the forefront of, progress at both national and European levels. Patient organisations have funded research, built infrastructure and helped bring therapies to patients where markets alone would not have delivered them, opening up therapeutic avenues that now benefit patients far beyond rare diseases.

Over the past decades, the EU has recognised rare diseases as a public health priority through their inclusion in health and research programmes, Regulation (EC) No 141/2000 on orphan medicinal products and the 2009 Council Recommendation on an action in the field of rare diseases. This has enabled further cooperation and investment, including shared infrastructures and initiatives such as Orphanet, the European Reference Networks (ERNs) and the European Rare Disease Research Alliance (ERDERA), as well as closer integration with national efforts through the JARDIN Joint Action. This ecosystem has also been shaped by EURORDIS – Rare Diseases Europe, the leading Europe-wide umbrella organisation representing rare disease patient organisations, which has benefited from long-standing EU support through operating grants, enabling it to train and support patient representatives and experts and to contribute to policy and regulatory developments.

This recognition of the strategic importance of rare diseases is also reflected in evolving legislative frameworks, including the revised pharmaceutical legislation, the HTA Regulation, the Critical Medicines Act, the European Health Data Space, and the proposed Biotech Act. However, these pillars have often developed in parallel. The remaining gaps stem less from a lack of initiatives than from weak coordination, limited continuity beyond project cycles and a disconnect between EU-level action and what patients experience in national and regional health and social systems.

An EU Action Plan would bring existing EU efforts under one framework, with shared goals, clear responsibilities and a common way of measuring progress. Europe's Beating Cancer Plan and the EU One Health Action Plan against Antimicrobial Resistance have shown the value of this approach, promoting national action, uniting stakeholders around common goals and creating momentum to tackle long-standing challenges.

Why now?

Europe is seeking to regain its competitive edge in life sciences while upholding its core values of solidarity and equal access to care. Rare diseases sit precisely where these ambitious goals meet. At the same time, the negotiation of the 2028–2034 Multiannual Financial Framework will determine whether rare disease priorities are adequately resourced for the next decade. An EU Action Plan would also signal to health systems, patient organisations, people living with rare diseases and investors alike that rare diseases are a high priority for the EU, supporting its strategic objectives in life sciences and biotechnology.

These developments respond to a longstanding demand: the rare disease community – comprising people living with rare diseases and their families, patient organisations, healthcare professionals, researchers, public authorities, industry and other stakeholders – has called for an EU Action Plan since the Rare2030 recommendations of 2021 (Kole et al., 2021). The European Parliament has since taken up this call through its legislative own-initiative report (European Parliament, 2026), as has the European Economic and Social Committee (European Economic and Social Committee, 2024). A large majority of Member States have also supported this direction through the 2022 call to action under the Czech Presidency of the Council of the EU (Czech Presidency of the Council of the European Union, 2022).

Moreover, in most EU countries, national plans or strategies for rare diseases have been adopted or renewed. These plans and strategies would greatly benefit from an EU policy framework guiding their implementation with similar measurable objectives. Beyond the EU, the 2025 World Health Assembly Resolution on rare diseases has opened the way to a Global Action Plan, giving the EU the opportunity to lead by example.

What is the Blueprint?

The Blueprint is a community-led initiative setting out the building blocks that the European Commission could consider in developing an EU Action Plan on Rare Diseases. It reflects contributions from across the rare disease community, including people living with rare diseases and their families, patient organisations, healthcare professionals, researchers, public authorities, industry and other stakeholders. Chapter 1 explains how the Action Plan could address challenges that existing EU initiatives have yet to tackle, within the wider EU, national and global policy frameworks. Chapter 2 sets out the proposed structural building blocks of the Plan: scope, vision and overarching goals, guiding principles, governance, funding, and monitoring and evaluation. Chapter 3 presents priority actions across six areas with the greatest impact on people living with a rare disease: diagnosis, specialised healthcare, integrated care and social inclusion, data, research, and access to medicines and medical devices.

Meaningful participation of people living with rare diseases and their representative patient organisations as equal partners is essential to an effective EU Action Plan. Patient organisations have helped build the rare disease ecosystem by bringing collective expertise, representing the priorities and lived experiences of their communities, and contributing to policy, research and service development. Their involvement should therefore be embedded across the Plan's priorities, governance and implementation. Accordingly, patient partnership is reflected as a cross-cutting principle and through specific actions throughout the Blueprint, rather than as a separate area.

How was it done and by whom?

The Blueprint is the result of a multi-stakeholder process led by EURORDIS – Rare Diseases Europe. A Core Group of 36 experts, bringing perspectives from across the rare disease community – including patient organisations and representatives, healthcare professionals, researchers and other relevant stakeholders – provided strategic direction and validated the final content, including the chosen priority actions. A Regional Taskforce, set up with Rare Diseases International, was consulted through a survey that received 236 responses from 33 countries. Finally, a pre-conference workshop held in Prague on 2 June 2026 brought together more than 150 participants to test and prioritise the proposed actions.

Building on 20 years of collective experience and work, including Rare2030, the Blueprint brings together existing studies, policy recommendations and initiatives into a comprehensive, actionable framework for the European Commission. It sets out what needs to be done to ensure that no major gaps or community priorities are overlooked, while avoiding duplication of existing work. Rather than defining highly detailed technical content for each chapter, the Blueprint takes a principle-based approach, leaving room for other expert groups, projects and initiatives such as JARDIN and ERDERA to build on this work. The full methodology is set out in Annex II.

How should it be read?

The Blueprint is the rare disease community's contribution to the Commission's work, not a substitute for it. It proposes what the community considers the essential building blocks of an effective Plan, while leaving the Commission full scope to frame and design it. Each thematic area follows the same logic. It first outlines the existing challenges and what the EU has already done. It then presents three priority actions, selected on the basis of stakeholder support, EU added value and gaps not already covered by existing initiatives. For each priority action, the Blueprint distinguishes the role of the EU from that of Member States. Other complementary actions discussed during the process but not prioritised are listed in Annex I.

The Blueprint covers the building blocks that will support EU-level cooperation in the rare disease field and its effective interaction with national rare disease plans, fully respecting Member States' competence over the organisation of their health and social systems. While complementary to this work, contributions from our community to the Global Action Plan for Rare Diseases, as envisaged by the 2025 World Health Assembly Resolution, will be published separately.

What is the main ask?

We ask the European Commission to propose an EU Action Plan on Rare Diseases and to consider our proposals, including the structural building blocks of the Plan outlined in our Blueprint: a shared vision with common goals, SMART targets, dedicated resources under the next MFF and patient partnership embedded in its governance. We also ask the Council to support this proposal, including through a renewed Council Recommendation on rare diseases by the end of 2027.



"Rare is Proud" - Hungary

1. CONTEXT: FRAMING THE EU ACTION PLAN

1.1 WHAT THE EU HAS BEEN DOING FOR RARE DISEASES

1.1.1 EU INITIATIVES IN RARE DISEASES

This section recognises the EU's contribution to improving the lives of people living with rare diseases through initiatives, projects and legislative and non-legislative files, highlighting the high added value of EU cooperation in this field. Rather than providing a comprehensive list of EU initiatives, this section provides a general overview of the main initiatives, while more detailed information on EU rare disease initiatives by thematic area is provided in Section 3.

Rare diseases are an area where European cooperation is essential, as no single Member State has all the necessary expertise, specialists, funding, knowledge or medical infrastructure to address these complex and low-prevalence conditions independently. Rare diseases are considered rare when their prevalence is "not more than five affected persons per 10 thousand", according to the threshold established in Regulation (EC) No 141/2000 on orphan medicinal products (European Parliament and Council of the European Union, 2000). Approximately 72% of rare diseases are of genetic origin (Nguengang Wakap et al., 2020); other rare diseases include rare adult cancers, paediatric cancers, some rare autoimmune and inflammatory diseases, some rare malformation syndromes and undiagnosed diseases. No country, including the largest Member States, can single-handedly ensure timely diagnosis, access to specialised care and essential treatments, or access to the relevant expertise for all rare diseases. The added value of EU action is therefore particularly evident in rare diseases, requiring supranational solutions and a pan-European architecture that enables Member States and other European countries that apply the EU acquis and/or participate in EU programmes and initiatives to pool resources, expertise and infrastructure and improve outcomes for patients and their families.

This is why rare diseases were recognised as an EU health policy priority more than 25 years ago. Since then, the EU has progressively developed a range of policies, legislation and initiatives to address the specific challenges of rare diseases and strengthen cooperation between Member States. The EU has demonstrated its ability to deliver for people living with rare diseases – both at Union level through legislation and initiatives such as the European Reference Networks (ERNs), and at Member State level through national action plans and policy initiatives. This experience demonstrates the tangible added value of coordinated EU and national action and provides a strong foundation for a new EU Action Plan for Rare Diseases.

1.2 EU ACTION PLAN, NATIONAL AND INTERNATIONAL COLLABORATION

1.2.1 THE EU ACTION PLAN: ADDRESSING EU CHALLENGES AND BRINGING ADDED VALUE TO NATIONAL ACTIONS

Despite the numerous initiatives taken so far, people living with rare diseases continue to face enormous barriers to diagnosis, treatment and care. They remain marginalised in society and endure significant inequalities throughout their lives, and progress towards closing these gaps must accelerate. The upcoming technological revolution in health and recent scientific breakthroughs must be matched by political will to ensure that these advances translate into tangible improvements in the lives of people living with rare diseases and their families, wherever they live in Europe.

The EU Action Plan for Rare Diseases will be key to addressing the unmet needs of the estimated 30 million people living with a rare disease across the Union. It can provide the political impetus and coordinated action needed to ensure that the promises of scientific and medical progress are translated into better outcomes for millions of citizens and their caregivers across Europe. Building on what already exists and has been achieved, the Plan should identify and prioritise the actions still needed to address persistent unmet needs, close remaining gaps and ensure that progress is delivered more consistently across Europe.

Moreover, the EU Action Plan on Rare Diseases shall create a coherent, pan-European framework to address fragmentation across existing initiatives, which are not sufficiently aligned. Through a holistic vision and a coherent plan, the impact of these initiatives and policy actions will be amplified, the ecosystem strengthened and the benefits for people living with rare diseases maximised. The Plan will serve as a tool to guide policy development and ensure consistency across different but mutually reinforcing domains, including healthcare, research and industrial policy. It will therefore contribute both to improving healthcare for citizens and to strengthening the competitiveness of the EU.

The scale and complexity of rare diseases mean that coordinated EU action in key areas can complement, reinforce or enhance Member States' efforts. Cross-border patient pathways, shared research infrastructure, coordinated data standards and coherent incentives for orphan medicine development cannot be built within a single country's borders. The EU dimension is not a complement to national ambition: it is a condition for sustaining it.

The Plan will:

- Provide a coordinated European framework, combining EU-level action and coordination with national implementation, and linking both through shared expected outcomes, common instruments and structured cooperation.
- Focus EU effort where it adds the most value, ensuring that existing and planned legislative and non-legislative initiatives are mutually reinforcing within a shared vision that, at every level, considers the implications for people living with rare diseases; support the development of novel orphan medicinal products (OMPs) and other health technologies; provide targeted funding; and develop guidance to support national stakeholders.

- Contribute to reducing inequalities across the EU while advancing innovation and competitiveness, including through the development of novel orphan medicinal products and other biotechnologies, the exchange of best practices, targeted EU support and guidance for national stakeholders.

The EU Action Plan on Rare Diseases therefore does not replace national strategies; rather, it makes them more effective by providing an enabling framework and coordination mechanisms, while Member States remain responsible for implementation and delivery within their national systems. This follows a well-established model in EU health policy – the same architecture that underpins initiatives such as Europe's Beating Cancer Plan (European Commission, 2021), the EU One Health Action Plan against Antimicrobial Resistance (European Commission, 2017a) and the EU Safe Hearts Plan (European Commission, 2025d).

1.2.2 NATIONAL PLANS: REDUCING INEQUALITIES ACROSS THE EU BY ADVANCING THE INTEGRATION OF EU AND NATIONAL STRATEGIES

National rare disease plans or strategies are essential to ensure sustained and coordinated action at national level. They provide the framework for translating a common European vision into national priorities and actions, while reflecting national contexts and competences. Their impact, however, depends on effective implementation, adequate resourcing, monitoring, accountability and regular renewal.

National cancer control plans must include rare adult cancers and paediatric cancers and ensure smart synergies with national rare disease plans, particularly on research involving small patient populations, cross-border patient pathways and access to innovative medicines. They should also align with Europe's Beating Cancer Plan and a future EU Action Plan on Rare Diseases.

Along the lines of the 2009 Council Recommendation on an action in the field of rare diseases, a renewed European push should encourage all Member States to establish, implement, monitor and periodically review meaningful and adequately resourced national plans and strategies for rare diseases. A new Council Recommendation on rare diseases, adopted by the end of 2027, could provide this renewed impetus and support greater convergence and continuity across Member States, while fully respecting national competences in health policy. It should encourage Member States to set measurable objectives, assess progress regularly, and identify unmet targets and implementation gaps. National plans should also be subject to regular, mandatory review and updating at defined intervals to ensure they remain aligned with evolving needs, evidence and advances in science and care.

National plans and strategies for rare diseases should also serve as the overarching framework for taking forward at national level the priorities and actions set out in the dedicated chapters of this Blueprint. The recommendations on areas such as access to healthcare, diagnosis, treatment, care pathways, data, research and social inclusion provide specific direction on how national plans and strategies can advance these priorities, without replacing or duplicating their role.

Together, stronger national planning and a more structured European dialogue can help establish a common European vision for rare diseases, while allowing sufficient flexibility for Member States to determine how this vision is translated into their national health and social systems. This combination of European direction, mutual learning and national ownership can support greater coherence, continuity and progress towards reducing inequalities for people living with rare diseases across Europe.

1.2.3 GLOBAL FRAMEWORK (UN AND WHO): MAKING EUROPE A LEADING REGION

The 2025 World Health Assembly Resolution on rare diseases (World Health Organization, 2025) mandates the development of a Global Action Plan for Rare Diseases, building on the political momentum established by the 2021 United Nations General Assembly Resolution on addressing the challenges of persons living with a rare disease and their families (United Nations General Assembly, 2021). Together, these developments provide a shared global framework – including common principles, goals and political commitments – on which regional and national action can build.

The EU is uniquely positioned to translate these global commitments into concrete, coordinated action: through dedicated funding, shared infrastructure (including European-level infrastructure for data and information), ERNs and common standards (including ORPHAcodes) across the 27 Member States, an EU Action Plan on Rare Diseases could operationalise at scale what the global framework sets out. Through this, the EU could feed back into the global evidence, demonstrating what coordinated rare disease policy looks like in practice and providing a model that other regions and the WHO can draw on, making the EU a leading region for rare diseases, in line with its established role in global health (European Commission, 2022a).

National plans are where patients experience the impact of both frameworks: shaped by global principles, enabled by EU coordination and delivered through national health systems – the three levels are mutually reinforcing, each giving the others greater reach and legitimacy than any could achieve alone.

1.2.4 LEGAL BASIS AND INSTITUTIONAL REFERENCES

Methodological note:

An EU Action Plan would normally set out the legal basis for EU action and for the European Commission to propose measures in this area, while also referring to relevant opinions, reports, resolutions and conclusions from EU institutions and bodies to provide further context. We have deliberately left this section for further development by the European Commission. This choice reflects the nature of our contribution, which focuses on the principles and building blocks of an EU Action Plan on Rare Diseases while leaving more specific and granular legal and institutional considerations to a later phase led by the European Commission.

2. BUILDING BLOCKS OF AN EU ACTION PLAN

2.1 SCOPE OF THE PLAN: DEFINING THE TARGET POPULATION AND THEIR NEEDS

2.1.1 DEFINITION OF RARE DISEASES

In order to address the needs of the rare disease population and avoid leaving anyone behind, it is important to define the target population of the EU Action Plan on Rare Diseases.

The definition of a rare disease currently used at EU level is laid down in Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999 on orphan medicinal products (the Orphan Medicinal Products Regulation), which refers to conditions affecting "no more than 5 in 10,000 people in the EU". The politically agreed text of the revised EU pharmaceutical legislation retains the existing prevalence threshold. Once formally adopted and applicable, the revised framework will replace Regulation (EC) No 141/2000 and maintain specific incentives for the development and authorisation of medicinal products for rare diseases.

At global level, the Operational Description of Rare Diseases, developed by a multi-stakeholder expert panel, defines a rare disease as a medical condition with a specific pattern of clinical signs, symptoms and findings affecting no more than 1 in 2,000 persons in any WHO-defined region (Wang et al., 2024). Its prevalence threshold is therefore identical to that of Regulation (EC) No 141/2000. Its clinical definition of "disease" draws on the WHO International Classification of Diseases and corresponds to the disorder level in the ORPHAcodes classification system. Aligning the EU Action Plan on Rare Diseases with this global reference would therefore support greater coherence between global, EU and national rare disease policy, without requiring any change to the EU prevalence threshold.

Recital 9 of the Clinical Trials Regulation (Regulation (EU) No 536/2014) refers to "ultra-rare diseases" as "severe, debilitating and often life-threatening diseases affecting no more than one person in 50,000 in the Union" (European Parliament and Council of the European Union, 2014). Approximately 85% of rare diseases affect fewer than 1 in 1,000,000 people (Nguengang Wakap et al., 2020), meaning that most are far rarer than the legal threshold for ultra-rare diseases. This suggests that the current definition of ultra-rare diseases may not fully reflect the distinct and specific needs of the very rarest conditions and has prompted discussion among stakeholders about whether ultra-rare diseases should be further distinguished. However, the rare disease community remains divided on this issue, as reflected in the multi-stakeholder discussions held to prepare the Blueprint.

2.1.2 KEY FIGURES ON RARE DISEASES AND THEIR IMPACT

Orphanet – the European reference database for rare diseases, coordinated by INSERM and designated an IRDiRC Recognized Resource – catalogues more than 6,500 clinically distinct rare diseases, each assigned a unique ORPHAcode (Orphanet, 2026). These diseases are heterogeneous in aetiology, clinical presentation, age of onset and organ system affected.

Epidemiological estimates exclude rare cancers, rare infectious diseases and rare poisonings (Nguengang Wakap et al., 2020). Rare cancers are nonetheless an integral part of the rare disease field and are fully covered by the European Reference Networks (ERNs), with specific figures provided below. The position of rare infectious diseases and poisonings is less settled, as their classification varies considerably across world regions. A dedicated reflection on whether they fall within the scope of the EU Action Plan on Rare Diseases should therefore underpin its drafting, taking the European context into account.

As for the impact of rare diseases, the landmark epidemiological analysis by Nguengang Wakap et al. (2020), published in the European Journal of Human Genetics and based on the Orphanet database, provides the most comprehensive evidence base to date on the global burden of rare diseases. Its findings underpin the scope and scale of the Action Plan:

29–56 million people living with a rare disease in Europe, including **18–34 million** in the EU (Orphanet, 2026)

329–624 million people affected worldwide, confirming rare diseases as a global public health priority (Orphanet, 2026)

4–7.6% of the population affected at any point in time – roughly between **1 in 25** and **1 in 13** people (Orphanet, 2026)

6,528 distinct rare diseases catalogued in Orphanet, with new conditions regularly described (Orphanet, 2026)

66% of rare diseases have an exclusively paediatric onset, making childhood onset a defining feature of the landscape (Orphanet, 2026)

Around **85%** of rare diseases affect fewer than **1 in 1,000,000** people, equivalent to fewer than **500** individuals in the EU (Nguengang Wakap et al., 2020)

Specific data on rare cancers:

Rare cancers have an incidence of fewer than **6 per 100,000** people per year, and the category includes all childhood cancers (RARECARE; Gatta et al., 2011). Together, they account for about **24%** of new cancer cases in Europe: around **650,000** new diagnoses each year, with **5.1 million** people living with a rare cancer. Five-year relative survival is **48%**, compared with **63%** for common cancers (RARECAREnet; Gatta et al., 2017).

Hereditary cancers and genetic tumour risk syndromes account for **5–10%** of all cancers. Carriers can face a lifetime risk of early-onset cancer of **up to 100%**, yet only **20–30%** have been diagnosed (European Commission, 2017b).

Childhood cancers are diagnosed in **35,000** children and young people in Europe each year. They are the leading cause of death by disease after the age of one, with **6,000** deaths annually. Survival now reaches **80%,** but at least two-thirds of Europe's **500,000** childhood cancer survivors experience long-term late effects (SIOPE and CCI Europe, 2024).

On the socio-economic impact of rare diseases, recent studies document a substantial burden that strengthens the case for coordinated strategic action at EU level. For example, a 2024 study covering 43 rare diseases in nine European countries estimated the cost of living with a rare disease at €121,900 per person per year, combining direct medical, direct non-medical and indirect costs (CRA, 2024). In practice, the EU Action Plan on Rare Diseases should comprehensively map existing and ongoing burden studies. It could build on the methodology for estimating the burden of rare diseases that the EU-funded European Rare Diseases Research Alliance (ERDERA) is expected to deliver in 2027.

2.1.3 POPULATION NEEDS AND CHALLENGES THAT WILL BE ADDRESSED BY THE PLAN

Methodological note:

The Blueprint and its priority actions draw on the challenges identified through its preparatory work, as described in Annex II (Methodology), and are complemented by findings from existing studies, including the Rare Barometer surveys conducted by EURORDIS with people living with a rare disease and their families across Europe. Together, these sources provide a comprehensive picture of the unmet needs of the rare disease population throughout the care pathway: from access to a timely and accurate diagnosis to specialised care, treatment, research and social and economic inclusion. These challenges are set out by thematic area in Section 3 of this Blueprint.

The EU Action Plan on Rare Diseases should build on this evidence base so that its objectives and actions respond directly to the needs expressed by the rare disease community.



"Painted Resilience" - England

2.2 VISION AND OVERARCHING GOALS

The aim of the EU Action Plan on Rare Diseases is to build a synergistic approach to rare disease policies at EU and Member State levels, so that the needs of the rare disease community are addressed effectively and holistically.

Vision: Better lives for people living with rare diseases in Europe

In line with United Nations General Assembly Resolution 76/132 on Addressing the challenges of persons living with a rare disease and their families and the UN Sustainable Development Goals, the Plan should look beyond diagnosis and treatment to quality of life, including physical and mental health, social participation and family resilience. It should enable people living with rare diseases to access appropriate care, attend school, work, take part in community life and live independently. At the same time, it should harness advances in science, research and innovation – including improved diagnosis, treatments, technologies, data and care pathways – to address unmet needs and improve health outcomes.

To turn this vision into measurable results, the Blueprint proposes a strategic architecture in which each level of the Plan has a distinct function:

- **Strategic Goals** define the outcomes Europe seeks to achieve for people living with rare diseases.
- **Operational Goals** define the system-level levers through which these outcomes are delivered.
- **Thematic areas** (Section 3) group the actions, including priority actions, that put the Operational Goals into practice. Each action is linked to deliverables and to KPIs or other indicators.

