Report

IRDiRC CONSORTIUM ASSEMBLY AND SCIENTIFIC COMMITTEE MEETING

Sofia, Bulgaria
18-19 March, 2026

IRDiRC
INTERNATIONAL
RARE DISEASES RESEARCH
CONSORTIUM

ACRONYMS

AAV – Adeno-associated viruses

AI – Artificial Intelligence

ACMG – The American College of Medical Genetics and Genomics

CA – Consortium Assembly

CCC – Companies Constituent Committee

CMC – Chemistry, Manufacturing and Controls

COVID-19 – Coronavirus disease 2019

DSC – Diagnostic Scientific Committee

ECRD – European Conference on Rare Diseases

EMA – European Medicines Agency

FDA – U.S. Food and Drug Administration

FCC – Funders Constituent Committee

GMP – Good Manufacturing Practices

GMO – Genetically Modified Organism

HR – Homologous Recombination

HTA – Health Technology Assessment

ISC – Interdisciplinary Scientific Committee

PACC – Patient Advocates Constituent Committee

RSC – Regulatory Scientific Committee

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EXECUTIVE SUMMARY

1. Parallel Sessions

Funders Constituent Committee (FCC)

The FCC discussion was framed around a roundtable among funders reviewing activity over the previous three years and looking ahead to the next three years. The purpose was to take stock of what has been funded, where momentum is building, and where funders may need greater alignment.
A major point that emerged was the growing interest among some funders in establishing more durable genomic infrastructures, described in the discussion as genomic institutes or fixed genomic programs. These are not seen as short-term projects but as more permanent platforms capable of providing genomic diagnosis for rare disease patients over time. An important observation was that these initiatives are often not rare-disease-only structures; rather, they are commonly shared with oncology and other health areas, while still incorporating rare diseases. The FCC saw this as a promising development and agreed that it would be useful to investigate these initiatives more systematically, compare how they operate, and understand what they could learn from one another in terms of plans, methods, and possible exchanges.
A second major theme was the problem of fragmentation and siloing among funded projects. FCC members noted that, within their own organisations, they often support many projects but struggle to make those projects communicate with one another. This challenge exists not only internally within a funder's own portfolio, but also across funding organisations internationally. The FCC expressed interest in identifying which clustering models have worked well, which have not, and whether any could be scaled to a more global level across multiple funders.

Key FCC themes

- Continued commitment of funders to rare disease research
- Interest in long-term genomic infrastructures rather than one-off projects
- Challenges arising from siloed project portfolios
- Need for clustering models that work both within and across funders
- Stronger strategic alignment among funders as a near-term priority

Patient Advocacy Constituent Committee (PACC)

The committee has been rethinking its direction under new leadership, and a survey conducted over the past six to eight months was presented back to the group to better understand members' needs, motivations, and expectations. The survey had participation from all global regions, which was highlighted as especially important for an international organisation.
The survey results and discussion pointed to several substantive priorities for patient organisations: patient outcomes, diagnosis, treatment-to-care pathways, and stigma. Beyond those topics, the committee asked a more foundational question: why do organisations join PACC and IRDiRC in the first place? From that discussion, five themes were distilled: networking and engagement; influencing research and ensuring diverse perspectives; being informed about the latest research; dissemination of information; and reducing the diagnostic odyssey. These themes were important because they moved the conversation from general aspirations to a clearer articulation of the committee's purpose.

A central issue in the PACC session was the relationship between PACC and the wider IRDiRC structure. The committee argued for much closer collaboration with the other committees, especially around shared priorities such as shortening the diagnostic odyssey.
Another notable point was the suggestion that PACC-led or PACC-linked activities may offer a compelling value proposition for non-government sponsorship, especially since patient participation is now increasingly expected in many funding structures. This was not developed into a firm plan during the session, but it clearly emerged as a possible avenue for supporting IRDiRC activities more broadly.

Key PACC themes

- Strategic repositioning of the committee under new leadership
- Strong demand for meaningful cross-committee collaboration
- Priorities centred on outcomes, diagnosis, stigma, and reducing diagnostic odyssey
- Possible future opportunity to leverage patient involvement for external sponsorship

Diagnostic Scientific Committee (DSC)