For each Strategic Goal, the Plan should include a clear description and SMART targets. Each target should specify who is responsible, by when it should be met, how progress will be tracked and which existing mechanisms support its achievement rather than leaving it merely aspirational (e.g. ERNs, Horizon Europe, the European Platform on Rare Disease Registration (EU RD Platform) and the Orphan Medicinal Products Regulation).

2.2.1 STRATEGIC GOALS: THE OUTCOMES EUROPE SEEKS TO ACHIEVE

SG1: Health, well-being and quality of life

Ensuring healthy lives and promoting well-being for all people living with rare diseases. This goal deliberately looks beyond diagnosis and treatment towards quality of life, including physical and mental health, independence, social participation and family resilience.

SG2: Equality and inclusion

Reducing inequalities affecting people living with rare diseases and promoting their full inclusion and participation in society.

SG3: Resilient systems, innovation and competitiveness

Building resilient infrastructure, promoting an inclusive, competitive and sustainable ecosystem and fostering needs-led research and innovation for people living with rare diseases.

2.2.2 OPERATIONAL GOALS: THE LEVERS FOR DELIVERY

OG1: Generate knowledge, evidence and innovation

Producing and sharing the data, evidence and scientific advances needed to understand, diagnose and treat rare diseases.

OG2: Ensure timely and equitable access and implementation

Ensuring that diagnosis, care, treatments and medical devices reach every person living with a rare disease, regardless of where they live.

OG3: Build connected, resilient and sustainable systems

Strengthening the networks, care pathways and social support structures that connect people living with rare diseases to expertise and services across borders.

Finally, each **thematic area** in Section 3 sets out actions, some of which are identified as priority actions, with an average of three per area. As noted in Section 3, the actions are cross-cutting and mutually reinforcing, and most thematic areas contribute to more than one Operational and Strategic Goal.

For each priority action, the Plan would specify deliverables, responsible actors, timelines and KPIs or other indicators. These indicators would feed into the monitoring framework described in Section 2.6, allowing progress to be traced from individual actions through to the Strategic Goals.



"My Glances Sing a Song" - Turkey

2.3 GUIDING PRINCIPLES OF THE EU ACTION PLAN

Subsidiarity, proportionality and EU added value

EU action supports and reinforces national action without replacing it. Member States retain full competence over the organisation of their health systems and the allocation of national resources. The EU should act where cooperation brings clear added value, building on existing structures, programmes, networks and successful practices rather than creating parallel mechanisms.

Whole-of-government approach

Rare diseases are not exclusively a health issue. Effective governance requires engagement across health, research, social affairs, industry, education and digital policy at both EU and national level. The Plan shall introduce a formal horizontal coordination model for rare diseases and cross-border healthcare across the relevant European Commission services, building on existing coordination, in particular between DG SANTE, DG RTD, DG CONNECT, DG EMPL and the Secretariat-General.

Meaningful partnership and balanced representation

People living with a rare disease, patient organisations and civil society are recognised as structural partners, formally involved in the design, implementation and evaluation of the Plan. Governance should also ensure balanced representation of all key stakeholder groups, including families, healthcare professionals, researchers, academia, Member States, regulators, HTA bodies, payers and industry. Appropriate support should enable effective participation where structural or resource-related barriers exist.

Science-led and evidence-based

The Plan will be grounded in strong scientific evidence and guided by the lived experience of people living with a rare disease. EU agencies, scientific and academic bodies and independent experts – including the EMA, ERNs, ERDERA, the Orphanet network and the European Platform on Rare Disease Registration (EU RD Platform), managed by the European Commission's Joint Research Centre (JRC) – provide the foundation for governance decisions.

Ownership, accountability and transparency

Responsibilities for implementation are clearly assigned at EU, national and, where applicable, subnational level. Progress against a limited set of key indicators is reported publicly and assessed through independent mid-term and final evaluations.

Continuous learning and improvement

New actions should be informed by lessons learned, evaluation of previous initiatives and identified gaps. Existing approaches should be strengthened, adapted or scaled up wherever appropriate.

2.4 GOVERNANCE

The implementation of the EU Action Plan on Rare Diseases will be the responsibility of the European Commission, supported by a structure or body, such as an Advisory Board, to advise, guide and support delivery of the Plan.

The Advisory Board will:

- Ensure effective oversight, policy steering, scientific grounding and national delivery without creating unnecessary administrative burden or duplication.
- Bring together representatives of the European Commission, including DG SANTE and relevant EU agencies, Member States and civil society – including patients, clinicians, academia and industry – with Member State representatives serving as the primary national interlocutors.
- Bridge EU-level guidance and national rare disease plans, drawing on existing EU agencies and technical bodies, including the EMA, JRC and European Health and Digital Executive Agency (HaDEA), and European-level structures such as the ERNs and Orphanet as implementation partners with defined mandates within the Plan's operational work programme, without requiring new institutional structures.
- Draw on the experience of EU rare disease governance bodies since 2004, such as EUCERD and the European Commission Expert Group on Rare Diseases, and follow the approach used in comparable EU health action plans, balancing ambition with operational feasibility.

2.5 FUNDING

A number of activities relevant to rare diseases are already supported through existing EU funding programmes, and only a limited number of new actions identified in the Plan are expected to require additional dedicated EU-level funding.

Importantly, by providing a common coordinating framework, the EU Action Plan on Rare Diseases can create synergies across existing initiatives and funding instruments, maximising their collective impact. The Plan would function as a cross-cutting policy framework to mobilise, coordinate and align existing EU and national funding streams around its three overarching objectives.

The Plan could build on and integrate a range of existing financial and policy instruments, including:

- MFF 2028–2034: health and research funding under negotiation, including the European Competitiveness Fund (ECF).
- Social, educational and investment dimensions of the Action Plan: EaSI, the European Programme for Employment and Social Innovation, Erasmus+ and InvestEU.
- European Investment Bank (EIB).
- National and Regional Partnership Plans (NRPPs), as an alternative source of funding requiring mobilisation at national level, including by Ministries of Health.

2.6 MONITORING AND EVALUATION

The Action Plan shall establish an integrated monitoring and evaluation framework linking EU and national levels, ensuring that both EU and national policies move towards the same measurable outcomes. The framework covers the Strategic and Operational Goals, priority actions, deliverables and outcomes and assesses progress consistently across Member States against a common set of measurable indicators. It serves to ensure accountability, support adaptive governance and identify and address inequalities between and within Member States.

Regular assessment

Progress is reviewed at predefined intervals. Reviews combine quantitative indicators with qualitative evidence, including implementation experience, the perspectives of patients and other stakeholders and emerging gaps.

Multi-stakeholder review

Results are reviewed by a representative multi-stakeholder body, with representatives of people living with rare diseases as full members. This body assesses implementation, identifies lessons learned and recommends corrective or additional action at EU and national level. It should be the Advisory Board foreseen in Section 2.4.

Periodic evaluation

Independent mid-term and final evaluations assess the effectiveness, coherence, equity and sustainability of the Plan and its progress towards the Strategic Goals.

Decision-oriented follow-up

Monitoring and evaluation are a basis for timely decisions, not a reporting exercise. Findings should identify where progress is insufficient or inequalities persist between and within Member States. They should lead to documented decisions on whether to maintain, adapt, scale up or discontinue actions and on whether new EU-level action is needed.

Indicators

A limited number of key indicators will be established, building on previous or ongoing work. This includes the 21 core indicators for monitoring national plans adopted in 2013 by the European Union Committee of Experts on Rare Diseases (EUCERD), as well as other relevant indicators, such as those under development by the JARDIN Joint Action, which specifically measure ERN integration into national health systems. The indicators will combine process indicators, assessing progress on the structures and measures put in place by the Plan, with outcome indicators, assessing achievement of targets, including for the complementary actions of national rare disease plans.

3. PRIORITY ACTIONS

Methodological note: The actions presented in the following areas have been identified through research and consultation with the different groups involved in the development of this Blueprint. These consultations also informed the prioritisation of actions with the highest relevance and added value at EU level (see Annex II for further details).

The Plan should focus on a workable number of clearly defined priorities, supported by detailed measures and actions. For each priority, it should set out the EU-level measures and the national rare disease plan measures that will contribute to delivery.

The priorities in this Blueprint are organised into six thematic areas that broadly follow the patient journey, from diagnosis through healthcare and care, research and data generation to access to treatment. In practice, these areas are closely interconnected, and many of the proposed actions are mutually reinforcing and cross-cutting. Patient partnership is a fundamental requirement throughout the Plan's development and implementation. In line with Rare2030's Partnership with Patients recommendation, this should include adequate resources and funding, evaluation of patient engagement and partnerships, and support for engagement and capacity building.

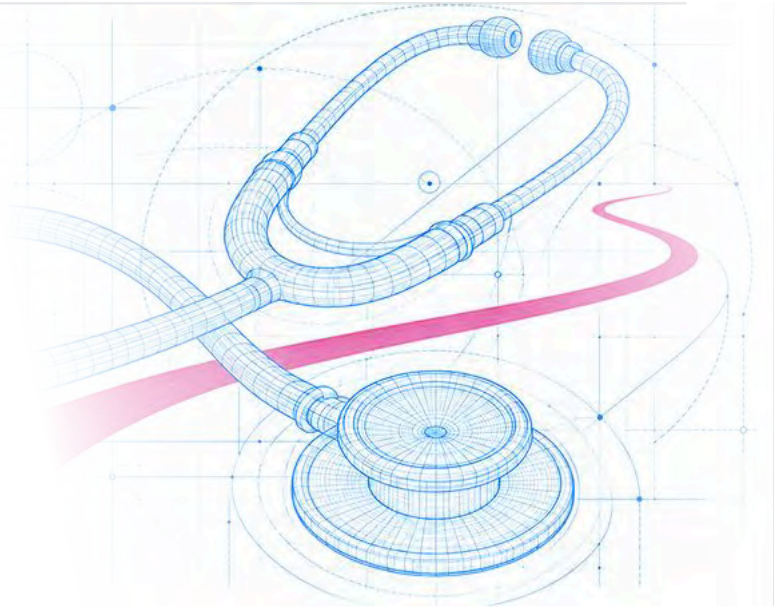


"To the Moon and Back" - Slovakia

3.1

EARLIER, FASTER AND MORE ACCURATE DIAGNOSIS

Shortening the diagnostic odyssey for people living with a rare disease



3.1.1 CHALLENGES

Earlier, faster and more accurate diagnosis for people living with a rare disease in Europe faces structural, persistent and interconnected challenges. The problems identified include:

- Diagnosing rare diseases is intrinsically complex: estimates have commonly ranged from 6,000 to 8,000 rare diseases, which are highly heterogeneous; the majority are genetic, many are multisystemic and individual conditions affect very small patient groups. This results in scarce expertise and makes recognition and confirmation difficult, contributing to delayed or incorrect diagnoses (EURORDIS – Rare Diseases Europe, 2020c).
- Early diagnosis can significantly reduce mortality and morbidity for certain rare diseases and improve quality of life through earlier access to effective care and treatment, yet for many people the search for a diagnosis still becomes a 'diagnostic odyssey'. On average, individuals wait nearly five years from first symptom onset to confirmed diagnosis, with women waiting even longer. During this time, many experience multiple misdiagnoses – 60% are initially misdiagnosed with another physical condition and 60% have symptoms dismissed or misattributed to psychological causes – and 25% undergo eight or more consultations before diagnosis is confirmed (EURORDIS – Rare Diseases Europe, 2020c; World Health Organization, 2025; European Economic and Social Committee, 2024; European Parliamentary Research Service, 2026; EURORDIS – Rare Diseases Europe, 2024a).
- Rare diseases are frequently misdiagnosed or diagnosed late, particularly when symptoms are non-specific or resemble more common conditions. Because each rare disease individually affects only a small number of people, most health professionals have limited exposure to them and may not recognise them promptly, underlining the need for stronger professional training and diagnostic guidance (European Parliament, 2024; EURORDIS – Rare Diseases Europe, 2020c).
- A key driver of diagnostic delay is slow or inefficient progression from primary care to specialised expertise and weakly structured routes to diagnosis. Access to specialist expertise, including Expert Centres and ERN-affiliated expertise, remains uneven across and within EU countries, contributing to unequal diagnostic outcomes and delays (European Parliamentary Research Service, 2026; EURORDIS – Rare Diseases Europe, 2020c; European Parliament, 2025).
- National referral pathways to Expert Centres and European Reference Networks (ERNs) are often insufficiently integrated into national health systems, limiting their impact on timely diagnosis and contributing to late referral and avoidable diagnostic delay. The Rare Barometer survey found that referral to a Centre of Expertise was associated with shorter diagnostic timelines, yet 40% of patients were never referred to such a centre (European

- Parliamentary Research Service, 2026; EURORDIS – Rare Diseases Europe, 2020c; World Health Organization, 2025; EURORDIS – Rare Diseases Europe, 2024a).
- Capacity, availability and quality of genetic testing – including differences in laboratory availability, quality management, interpretation capacity and reimbursement – vary substantially across Member States, with some countries offering only a few dozen tests and others thousands. These disparities generate unequal access to molecular diagnosis and contribute to the persistence of undiagnosed cases (European Union Committee of Experts on Rare Diseases, 2015; EURORDIS – Rare Diseases Europe, 2020c; World Health Organization, 2025; European Parliamentary Research Service, 2026).
- Implementation of next-generation sequencing (NGS) is uneven and often slow, despite its ability to shorten the diagnostic odyssey. Scalable implementation is constrained by challenges in variant interpretation, bioinformatics and workforce capacity, inconsistent clinical utility standards, fragmented and inadequate data governance and storage, and reimbursement pathways (EURORDIS – Rare Diseases Europe, 2020c; European Parliamentary Research Service, 2026).
- The use and accessibility of effective diagnostic tools and technologies, best practices and programmes remain uneven across Europe and are often not integrated into a continuum of health strategies throughout the life course of people living with a rare disease (Czech Presidency of the Council of the European Union, 2022). Member States tend to consider the reimbursement of medical devices and therapies in isolation; greater horizon scanning of therapies and diagnostics developed in parallel could help ensure that, where both are being developed for the same condition, reimbursement for both is explored together, rather than one being reimbursed and the other not.
- Newborn screening programmes (NBS) for rare diseases vary widely in scope and approach across EU Member States, and even within countries, leading to unequal opportunities for early diagnosis and intervention. There is no common European approach to expanding and updating NBS programmes, nor sufficient European collaboration in areas where this could be beneficial, while respecting the principle of subsidiarity and Member States' competences (European Union Committee of Experts on Rare Diseases, 2013; EURORDIS – Rare Diseases Europe, 2021; European Parliament, 2025; European Parliamentary Research Service, 2026; World Health Organization, 2025). The lack of Europe-wide standards (e.g. timing, sample collection, follow-up and information to parents) contributes to uneven quality and outcomes (EURORDIS – Rare Diseases Europe, 2020c; EURORDIS – Rare Diseases Europe, 2021b).
- A substantial number of people remain undiagnosed – either because their clinical team has not yet 'solved' their case despite the condition being diagnosable, because the condition is not yet scientifically characterised, or because existing tools cannot identify its cause (EURORDIS – Rare Diseases Europe, 2020c; European Parliamentary Research Service, 2026; World Health Organization, 2025).
- Primary prevention options (e.g. preconception carrier screening, prenatal testing and preimplantation genetic diagnosis) raise ethical, legal and social sensitivities for patients and families, requiring careful governance and rights-based approaches (EURORDIS – Rare Diseases Europe, 2020). Ethical, legal and psychosocial challenges related to genetic testing – including consent, incidental findings, stigma and discrimination – are inconsistently addressed across Member States, affecting trust, uptake and equitable use of advanced diagnostics (European Parliamentary Research Service, 2026; World Health Organization, 2025; EURORDIS – Rare Diseases Europe, 2020c).
- Persistent diagnostic delays and unequal access to diagnostic tools and services across countries remain a major source of health inequity, limiting the ability of health systems to provide timely diagnosis and care and undermining progress towards universal health coverage (World Health Organization, 2025).

3.1.2 WHAT THE EU HAS DONE

The following actions are substantially or partially addressed by ongoing EU legislative or programmatic instruments, or by existing or recently concluded initiatives, such as the Joint Action JARDIN, the IMI project Screen4Care, the recently concluded Solve-RD project and the ERDERA co-funded partnership. The Action Plan should acknowledge these, monitor their implementation and address residual gaps.

Develop and implement a structured diagnosis pathway with referral criteria linking primary care to ERNs and Expert Centres	Ongoing work under JARDIN, the EU4Health Joint Action on integrating ERNs into national healthcare systems, explicitly includes optimising patient pathways and referral systems to ERNs, facilitating national reference networks and programmes for undiagnosed diseases, and developing organised pathways intended to turn 'diagnostic odysseys' into structured 'highways to diagnosis' (European Health and Digital Executive Agency, 2026; EURORDIS – Rare Diseases Europe, 2024b). Residual gap: EU-wide clinical decision-support tools and harmonised 'red flag' referral criteria for primary care remain to be developed.
EU-level coordination and evidence generation on newborn screening	A standing EU body with a mandate to issue recommendations on screening panels, quality standards and equitable follow-up care does not yet exist. Nevertheless, in 2013 the European Union Committee of Experts on Rare Diseases (EUCERD) adopted an opinion identifying areas where a shared European approach to newborn screening could add value while respecting national competences. An EU-funded study concluded that European cooperation could add value by enabling systematic assessment and sharing of scientific, economic and ethical evidence, fostering common approaches and best practices, and supporting more consistent quality and follow-up, while leaving decisions and implementation to national authorities (Cornel et al., 2014). The study proposed a framework for debate on EU neonatal screening policies and the evidence base on which a future EU-level governance mechanism could draw.
Systematic reanalysis of undiagnosed patients' genomic data	Solve-RD, a Horizon 2020-funded flagship project bringing together clinical and molecular experts from 37 centres across four founding ERNs, has already reanalysed genomic data for over 6,000 previously undiagnosed families, yielding several hundred new diagnoses (Solve-RD, 2025). This reanalysis infrastructure and methodology has been adopted as the core framework for undiagnosed-case reanalysis under ERDERA's Clinical Research Network, which aims to extend the approach to all 24 ERNs and reanalyse over 100,000 datasets. Residual gaps concern sustainable, long-term funding for periodic (rather than one-off) reanalysis and extending coverage beyond the four founding ERNs.

Comparative evidence and shared diagnostic/registry infrastructure

Orphanet, the EU Rare Diseases Platform and ERDERA's Data Services Hub already provide a shared evidence base on nomenclature, prevalence and expert-centre/ERN coverage across Member States, and JARDIN's national competent-authority structure is generating comparable national data on ERN integration and referral pathways as part of its national roadmap process. The Action Plan shall build on and reference these ongoing sources rather than commission new comparative-indicator work from scratch.

3.1.3 PRIORITY ACTIONS

Based on workshop discussions, survey feedback and an assessment of EU added value, focusing on actions not already substantially addressed at EU level, three actions emerge as the highest EU-level priorities.

Implement a structured 'diagnosis pathway' from primary to specialised care, including clear referral criteria to centres/ERNs and use of clinical decision support

PRIORITY ACTION

Action description

- National networks of expert centres to support efficient diagnostic pathways and shorten the diagnostic odyssey.
- Clinical decision-support tools and clear referral/escalation criteria, including a 'red flags' system for primary care.
- Harmonisation of diagnostic pathways across countries to reduce variation between centres.
- Greater focus on the pre-diagnosis period (recognising non-specific symptom patterns across multiple healthcare interactions) and on rare or under-recognised iatrogenic conditions, including improved informed consent and long-term outcome monitoring.

How this responds to the challenges

This action responds directly to the identified challenges by reducing diagnostic delays through stronger early recognition of rare conditions and improved referral pathways from primary care to specialised expertise, and by ensuring timely and equitable access to specialised diagnostic expertise across Europe, including through stronger integration of Expert Centres and ERNs within national health systems. It directly targets the diagnostic-odyssey evidence: an average of nearly five years from first symptom to confirmed diagnosis, 60% of patients initially misdiagnosed with another physical condition and 40% of patients never referred to a Centre of Expertise, despite referral being associated with shorter diagnostic timelines.

Establish an EU-level Newborn Screening (NBS) Expert Advisory Committee and common guidance to support coordinated, high-quality screening across Europe

PRIORITY ACTION

Action description

- Establish an EU-level NBS Expert Advisory Committee (or multistakeholder steering group), including patient representatives, to provide non-binding recommendations on minimum requirements for screening panels, quality standards and ethical safeguards (European Parliamentary Research Service, 2026).
- Develop EU guidance on evaluating and implementing screening for rare diseases, including ethical considerations and patient involvement.
- Support the expansion and harmonisation of newborn screening and early diagnosis programmes across Europe, supported by governance mechanisms that ensure equitable access and appropriate follow-up care, and encourage programmes to monitor emerging technologies, follow good clinical and research practices and consider the inclusion of actionable diseases where early action provides benefits – improved health outcomes, faster diagnosis or informed reproductive choices – despite the absence of an available treatment (European Parliamentary Research Service, 2026).
- This action should also involve issuing EU guidance on minimum standards for confirmatory testing, clinical follow-up and psychosocial support pathways after a positive newborn or other screening result, to be considered alongside the work of the proposed NBS Advisory Committee.

How this responds to the challenges

This action responds to the need to promote coordinated and high-quality newborn screening programmes across Europe, supporting early identification of actionable rare diseases and timely access to appropriate care and treatment. It addresses the major differences in newborn screening programmes across Europe – what conditions are screened for, how programmes are run and how results are followed up – as well as the lack of a common European approach, shared standards and better exchange of data and good practices. The principle of subsidiarity and Member States' competences is upheld, avoiding the risk of over-centralising NBS at EU level.

EU added value

Newborn screening panels and programme design are, and should remain, a national competence closely tied to national health-system organisation and resourcing, in line with the principle of subsidiarity. However, 27 Member States are each independently evaluating the same emerging screening technologies, ethical questions and follow-up-care models, generating duplicated effort and highly uneven outcomes for children born in different countries. The EU adds value not by centralising decision-making but by providing a shared, non-binding platform – the proposed Advisory Committee – to pool horizon scanning, evidence review and ethical guidance so that Member States can decide on national implementation with better information. Ongoing work under Screen4Care, an IHI/IMI-funded consortium including EURORDIS, piloting genetic newborn screening and AI-based symptom-recognition tools across a large European cohort, already illustrates the scale at which this kind of evidence generation is more efficient when pooled at EU level, but a standing EU governance mechanism with a mandate to issue recommendations does not yet exist.

EU added value

Diagnostic pathways and referral criteria are implemented nationally, but the problem this action addresses is itself cross-border in nature: the small, dispersed patient population for any single rare disease means no Member State can build and validate a full set of clinical decision-support tools and 'red flag' referral criteria on its own. The EU adds value by pooling clinical knowledge and evidence across the 24 ERNs and Member States to produce a common framework and shared tools that no individual health system could develop as efficiently alone, while implementation within national referral and reimbursement systems remains a Member State responsibility. Some of the groundwork on referral pathways to ERNs is already underway under JARDIN.

Delivery roles

What the EU should do

Establish standardised guidelines and criteria for developing clinical decision-support tools and referral pathways. These can be embedded in Electronic Health Records (EHRs) and included as core functional specifications in EHR procurement tenders; issue guidance/templates for structuring pathways to ERNs and Expert Centres; set EU-level indicators to monitor diagnostic delay and referral rates across Member States.

What Member States should do

Integrate ERNs and expert centres into national referral systems and reimbursement structures; deploy decision-support tools in primary and emergency care; resource and staff national diagnostic pathways; integrate EU-level standardised guidelines and criteria for developing clinical decision-support tools and referral pathways as core functional requirements in public tenders to procure new or update existing EHR systems.

Other measures could be identified at national level and embedded in national plans or strategies for rare diseases and rare cancers, with the aim of closing the national referral gap reflected in the 40% non-referral figure.



"Never Give Up" - USA

Delivery roles

What the EU should do

EU (non-binding, coordinating role): establish the Advisory Committee to issue non-binding recommendations on screening panels, quality standards, ethical safeguards and the responsible use of genetic newborn screening technologies; facilitate shared learning and best-practice exchange, including by supporting the scaling-up of successful national pilot projects; provide guidance on the evaluation and adoption of new technologies; support Member States in learning from and building on each other's pilot projects and share recommendations on how mutual recognition could be achieved; propose a harmonised, best-in-class reference panel for voluntary adoption and periodic review.

To strengthen follow-up care after screening, guidance on minimum standards for confirmatory testing, clinical follow-up and psychosocial support pathways after a positive newborn or other screening result should also be considered alongside the work of the NBS Advisory Committee.

What Member States should do

Member States (retain core competence): decide on the adoption, scope and expansion of national screening panels; fund and deliver screening and confirmatory follow-up care; ensure ethical and equitable implementation nationally; feed national data and experience into the EU-level shared-learning process.

To ensure follow-up care after screening, Member States shall also resource and organise follow-up care pathways – including confirmatory testing, treatment initiation and psychosocial support to families – integrated with national referral pathways to expert centres.

Improve access to genetic testing and genomic sequencing based on clinical need, with agreed quality standards

PRIORITY ACTION

Action description

- Ensure equitable access to genetic testing and genomic sequencing across all countries, including under-resourced settings.
- Offer free cascade genetic testing to at-risk relatives to support prevention and early detection.
- Promote earlier access to genomic testing to reduce diagnostic delays, unnecessary investigations and repeated referrals.
- Establish EU-wide quality standards for accurate, reliable and safe genetic diagnostics.
- Improve timely diagnosis, care planning, targeted management and access to research and clinical trials.
- Ensure high standards of data protection, privacy and protection against genetic discrimination.
- Reduce inequalities in access to genetic expertise and specialised diagnostic services.

How this responds to the challenges

This action responds to the call to expand equitable access to advanced genomic and genetic diagnostic technologies, including next-generation sequencing and related bioinformatics capacities. It directly addresses disparities in genetic-testing capacity, quality management, interpretation capacity and reimbursement across

Member States, as well as the uneven and often slow roll-out of next-generation sequencing, constrained by variant interpretation and bioinformatics capacity, inconsistent clinical utility standards and fragmented data governance and reimbursement pathways. It also addresses the inconsistent handling of ethical, legal and psychosocial issues around genetic testing across Member States.

EU added value

Rare disease patient populations for any single condition are small and geographically scattered, so no Member State alone can generate the case volumes needed to validate variant interpretation, maintain state-of-the-art bioinformatics pipelines or negotiate favourable terms for advanced sequencing technologies. The EU can achieve economies of scale and quality assurance that individual national laboratories cannot by setting shared interpretation and quality standards, co-funding bioinformatics infrastructure and enabling cross-border access to expertise, while Member States remain responsible for delivering and reimbursing testing within their health systems.

Delivery roles

What the EU should do

The EU should set EU-wide quality and interpretation standards for genetic and genomic testing; invest in shared bioinformatics and variant-interpretation infrastructure; support harmonisation of reimbursement principles and cross-border capacity building; issue guidance on consent, incidental findings and non-discrimination.

What Member States should do

Member States should implement the agreed quality standards in national laboratories; expand testing capacity and reimbursement coverage to close the current gap between countries; invest in national bioinformatics and workforce capacity; apply data-protection and anti-discrimination safeguards in practice.


"Looking Out & Looking In" - USA

3.2

ACCESS TO SPECIALISED AND HIGHLY SPECIALISED HEALTHCARE

Closing the distance between people living with a rare disease and the expertise they need



3.2.1 CHALLENGES

Access to specialised and highly specialised healthcare for people living with a rare disease in Europe faces structural, persistent and interconnected challenges. The challenges identified are:

- A scarcity of specialists and expert centres creates significant access barriers, resulting in medical deserts, long travel distances and extended waiting times (European Parliament, 2025; EURORDIS – Rare Diseases Europe, 2019; World Health Organization, 2025).
- Non-existent or inadequately structured referral pathways across Member States mean that people rely on ad hoc navigation and repeated visits to non-expert services. Referral to an expert centre measurably reduces diagnostic delay; patients referred to an expert centre wait, on average, 4.3 years for diagnosis compared with 5.4 years for those not referred (Faye et al., 2024).
- Variation in access policies across Member States may result in unequal health outcomes: not all EU countries have formal systems to designate and accredit expert centres, referral pathways are non-mandatory, and patients often bear non-medical travel costs not covered by health systems, producing persistent geographic and financial barriers to timely and adequate care services (EURORDIS – Rare Diseases Europe, 2019; European Parliamentary Research Service, 2026; World Health Organization, 2025).
- While the current EU legal framework for cross-border healthcare may function adequately for high-volume, low-complexity procedures, it remains insufficient for low-volume, specialised or complex healthcare services and procedures. Awareness of cross-border healthcare rights is low among both patients and clinicians, while administrative barriers, variable national procedures and insufficient integration of ERNs into national pathways limit timely and equitable access to specialist care across borders (EURORDIS – Rare Diseases Europe, 2019a; European Parliamentary Research Service, 2026; European Commission, 2022b).
- Evidence on inequities in access to specialised care, nationally and cross-border, is limited, particularly regarding the impact of socioeconomic status, education, gender, age or geography, hindering targeted policymaking and monitoring of progress (EURORDIS – Rare Diseases Europe, 2019a; European Parliamentary Research Service, 2026).

- There is no common EU framework for monitoring access, equity, quality or patient-reported experience and outcomes in rare disease care, limiting the ability to benchmark and improve services. Available evidence shows that people living with rare diseases report markedly better healthcare experiences when treated in ERN-affiliated hospital units: on a scale from 1 to 5, the average score was 3.4 compared with 2.6 in non-ERN units, yet this evidence remains under-used (EURORDIS – Rare Diseases Europe, 2021a).
- Care coordination remains fragmented: patients and families often act as the main link between healthcare, allied health, community care and social care professionals, while poorly managed transitions between levels of care can lead to loss of information and continuity, gaps in services and interruptions to treatment (EURORDIS – Rare Diseases Europe, 2019a; European Parliamentary Research Service, 2026; World Health Organization, 2025). Many people living with a rare disease continue to experience significant difficulty in accessing effective adult care, underlining the need for a true continuum of expertise and care across the entire patient journey. This continuum must also address the growing number of people living with a rare disease who are now living into old age, as a direct consequence of medical progress and therapeutic innovation.
- Workforce planning and forecasting remain insufficient: health systems struggle to address specialist shortages, ensure sustainability and retention, maintain an appropriate skill mix and prevent the loss of expertise when experts retire (EURORDIS – Rare Diseases Europe, 2019a; European Parliamentary Research Service, 2026; World Health Organization, 2025).

3.2.2 WHAT THE EU HAS DONE

The following actions are being substantially or partially addressed by ongoing EU legislative or programmatic instruments, or by existing projects and initiatives such as JARDIN and ERDERA. The Action Plan should acknowledge these, monitor their implementation and address residual gaps

Improve ERN geographical coverage and expand to under-represented disease areas through targeted outreach	Ongoing work is underway to address geographic gaps via Affiliated Partners. Work to address gaps in disease coverage also appears to be underway, with a recent disease expansion having been approved for some ERNs alongside the possibility for ERN members to claim expertise in these conditions, but without the possibility for other expert centres to join the network through a new call. Information on this process is not publicly available, so this should be confirmed by DG SANTE.
Amend Social Security Regulations / the Cross-Border Healthcare Directive to cover virtual consultation time	The Cross-Border Healthcare Directive is an existing EU legal instrument; this action proposes a specific amendment – payment for time spent on cross-border virtual consultations – rather than new legislation. Ongoing work is underway through the legislative own-initiative report tabled by the European Parliament, which seeks to amend Directive 2011/24/EU. To guarantee real impact and improve access for people living with rare and complex conditions, the Action Plan should refer to a revision of Social Security Regulation (EC) No 883/2004 that would address the specific needs of this patient population.

Work is underway through JARDIN for 13 out of the 25 actions proposed

The remaining gaps to be addressed by the Action Plan, as well as the actions required from Member States, will need to be addressed alongside these ongoing activities.

- Develop and implement clear referral pathways to reduce navigation burden and ensure integration with ERNs;
- Strengthen telemedicine and virtual case discussion to preserve cross-border access while reducing unnecessary travel;
- Update and implement national rare disease and rare cancer plans, aligned with EU guidance and ERN integration;
- Member States should establish a roadmap for integrating ERNs into national health systems;
- Invest sustainably and proportionately in expert centre capacity and ERN competencies from national and EU budgets;
- Supplement continuous ERN monitoring with more nationally relevant and disease-relevant indicators;
- Establish a formal ERN sustainability framework, including stable EU and national funding, clearer operational status, protected expert time and accountability;
- Strengthen registries and data linkage;
- Develop and implement generic care pathways for rare conditions grounded in patient community needs;
- Develop EU guidance and implementation tools for multidisciplinary, person-centred integrated care pathways, with measurable indicators;
- Support Member States to scale care-coordination roles (e.g. case managers) and shared care plans, including paediatric-to-adult transition;
- Encourage training of healthcare professionals outside the rare disease field, including rare cancers, to promote awareness and earlier referral.

Systematic use of patient-generated evidence, including patient-reported outcome measures (PROMs) and patient-reported experience measures (PREMs), in rare disease policy, care and EU HTA processes

Regarding PROMs, substantial work has been done or is ongoing in this area, including the PROMs repository developed under ERICA, work developed by ERNs to validate and adapt existing PROMs and integrate them into registries, as well as ongoing work on patient-centred measures being expanded and continued under ERDERA through its Clinical Research Network. On PREMs, Rare Diseases Ireland will complete the development of the first generic PREM for rare diseases in 2027.

Strengthen telemedicine and virtual case discussion to preserve cross-border care access while reducing unnecessary travel	In addition to JARDIN's ongoing work on developing guidance on referral systems to ERNs and on the incorporation of advice from the ERN Clinical Patient Management System (CPMS), MyHealth@EU will support cross-border telemedicine services, including teleconsultations. There is also ongoing work on cross-border telemedicine services under the Xt-EHR Joint Action.
Support ERNs to educate and train future rare disease experts, including clinical, surgical and holistic training	There is ongoing work under EU4Health to position ERNs as rare disease workforce training hubs.



"Rarely Together - Lotte and Salomon" - Germany

3.2.3 PRIORITY ACTIONS

Based on workshop discussions, survey feedback and an assessment of EU added value, three priorities emerge for EU-level action, focusing on areas not already substantially addressed at EU level.

Update and implement national rare disease plans aligned with EU guidance and ERN integration

PRIORITY ACTION

Action description

Update and implement national rare disease plans, and national cancer plans with respect to rare cancers, to improve access to specialised healthcare. These plans should include measurable objectives, align with EU guidance, strengthen ERN integration and provide adequate financial incentives, greater visibility and stronger national-level engagement (Council of the European Union, 2009; European Commission, 2008; EURORDIS – Rare Diseases Europe, 2019a; European Parliamentary Research Service, 2026).

How this responds to the challenges

This action directly addresses variation in access policies and the absence of formal expert centre designation systems across Member States; weak referral pathways and the diagnostic odyssey; insufficient evidence on timely and adequate access to specialist healthcare; and fragmented care coordination. Updating national rare disease plans and cancer plans is the primary lever through which Member States translate EU guidance into measurable national commitments.

EU added value

National plans are, by definition, national instruments, but this action explicitly calls for them to be aligned with EU guidance and ERN integration. The EU could play a coordinating and standard-setting role, requiring plans to include a set of common measurable objectives on access to specialised healthcare, including, but not limited to, specific ERN-integration commitments. Some of this groundwork is already being undertaken through JARDIN, which supports countries in integrating sustainable approaches into national rare disease plans and strategies, as well as into national cancer plans, including through bilateral meetings.

Delivery roles

What the EU should do

The EU should issue common guidance and minimum content standards for national rare disease plans and national cancer plans with respect to rare cancers. These should include measurable objectives for access to specialised healthcare, ERN-integration commitments and a minimum set of indicators to monitor implementation across Member States.

What Member States should do

Member States should update and implement their national rare disease plans and cancer plans to meet these standards, with regular reporting, dedicated national financing and greater visibility.

Establish an ERN sustainability and integration framework

PRIORITY ACTION

Action description

This priority brings together several actions recognised as intertwined under the overarching theme of ERN sustainability and integration: (i) establish a formal ERN sustainability framework, including stable EU funding, clearer operational status, protected expert time and accountability for care, training, data and research functions; (ii) improve cross-border collaboration via ERNs, including shared clinical pathways and access to expertise; and (iii) ensure stable national funding for expert centres participating in ERNs.

How this responds to the challenges

This action directly responds to the scarcity of specialists and expert centres, which is addressed through ERN capacity, as well as to the complexity of cross-border access and weak integration of ERNs into national pathways.

EU added value

ERNs are inherently an EU-level, cross-border structure. No single Member State can fund or sustain a network whose value comes precisely from pooling scarce expertise across borders, facilitating cross-border collaboration and generating knowledge. At the same time, expert centres involved in the ERNs are subject to national legal frameworks and operate within the health systems where they are located. Therefore, guaranteeing the long-term sustainability of the ERNs requires concerted efforts at both EU and national level, supported by EU funding and national health budgets. The Cross-Border Healthcare Directive (2011/24/EU) and related legislation established the framework for ERNs, setting criteria for assessing networks and expert centres, but neither the Directive nor the related legislation currently guarantees stable long-term funding, protected expert time or accountability mechanisms for ERNs. This is the residual, unaddressed gap that this action targets.

Delivery roles

What the EU should do

The EU should establish a formal sustainability framework for ERNs, providing stable, multiannual funding and clear accountability mechanisms, and incorporating requirements for registries and data linkage. This framework should build on, while going beyond, the existing ERN legal framework and relevant data provisions of the Biotech Act.

What Member States should do

Building on JARDIN's recommendations and sustainability strategy, Member States should commit stable national funding for designated expert centres, both members and non-members of ERNs, and establish the necessary governance and operational arrangements to allow health systems to fully benefit from cross-border collaboration through the ERNs.

Investigate the feasibility of EU-level approaches to support cross-border access to ultra-rare and highly specialised care

PRIORITY ACTION

Action description

Highly specialised care for ultra-rare conditions and complex procedures remains fragmented across Europe. Patients often face long diagnostic and referral delays, limited clinical expertise in their home country and significant administrative barriers to travel for cross-border treatment. At the same time, evidence has consistently shown that outcomes for highly specialised interventions improve when care is concentrated in centres with sufficient expertise and caseload. This action proposes to explore a structured approach to centralising selected highly specialised services at European level while ensuring equitable access for patients across Member States. Specifically, this action would contribute to designing some of the operational framework required to enhance cooperation between Member States to plan, contract and provide highly specialised healthcare services for:

- people living with a disease that affects fewer than 500 people across the EU;
- people who require complex interventions where fewer than 500 procedures are performed each year across the EU;
- people who require innovative treatments that are typically delivered in only a few centres across the EU.

How this responds to the challenges

This action directly responds to the scarcity of specialists and expert centres, which can be addressed through concentration of expertise; limitations in the current legal and operational framework for cross-border access to low-volume, highly specialised or complex healthcare services, which could be addressed through enhanced cooperation and a specific operational model; and variation in access policies across Member States leading to unequal health outcomes.

EU added value

Building on the current legal framework for cross-border healthcare and the national and European Reference Networks for rare and complex diseases, there is scope to create an EU model for advanced cooperation in the organisation and provision of low-volume, highly specialised healthcare services ("European Rare Disease Lighthouses"). Greater cooperation in this area is not only important for guaranteeing universal health coverage for people living with very rare conditions, but also represents an opportunity for the EU to be at the forefront of healthcare innovation while increasing the effectiveness of public spending, securing a sustainable workforce and improving health-system performance.

Delivery roles

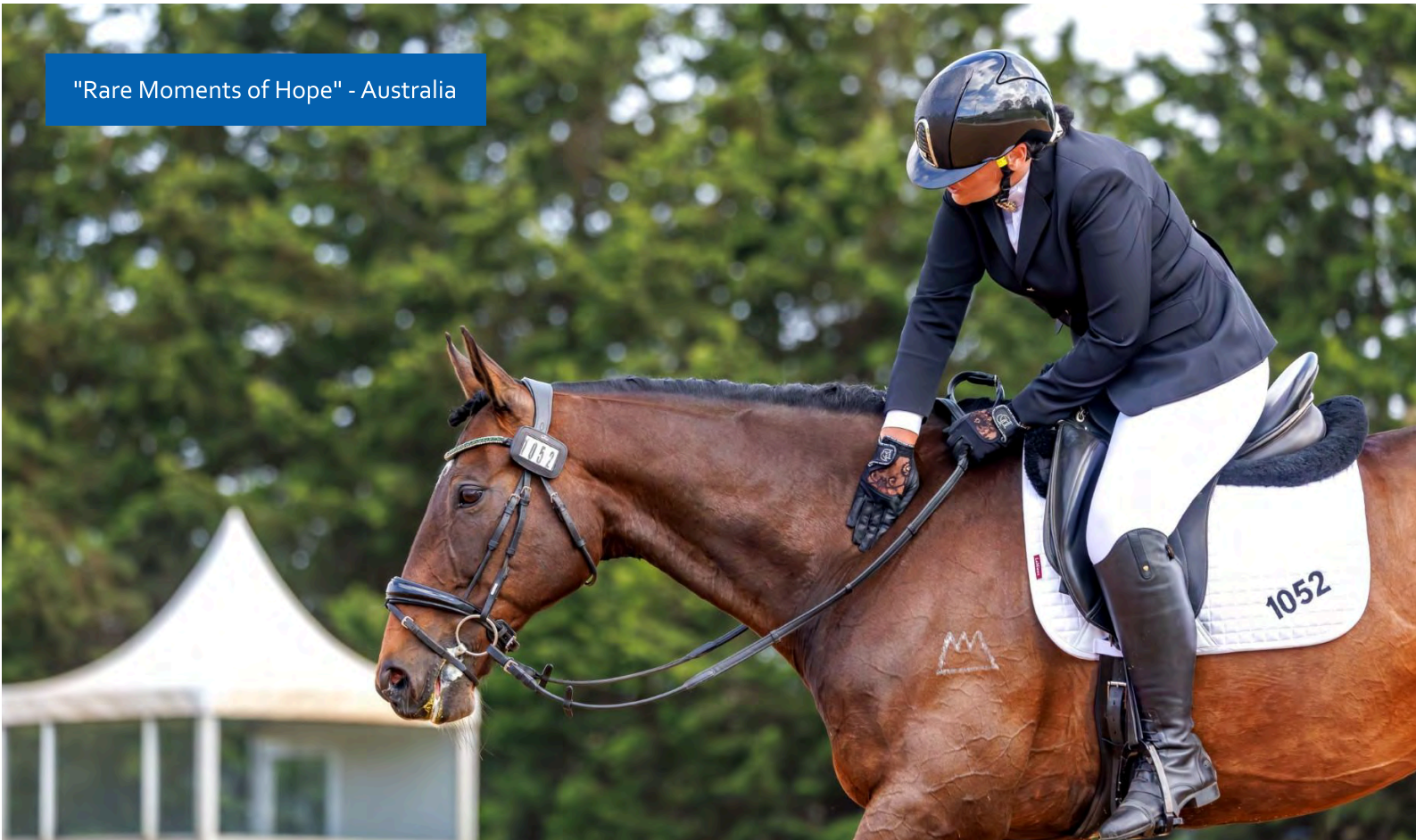
What the EU should do

The EU should allocate funding to develop a pilot project that would lay the groundwork for an EU model for advanced cooperation in organising and delivering highly specialised healthcare for ultra-rare conditions and complex low-volume surgeries ("European Rare Disease Lighthouses"). The pilot project would:

- generate additional evidence on low-value healthcare under the current national and cross-border care delivery model; and
- develop key elements of the Rare Disease Lighthouse model's operational framework. Specifically, the project would develop high-level service specifications and standards of care for two selected conditions and define a core set of key performance indicators (KPIs) for each condition to support quality monitoring and accountability. It would also serve to design a reference or model access pathway, outlining how patients could move through a future Lighthouse system, from referral and eligibility assessment by expert clinical panels, through treatment delivery, to coordinated follow-up with local healthcare providers.

What Member States should do

At this stage, Member States should endorse the action to secure political support. In a second step, building on the results of the feasibility pilot, interested Member States could agree to scale up the model and articulate collective action to plan, organise, fund and monitor the provision of cross-border, low-volume, highly specialised healthcare services.