The committee emphasised that its role is not only to speed up diagnosis but also to ensure diagnoses are correct, with a particular focus on reducing the "misdiagnostic odyssey" and the harm caused by wrong diagnoses or misinterpreted genetic data.
Three main topics were discussed. First, the committee reviewed a survey on the international laboratory genetics landscape, sent to IRDiRC members and to clinical, laboratory, and quality-control professionals. The aim was to map accreditation systems, quality standards, participation in external quality assessment, and oversight structures across countries. The discussion showed that even where laboratories are accredited and follow ISO-based quality systems, errors and near misses still occur. The committee plans to analyse the data further and produce a paper from this work.
Second, the committee examined misdiagnosis in genetics, especially with emerging technologies. Members noted that new technologies are not fully robust at first, and that sequencing has exposed much more human variation than previously understood, increasing the risk of interpretive error. Different laboratories may still classify the same variant differently, even under The American College of Medical Genetics and Genomics (ACMG) guidance. The group stressed that non-specialist clinicians may place too much confidence in genetics reports without recognising the uncertainty behind some classifications. This can have serious consequences, including harmful treatment decisions or inappropriate reproductive choices.
Third, the committee discussed how to turn these concerns into a practical output. It proposed a paper on misdiagnosis built around selected steps in a 22-step clinical genetics pathway, using clinical vignettes to show what can go wrong, the consequences, the lessons learned, and the safeguards needed. A member of DSC, based in South America, agreed to lead this effort, with members invited to contribute with real-world examples.
A wider discussion then addressed AI, data sharing, and long-read sequencing. AI was seen as potentially useful, but not as a substitute for better shared variant data. Better access to national and international datasets was viewed as essential, and the lack of genomic background data for underrepresented populations, including African populations, was identified as a major limitation. Long-read sequencing was seen as promising, but still largely at the research stage rather than routine clinical practice. The committee acknowledged the tension between the urgency of helping undiagnosed families and the need for caution when introducing new technologies into validated diagnostic settings.

Key DSC themes

- Move from reducing diagnostic delay to also reducing misdiagnosis

- Need for a global map of laboratory accreditation and quality frameworks
- Recognition that quality systems help but do not eliminate diagnostic error
- Concern about variant interpretation and real-world harm from misclassification
- Strong emphasis on data sharing as a prerequisite for better AI and better diagnosis
- Long-read sequencing seen as promising but not yet mature for broad clinical deployment
- Decision to develop a practical paper using misdiagnosis vignettes and safeguards

Interdisciplinary Scientific Committee (ISC)

The ISC session focused on the concept of "adaptive diagnosis and care," which was presented as integrating evolving molecular knowledge into lifelong rare disease management. The committee argued that diagnosis should no longer be seen as a one-time event, but as an ongoing process that changes as science, technology, and interpretation improve.
From this perspective, the committee proposed diagnostic checkpoints across the life course, where cases could be reviewed or re-analysed. Examples included the transition from paediatric to adult care, entry into palliative care, major changes in school attendance, and routine reanalysis every 18 months to two years. The committee summarised this approach by describing diagnosis and care as dynamic, cross-sectional, and lifelong.
The discussion also went beyond the clinical setting to include disability services, education systems, and service eligibility frameworks. Members noted that in many settings, even an undiagnosed rare disease code can help unlock support. This means the issue is not only scientific, but also linked to policy, social protection, and administrative systems. The committee also recognised that continuous retesting of everyone is unrealistic, so a more structured framework would be needed.
Patient and family perspectives were seen as essential. Members noted that some patients do not want to remain on a permanent diagnostic journey, and that re-diagnosis can bring both benefits and risks by affecting treatment eligibility or access to support. This led to discussion of the tension between correcting a diagnosis and preserving access to services. The example of cerebral palsy was used to show how a molecular diagnosis can sometimes be added to an existing diagnosis rather than replacing it.
The committee agreed that this topic should be developed further, potentially as a white paper, commentary, or perspectives paper. It also identified future areas of interest, including AI across diagnosis and therapy, the overlap between congenital anomalies and rare diseases, patient involvement in new drug development, and the alignment of health and social systems. Some of these topics were seen as requiring closer discussion with PACC.

Key ISC themes

- Reframing diagnosis as iterative, lifelong, and linked to care
- Proposal for life-course diagnostic checkpoints
- Recognition that diagnosis affects not only medicine but also education, disability, and services
- Need to build frameworks that are sensitive to different resource settings
- Strong emphasis on patient and family perspectives
- Tension between correcting diagnosis and preserving access to support
- Interest in turning the discussion into a formal publication or recommendation document

Therapies Scientific Committee (TSC)

The TSC session focused on reviewing recent work, clarifying current priorities, and narrowing future strategic choices. The 2026 priorities will focus on the digital twin task force and the digital biomarkers working group.
The central part of the discussion concerned planning for 2027. The committee had started with a list of nine possible topics, then worked over several months to reduce that to four. Those four were:

1. Equity by design – ensuring inclusive rare disease therapy development
2. Real-world evidence in rare disease trials and therapy development
3. Platform technologies for orphan drugs
4. Ethical and regulatory readiness for AI-based tools in rare disease therapy development.