"Rare Moments of Hope" - Australia

3.3

INTEGRATED CARE AND SOCIAL INCLUSION

Delivering integrated and person-centred care and ensuring inclusion and participation in society for people living with a rare disease



3.3.1 CHALLENGES

Delivering integrated, person-centred care and full social inclusion for people living with a rare disease in Europe faces structural, persistent and interconnected challenges. The problems identified in the working document are:

- The need for integrated social care and somatic healthcare is widely recognised as essential for all conditions, but gaps in integration disproportionately affect people living with a rare disease, whose complex care needs require a high level of coordination. Holistic, person-centred care covering the full spectrum of needs – preventive, curative, rehabilitative, palliative, social and daily-life support, including for progressive and life-limiting conditions, paediatric palliative care, respite and bereavement support for families – remains the exception rather than the rule across Member States.
- Care pathways are complex, fragmented and hard to manage, with weak coordination between health, social and community providers and gaps at key transition points (e.g. child-to-adult, adult-to-older-age, and hospital-to-community). People living with a rare disease and their carers are often forced into the time-consuming role of coordinating care themselves – 65% of respondents to a EURORDIS survey reported having to visit different health, social and local services within a short period of time – and health and social data systems remain fragmented, further limiting continuity of care and access to expertise (EURORDIS – Rare Diseases Europe, 2017).
- Healthcare, social care and community professionals often lack the knowledge and skills required to recognise, manage and coordinate rare and complex conditions, while responsibilities are fragmented across sectors and levels of governance, resulting in gaps in service delivery and accountability.
- Disability related to rare diseases is insufficiently and inconsistently recognised across Member States: eight in 10 people living with a rare disease live with disabilities, yet 53% found it difficult or very difficult to obtain publicly funded support (EURORDIS – Rare Diseases Europe, 2025), and many rare diseases – though incapacitating or degenerative – are not included on official national disability lists. Disability recognition is nevertheless an important route through which people living with a rare disease may gain access to legally recognised rights and benefits within welfare and healthcare systems. For people living with rare diseases and disabilities, timely and needs-based disability assessment and recognition are decisive for whether they can live independently, access the right care services and exercise their rights. Many people have invisible, fluctuating or progressive conditions that do not fit rigid medical criteria, leading to delayed, inadequate or denied recognition and limited or no access to developmental and rehabilitative therapies, social services and social protection, directly undermining dignity, autonomy and inclusion.

- The barriers to disability assessment and recognition have serious consequences, hindering access for persons with disabilities to key rights, including those deriving from the flagship initiatives of the European Strategy for Persons with Disabilities.
- Rare diseases generate a significant social participation and economic burden: 85% of people living with a rare disease experience impacts across several aspects of health and everyday life, seven in 10 patients and family carers reduce or stop their professional activity and 69% experience a decrease in income (EURORDIS – Rare Diseases Europe, 2017). School inclusion is problematic for 79% of students living with a rare disease, and the unemployment rate among people living with a rare disease is 23%, compared with an EU average of 6.1% in 2023 (EURORDIS – Rare Diseases Europe, 2025).
- Women, particularly mothers, bear a disproportionate and often invisible burden as informal carers — they are more likely to reduce or leave paid employment and shoulder long-term caregiving responsibilities — while women and children living with a rare disease also face additional barriers as patients, including later diagnosis and bias in symptom assessment.
- There is a persistent lack of public awareness about rare diseases, particularly regarding non-visible symptoms. Many people living with a rare disease report feeling dismissed, misunderstood or stigmatised throughout their diagnostic and care journeys, further limiting participation in education, work and community life and contributing to social isolation and discrimination.
- People living with a rare disease and their carers experience a significant mental health burden: psychosocial risk, medical uncertainty and economic hardship frequently intersect, and mental health comorbidities create a significant unmet need affecting not only the individual but the whole family.
- Emotional and psychological support is essential for people living with a rare disease and their families during the diagnostic journey and at the point of diagnosis. Such support may also enable faster diagnosis – improving access to appropriate care – and facilitate acceptance when no treatment is available. Yet only 25% report having access to professional psychological support during their search for a diagnosis (EURORDIS – Rare Diseases Europe, 2026). Beyond the diagnostic journey, people living with a rare disease and their families often have ongoing psychological support needs that remain largely unmet. Nearly three in four (73%) report needing professional psychological support, yet only 49% receive it. In addition, 55% report barriers to accessing professional psychological support (EURORDIS – Rare Diseases Europe, 2026).
- Current funding mechanisms are often fragmented and do not incentivise coordination, prevention or long-term support, particularly for complex and lifelong conditions such as rare diseases.

3.3.2 WHAT THE EU HAS DONE

The following actions are substantially or partially addressed by ongoing EU legislative or programmatic instruments, or by existing projects and initiatives such as JARDIN and ERDERA. The Action Plan should acknowledge these, monitor their implementation and address residual gaps – rather than duplicate them.

Disability recognition for rare diseases	Under the May 2026 EU 'Enhanced' Disability Strategy 2021–2030, Member States receive support-level measures for disability assessment: continued technical assistance via the Technical Support Instrument to improve national assessment methodologies and procedures, mutual learning and exchange of best practices among Member States, and targeted guidance through the European Semester tied to UNCRPD implementation commitments. A gap remains regarding convergence of Member States' disability assessment schemes towards an EU framework beyond funding support and mutual learning alone, potentially through dedicated EU guidance in the context of implementation of the Strategy. The Action Plan's residual role would then be to ensure that the review addresses rare-disease-specific gaps: consistent recognition of invisible, fluctuating and multiple impairments, and inclusion of incapacitating or degenerative rare conditions on national disability lists.
Social participation in education, work and community	Partially addressed by the EU Work-Life Balance Directive and the European Pillar of Social Rights Action Plan. The Action Plan should focus on rare-disease-specific reasonable-adjustment guidance for education and employment, rather than new general legislation.
Mental health and psychosocial support	Partially addressed by the European Commission's Comprehensive Approach to Mental Health, which, however, does not explicitly recognise people living with existing physical health conditions, including chronic and rare conditions, as a population living in vulnerable situations. This includes the 30 million people living with a rare condition in the European Union. The Action Plan should confirm alignment and ensure that actions specific to people living with a rare disease, together with dedicated funding, are added within the existing EU mental health strategy rather than creating a parallel one.
Socioeconomic burden of rare diseases	Numerous studies on the burden of rare diseases already exist, often focusing only on certain rare diseases and/or countries; this should be complemented by a meta-analysis to consolidate the evidence base. ERDERA also plans to develop a methodology for assessing the burden of rare diseases in 2027. The Action Plan should ensure that this study's findings feed directly into policy and resource-allocation decisions, while identifying any residual gaps (e.g. gender-related impacts) that the ERDERA study may not fully cover.

3.3.3 PRIORITY ACTIONS

Based on an assessment of EU added value, focusing on actions not yet substantially addressed at EU level, three actions stand out as the highest priorities for EU-level action

Develop EU implementation tools for generic, person-centred integrated care pathways, with measurable indicators

PRIORITY ACTION

Action description

- Develop EU guidance and implementation tools to support Member States in developing multidisciplinary, person-centred rare disease integrated care pathways, including social care (EURORDIS – Rare Diseases Europe, 2021a; Council of the European Union, 2009; EURORDIS – Rare Diseases Europe, 2020b; European Economic and Social Committee, 2024; European Parliamentary Research Service, 2026).
- This guidance will: build on and integrate the JARDIN Generic Care Pathway framework; recommend mechanisms to guarantee coordination between relevant sectors (health, social affairs, employment, education and research); integrate a gender-sensitive approach; embed mental healthcare and psychological support; support recognition of informal carers' roles; develop EU-level guidelines on case management, including formal recognition of the case-manager profession within national occupational codes and dedicated training and financing; and support Member States in developing shared care plans, including structured transition pathways from paediatric to adult services and from adult services to geriatric care.
- The toolkit should also define a shared minimum set of measurable indicators, co-developed with Member States, covering both process measures (e.g. time to a coordinated care plan, share of patients with a recognised case manager) and outcome measures (e.g. avoidable hospitalisations, patient- and carer-reported quality of life), reportable in a standardised format to enable EU-level monitoring without adding a new reporting burden on national systems.

How this responds to the challenges

This action aims to make holistic integrated care the rule rather than the exception and to address fragmented pathways, weak coordination, fragmented data systems and the burden placed on families to coordinate their own care. It also contributes to addressing professional knowledge and coordination gaps through case-manager training and recognition, as well as unmet healthcare needs, while incentivising coordination.

EU added value

JARDIN's Generic Care Pathway framework and case-management recommendations are a starting point. The EU should move from information design and general guidance to implementation support for Member States. The work left to design and implement generic integrated care pathways should be primarily driven by Member States, but having an implementation-support layer and learning system at EU level would contribute to accelerating national reforms, avoiding duplication of work and facilitating the work of national teams tasked with designing and implementing generic integrated care pathways.

Delivery roles

What the EU should do

The EU should transform JARDIN's Generic Care Pathway Framework static table into an online decision-support toolkit featuring different levels of detail depending on the user (high-level executive roadmaps for health authorities, detailed operational workflows and downloadable technical templates for operational teams). The tool should be equipped with modular resources such as decision trees, built around practical steps to design and later implement generic rare disease pathways at local level, a list of red flags, examples of indicators to assess impact and self-assessment checklists that national teams can download and immediately adapt. Finally, the EU should offer countries active implementation support: establish peer-learning twinning programmes, interoperable data and learning-system standards to support care coordination and provide targeted technical assistance (such as via DG REFORM) to guide countries through rollout.

What Member States should do

Member States should prioritise in their national rare disease plans the development of generic integrated care pathways, either as a single generic care pathway or as generic pathways for clusters of conditions. They should leverage the EU toolkit to drive the design of generic integrated care pathways and then their implementation at local level, including systematic monitoring of their impact in terms of time to diagnosis, care coordination, patient experience and health outcomes. Countries should mobilise investment and resources to implement the organisational, technical and legal reforms required, including the formal recognition of the case-manager profession within national occupational classifications and adequately resourced shared care plans within national health and social systems.

Ensure access to adequate social services and social protection for people living with a rare disease and their carers

PRIORITY ACTION

Action description

- Implement specific measures to ensure that people living with a rare disease and their carers have access to adequate social services and social protection. European countries must guarantee that all people living with a rare disease and their carers are entitled to access support from a social worker and adequate social protection and social inclusion provisions, adapted to their individual needs and the cost of living. These provisions must aim to support independent living while also covering the needs of severely affected individuals (European Commission Expert Group on Rare Diseases, 2016).
- To achieve this, Member States should support the development of integrated care services for people living with a rare disease and integrate social services into the national rare disease networks currently under development, so that health and social care are delivered together as part of a holistic care pathway.
- This action constitutes a building block of the decision-making tool described under the previous priority and can be implemented as one of its sub-actions. It is also closely linked to a complementary action listed in Annex I – List of Complementary Actions, which likewise contributes to that priority: "Establish EU guidance for Member States on disability assessment procedures (or equivalent entitlement mechanisms) to ensure that persons with rare disease-related disability and functional limitations receive consistent and timely recognition."
- EU guidance should set out common principles for assessing disability and functional limitations arising from rare diseases, taking into account their often invisible, fluctuating and multisystemic nature, and drawing on

the expertise of European Reference Networks and national expert centres. This would ensure that rare disease-related disability is recognised more consistently across Member States and is therefore adequately supported through social security and social protection schemes.

How this responds to the challenges

This action directly contributes to making holistic and cross-sectoral care the rule rather than the exception and to addressing the social participation and economic burden of rare diseases, including reduced employment and income. It also contributes to addressing the lack of access to disability-related support.

EU added value

The relevant legal frameworks – the UN Convention on the Rights of Persons with Disabilities (UN CRPD), the EU Charter of Fundamental Rights (Articles 21 and 26) and the European Social Charter – set out general disability and social rights principles but does not translate them into rare-disease-specific guidance on access to social workers or social protection. Without EU-level guidance, Member States have limited incentive to adapt general social protection frameworks to the specific, often invisible and fluctuating needs of people living with a rare disease and their carers, leaving genuine residual EU added value in providing that translation.

Delivery roles

What the EU should do

The EU should issue guidance translating existing disability and social rights instruments (UN CRPD, EU Charter of Fundamental Rights and European Social Charter) into rare-disease-specific standards for access to social workers and social protection, adapted to fluctuating and invisible needs.

What Member States should do

Member States should support the development of integrated care services for people living with a rare disease, fostering the integration of social services into national healthcare networks for rare diseases. Member States should guarantee access to the support of a dedicated social worker and adequate, needs-adapted social protection and inclusion provisions for people living with a rare disease and their carers, covering both independent living support and the needs of severely affected individuals.

Establish formal mechanisms for representatives of people living with rare diseases and their families, and patient organisations, to co-design rare disease policies and services

PRIORITY ACTION

Action description

- Establish formal mechanisms for representatives of people living with a rare disease and their families, patient organisations and civil society to co-design rare disease policies and services, with minimum standards for meaningful participation (EURORDIS – Rare Diseases Europe, 2021a; Council of the European Union, 2009; EURORDIS – Rare Diseases Europe, 2020d). This includes providing sustainable support for participation – capacity building, compensation for time and transparent consultation processes – and funding EU-level training activities on patient partnerships, co-design, governance skills and multi-stakeholder collaboration (EURORDIS – Rare Diseases Europe, 2021a; European Parliamentary Research Service, 2026).

How this responds to the challenges

By engaging people living with a rare disease and their representative organisations in the design, implementation and monitoring of policies and services, this action cuts across nearly every problem: patient organisations are a key mechanism through which unmet needs are identified and fed back into policy.

EU added value

Only EU-level coordination can set minimum participation standards that are consistent across Member States and EU governance bodies, including ERNs, expert centres, research programmes, policy advisory bodies and social security bodies and schemes. The EU added value here lies in sustaining and scaling rather than creating from scratch, for instance by building on existing patient training initiatives such as the EURORDIS Open Academy and EUPATI. However, a formal co-design mechanism to involve patient organisations, together with its governance and sustainable funding, remains a substantial gap that can only be filled at EU level.

Delivery roles

What the EU should do

The EU should establish minimum standards for meaningful patient and civil society participation in rare disease policymaking, embedded across ERNs, expert centres, research programmes and policy advisory bodies, with a funded compensation model for participating patient organisations.

What Member States should do

Member States should embed the EU participation standards in national rare disease governance structures and provide sustainable national funding and capacity-building support to national patient organisations so they can participate on an equal footing with institutional, academic and industry stakeholders.

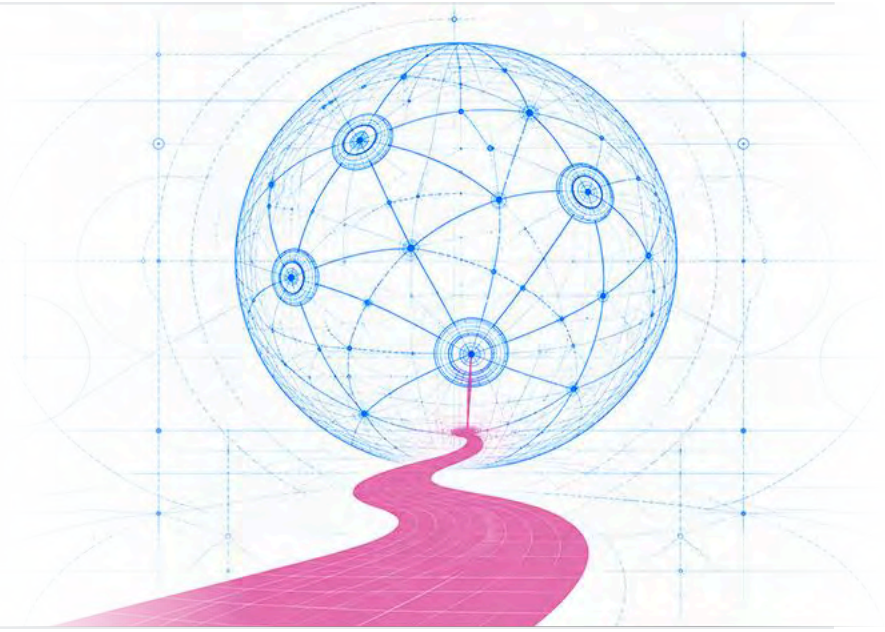


"Princess of the light" - Algeria

3.4

OPTIMISING THE DATA ECOSYSTEM

Building a connected, interoperable and patient-centred rare disease data infrastructure across Europe



3.4.1 CHALLENGES

Rare disease research and healthcare rely on diverse types of data, including quality of life, health economics, natural history, genomics and clinical information, but the rarity and geographic dispersion of patients make it difficult to collect sufficiently large and robust datasets (EURORDIS – Rare Diseases Europe, 2020a).

- While the volume of data generated across health systems is expected to continue growing, including through opportunities linked to the European Health Data Space (EHDS), limited visibility of people living with a rare disease in health systems, limited interoperability, uneven development of infrastructures and barriers to cross-border data sharing – legal, financial, technical, administrative and organisational – risk inhibiting the ability to generate the critical mass of knowledge needed to accelerate research, diagnosis and therapy development, support evidence-based care and policy decision-making, and improve the visibility of people living with a rare disease in health systems (EURORDIS – Rare Diseases Europe, 2020a; European Parliament, 2025; European Parliamentary Research Service, 2026).
- Artificial intelligence and other technologies building on this data ecosystem also have the potential to bring benefits for people living with a rare disease, while creating new challenges and increasing the urgency of addressing current gaps. The following key problems have been identified:
- The limited and inconsistent use of common data standards, harmonised minimum datasets and rare disease coding systems, notably ORPHAcodes, prevents data from being meaningfully linked or compared across institutions and Member States (EURORDIS – Rare Diseases Europe, 2020a; High-Level Meeting on a European Innovation and Care Ecosystem for Rare and Complex Diseases, 2025). The 2025 ERN monitoring report shows highly heterogeneous adoption of rare disease coding across expert centres and countries, confirming that even Europe's most specialised rare disease centres – those participating in the ERNs – have highly uneven implementation of ORPHAcodes, with some countries reporting adoption below 20% and a high proportion of "not available" responses in several countries (European Commission, 2025). These data appear to point to a range of technical and organisational barriers, including lack of awareness, limited coding literacy, technical and financial constraints and the absence of a mandate or obligation to use rare disease coding systems (Vohora et al., 2026; European Commission, 2025).
- The lack of systematic use of rare disease codes in electronic health records (EHRs), national and regional health information systems, hospital discharge records and mortality data means that most people living with a rare disease, including those in a diagnostic dead end (so-called 'undiagnosed patients'), remain unidentifiable at population level, making rare diseases largely invisible in health data systems (European Commission, 2008; EURORDIS – Rare Diseases Europe, 2020).

- Data are siloed across healthcare systems, registries, biobanks and research platforms, and the fragmentation and uneven development of these infrastructures across Europe limit the ability to link clinical care, research and innovation across the rare disease ecosystem.
- Rare disease registries are a primary source of natural history data, real-world evidence and patient cohorts. While significant resources are required for registry development and long-term maintenance, rare disease registries are perceived as one of the most valuable resources for research and care (EURORDIS – Rare Diseases Europe, 2020a; European Parliament, 2025; European Parliamentary Research Service, 2026). Yet, despite their strategic importance, most lack sustainable funding, are unsustainably governed and are unevenly developed across Member States.
- Cross-border healthcare data exchange and research data sharing face persistent legal, administrative and governance barriers. The EHDS creates a major opportunity to address these gaps but would require dedicated attention to rare diseases, including harmonised minimum datasets and appropriate governance provisions. Otherwise, the EHDS could deliver a data infrastructure that systematically excludes or misrepresents people living with a rare disease.
- Secondary use of health data and real-world evidence is underexploited for rare diseases, mostly due to the lack of governance frameworks that enable secure and trusted secondary use of health data. Potential inconsistencies between different EU and national legislative frameworks, such as the GDPR, the EHDS and national legislation governing the secondary use of data, could further impede progress.
- Patients and patient organisations are rarely recognised as meaningful partners in decisions about how their data are governed, accessed and used. Trust in data sharing is insufficiently supported through clear communication, patient information and participatory governance. People living with a rare disease strongly support responsible data sharing to improve healthcare and foster research, but their willingness to share data depends on transparency, trust and safeguards that respect their privacy, preferences and expectations regarding how their data are used (Courbier et al., 2019; EURORDIS – Rare Diseases Europe, 2020a). The implementation of new European data governance frameworks such as the European Health Data Space (EHDS) will require careful governance and stakeholder engagement to ensure that increased data availability for research and innovation is balanced with appropriate safeguards for people living with rare and ultra-rare conditions, including protection against risks of misuse, re-identification and discrimination (European Parliamentary Research Service, 2026; EURORDIS – Rare Diseases Europe, 2020).
- AI and digital tools hold major potential for rare diseases, including for case finding, diagnosis, clinical decision support and research. However, the use of AI-based approaches, alongside a well-functioning data ecosystem to underpin these tools, requires consistent governance, including validated frameworks, community-led governance standards and equity monitoring.

3.4.2 WHAT THE EU HAS DONE

The following actions are substantially or partially covered by existing EU instruments or initiatives. The Action Plan should acknowledge these, build on them and address residual gaps – rather than duplicate them.

Integrate rare diseases into the EHDS	The EHDS Regulation (2025) creates the legal framework for the primary and secondary use of health data and cross-border data sharing, but rare diseases are not explicitly identified as a priority use case within the EHDS. The functional specifications of the eHealth Network guidelines on the European Electronic Health Record exchange format (EEHRxF) include ORPHAcodes for inclusion in the Patient Summary. As such, ORPHAcodes, at disorder and subtype level, are included in the MyHealth@EU code system and the eHealth Digital Service Infrastructure (eHDSI) for the exchange of patient summaries and other health datasets for primary use. In addition, the JARDIN Joint Action on Integration of ERNs into national healthcare systems is devising a rare disease dataset to be included in EHRs for both primary and secondary use, in alignment with the requirements of the EEHRxF. JARDIN's work in this area will provide a foundation for primary data use, while for secondary data use, the EHDS2 Pilot Project, THEDAS Joint Action, QUANTUM and SHAIPED projects and the ERDERA Policy Think Tank will provide a basis on which to build further.
EHR and registry interoperability	JARDIN Work Package 8 (Data Management) specifically addresses the fragmentation of ERN registries, rare disease databases and health data sources through improved technical and semantic interoperability.
Registry harmonisation and data infrastructure	ERDERA's Strategic Research and Innovation Agenda advances registry harmonisation, FAIR data practices and federated data infrastructures for rare diseases. Remaining challenges include the sustainability of funding, governance and operational models beyond project cycles; the integration of rare disease registries and data services into the European Health Data Space architecture; consistent data quality and regulatory-readiness standards; and stronger interoperability between healthcare and research data ecosystems.
Secondary use of health data	The EHDS Regulation establishes a framework for the secondary use of health data, including for research. Residual gaps include harmonisation of Informed Consent Form (ICF) templates, addressing the re-identification risks for small rare disease populations and explicit provisions for rare disease research use cases.

Patient-reported outcomes and patient-reported experience measures

The HTA Regulation creates partial provisions for patient-generated evidence. The ERICA project developed a database of rare disease patient-reported outcome measures (PROMs), and ERDERA is scaling up this effort. The Rare Disease Catalyst Consortium in Ireland is in the final phase of developing a patient-reported experience measure for people living with rare diseases and their carers (RD-PREM), to understand experiences of care from the perspective of a person living with a rare disease or a caregiver. However, the systematic integration of PROMs, patient-reported experience measures (PREMs) and n-of-1 patient-led research data as recognised evidence sources for rare diseases is not yet standard practice.