Participants indicated that two of these topics would likely become the main priorities for 2027, but discussion with the broader group was still needed before finalising that choice.
TSC also discussed its own membership and capacity gaps. Following a gap analysis, the committee identified three areas of expertise it wants to recruit: digital health and data governance, methodological expertise for evidence generation in small populations, and regulatory expertise.

Key TSC themes

- Consolidation under new leadership
- 2026 priorities: digital twin task force and biomarker-related work
- Structured narrowing of 2027 priorities from nine topics to four
- Strong interest in equity, real-world evidence, platform technologies, and AI readiness
- Targeted recruitment to close expertise gaps

Regulatory Science Committee (RSC)

The RSC also reviewed its work to date. It described one completed manuscript as a landscape analysis of orphan drugs approved in different regions of the world, comparing whether medicines approved in one region were also approved in others. An important finding from that work was that the type and level of evidence in regulatory dossiers were often broadly similar across regions, yet access outcomes still differed: medicines sometimes reached one market later than another, or never reached some markets at all. This raised the question of why convergence in evidence does not necessarily produce convergence in access.
A second paper is underway and is intended to examine the “right side of the story,” meaning the positive incentives and drivers behind successful cases, rather than focusing mainly on failures. That shift in emphasis suggests the committee is trying to identify enabling conditions that can be replicated. At the same time, the committee recognised the difficulty of obtaining data from companies, particularly around why they do or do not pursue parallel submissions across agencies.
In terms of future topics, the RSC reported overlap with topics being considered by other committees. Among the issues under consideration were AI in the regulatory process, alternative trial designs including N-of-1 and small-N approaches, and links to recent work on platform approaches. However, the committee’s stance on AI was more cautious than some others’: members emphasised the need to define scope carefully, validate tools, and be confident that AI systems are fit for regulatory purpose before relying on them. This was an important note of caution in a meeting where AI was repeatedly raised as an attractive solution.
Finally, the RSC noted that it had three vacancies and was seeking committed members with scientific and regulatory expertise, ideally including underrepresented regions, though expertise and commitment were seen as the first priorities.

Key RSC themes

- Ongoing comparative work on orphan drug approvals and access divergence

- New focus on understanding positive incentives behind successful market access
- Cautious but active interest in AI and alternative trial designs
- Clear overlap and potential for stronger cross-committee work
- Continued need to strengthen committee membership and expertise

2. Topic session on Gene, base, and prime editing

New generation sequencing has opened the accession to whole genome determination allowing to envision revolutionary personalized medicine, where genetic mutations might be identified and corrected at individual level. Targeted gene modifications via homologous recombination represents the key necessary tool for personalized genetic correction. In the last years, numerous techniques have been developed, involving proteins and nucleoprotein complexes. The presentation touched base on what is the homologous recombination (HR), RNA-guided CRISPR/Cas9 endonuclease system, prime editing, offering concrete examples from 2023-2025 advances using CRISPR/Cas9, base editing, and prime editing technologies, noting that between 2024-2026, the field of genome editing has transitioned from experimental “proof-of-concept” to a tangible clinical reality. CRISPR/Cas9 could be applied in a large panel of potential therapeutic applications including in genetic or infectious diseases affecting liver, central nervous system, retina or muscle.

3. Cross-Committee Topic Sessions

1. Patient partnership in research funding

This session focused on a draft paper on patient partnership in rare disease research. Its main argument was that research progress depends not only on science and technology, but also on patients’ lived experience, priorities, and care needs. The discussion reflected a shift from seeing patients as passive beneficiaries to treating them as partners in shaping research agendas, funding, and data generation.

The presentation described patient partnership as a spectrum with three forms: consultative engagement, collaborative partnership, and patient leadership. These were not presented as fixed stages, but as different approaches suited to different contexts. The session also stressed that the relationship between patients and funders is now increasingly two-way, since patient organisations are also becoming research funders.

The draft paper proposed five pillars for stronger partnership: compensation and recognition, fair representation, data stewardship, education and training, and evaluation frameworks. In discussion, participants argued that training should not focus only on patients. Researchers, clinicians, and funders also need to learn how to communicate clearly, use accessible language, and work with patients more effectively.

A major concern was sustainability. Participants noted that patient involvement is often strong at the proposal stage but weakens later. They called for more continuous engagement through regular updates and structured opportunities to stay involved. Another key issue was early involvement in data and endpoint development. Speakers stressed that patients should help shape outcomes, endpoints, trial design, and registry strategy from the start, not only after approval.