AI in rare diseases

The AI Act provides a regulatory framework for high-risk AI applications in health. The Biotech Act proposes specific measures to support the application of AI in biotechnology, including for rare diseases, and there is further political momentum at EU level to prioritise the value of AI in health innovation and care. Guidance for specific AI applications with potential impacts on people living with rare diseases would be needed to ensure that potential benefits and risks are appropriately balanced.



"A Helping Hand" - Czech Republic

3.4.3 PRIORITY ACTIONS

Accelerate the systematic use of ORPHAcodes across EU health information systems, registries and other relevant datasets

PRIORITY ACTION

Action description

- Accelerate the systematic adoption of ORPHAcodes as the standard for rare disease coding across the EHDS and national health information systems, in line with existing EU and WHO recommendations. The consistent use of ORPHAcodes shall be accompanied by ICD-11, and ICD-O where relevant, for disease identification, and SNOMED for health system records.
- Promote the systematic capture of rare disease codes in relevant clinical and demographic datasets, such as hospital discharge records, EHR systems used in tertiary, secondary and primary care, mortality information systems and the social care sector, to improve visibility and comparability.

How this responds to the challenges

This action addresses fragmentation and the absence of common data standards and contributes to making rare diseases visible in mainstream health information systems. ORPHAcode adoption is the single most enabling technical step for rare disease data interoperability: without a shared coding standard, data from different systems cannot be linked, patients cannot be identified across settings and disease burden cannot be measured. Mapping existing coding systems and promoting the systematic adoption of rare disease codes in electronic health records (EHRs) are also complementary but essential actions to fully unlock the potential of harmonisation through ORPHAcodes.

EU added value

ORPHAcodes are already recognised in EU policy and interoperability frameworks and are aligned with WHO and ICD classifications. Achieving a critical mass of ORPHAcode adoption in health information systems, registries and other relevant datasets requires EU-level coordination, including regulatory enforcement, co-funding for implementation and alignment with the EHDS. Likewise, mapping existing coding systems is a technical and governance task that individual Member States cannot achieve alone.

Delivery roles

What the EU should do

Through implementing acts under the EHDS, the European Union should:

- Continue supporting the adoption of common semantic standards to ensure that rare diseases are accurately identified and searchable across all EU health systems.
- Continue funding Orphanet's core activities to ensure the long-term sustainability of ORPHAcodes and mappings with other coding systems (e.g. ICD-10 and ICD-11), supporting countries that use different coding systems while enabling interoperability.
- Consider adopting EU legislation to mandate the use of ORPHAcodes in data categories to be exchanged under the EHDS (e.g. patient summaries, electronic prescriptions, electronic dispensations and discharge reports) across all EU Member States (technical harmonisation).
- Consider making the consistent use of ORPHAcodes a mandatory requirement in funding calls and monitoring systems to ensure compliance.
- Encourage Member States, through guidance, to require certain standards, including ORPHAcodes, in public procurement of software and IT solutions.
- Promote the adoption of ORPHAcodes and other interoperable coding systems through conditionalities attached to EU funding.
- Provide targeted co-funding for cross-mapping between ORPHAcodes and other interoperable coding systems and standards.

What Member States should do

Implement ORPHAcodes in EHR systems and health information systems, including, for example, the social sector, emergency departments and pharmacies, ensuring systematic capture of rare disease codes in hospital, primary care and mortality datasets, and designate national focal points for rare disease coding compliance.

Require hospitals, primary care providers and expert centres to systematically use ORPHAcodes in EHRs and clinical coding.

Require ORPHAcodes and other coding systems and standards as a condition for receiving national funding, including for publicly funded registries or those operating under national health authority oversight.

Strengthen registries and data linkage to support care quality, research and service planning

PRIORITY ACTION

Action description

This action focuses on strengthening registries and data linkage to support care quality, research and service planning, including by developing sustainable funding models for registries in the context of the EHDS and exploring how appropriately governed data access could contribute to long-term sustainability. This could position registries as strategic EU assets for competitiveness, innovation and evidence generation.

How this responds to the challenges

Rare disease registries are an irreplaceable foundation for natural history data, patient cohort identification and post-authorisation evidence. Sustainable funding and quality management for registries are required for them to become a strong infrastructure within the EU data ecosystem and to address challenges related to evidence generation and data linkage for monitoring equity, access and quality of care.

EU added value

Patient populations for individual rare conditions are small and geographically scattered across 27 Member States, and no single country possesses sufficient clinical data, sample sizes or expertise to build comprehensive registries. EU added value lies in the ability to overcome national borders by pooling data, expertise and infrastructure. This enables the creation of sufficiently large patient cohorts for clinical trials, real-world evidence generation and epidemiological monitoring. Registry sustainability and harmonisation also cannot be achieved by individual Member States or disease communities acting alone. EU-level co-funding and support through common quality standards, harmonised Informed Consent Forms' (ICF) requirements and integration into the EHDS are essential to achieve impact.

Delivery roles

What the EU should do

Establish a dedicated, sustained co-funding stream for rare disease registry infrastructure, linked to EHDS implementation and to ERDERA, or its follow-up, with harmonised quality standards, common ICF frameworks enabling data reuse and clear data access governance models that contribute to long-term sustainability.

Establish harmonised rare disease registry data standards and minimum datasets at EU level, building on ERDERA Policy Think Tank recommendations and forthcoming JARDIN recommendations, with explicit links to the European Platform on Rare Disease Registration and the ERDERA Data Services Hub.

Continue funding and upgrading common infrastructures that facilitate federated data queries, including the European Platform on Rare Disease Registration, the ERDERA Data Services Hub, the ERDERA Virtual Platform and ERNs; provide sustained financing for research consortia that bridge clinical registries, basic science and therapy development; and establish clear, harmonised rules under the EHDS framework for cross-border secondary data access, while maintaining strict GDPR compliance.

What Member States should do

Member States should ensure that national rare disease registries receive adequate and sustainable public funding, implement harmonised quality standards and ICF frameworks, and connect national registries to EU-level data infrastructure, including the EHDS and ERDERA's federated ecosystem.

Connect national rare disease registries to EU platforms and ensure that existing and new national and disease-specific registries adopt FAIR data principles and common standards and share their metadata with European platforms.

Designate and resource national Health Data Access Bodies (HDABs) under the EHDS framework to handle cross-border rare disease data access requests efficiently.

Implement JARDIN recommendations, including those aimed at improving semantic accuracy across national systems and ERN registries and the interoperability of rare disease health data.

Adopt harmonised registry standards and minimum datasets nationally, connecting national registries to EU-level infrastructure.

Support registries through national rare disease plans and existing national health data information systems, and incentivise data collection and data sharing through dedicated human resources, funding or technical support.

Enhancing EHR systems for standardised rare disease data integration into the European Health Data Space

PRIORITY ACTION

Action description

- Support Member States in strengthening and fully implementing EHR systems to capture structured data relevant to rare diseases, ensuring compatibility with registries and the EHDS and the systematic use of ORPHAcodes. Specifically, this action should support the implementation in EHR systems of the JARDIN standardised rare disease dataset to improve interoperability and data integration across national health information systems, EHR systems and ERN registries.
- In parallel, the EHDS should integrate a dedicated rare disease module, adopting the JARDIN-recommended minimum rare disease dataset, harmonised across Member States.

How this responds to the challenges

This action directly addresses the invisibility of rare diseases in mainstream health data systems and the fragmentation of data, while contributing to ensuring that EHDS implementation meets rare disease needs. EHR systems are the primary point of data capture for clinical care: if rare disease data are not captured at source with appropriate structure and coding, no downstream interoperability, registry or EHDS integration can compensate.

EU added value

Only EU-level action can ensure that the JARDIN rare disease dataset and ORPHAcode implementation are adopted consistently across the different EHR systems of all 27 Member States in a way that enables the full potential of the EHDS to be realised for rare disease research and care.

Delivery roles

What the EU should do

Mandate the inclusion of the JARDIN rare disease dataset and ORPHAcode fields in EHR systems, building on JARDIN Work Package 8 outputs for technical and semantic interoperability standards, and provide targeted funding for Member States to support the implementation of these requirements.

Develop EU-level guidance and tools for integrating rare disease information into EHR-based primary care workflows, including referral prompts and decision support. Explore the use of AI tools, where appropriate, to support primary care professionals in detecting potential rare disease cases.

Integrate rare diseases explicitly as a priority use case within the EHDS, establishing a dedicated JARDIN rare disease module, including the use of ORPHAcodes, and explicit provisions for patient-generated data, PROMs, PREMs and lived experience data, while ensuring that the rare disease community is represented and involved in its implementation.

What Member States should do

Upgrade EHR systems used across primary, secondary and tertiary care settings to capture structured data relevant to rare diseases, including, at a minimum, the rare disease dataset module resulting from JARDIN; implement ORPHAcodes at local and national levels; and enable the use of EHR data in registries and the EHDS, with dedicated support for healthcare providers in less-resourced settings, including funding and human and technical resources.

Build on JARDIN Work Package 8 (Data Management) outputs to improve data capture, data linkage and large-scale rare disease data integration through improved technical and semantic interoperability, secure data integration and sustainable governance frameworks adopted by rare disease registries, EHR systems and other relevant health information systems.

What the EU should do

Ensure that the dedicated rare disease module also enables interoperability with verified registries and external databases rather than duplicating data collection, and supports the development of minimum national datasets to improve interoperability, increase cohort sizes across rare diseases, measure disease burden collectively and evaluate the impact of healthcare interventions.

Allocate adequate funding and appropriate mechanisms to ensure consistent implementation of the EHDS, including technical assistance and capacity building for IT and clinical teams.

What Member States should do

Strengthen primary care capacity through dedicated funding and an adequate legal and regulatory framework for rare disease identification and referral, and ensure that EHR systems include referral prompts to specialist rare disease centres and ERNs.

Ensure that national EHDS implementation plans include the JARDIN rare disease minimum dataset and patient data governance provisions, and that rare disease patient organisations are represented in national EHDS governance.



"My Lonesome Self" - Guyana

3.5

INNOVATIVE AND NEEDS-LED RESEARCH

Making the EU a global leader in rare disease innovation



3.5.1 CHALLENGES

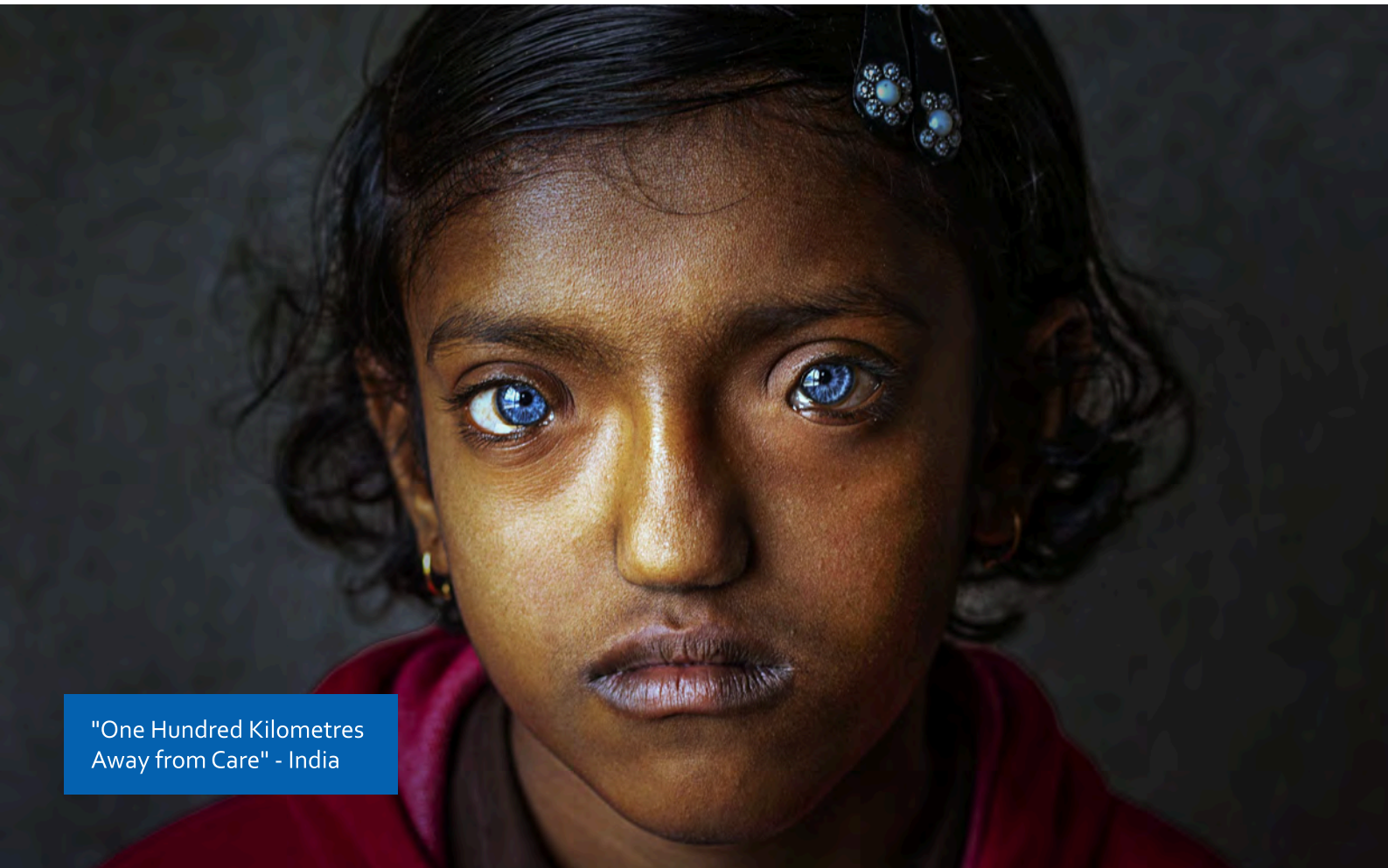
Research, diagnosis and treatment access form a continuous and interconnected pathway. The quality and long-term sustainability of the research ecosystem determine the development, evaluation, approval and availability of diagnostic tools and therapies. It is therefore essential to keep this interconnection in mind when addressing the issues covered in this section.

Europe does not lack rare disease initiatives. What is missing is greater continuity, integration and prioritisation across the research and innovation pathway. While significant progress has been made over recent decades, rare disease research continues to face structural and interconnected challenges. At the same time, the evidence base remains limited for most rare diseases. Expanding knowledge must therefore remain a priority. Focusing funding primarily on late-stage research or short-term opportunities will not be sufficient to address these gaps. The core problems are:

- Long-term funding continuity across the research continuum remains inadequate. Underinvestment and fragmented funding across the research continuum disproportionately affect commercially less researched disease areas, including many ultra-rare conditions, where limited incentives can slow the translation of research into diagnostic and therapeutic advances. Public funding is predominantly short-term and project-based, making it difficult to sustain the infrastructures, careers and long-term partnerships that rare disease research requires. Low investment in basic research is a particular concern, as it can constrain further R&D and intensify competition for limited overall funding (EURORDIS – Rare Diseases Europe, 2019b; Council of the European Union, 2009; European Parliamentary Research Service, 2026; European Parliament, 2025; Aartsma-Rus et al., 2021).
- Despite substantial regulatory harmonisation through the EU Regulation 536/2014 or EU Clinical Trials Regulation (CTR), residual differences in national implementation, ethics, contracting, site activation, data governance and other administrative requirements continue to create complexity and reduce Europe's relative attractiveness for multinational clinical trials (European Parliamentary Research Service, 2026; UCB, 2024; Letta, 2024).
- The heterogeneity of rare diseases, combined with small patient numbers for each condition, creates intense competition for limited funding and makes it structurally difficult to achieve the critical mass of patients, data and expertise needed for robust studies. This fragmentation is compounded by a structural gap for diseases that remain at the fundamental research stage, where registries may not yet exist and natural history is uncharacterised. These diseases can therefore be excluded from registry-based trials and evidence-generation frameworks, risking leaving some patients behind even as the broader research ecosystem advances (EURORDIS – Rare Diseases Europe, 2019b; Council of the European Union, 2009; European Parliamentary Research Service, 2026; European Parliament, 2025; Ardigò et al., 2026). Research priorities, outcomes and

evidence-generation strategies are also not consistently shaped with patients from the earliest stages, contributing to mismatches between research outcomes and what matters to people living with rare diseases (Kole et al., 2021; European Parliamentary Research Service, 2026; UCB, 2024). As a result, unmet needs in rare diseases extend beyond the lack of medicines to include delayed diagnosis, absent natural history data, caregiver burden and transition gaps, among others.

- Registries, biobanks and data platforms are underdeveloped, non-interoperable and unevenly governed. The absence of FAIR, linked and federated data slows discovery, trial design and evidence generation – all prerequisites for innovation (Czech Presidency of the Council of the European Union, 2022).
- Many promising innovations fail to progress because conventional commercial incentives are insufficient, highlighting the need for dedicated pathways for ultra-rare conditions, n-of-1 therapies, repurposing and other commercially fragile areas. The 'valley of death' between early- and late-phase development remains poorly addressed (European Parliamentary Research Service, 2026; UCB, 2024).
- Over the past 20 years, Europe has progressively built one of the world's most advanced cross-border rare disease research ecosystems through successive initiatives, including E-Rare, EJP RD, ERDERA, rare disease expert centres across the EU, the 24 European Reference Networks (ERNs) and major European Research Infrastructures such as BBMRI, ECRIN and EATRIS. However, many of these critical infrastructures remain insufficiently recognised, not fully leveraged or inconsistently embedded at national level, limiting their research potential. The main remaining challenge is therefore to ensure the long-term sustainability, optimisation and equitable uptake of existing collaboration mechanisms across Member States, while addressing persistent geographical inequalities in research expertise and capacity. This is essential to ensure that people living with rare diseases in smaller or less-resourced countries are equally able to benefit from research progress or access clinical trials. Achieving this will require addressing fragmented governance, limited funding and limited digital interoperability across key research infrastructures (European Parliamentary Research Service, 2026; European Parliament, 2024; UCB, 2024; Nordic Rare Disease Summit, 2025; European Parliament, 2025).



"One Hundred Kilometres Away from Care" - India

3.5.2 WHAT THE EU HAS DONE

The following actions are substantially or partially addressed by ongoing EU legislative or programmatic instruments. The Action Plan should acknowledge these, monitor their implementation and address residual gaps – rather than duplicate them.

Coordinate rare disease research	The European Rare Disease Research Alliance (ERDERA) has developed the Strategic Research and Innovation Agenda as the foundation for a coordinated rare disease research ecosystem in Europe, and any European Rare Disease Research Agenda should build on it rather than create parallel structures (ERDERA, 2025). IRDiRC provides international coordination, while implementation of the Life Sciences Strategy offers an additional policy mechanism that could be leveraged at EU level (European Commission, 2025a).
Strengthen ERNs as research infrastructure	The Biotech Act, still under discussion by the EU co-legislators, creates an opportunity to introduce provisions linking the ERNs to the EU research infrastructure. These should be used to give ERNs an explicit, sustainably funded research-infrastructure function covering natural history cohorts, registries, biobanks, trial-readiness platforms and FAIR data access, building on models such as Solve-RD. While the Biotech Act remains under negotiation and the final text could change, the proposed strategic projects could provide funding and foster relevant partnerships (European Commission, 2025c). ERDERA's National Mirror Groups offer an additional mechanism for broader national linkage to EU structures.
Enable innovative trial designs	Innovative trial designs and regulatory science for small populations are partially addressed by the EU Clinical Trials Regulation, ACT-EU and the proposed Biotech Act, including FAST-EU pilots, a regulatory sandbox and a centralised voluntary procedure for rare disease trials. The Biotech Act also opens the door to an academic-led development pathway for commercially fragile areas, including ultra-rare diseases, n-of-1 therapies, repurposing and platform trials, and these measures could complement existing mechanisms.
Support multi-country studies	Multi-country studies and shared protocols are partially addressed through ERDERA-aligned calls and joint evaluation, and through the CTR shared protocol regime. Patient pool pre-identification and trial-site readiness are also being addressed through the RealiseD project (WP1 and WP3).

Enable remote participation in studies

Remote and digital participation in clinical studies is partially addressed through decentralised clinical trial provisions in the CTR and illustrated by national best practices, such as the German virtual-site and Principal Investigator model with homecare integration. The Action Plan should promote uptake while addressing equity concerns: digital platforms must not replace in-person specialist care, should be accessible to patients without adequate devices or connectivity, should use language that is accessible regardless of digital literacy and must not create or deepen a digital divide. Citizen science-led approaches should also be explored as the AI era makes conventional digital research platforms increasingly fragile.

Support public-private research partnerships

Public-private partnerships for rare disease research are partially addressed through ERDERA, IHI and Horizon Europe PPP mechanisms. The Commission has been called upon to actively support ERNs in building PPPs and to embed shared-risk mechanisms, open-science principles and clear benefit-sharing frameworks. This aim, however, should be treated as a component of the broader co-investment ecosystem rather than as a standalone action, with a global scope given that ultra-rare diseases require partnerships extending beyond EU borders.

Support responsible AI and digital tools

While the AI Act provides the specific framework for AI applications and the Medical Devices Regulation provides specific rules for medical devices using AI, the use of AI and digital tools for rare diseases is also being facilitated through the proposed Biotech Act. Given this fairly complex framework, the Action Plan could further facilitate AI deployment under key conditions, such as data infrastructure readiness and meaningful patient involvement in tool design, development, piloting and validation.



"Júvan's Miracle Mission" - South Africa

3.5.3 PRIORITY ACTIONS

Based on workshop discussions, survey feedback and an assessment of EU added value, focusing on actions not already substantially addressed at EU level, three actions emerge as the highest EU-level priorities.

Strengthen and better align EU co-investment across the rare disease research and innovation continuum

PRIORITY ACTION

Action description

Establish a mechanism to ensure sustained, long-term EU co-investment in rare disease research, aligned with patients' needs and spanning the full innovation pipeline from basic and translational science to clinical and social research. The mechanism should leverage effective public-private partnership models, ERDERA's federated ecosystem as the rare-disease-specific infrastructure anchor, European expert centres for rare diseases and ERNs, and the broader European research infrastructure landscape (e.g. BBMRI, EATRIS and ECRIN) as complementary resources for rare disease communities. Long-term public-private partnerships should contribute to innovation, with explicit prioritisation of commercially fragile areas.

How this responds to the challenges

This action directly responds to chronic underinvestment and fragmented, short-term funding in the sector, declining EU attractiveness for rare disease R&D, translational bottlenecks and the 'valley of death' for commercially fragile areas, and the underfunded research function of key infrastructures, including rare disease expert centres and ERNs. Long-term EU co-investment is an enabling condition for almost all other research actions: infrastructure, trial readiness, patient involvement and regulatory innovation cannot be sustained without predictable, non-project-based funding. As most rare diseases do not have a viable financial model, public co-investment remains essential to advance research and development, including innovative trial designs for small populations.

EU added value

Only EU-level co-investment mechanisms can achieve cross-border, multi-disease coordination at a scale that no single Member State can sustain. Horizon Europe and equivalent instruments uniquely enable the pooling of resources across Member States and provide the neutral governance necessary for fair access.

Delivery roles

What the EU should do

Establish a dedicated, sustained co-investment mechanism for rare disease research within the next Multiannual Financial Framework, drawing from FP10 and other relevant funding lines, sufficiently covering the full innovation pipeline and explicitly prioritising commercially fragile areas.

Ensure funding for key rare disease research infrastructures, building on and complementing ERDERA's federated ecosystem and involving European expert centres, ERNs and the broader European research infrastructure landscape, alongside a dedicated academic-led development pathway for ultra-rare diseases, n-of-1 therapies, repurposing and platform trials.

What Member States should do

Develop and implement national rare disease research funding strategies with multi-year commitments, aligned with the EU mechanism and ERDERA's Strategic Research and Innovation Agenda, and co-invest in the integration of national research centres into ERDERA's federated ecosystem.

Establish national compensation mechanisms for clinicians and researchers undertaking research-related workloads – including registry participation, data contribution and patient recruitment – to stimulate participation in registries and trials.

Build a strong culture of meaningful patient partnership and patient-relevant evidence across rare disease research

PRIORITY ACTION

Action description

Strengthen meaningful patient involvement in rare disease research by building a strong culture of patient partnership, including patients in priority-setting, project governance, study design, outcomes and dissemination, with clear guidance and resources to help patient organisations build capacity and contribute effectively, while incentivising similar approaches at national level. This would entail leveraging EU funding requirements as one of the strongest levers available at EU level to ensure that the desired standards of involvement apply across the wider European research ecosystem. It would also involve promoting the systematic use of patient-generated evidence, including patient-reported outcome measures (PROMs), patient-reported experience measures (PREMs) and quality-of-life (QoL) measures, in research and clinical trials. These measures can improve understanding of diseases, identify unmet needs and support better research and clinical decisions.

How this responds to the challenges

This action directly responds to insufficient understanding of patient-relevant outcomes and natural history, and to a fragmented landscape in which patient data and priorities are not systematically integrated. Patient involvement is also the mechanism through which funding decisions, research design and evidence standards can align with actual unmet needs, making it a structural prerequisite for all other priorities in this area. In the context of ultra-rare and personalised therapy development, where the boundary between research and clinical care is blurred, structured patient involvement is also an ethical and safety imperative.

EU added value

The EU can establish a common European expectation for meaningful patient partnership across rare disease research and use its funding programmes, regulatory and methodological guidance, research infrastructures and support to Member States to promote consistent implementation across sectors and countries. EU funding

conditions and framework programmes are also an effective lever for mandating patient involvement standards consistently across Member States. A harmonised EU standard – embedded in research funding conditions – can cascade into national programmes and create a virtuous cycle in which patient-generated evidence becomes a structural feature of the rare disease research ecosystem. This action is only partially addressed by existing instruments and requires explicit, binding EU-level guidance and resourcing.

Delivery roles

What the EU should do

Mandate structured patient involvement – including a mandatory percentage of funding allocated to patient organisations, reimbursement mechanisms, capacity building for patient organisations, inclusion of patients as experts in evaluation and transparent impact reporting – as a binding condition of all EU-funded rare disease research.

Develop harmonised EU guidance on patient-generated evidence tools (PROMs, PREMs and QoL measures), with patients and patient organisations involved in selecting, designing, validating and interpreting these tools, building on the EMA Reflection Paper on Patient Experience Data.

Ensure that clear responsibility for overseeing meaningful patient involvement is explicitly assigned in all research protocols, whether to ethics committees, regulators or independent patient advocacy structures, building on available resources such as the toolbox developed by the IMI-funded PARADIGM project.

What Member States should do

Develop national frameworks for patient involvement in publicly funded rare disease research, consistent with EU-level guidance, alongside dedicated funding for national patient organisations to support training and appropriate, adapted reimbursement and compensation schemes. As part of their meaningful involvement, patients should also be involved in post-trial access discussions.

National frameworks should incentivise the adoption of similar patient involvement and patient-generated evidence standards in non-EU-funded projects.

Consolidate, connect and sustain the European rare disease research infrastructure ecosystem

PRIORITY ACTION

Action description

Europe should prioritise the coordination, connection, visibility and sustainable use of existing rare disease research and clinical infrastructures, ensuring that researchers, clinicians, patients, industry and policymakers can identify and access available networks, data resources, expertise, platforms and services before new structures are created. EU-supported initiatives should be required to provide clear pathways for the continuation, integration, reuse and visibility of outputs beyond the lifetime of individual projects, reducing duplication and preserving institutional knowledge.

How this responds to the challenges

This action directly responds to the fragmented research landscape; scarce, dispersed and non-interoperable data and expertise; the underused research role of ERNs and other expert centres; and geographical inequalities in

research capacity. Interconnected and interoperable registries, biobanks and trial networks, supported by sustainable governance and funding and common data standards, are prerequisites for nearly every other research ambition – from innovative trial designs to international collaboration, AI deployment and ERN-based trial readiness.

EU added value

Only EU-level support and coordination can achieve the scale and interconnection required across existing EU- and national-level infrastructures connecting the systems of all 27 Member States. The proposed Biotech Act may contribute to scaling up some key initiatives but does not address current governance, funding and research-mandate gaps in existing infrastructures, including both rare-disease-specific and general EU research infrastructures. In addition, an EU equity mechanism targeting these actions in smaller Member States has clear EU added value – national governments in smaller Member States cannot solve the critical-mass problem unilaterally.

Delivery roles

What the EU should do

Provide guidance and sustainable funding for the coordination, connection, visibility and sustainable use of existing rare disease research and clinical infrastructures.

Consider an EU rare disease research equity mechanism with ring-fenced support for EU13 and smaller Member States to build research capacity, registry interoperability, diagnostic integration and trial participation, and ensure adequate coordination between EU and national levels.

Provide support, including funding, for the uptake and implementation of common data standards and existing standards such as ORPHAcodes, and for connecting key rare disease infrastructures (e.g. expert centres, ERNs, ERDERA, registries and biobanks) with other general EU and national research infrastructures through clear interoperability pathways. This action would complement those proposed for optimising the data ecosystem.

Establish a clear, funded research mandate for ERNs within EU infrastructure legislation and support national centres and networks in connecting to EU infrastructures, with clear pathways for data and sample access and requirements for demonstrable data-sharing and sample-exchange outcomes.

Explore how the collaboration model proposed in the European Parliament's STOA study Addressing challenges to European multi-country collaboration models for rare diseases could complement the work of ERNs and ERDERA. This model relies on small transnational ecosystems of complementary centres and the critical mass that highly integrated communities can achieve for care and research (Schmiegelow et al., 2024).

What Member States should do

Member States should co-invest in national rare disease research centres and networks with clear mandates, work with existing ERDERA National Mirror Groups and National Alliances of rare disease patients to strengthen national links to EU structures, and develop interoperable national registries with harmonised data standards. Member States should establish national funding obligations to compensate clinicians and researchers for research-related workloads – as lack of compensation is often identified as a structural driver of non-participation in registries and trials.

3.6

AVAILABLE, ACCESSIBLE AND AFFORDABLE MEDICINES AND MEDICAL DEVICES

Ensuring that people living with rare diseases can access authorised treatments equitably across Europe



3.6.1 CHALLENGES

Access to diagnosis and treatment cannot be fully separated from research and development: the quality and sustainability of the research ecosystem directly determine whether therapies and diagnostic tools are developed, trialled, approved and ultimately made available to patients. This interconnection should therefore be borne in mind throughout this section.

Access to treatments and medical devices for people living with rare diseases faces multiple, compounding barriers that operate at every stage, from development through to delivery to patients. In addition to the access challenges affecting more common diseases, the rarity of conditions creates structural market failures, while small patient populations make both development and evidence generation inherently more difficult. Europe has increasingly effective mechanisms for developing and authorising rare disease innovation, but still lacks a sufficiently coordinated and conducive pathway to convert innovation into timely, equitable and sustainable patient access across Member States. The core problems are:

- Lack of authorised treatments for the vast majority of rare diseases. Persistent scientific, economic and regulatory challenges mean that most rare diseases have no approved therapy, reflecting both limited commercial incentives and the scientific difficulty of characterising rare conditions and generating evidence in small populations (Joint Action on Rare Cancers, 2019; Czech Presidency of the Council of the European Union, 2022; European Parliamentary Research Service, 2026; European Parliament, 2024; Ardigò et al., 2026).
- Significant and persistent disparities in access to authorised treatments across EU Member States. Even where treatments are centrally authorised, pricing and reimbursement decisions remain national. As a result, fewer than half of innovative medicines actually reach patients across Europe. Access is strongly determined by country of residence, driven by divergent national pricing, reimbursement, HTA and budget decisions. Differences in national interpretation of clinical evidence can also create availability gaps within approved indications, for example between paediatric and adult populations (European Parliament, 2025; EURORDIS – Rare Diseases Europe, 2019a; High-Level Meeting on a European Innovation and Care Ecosystem for Rare and Complex Diseases, 2025).
- Long and highly variable delays persist between EU marketing authorisation and national pricing and reimbursement decisions, which can themselves precede patient access by a further six months to a year or

more. Patients experience an average delay of 578 days between marketing authorisation and reimbursement decisions, rising to 900 days or more in some Member States, particularly smaller and lower-income countries (Czech Presidency of the Council of the European Union, 2022; European Parliament, 2024; Newton et al., 2025).

- Conventional HTA frameworks – designed around large randomised trials, established comparators and long-term outcome data – can be structurally inadequate for rare diseases, where patient numbers are small, natural history is poorly characterised and conventional evidence packages may simply be infeasible. Significant progress has been made since the early work of EUnetHTA: HTA bodies now accept a range of comparators, including off-label medicines where no authorised alternative exists, and guidance allows for sources of evidence beyond the large randomised trials traditionally used for common diseases.
- The emerging EU HTA framework provides important methodological tools and opportunities for greater flexibility and alignment, but its application to orphan medicines remains at an early stage and will only become systematic from 2028. Implementation remains uneven across industry, and methodological adaptation is not always applied with the required scientific rigour, leading to high uncertainty in the assessment of new technologies. This applies, for example, to slowly progressive conditions, where sufficiently sensitive outcome measures for regulatory and HTA purposes may not yet exist, and to rapidly evolving conditions, such as acute cancers or amyotrophic lateral sclerosis, where clinical trial design can be challenging. The HTA Regulation has introduced parallel assessment and information exchange between the EMA and HTA bodies – a significant advance with the potential to reduce delays by up to six months. However, regulatory, HTA and national pricing and reimbursement processes can still operate with misaligned evidence requirements, timelines and outcome measures, prolonging delays and creating uncertainty for developers and patients. Evidence requirements should therefore be aligned prospectively across the development pathway rather than reconciled retrospectively once pivotal evidence has been generated (Czech Presidency of the Council of the European Union, 2022; European Economic and Social Committee, 2024).
- Weak post-authorisation evidence generation and inadequate use of real-world evidence. Post-marketing evidence plans for rare disease products are inconsistent, underfunded and not systematically linked to registries or ERN infrastructures, in part because of the lack of systematic use of ORPHAcodes and limited awareness of requirements for establishing real-world databases for use by regulators and/or HTA bodies. While methodological guidance exists and regulatory and HTA bodies have published frameworks for real-world evidence in rare diseases, more consistent investment in appropriate data sources and the expertise needed to apply these methods in practice is required. Uncertainty at launch is often high in rare diseases, but it should be actively managed rather than used as a reason to deny or indefinitely delay access. Where uncertainty is the principal barrier to access, outcome-based or evidence-generating Managed Entry Agreements (MEAs) should be designed as genuine uncertainty-management and access tools, with predefined evidence requirements, timelines and consequences for reassessment, rather than functioning solely as confidential price-discount mechanisms (Kole et al., 2021; UCB, 2024).
- Structural barriers to cross-border access, including for specialised treatments and highly specialised care. Reimbursement mechanisms require upfront patient payment under the Cross-Border Healthcare Directive. While the S2 route (under Regulation (EC) 883/2004) reimburses in full, with no upfront cost for the patient, it requires prior authorisation, which often entails a complex and lengthy process, with frequent refusals on cost grounds. For ultra-rare diseases requiring highly specialised expertise available in only a handful of EU centres, cross-border access is not a choice but a structural necessity – yet neither framework reflects this. The concentration of expertise must not itself become a barrier through unaddressed travel and accommodation costs, which remain uncovered under both instruments.
- Innovative therapies often have strong supply chains, with reliable sources and around 75% of manufacturing taking place within the EU, US or other like-minded partner countries, resulting in less dependence on other countries or regions. Nonetheless, small manufacturing volumes, unique manufacturing sites and fragile supply chains with limited substitutability make rare disease products vulnerable. In addition, shortages affecting other critical medicines, such as anti-infectives and anaesthetics, are particularly serious for people living with rare diseases, as even temporary unavailability can cause disease deterioration, hospitalisation or treatment interruption.

- Inequities between Member States, particularly for smaller and lower-income countries. Smaller Member States face structural disadvantages in pricing and reimbursement negotiations, including limited negotiating power, budget constraints and lower market attractiveness, while industry may prioritise larger markets when launching products. Even where a product is authorised, it may never reach patients in a significant proportion of the EU.
- Risk of regression in existing access, as access can also be lost where it already exists. Evergreening, product withdrawal from smaller markets and reimbursement reversals can all result in patients losing access to treatments they currently depend on, calling for explicit safeguards.
- Although the EU has begun to recognise the specific challenges of orphan devices through dedicated Medical Device Coordination Group guidance and the proposed revision of the MDR/IVDR framework, a predictable and economically sustainable development, evidence-generation and market-access pathway for orphan and paediatric devices remains insufficiently developed.



"The world has the colours that we paint" - Brazil

3.6.2 WHAT THE EU HAS DONE

The following actions are substantially or partially addressed by ongoing EU legislative or programmatic instruments. The Action Plan should acknowledge these, monitor their implementation and address residual gaps – rather than duplicate them.

Improve regulatory efficiency	Regulatory efficiency for rare disease products is substantially addressed by the implementation of the revised General Pharmaceutical Legislation (GPL), the Medical Devices Regulation revision, the Biotech Act proposal and the HTA Regulation implementation. Residual gaps include monitoring and periodic evaluation of the regulatory landscape's impact on rare disease therapy development, and ensuring coordination between regulatory reform and HTA and reimbursement processes, including for slowly progressive conditions lacking adequate outcome measures.
Strengthen incentives for unmet needs	Improved incentives for the development of therapies for areas of unmet needs and for breakthrough innovations are partially addressed by the GPL and the proposed Biotech Act. The Action Plan should focus on ensuring monitoring of existing incentives for medicinal products, addressing the remaining gaps for people living with rare diseases, ensuring that reformed incentives reach ultra-rare diseases and non-commercial developers, and attaching access conditions to public incentives. This includes academic ATMP developers using the hospital exemption pathway under Regulation (EC) No 1394/2007, who can typically develop therapies but may struggle to sustain post-approval maintenance requirements, including pharmacovigilance and quality systems, risking loss of market access once a therapy is developed.
Align regulatory, HTA and payer decisions	Coordinated mechanism for EMA, HTA and payer alignment. The HTA Regulation already establishes Joint Clinical Assessments and Joint Scientific Consultations. Residual gaps include meaningful patient involvement, including funding for training, adapting the process for rare diseases, aligning payer decisions with JCA outputs at national level and strengthening existing early dialogue mechanisms rather than creating new ones. Another illustrative example is the EMA PRIME (Priority Medicines) designation, which provides support and accelerated assessment for priority medicines, 60% of which are for rare diseases. However, enhanced regulatory support currently stops at marketing authorisation, with no equivalent continuity mechanism into HTA and payer decision-making.

Strengthen post-authorisation evidence	Incentives for post-authorisation evidence generation. Partially addressed by the revised GPL, the proposed Biotech Act, the HTA Regulation (including post-market evidence requirements) and DARWIN EU. The Action Plan should strengthen coordination and ensure that ERN and ERDERA registries are used as the primary infrastructure for evidence generation.
Improve cross-border treatment access	While cross-border access to treatments has been addressed through the Cross-Border Healthcare Directive and Regulation (EC) No 883/2004, several critical gaps remain, including prior-authorisation refusals on cost grounds for ultra-rare treatments and ensuring that the concentration of expertise does not itself become a barrier through travel and accommodation costs.
Strengthen shortage prevention	Shortage early-warning and mitigation measures are substantially addressed by the Critical Medicines Act and the GPL's shortage-related requirements.
Support collaborative procurement	The Critical Medicines Act also partly addresses unequal access to orphan medicines across Member States, as it extends its collaborative procurement mechanism to orphan medicinal products and allows the Commission to procure on behalf of Member States when at least five request it. The Action Plan should monitor its uptake for rare disease therapies, including ultra-rare therapies, and ensure that patient organisations are involved in identifying priority products.



"Visible in the Invisible A Rare Journey" - Sweden

3.6.3 PRIORITY ACTIONS

Based on workshop and survey results, three actions were identified as the highest EU-level priorities, combining high scores for EU added value, top workshop rankings and clear gaps not already addressed by existing EU legislation or programmes.

Improve the alignment, quality and predictability of evidence generation and assessment for rare disease health technologies

PRIORITY ACTION

Action description

Generate the right evidence through better alignment of regulatory, HTA and payer requirements and fit-for-purpose evidence generation for rare disease technologies, building on the significant progress already achieved through EUnetHTA, European projects on HTA and the HTA Regulation framework. This should address implementation gaps by ensuring that adapted methodologies are systematically applied in practice, that both industry teams and HTA assessors share the same objective of rigorous scientific analysis of the data, and that patients are meaningfully involved in early dialogue with developers, for example by expressing their unmet needs and defining meaningful outcomes. This would also require establishing clear links between regulatory, HTA and payer decision-making processes for rare disease therapies, in particular through parallel EMA/HTA scientific advice, and increasing the capacity to offer Joint Scientific Consultations to health technology developers.

How this responds to the challenges

This action directly responds to inadequacies in HTA methodologies for rare diseases and to remaining fragmentation between EMA, HTA and payers. While HTA frameworks already exist, their incomplete and uneven implementation remains a practical challenge, particularly for rare diseases. Without fit-for-purpose HTA, even well-designed rare disease therapies may struggle to demonstrate value and reach patients.

This also responds to the identified weakness in post-authorisation evidence generation and inadequate use of real-world evidence, highlighting the need for appropriate data sources and expertise.

EU added value

Significant progress has been made in HTA methodology for small populations since the early work of EUnetHTA. The HTA Regulation creates the institutional framework – Joint Clinical Assessments and Joint Scientific Consultations – that, if fully and consistently implemented, can align evidence requirements across 27 Member States and reduce duplicative national assessments. Only EU-level guidance can ensure that this alignment is achieved in practice for rare disease products and translate the existing methodological consensus into systematic implementation.

Delivery roles

What the EU should do

Promote the systematic involvement of patient advocates – preferably through Community Advisory Boards – throughout the R&D of health technologies, from early discussions on development plans and outcome measures to clinical study design and comparator selection, with dedicated funding, clear procedural rights and transparent feedback on how patient input shaped final assessments, in line with the 'quality by design' principle embedded in ICH E8 General Considerations for Clinical Trials.

Establish a workable re-examination mechanism where a health technology developer has significant disagreements with the JCA report before publication, ensuring that disagreements over appropriate evidence standards for rare diseases can be resolved in a structured, transparent and timely way.

Support training and capacity building to improve the quality of evidence submitted by SMEs and non-profit developers, helping them to better meet regulatory and HTA standards and requirements through partnerships with existing initiatives, such as More-Europa, the GetReal Institute Academy and IHI projects. This should include shared forums for exchanging experience and support for investment by developers in real-world data, registries or cohorts where these are missing or outdated by more than two years.

What Member States should do

Actively participate in Joint Scientific Consultations (JSCs) for rare disease products and reduce duplicative national assessment and the delays it causes.

Ensure that patient organisations are resourced and supported to participate in national HTA processes, especially as not all products and developers will go through JSCs.

Strengthen compassionate use frameworks across Member States as a priority measure to improve access to rare disease therapies

PRIORITY ACTION

Action description

Enable timely patient access while uncertainty remains and regulatory, HTA, pricing and reimbursement processes are still ongoing by supporting the sharing of best practices between Member States on compassionate use (CU) frameworks as a priority measure to improve access for people living with rare diseases, and by developing EU-level frameworks to ensure that early access schemes include patient-informed criteria, transparent eligibility and timelines, and structured evidence collection.

How this responds to the challenges

This action directly addresses the needs of patients in urgent need of a treatment option, both in parallel to clinical trials prior to marketing authorisation and during the delays between regulatory approval, pricing and

reimbursement decisions, and patient access once a product is placed on the market. It also addresses existing disparities in access across Member States. Compassionate use frameworks are one of the most immediate mechanisms for ensuring that patients with no alternative can access therapies while definitive evidence is generated, and early access can help ensure that patients have access before pricing and reimbursement decisions are made.

EU added value

The EU legal framework for CU under Article 83 of Regulation (EC) No 726/2004 (to be updated to reflect the relevant article of the revised EU pharmaceutical legislation once applicable) provides an established legal basis, but implementation is uneven across Member States. Only EU-level guidance can help ensure that CU is consistently available and equitably implemented. EU guidance and voluntary pilots can create the conditions for greater convergence and more equitable access.

Delivery roles

What the EU should do

Support the sharing of best practices on CU across Member States and develop EU-level guidance to strengthen and harmonise CU frameworks, building on the revised General Pharmaceutical Legislation.

Update EMA guidelines on compassionate use, including extending CU to use on a named-patient basis; develop common standards for data collection within CU programmes so that evidence generated feeds into marketing authorisation and HTA assessments; and align industry practices and ethical standards, including mandatory patient organisation involvement in defining eligibility criteria and monitoring access.

Support consistent enforcement of Article 83(8), EU Reg. 726/2004, continuity obligations, guaranteeing that patients in CU programmes retain access between authorisation and market launch. Where national early access schemes exist, the EU should establish common patient-informed eligibility criteria, transparent timelines and structured evidence-collection requirements.

What Member States should do

Review and strengthen their national compassionate use frameworks, drawing on EU guidance, with patient organisations involved in defining eligibility criteria and monitoring whether CU translates into sustained access.

Where national early access schemes exist, Member States should ensure that they include patient-informed eligibility criteria, transparent timelines and structured evidence generation, and that Article 83(8) continuity obligations are consistently applied.

Develop EU solidarity and coordinated access mechanisms for ultra-rare disease therapies and Member States facing structural access barriers

PRIORITY ACTION

Action description

Mandate a multi-stakeholder discussion on a potential EU Rare Disease Solidarity Fund to support access to rare disease treatments authorised in the EU, particularly where ultra-rare conditions and/or structural constraints –

including limited negotiating power, small patient populations and budget constraints – may prevent market launch or timely reimbursement, especially in lower-income Member States. Such discussions could also benefit larger and/or higher-income Member States that are struggling to reimburse all new medicines. The multi-stakeholder discussion should explore how such a Fund could primarily facilitate access and reduce market-entry barriers, including by coordinating price negotiations, supporting simultaneous market entry across Member States and exploring a minimum guaranteed price mechanism based on common methodologies.

How this responds to the challenges

This action directly addresses inequities between Member States, existing barriers to cross-border access and lack of development for commercially fragile conditions. EU marketing authorisation without market access in a significant proportion of the EU represents a structural failure of the single market.

EU added value

Only EU-level coordination can address the structural disadvantage faced by smaller Member States in pricing negotiations and market-launch decisions. For ultra-rare diseases and lower-income Member States, a targeted EU fund could provide a mechanism to support more equitable access. The rationale is to use European scale to address access problems that individual national markets cannot efficiently solve alone. The MFF and EU investment instruments could provide an appropriate vehicle, while the Critical Medicines Act may create partial openings that such a Fund could complement and operationalise. In addition, the Biotech Act, as currently negotiated, may provide further opportunities to complement this Fund.

Delivery roles

What the EU should do

Establish a multi-stakeholder group to discuss a dedicated Rare Disease Solidarity Fund under the next MFF, focused on facilitating market launch and access in smaller and lower-income Member States.

The Fund should help Member States negotiate a reasonable price with health technology developers, respecting national competences and coordinating across Member States to support faster and more simultaneous uptake across the EU.

National authorities, via NCAPR, could lead the estimation of minimum guaranteed prices based on common methodologies and enable developers to opt into a fast-uptake, EU-coordinated pathway in exchange for a negotiated minimum price. As an optional pathway, developers would remain free to choose between the minimum-guaranteed pathway and the regular pathway.

The Fund could also support access to ultra-rare disease therapies, orphan and paediatric devices and IVDs, and complex low-volume health delivery interventions such as those addressed by European Lighthouses.

What Member States should do

Engage actively in discussions on the proposed Rare Disease Solidarity Fund, as well as in EU-level price-coordination mechanisms and the voluntary fast-uptake pathway.

Support simultaneous market entry where EU coordination is provided and use EU funding to reduce time to access for rare disease products.

Involve patient organisations in monitoring whether financial support translates into real patient access.

ANNEX I – LIST OF COMPLEMENTARY ACTIONS

This annex includes the full list of actions identified and discussed with all stakeholders involved, organised according to the same six thematic areas presented above in Section 3.

Readers may notice that some actions in this annex appear to repeat one another or appear under more than one thematic area. Many actions cut across several areas and cannot be neatly assigned to a single one. They have nonetheless been classified by thematic area to provide greater clarity and support the next steps in the policy work. Where similar actions appear in different areas, they often reflect different nuances, levels of granularity or perspectives on the same issue and have been retained to preserve that complementarity.

EARLIER, FASTER AND MORE ACCURATE DIAGNOSIS 1

Strengthen patient registries and data sharing to support undiagnosed patients

EU action

Extend and financially support EU-funded registry and data-linkage infrastructure (e.g. the EU Rare Diseases Platform, Orphanet and the secondary-use provisions of the EHDS) to systematically capture undiagnosed rare disease cases.

Fund cross-border matchmaking tools – building on the Solve-RD/ERDERA infrastructure – to link undiagnosed patients' data internationally and increase the likelihood of a diagnostic match.

National (MS) action

Connect national undiagnosed-disease programmes and registries to EU platforms.

Ensure that undiagnosed patients' data are captured, coded and made available for cross-border matching, subject to patient consent and GDPR safeguards.

Develop structured pathways for undiagnosed patients, including periodic reanalysis of genomic data

EU action

Building on Solve-RD and its continuation under ERDERA's Clinical Research Network (see Section 3), secure sustainable EU funding for periodic, rather than one-off, reanalysis of previously undiagnosed cases across all 24 ERNs.

Support EU-level matchmaking tools connecting undiagnosed patients internationally.

National (MS) action

Establish or strengthen national undiagnosed-disease programmes connected to ERNs.

Ensure that patients whose cases remain unsolved are flagged for periodic reanalysis rather than closed out of the diagnostic process.

Advance diagnostics through multi-omics approaches

EU action

Fund research and pilot deployment of multi-omics diagnostic approaches, including transcriptomics, proteomics and metabolomics alongside genomics, through Horizon Europe, EU4Health (or equivalent future EU funding programmes) and ERN research networks.

Support shared standards for clinical interpretation.

National (MS) action

Build national capacity and reimbursement pathways to adopt validated multi-omics diagnostic approaches as they mature, prioritising expert centres and ERN-affiliated laboratories.

Support primary prevention and genetic counselling

EU action

Support the development of EU guidance on ethical, non-directive genetic counselling standards and on the governance of primary prevention options, including carrier screening, prenatal testing and preimplantation genetic testing, while respecting national legal and ethical frameworks. This action could be supported by the NBS Advisory Committee mentioned in Section 3.1.3, Priority Action 2.

National (MS) action

Ensure access to qualified genetic counselling before and after genetic testing, within national legal and ethical frameworks.

Safeguard against discrimination on genetic grounds.

Support comparative research on diagnostic delay across Member States

EU action

Fund comparative research on diagnostic delay, referral rates and access to specialised diagnostic services across Member States, building on Orphanet, the EU Rare Diseases Platform and JARDIN's national roadmap data (see Section 3).

Define a shared set of diagnostic indicators for monitoring.

National (MS) action

Contribute national data on diagnostic delay, referral and testing capacity to the shared EU indicator set.

Use the shared indicators to benchmark and improve national diagnostic pathways.

Establish governance for AI in diagnosis

EU action

Ensure that any EU support for AI-based diagnostic tools, including symptom checkers and decision-support algorithms developed under projects such as Screen4Care, is accompanied by clear governance, validation and oversight requirements developed with clinicians and, crucially, with patient input.

National (MS) action

Apply agreed EU governance and validation requirements when deploying AI-based diagnostic tools in national health systems.

Monitor their real-world performance and equity impacts.

ACCESS TO SPECIALISED AND HIGHLY SPECIALISED HEALTHCARE 2

Improve ERN geographical coverage and expand to under-represented disease areas through targeted outreach

EU action

Maintain a dynamic and updated information system on disease coverage per ERN (operational coverage: diseases represented by an expert centre in the ERNs; potential coverage: conditions not represented by an expert centre in the ERN), with the support of Orphanet, to identify gaps and overlaps dynamically and allow the planning and monitoring of ERN disease expansion.

Instruct ERNs to develop strategies to cover disease gaps and develop specific criteria for new conditions. Each ERN should develop a stepwise expansion roadmap to complete coverage of the diseases clustered under its disease grouping (thematic and sub-thematic areas). For each new disease, ERNs should define specific criteria to assess expert centres and commit to undertaking specific collaborative activities. Adequate funding should be secured to ensure that this stepwise operational expansion translates into concrete activities for any new diseases incorporated into the operational coverage of each ERN.

Open regular calls for full membership to allow expert centres not currently involved in the ERNs, but with expertise in the new set of conditions, to join.

Open a new call for an ERN on rare gynaecological and obstetrical diseases and complex pregnancies.

Open a new call for an ERN on rare infectious diseases.

Continue work to improve geographical coverage through the call for Affiliated Partners (see Section 3 above).

Scale up EU-level mechanisms to improve cross-border access to ultra-rare and highly specialised treatments (e.g. 'European Rare Disease Lighthouses')

EU action

Allocate EU funding to scale up the Rare Disease Lighthouse model and articulate collective EU action to improve cross-border access to ultra-rare and highly specialised treatments, building on the results of the feasibility pilot.

Assess the value and operational implications of scaling up European treatment eligibility panel-type approaches for ultra-rare diseases and piloting the 'European Lighthouses' concept – concentrating highly specialised expertise and care delivery in a limited number of centres on a voluntary, complementary basis.

National (MS) action

Building on the results of the feasibility pilot, interested Member States should agree on how to articulate collective action to plan, organise, fund and monitor the provision of cross-border highly specialised healthcare services when one or more of the following three factors arise:

- **Lack of sufficient cases:** national health systems are unable to adequately assess population needs at national level due to very small patient populations and infrequent cases.
- **Safety risks and poor clinical viability:** not all countries have an expert team with the competencies and expertise to provide a safe and sustainable service.

National (MS) action

- **Limited financial capacity of individual countries:** individual health systems lack the financial and innovation capacities required to provide and maintain high-cost, highly specialised and innovative healthcare services, including workforce training and adequate replacement rates.

Strengthen telemedicine and virtual case discussion to preserve cross-border access to diagnosis and care while reducing unnecessary travel

EU action

Develop guidance on referral systems to ERNs and on the incorporation of CPMS advice, and strengthen the use and sustainability of CPMS, including for diagnostic case discussion. This is ongoing work under JARDIN and ERNs.

Leverage MyHealth@EU to support cross-border telemedicine services, including teleconsultations and virtual case discussion, throughout the diagnostic process and care pathway. This is ongoing work under the EHDS and Xt-EHR Joint Action.

National (MS) action

Establish clear referral pathways for CPMS discussion so that people living with a rare disease can benefit from specialised knowledge for both diagnosis and care, regardless of geographical location.

Integrate telemedicine and virtual case discussion into national diagnostic and care pathways and establish the legal, organisational, technical and reimbursement requirements needed to provide cross-border telemedicine services.

Amend the Social Security Regulations and/or the Cross-Border Healthcare Directive to allow payment for time spent on cross-border virtual consultations

EU action

This action proposes a specific amendment (payment for time spent on cross-border virtual consultations) rather than new legislation. Ongoing work is underway through the own-initiative legislative report tabled by the European Parliament, which seeks to amend Directive 2011/24/EU. The Action Plan should refer to an overall amendment of Regulation (EC) No 883/2004 on the coordination of social security systems to ensure timely access and a uniform exercise of the right to access cross-border healthcare, going beyond the narrow scope proposed in this action (reimbursement of experts' time for cross-border consultations). This would entail a revision of Regulation (EC) No 883/2004 to address the needs of people living with rare and complex conditions. The amended Regulation should establish a standardised, time-bound cross-border clinical and administrative care pathway, guaranteeing maximum timeframes for the clinical evaluation that precedes prior authorisation, comprehensive coverage for diagnostic tests, medical interventions and follow-up care, support for families and patients to navigate the cross-border healthcare system and financial support to cover non-clinical expenses. The new Regulation should also establish an EU-wide procedure for competent national authorities to seek expert advice to inform prior authorisation decisions.

Strengthen the designation of expert centres/ Comprehensive Centres, ensuring multidisciplinary care

EU action

Clarify EU-wide definitions and develop a taxonomy to classify national or regional accreditation and designation systems for expert centres.

National (MS) action

Develop and implement national designation systems for expert centres, including the definition of specific criteria, assessment methodology and regular audits to monitor compliance with the defined criteria.

Ensure sustainable and proportionate investment from national and EU budgets in expert centre capacities and ERN competencies

EU action

Develop recommendations on existing mechanisms to support expert centres (working conditions, research and education, quality of care, designation, development strategies and funding mechanisms). This is ongoing work under JARDIN – although the recommendations only refer to expert centres that participate in the ERNs.

National (MS) action

Provide support and proportionate national budget contributions to expert centres based on performance. Support should reach all designated expert centres, both those participating in ERNs and those that are not.

Supplement continuous ERN monitoring with more nationally relevant and disease-relevant indicators

EU action

Incentivise ERNs to define disease-specific indicators that can then be implemented in different expert centres and monitored across each ERN for benchmarking and quality improvement. This is ongoing work in some ERNs.

Define ERN integration monitoring indicators. This is ongoing work under JARDIN.

National (MS) action

Support expert centres to implement and monitor disease-specific indicators (structure, process and outcomes).

Integrate ERN integration indicators into national and regional healthcare system monitoring.

Develop and implement generic care pathways for rare conditions grounded in patient community needs

NB: This action largely complements Section 3.3.3, Priority Action 1.

EU action

The EU needs to move from information design to product design and implementation support; it should transform the static table developed by JARDIN into an online decision-support tool featuring different layers of detail depending on the user (high-level executive roadmaps for decision-makers, detailed operational workflows and downloadable technical toolkits for operational teams). Operationally, the

National (MS) action

Member States should identify the development of generic care pathways (either one pathway or generic pathways for clusters of conditions) as a priority in their national rare disease plans and, with respect to rare cancers, cancer plans; allocate adequate funding to design and implement them; and leverage the EU implementation ecosystem (online decision-support tool and technical support) to drive the design and

EU action	National (MS) action
framework must be equipped with modular resources such as decision trees, examples of indicators, guidance on involving patient organisations, lists of red flags and self-assessment checklists that national teams can download and immediately adapt. Finally, the EU should offer countries active implementation support by establishing peer-learning twinning programmes and providing targeted technical assistance (such as via DG REFORM) to guide countries through rollout. This is ongoing work under JARDIN.	implementation of generic pathways within their own national health systems.

Develop strategies to minimise disparities between European regions in access to high-quality healthcare

EU action	National (MS) action
Agree EU-wide definitions, methodology and metrics to monitor disparities in access to high-quality healthcare.	Implement agreed EU-wide metrics and capacities in national information systems to capture socioeconomic and stratifying variables that allow inequities and disparities to be measured (educational attainment, socioeconomic status, income, poverty status, main activity status, etc.).

Adopt and implement guidelines developed or reviewed by ERNs at national/regional level

EU action	National (MS) action
Instruct ERNs to establish Central Implementation Support Teams to drive clinical guideline adoption and oversee the network's quality cycle, helping member hospitals reduce care variability (building on the ERNICA model).	Establish mechanisms, where needed, and support the adoption and implementation of clinical practice guidelines developed or reviewed by ERNs within national and regional care systems.

Encourage systematic use of patient-generated evidence (PROMs/PREMs) in rare disease policy, care and EU HTA processes

EU action	National (MS) action
Allocate targeted grants through ERDERA (European Rare Diseases Research Partnership) and Horizon Europe to fund international consortia developing and psychometrically validating disease-group-specific PROMs. Work directly with patient groups to ensure that measures reflect what matters most to patients and avoid overly generic metrics that miss key symptoms. This work is already being advanced	Mandate the collection of PROMs/PREMs during routine hospital visits at designated expert centres. Support expert centres to systematically capture and register PROMs and PREMs and use them to improve the quality of care provided.

EU action

through ERDERA, whose Clinical Research Network plans to develop patient-centred outcome measures to guide future interventions.

Allocate Horizon Europe funding to validate the Rare Disease PREM currently being developed by Rare Diseases Ireland, including its validation across EU languages.

Instruct the 24 ERNs to routinely embed standardised electronic PROMs/PREMs into their clinical registries. Use ERNs to run longitudinal, cross-border natural history studies driven by patient-reported data, establishing essential baselines for future HTA appraisals.

Allocate Horizon Europe funding to support the implementation of PROMs and PREMs in expert centres and national rare disease registries.

Develop EU-wide standards for validating qualitative and proxy PROMs (e.g. caregiver-reported outcomes for paediatric or cognitively impaired rare disease patients) so that they carry appropriate scientific weight during Joint Clinical Assessments.

National (MS) action

Establish nationwide information systems and registries to allow the use of PROMs and PREMs to support policymaking and HTA processes.

Explore the feasibility of Comprehensive Rare Disease Infrastructure Clusters (CoRDICs)

EU action

The European Commission should support feasibility studies to test the CoRDIC concept and develop a framework setting out its constituent elements, the minimum requirements for implementation and the arrangements for their articulation with the ERNs and ERDERA. CoRDICs are meant to bring together, in a coordinated structure, the resources needed for rare disease research, innovation and care: translational research facilities, advanced diagnostic laboratories and clinical trial infrastructure able to run Phase I to IV trials

National (MS) action

Member States should develop pilot CoRDICs within their national health systems, based on existing infrastructure and national capacity, and share the results to inform the EU framework.

Support lifelong education of a healthcare workforce sensitive to and specialised in complex and rare disease needs

EU action

Fund EU-level lifelong education content and training standards for the rare disease workforce. This is ongoing work under the ERNs.

National (MS) action

Deliver lifelong education on rare and complex conditions within national continuing education systems.

Support ERNs to educate and train future rare disease experts, including clinical, surgical and holistic training

EU action

Provide sustainable ERN funding for training and position ERNs as rare disease workforce training hubs. This is ongoing work under the ERNs.

National (MS) action

Support expert centres to develop training activities, including clinical, surgical and holistic training. Leverage the ERNs to complement national training capacities.

Provide training, education and tools for primary care, emergency care and other healthcare professionals outside the rare disease field to recognise rare diseases and refer earlier, in collaboration with specialists

EU action

Fund the development of EU-level training frameworks, curricula and continuing education content, together with awareness materials, lists of 'red flags' and digital tools, to help primary care professionals, emergency clinicians, nurses and other non-specialist healthcare professionals recognise rare disease presentations, raise suspicion of a rare disease and navigate referral pathways to expert centres and ERNs. This is ongoing work under the ERNs and JARDIN.

National (MS) action

Fund national training programmes on rare disease awareness, recognition and referral, tailored to national health system structures, and integrate rare disease modules into primary care, emergency medicine and other non-specialist training and continuing education for doctors and nurses, using EU-developed materials.

Formalise Member State collaboration in strategic and workforce planning

EU action

Facilitate formal EU-level collaboration structures for workforce planning in rare diseases and cooperation in this area.

National (MS) action

Define and implement information systems to systematically capture workforce retention and workforce mix indicators, as well as measures to support supply-demand forecasting.

INTEGRATED CARE AND SOCIAL INCLUSION 3

Establish EU guidance for Member States on disability assessment procedures, so that persons with rare disease-related disability and functional limitations receive consistent and timely recognition

EU action

Embed rare-disease-specific guidance within the mid-term review of the EU Disability Strategy 2021–2030.

Support the further development, up to completeness, of the Orphanet database and ontology of rare disease-related disabilities as the evidence base for a common disability assessment tool to be developed, or adapted from existing generic tools, by an EU/Member State expert body including patients, scaling up work partially supported by ERDERA.

National (MS) action

Apply EU guidance within national disability assessment procedures and update national disability lists to include incapacitating or degenerative rare conditions.

Develop practical guidance and monitoring instruments for Member States to embed reasonable adjustments to the specific needs of people living with rare diseases in mainstream education and employment policies

EU action

Issue practical guidance and self-assessment tools translating 'reasonable adjustments' into concrete measures: flexible work arrangements, reasonable leave, career counselling, workplace accommodation and adapted schooling.

Introduce indicators in the Social Scoreboard to monitor uptake across Member States.

National (MS) action

Enshrine non-discrimination in education and employment law and implement it through flexible work arrangements, reasonable leave, workplace accommodation and adapted schooling, coordinated across health, social, education and employment ministries.

Within the implementation of the EC Comprehensive Approach to Mental Health, identify and add dedicated supporting actions and adequate financial support for people living with a rare disease as a population in vulnerable situations

EU action

Expand the scope of the EC Comprehensive Approach to Mental Health to explicitly recognise Europeans living with existing physical health conditions, including chronic and rare conditions, and specifically the 30 million people living with a rare condition in the

National (MS) action

Increase the visibility of mental health in the revision of national rare disease plans and strategies, and national cancer plans with respect to rare cancers, and commit to actions to address the unmet mental health needs of people living with rare diseases and their

EU action

European Union, as a population living in vulnerable situations, and take action to address these severe unmet needs in order to better protect mental health, prevent mental health problems and reduce further exclusion and marginalisation.

National (MS) action

families. At the same time, in compliance with the UN General Assembly Resolution on rare diseases (A/RES/76/132), develop effective programmes and national strategies to promote mental health and psychosocial support for people living with a rare condition, and coordinate EU action to develop and promote policies and programmes that enhance the wellbeing of their families and caregivers.

Socioeconomic burden of rare diseases

EU action

Conduct EU-wide research on the socioeconomic burden of rare diseases, building on ERDERA's planned study.

Develop indicators to measure the costs of diagnosis, care pathways and timely access to treatment, including gender-related impacts.

OPTIMISING THE DATA ECOSYSTEM 4

Develop common approaches to patient-reported outcomes (PROMs) and quality-of-life measures to support comparative evidence generation

NB: Actions on the systematic use of patient-generated evidence, including PROMs and PREMs, appear in several thematic areas. This reflects their cross-cutting importance across diagnosis, care, data, research and access to treatments.

EU action

Develop EU-level common approaches to PROMs and QoL measures for rare diseases, including recognition of structured n-of-1 patient-led research as a valid evidence source.

Integrate PREMs alongside other patient-reported measures.

National (MS) action

Member States should ensure that national health data systems and HTA processes include rare disease PROMs and PREMs as standard evidence inputs.

Support validated AI applications for case finding, decision support and research, built on high-quality datasets; monitor AI performance and equity impacts with transparency requirements

EU action

Support the development and deployment of trustworthy AI and digital tools for rare diseases, conditional on robust interoperable data infrastructure being in place, with EU governance frameworks for AI monitoring, transparency and equity impact assessment, and a Rare Disease AI Validation Commons for benchmarking algorithms on federated, multi-country datasets before adoption.

Develop EU best-practice and governance frameworks for AI use in rare diseases, including clear definitions of validated AI tools, legal and data protection requirements, community-led guidance on responsible AI use and mandatory transparency and equity monitoring.

Promote digital sovereign AI approaches that prioritise patient needs.

Clarify AI's role as a means, rather than an end, towards improved data reuse, case detection, referral and care.

National (MS) action

Member States should ensure that national AI governance frameworks include rare disease provisions and that AI tools deployed in rare disease clinical settings are subject to EU transparency and equity monitoring requirements.

Implement and support a meaningful partnership for data governance with patients at its core

EU action

In line with Chapter IV of the EHDS Regulation, and as part of the EU minimum standards for meaningful patient and civil society participation proposed under Section 3.3.3, Priority Action 3, develop EU-level standards for patient partnership in rare disease data governance. These should recognise patients as key actors, enable meaningful representation of patient organisations in EHDS and EU data access governance bodies and be backed by capacity building, compensation for time and transparent consultation processes.

Develop clear patient-facing information standards to build trust and a coherent EU framework for trustworthy, patient-centred governance of the secondary use of rare disease data, including measures to mitigate re-identification risks in small rare disease populations.

Clarify and formalise access rules for the European rare disease data hub and registry ecosystem, recognising patient organisations as key governance stakeholders, in line with WHO recommendations.

National (MS) action

Apply the EU participation standards in national health data access governance, building on the representation of rare disease patient organisations in national EHDS governance under Section 3.4.3, Priority Action 3, and support patient organisations to participate on an equal footing with institutional, academic and industry stakeholders.

Designate rare disease data governance focal points and provide clear, accessible information to people living with a rare disease on how their data are used and on their rights.

INNOVATIVE AND NEEDS-LED RESEARCH 5

Develop a European rare disease research strategy spanning the full rare disease pathway in co-creation with stakeholders (including patients)

EU action

Develop a coordinated EU rare disease research strategy building on ERDERA's Strategic Research and Innovation Agenda and aligning with IRDiRC to guide responsive, evidence-based funding across EU and national programmes, covering all rare diseases (including non-genetic and ultra-rare conditions). The strategy should cover the full pathway from discovery to patient benefit, in co-creation with patients and including underrepresented and undiagnosed patients.

National (MS) action

Inform national rare disease research agendas and funding strategies through the EU research strategy, with multi-year commitments covering all research stages, including basic science.

Create a structured EU platform to enable public-private partnerships (PPPs) focused on unmet rare disease needs

EU action

Create a structured EU platform to enable PPPs for unmet rare disease needs, with shared-risk mechanisms, open science principles and clear benefit-sharing frameworks, embedding patient organisation involvement in PPP governance. The platform should be developed as a component of the co-investment mechanism proposed under Section 3.5.3, Priority Action 1, which already includes long-term PPPs.

Promote innovative trial designs and regulatory science for small populations with early dialogue and learning cycles

EU action

Promote innovative trial designs and regulatory science for small populations – including adaptive trials, platform trials and external control arms – with structured EU-level dialogue between regulators, HTA bodies, payers, researchers, sponsors and patients, and monitoring of EMA progress on flexibility for rare disease trials.

Facilitate trial readiness in ERNs and expert centres

EU action

Support EU-level coordination of trial readiness in ERNs and expert centres, including support for site networks, harmonised protocols and patient recruitment through interoperable ERN registries enabling patient identification across countries and addressing the needs of both commercial and non-commercial sponsors.

National (MS) action

Ensure national competent authorities and ethics committees have adequate resources and meeting schedules to implement EU clinical trial authorisation timelines equitably; provide dedicated procedural support for non-commercial and academic rare disease sponsors at national level.

Incentivise multi-country studies and shared protocols to reduce fragmentation and improve scalability

EU action

Incentivise multi-country studies and shared protocols through aligned EU and national funding calls and joint evaluation mechanisms, pursued through ERDERA and focusing on the residual barriers not addressed by the CTR (e.g. patient pool pre-identification and clinical trial site readiness), and building on existing initiatives such as Accelerating Clinical Trials in the EU (ACT EU).

Support the deployment of digital platforms for remote participation in studies and follow-up

EU action

Support EU-level frameworks and coordination for digital platforms enabling remote participation in rare disease studies and follow-up to reduce the burden on patients and carers, while ensuring equity safeguards and complementarity with in-person specialist care.

National (MS) action

Member States should ensure that digital platforms are accessible to patients with limited digital literacy or connectivity and do not create a divide between well-resourced and less-resourced patient communities.

AVAILABLE, ACCESSIBLE AND AFFORDABLE MEDICINES AND MEDICAL DEVICES

6

Improve regulatory efficiency for rare disease products (orphan medicinal products, advanced therapies and orphan and paediatric devices)

EU action

Establish a mechanism for continuous monitoring and periodic evaluation of the regulatory landscape and its impact on rare disease therapy development, coordinated with strengthened EU HTA processes and clinical trial facilitation. Include specific attention to slowly progressive conditions lacking adequate regulatory outcome measures.

National (MS) action

Member States should support implementation of the GPL and MDR revisions at national level and ensure that national regulatory and HTA bodies participate in EU coordination mechanisms.

Promote, tailor and improve targeted incentives to support development addressing unmet needs, including for ultra-rare diseases and repurposing

EU action

Establish targeted EU funding streams and incentive mechanisms, including scientific advice, to support development, including repurposing and translation of therapies for ultra-rare diseases where commercial incentives are insufficient.

Include special measures to support the development of medicines for ultra-rare diseases by academics and non-profits, including support for research, market access and the continued availability of their ATMP products on the market.

Link public funding to commitments on equitable access, patient involvement and real-world evidence generation.

Organise EU-level generation and monitoring of post-marketing evidence for rare disease treatments, building on DARWIN EU, ERN registries and ERDERA

EU action

Establish a coordinated EU-level mechanism and co-funding stream for post-marketing evidence generation and surveillance for rare disease treatments, leveraging GPL provisions, DARWIN EU and ERN/ERDERA registries and long-term monitoring.

Develop EU guidance and funding support for rare disease real-world evidence plans, building on GPL provisions and DARWIN EU and linked to ERN/ERDERA registries.

Require ERN/ERDERA-linked real-world evidence plans for selected rare disease products, using common core outcomes, natural-history comparators, PROMs/PREMs and long-term safety and effectiveness monitoring.

Provide funding mechanisms for patients to contribute to regulatory, value assessment and reimbursement decisions

EU action

Establish EU-level funding mechanisms to enable patient organisations to participate fully and on equal terms in HTA, value assessment and reimbursement decision-making processes, including capacity building, reimbursement of participation costs and training. Patient advocates should be included as full members of advisory boards and access decision-making bodies.

Improve cross-border access to specialised expertise, treatments and devices

EU action

Strengthen EU-level frameworks for cross-border access to rare disease treatments – including streamlined prior authorisation, coordination between ERNs, expert centres and national payers, and the proposed amendment to Regulation 883/2004 (Social Security Regulation) to prevent unjustified refusals of S2 requests under this Regulation for authorisation of ultra-rare disease treatments. Ensure that centralisation of expertise does not become a barrier due to travel and accommodation costs.

Strengthen EU coordination on cross-border access pathways, building on Critical Medicines Act collaborative procurement provisions and the EHDS on interoperability. Develop a common rare disease documentation framework for cross-border reimbursement using ORPHAcodes.

National (MS) action

Member States should designate and resource national contact points for cross-border rare disease access, implement streamlined prior authorisation procedures for ERN-referred rare disease patients and ensure coordination between referring and treating centres.

Member States should reduce administrative barriers to cross-border reimbursement and implement EHDS interoperability standards for rare disease clinical summaries and prescriptions.

Pilot joint negotiation and aligned decision-making and facilitate voluntary joint procurement for selected rare disease treatments and devices

EU action

Facilitate voluntary joint procurement and coordinated access approaches for selected rare disease treatments and devices – particularly for ultra-rare diseases and small Member States – building on Critical Medicines Act mechanisms and EU-funded initiatives such as the "Competent Authorities for Pricing and Reimbursement to coordinate Involvement of clinical experts and patients, to manage uncertainty and the challenges associated to Orphan medicinal products" (CAPRICORD) project. Link these approaches to fair pricing, real-world evidence, reassessment and access commitments.

National (MS) action

Member States should participate voluntarily in joint negotiation and procurement pilots, with patient organisations identifying priorities and monitoring whether collaborative approaches translate into real patient access.

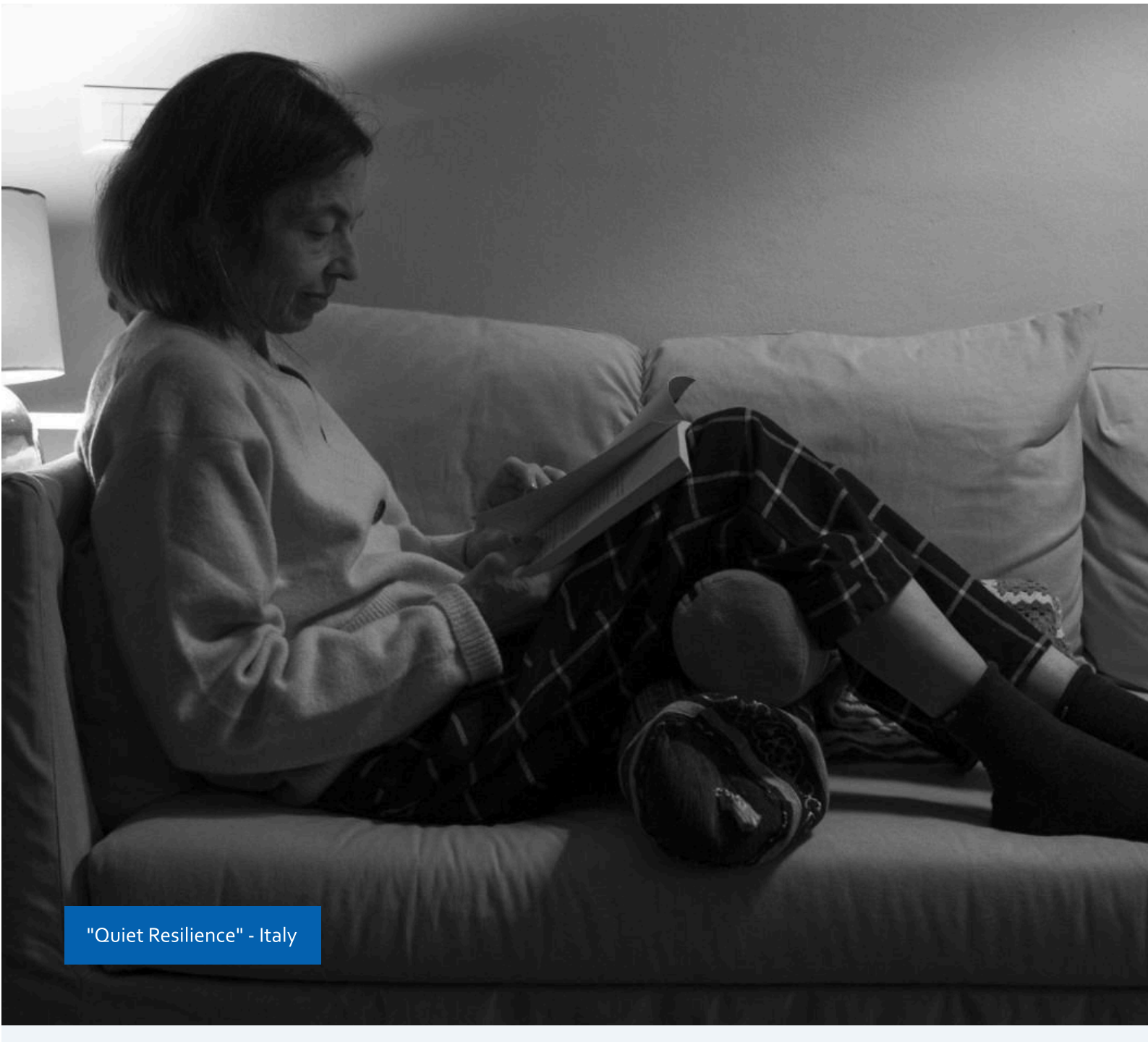
Strengthen early warning and mitigation for shortages of treatments, devices and IVDs relevant to rare diseases

EU action

Develop EU-level rare-disease-specific shortage prevention and communication mechanisms, building on the General Pharmaceutical Legislation and Critical Medicines Act framework; formalise ERN coordination models for shortage management and reporting channels for patients and clinicians; and improve patient and clinician communication on availability, duration and alternatives during shortages.

National (MS) action

Member States should designate rare disease focal points within national shortage management systems, resource ERNs to act as shortage alert and coordination hubs, develop national contingency plans for treatments with no substitutes and implement reporting channels for patients and clinicians.



"Quiet Resilience" - Italy

ANNEX II – METHODOLOGY

The European Blueprint for Rare Diseases was co-created by a multi-stakeholder group led by EURORDIS – Rare Diseases Europe and focuses on presenting the main proposed structural elements for an EU Action Plan on Rare Diseases, including prioritised actions at EU level. The same process described here also served to compile contributions from members of the rare disease community in the WHO European Region to the Global Action Plan on Rare Diseases; however, these will be included in a forthcoming document.

The co-creation of the Blueprint entailed a structured process, with different groups providing strategic direction, supporting the development of the content, being consulted and validating the results of these consultations.

This approach rested on two principles. The first principle is that the process should build on the substantial body of work already produced on rare diseases in Europe. To ensure this, all documents used for discussion and consultation with the multi-stakeholder groups involved (i.e. the draft documents, the survey and the preparatory documents for the workshop) brought together existing studies, policy recommendations and initiatives, building on 20 years of collective experience and work, including the Rare2030 foresight study. This first part was carried out through desk research by EURORDIS staff.

The second principle is that meaningful policy development on rare diseases requires bringing together a group representing all members of the community. To ensure this, between November 2025 and September 2026, EURORDIS worked with the support of the Core Group and the European Regional Taskforce to put these principles into practice. In addition, a pre-ECRD conference workshop complemented the prioritisation of proposed policy actions for this Blueprint. The process and activities undertaken by each group, as well as the main objectives of the workshop, are described below.

The Core Group: providing strategic input and validation

A Core Group of 36 experts and stakeholders provided strategic input and direction throughout the process. The Core Group met four times in 2026: 1) an initial meeting to co-create the Blueprint's scope, objectives and thematic structure; 2) a second meeting to take stock of progress; 3) a third meeting to review and discuss members' input to preparatory documents covering challenges, common goals and proposed actions for key thematic areas affecting people living with rare diseases, as reflected in the final content of Section 3 of this Blueprint; and 4) a final meeting to validate the final set of priority actions to be included in the Blueprint. Between meetings, members provided written input to each thematic area of the Blueprint, which formed the working basis for the wider consultation that followed, and contributed to validation of the final document. The Core Group was informed, consulted and involved in the work of the Regional Taskforce. A full list of Core Group members and EURORDIS staff involved is provided below.

The European Regional Taskforce: broader consultation and prioritisation across the WHO European Region

EURORDIS, in collaboration with Rare Diseases International, established a European Regional Taskforce through an open call for expressions of interest launched in February 2026 and open until 26 February. The Taskforce held its kick-off webinar on 6 March 2026. The call was directed to patient organisations, civil society groups, healthcare professionals, researchers, policymakers, public authorities and industry partners working on rare diseases within the WHO European Region.

The Taskforce was consulted through an online survey mirroring the structure of the preparatory documents shared with the Core Group. The survey asked participants to rate the priority of each proposed action for a future EU Action Plan, assess its relevance for a Global Action Plan on Rare Diseases and add comments or share best practices. The survey was open for several weeks in spring 2026 and was supported by an informative webinar. A total of 236 stakeholders from more than 30 countries responded to the survey, providing broad geographical representation.

The pre-ECRD Conference Workshop in Prague: prioritisation and consensus

A dedicated pre-conference workshop held on 2 June 2026 in Prague, ahead of the European Conference on Rare Diseases and Orphan Products (ECRD 2026), brought together over 150 participants from the Core Group, the Regional Taskforce and the wider rare disease community. The workshop tested the Blueprint's proposed policy actions across each of the themes developed in the documents shared with the Core Group and the survey questions circulated to the Regional Taskforce. Through plenary sessions and six thematic breakout discussions – covering all the thematic areas of the Blueprint – participants applied a shared set of prioritisation criteria (e.g. the extent of unmet need addressed, the severity of the problem, the expected impact of the action and its potential to enable progress in other areas) to confirm, amend or challenge the proposed actions. Each breakout table identified up to three priority actions at EU level and at least one at global level, while explicitly recording areas of consensus or potential disagreement ahead of the Blueprint's finalisation. Participants were also asked whether they agreed with the proposed prioritisation criteria. The Workshop Report is available online.

An iterative, cumulative process

After these phases of drafting and consultation, EURORDIS staff, with the final validation of the Core Group, reconciled all the input received into a final document, which was submitted for final review by the Core Group in August and September 2026. The list of prioritised actions was also shared with members of the European Regional Taskforce during a webinar in September 2026.

Full list of Core Group Members

Name	Surname	Affiliation
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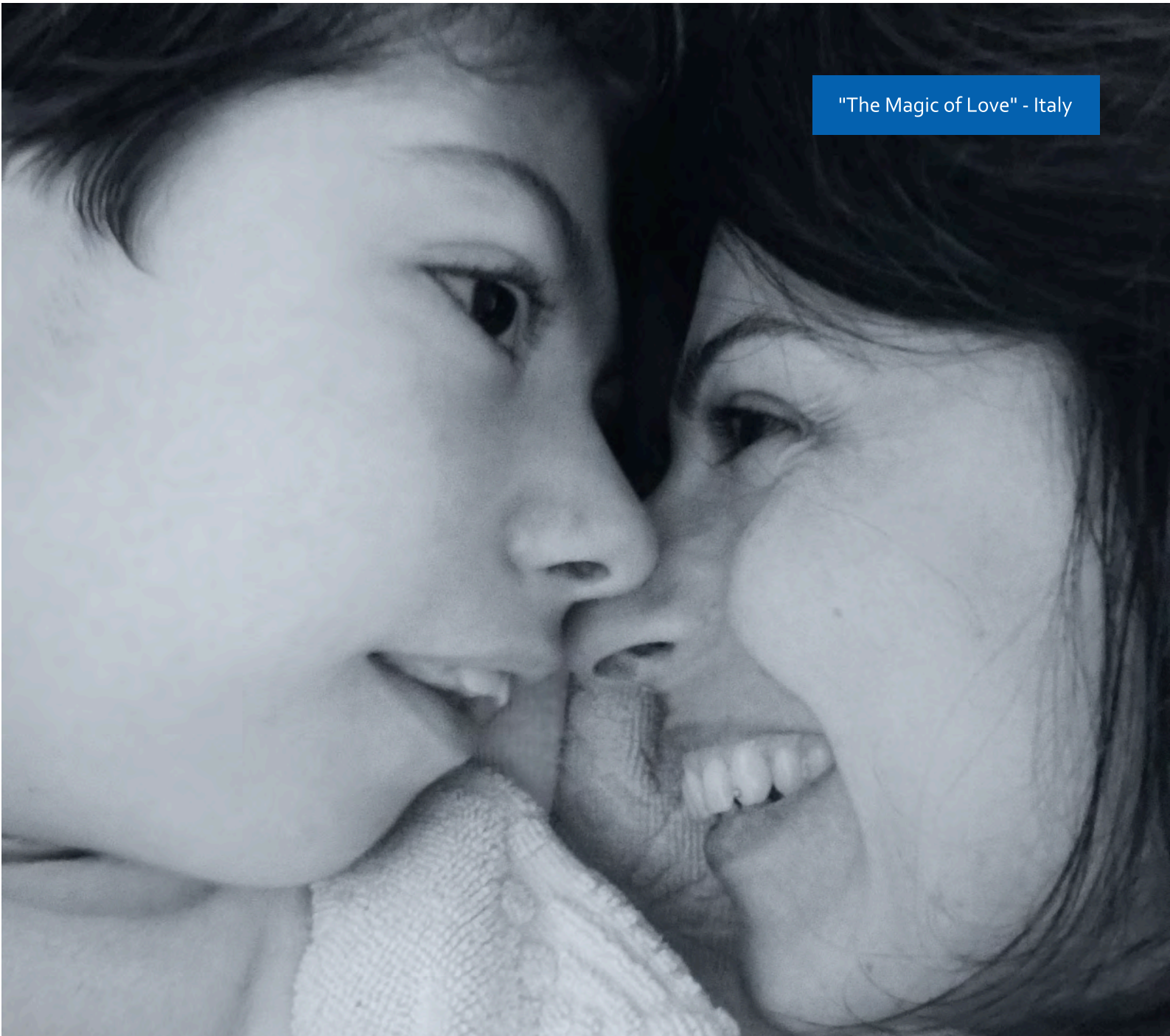
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Ruth	Ladenstein	ERN PaedCan
Simona	Bellagambi	UNIAMO – Federazione Italiana Malattie Rare
Simone	Louisse	ERN GUARD-Heart, ePAG Steering Committee

Name	Surname	Affiliation
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"The Magic of Love" - Italy

ANNEX III – COMMUNITY CONSULTATION ON THE EUROPEAN BLUEPRINT FOR RARE DISEASES (THE SURVEY)

1. Context and purpose

To ensure that the European Blueprint for Rare Diseases represents the voices of the rare disease community and reflects a community-led vision for future policy action, EURORDIS – Rare Diseases Europe launched a dedicated multi-stakeholder consultation survey. Members of the Regional Taskforce received the survey link on 30 April, and the consultation remained open until 24 May, when submissions closed.

The survey gathered feedback, priority rankings and qualitative insights across key policy pillars. The EURORDIS Rare Barometer team supported the design, development, dissemination and analysis of the survey and its results.

2. Scope and respondent profile

The consultation received a total of 236 valid responses.

Most responses were submitted on behalf of formal entities, with organisational representation accounting for 65% of the total. These entities included national rare disease alliances, clinical expert centres, European patient federations and private industry developers. Individual advocates, experts and clinicians submitted 32.7% of the responses, providing direct experiential and professional insights.

Responses also reflected a balanced multi-stakeholder distribution. Patient organisations formed the largest single group of contributors, accounting for 38% of participants. Private-sector developers and research sponsors represented 25%, followed by healthcare professionals at 16%. Academic institutions and research bodies comprised 9% of respondents, while public authorities and policymakers together accounted for 7%. Independent advocates made up the remaining 4%.

3. Geographical reach and level of operation

The survey achieved broad geographic coverage, drawing input from stakeholders across 33 countries. Participation spanned Western, Southern, Central and Eastern Europe, as well as international partner countries. The largest numbers of contributions came from Belgium, the United Kingdom, France, Germany, Italy, Slovakia, Spain, Georgia, Austria and Portugal, reflecting diverse national healthcare systems and varying stages of rare disease policy development.

The majority of responding organisations and individuals operated at national level (44%), providing important insights into the implementation of health policies in practice. Stakeholders with a global remit represented 26% of respondents, while those operating primarily at EU or European level accounted for 25%. Local and regional actors comprised the remaining 5%.

4. Analytical Role in the Blueprint Architecture

The input gathered through the survey was critical to the co-creation of the Blueprint's content. The survey supported the prioritisation of a longlist of policy actions across each thematic pillar of the Blueprint. By prompting respondents to evaluate each measure against criteria of unmet need, severity, expected impact and cross-sectoral enabling potential, the survey also highlighted areas of strong multi-stakeholder alignment. Additionally, the open questions allowed for the collection of more detailed input about the challenges at different levels (e.g., European, EU, national, regional), potential policy solutions and existing best practices.

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