The session also highlighted the growing value of patient preference and patient perspective studies, which were described as becoming a form of foundational science for endpoint selection and development strategy. Participants supported stronger use of shared repositories and existing disease registries so that patient groups are not repeatedly asked the same questions by different organisations.

The discussion ended with practical points: use simpler language, reduce administrative burden, and avoid treating patient organisations as only vulnerable groups. Many patients and carers are already strong leaders, but they still need time, support, and fair conditions to participate.

2. How patients are involved in regulatory decision-making

This session used the EMA model to discuss how patient participation in regulatory processes can be structured more broadly in rare diseases. The presentation showed that, in the EU system, patients can be involved throughout the regulatory lifecycle, from early development and scientific advice to marketing authorisation and post-authorisation activities. The main message was that patient engagement should not be limited to the final approval stage.

A key strength of the EU model is that patient representatives can serve as full members of some committees, including in the orphan products area. This allows them to build real expertise in regulatory thinking, evidence requirements, and benefit-risk assessment. The discussion suggested that the goal is not simply to "educate" patients, but to integrate them meaningfully into regulatory systems so their expertise can be used effectively.

The EMA pilot on early dialogue with patient organisations for orphan marketing authorisation applications was highlighted as a useful example. Patient groups were asked to provide input on unmet needs, treatment options, quality of life, daily impact, and desired benefits. This input proved especially valuable for understanding what matters most in daily life. The broader conclusion was that such input is even more valuable earlier, when trial design and outcome measures are still being defined.

As a result, timing became one of the central themes of the session. Participants repeatedly argued that patient input has the greatest value before pivotal studies are fixed, when it can influence endpoints, study burden, trial design, and the use of alternatives such as single-arm studies or external controls. Later input remains useful for benefit-risk assessment and product information, but often comes too late to shape the core design of studies.

The discussion also distinguished between an individual patient and a patient representative. A representative should speak for a broader community and stay connected to patient organisations and families, not only bring personal experience. One example showed that while clinicians may focus on motor outcomes, patients may prioritise respiratory or swallowing function because these matter more for survival and daily life.

Other important issues included conflicts of interest, which are especially challenging in rare diseases because communities are small and interconnected. The view expressed was that different degrees of conflict should lead to different roles, rather than automatic exclusion. Accessibility was another concern: even where many patient-engagement resources exist, they may be hard to find or navigate. The FDA contribution showed that the US is also developing multiple programmes and resources, using a similar lifecycle approach.

The session also stressed burden versus benefit. Participation can require significant time, travel, and energy, so flexible engagement methods are needed, including in-person, online, written, and survey-based input. Young people's participation was also highlighted as important but still underused. Overall, the conclusion was that the EMA and FDA models show real progress, but patient involvement remains uneven across jurisdictions, leaving clear scope for IRDiRC to help identify, compare, and spread workable models.

3. Platform technologies for orphan drugs

This session explored whether platform technologies should become a future IRDiRC initiative. The framing was that platform approaches allow established components or manufacturing methods to be reused while adaptable elements change, potentially speeding up development and regulatory assessment. The COVID-19 vaccine experience was used as the clearest proof that such approaches can work. For rare diseases, where very few conditions have approved treatments, this was presented as a potentially important strategic opportunity.

The presentation identified several possible benefits: faster medicine development, more personalised treatments including N-of-1 or N-of-a-few approaches, improved patient access, more efficient regulation, and reduced duplication of animal studies. Examples particularly relevant to rare diseases

included vaccines, gene therapies, cell-based therapies, and antisense oligonucleotides. The discussion also connected the topic to earlier IRDiRC interest in repurposing and highly personalised therapies.
The topic was also seen as timely because of emerging policy developments. The session referred to platform marketing authorisation language in the EU's draft pharmaceutical legislation and to the FDA's 2024 draft guidance on platform technologies. These developments suggested that regulators are beginning to create more formal space for approaches where a fixed component and a variable component can be assessed together. Participants saw this as especially relevant in rare disease areas where vectors, backbones, or manufacturing elements may stay constant while the disease-specific or mutation-specific component changes.
At the same time, one of the clearest messages was that the concept is still underdefined. Participants noted that there is no single stable definition of what counts as a platform. One important distinction raised was between using "prior knowledge" to support a new but separate product, and treating the platform itself as a more central regulatory object. That distinction matters because the implications for rare disease development could be modest in the first case and potentially transformative in the second.
Examples discussed included gene therapies where the vector stays fixed but the inserted sequence changes, and antisense therapies where the backbone stays fixed but the sequence changes. These examples showed why rare disease stakeholders are interested: if the platform is already validated, additional variants might be developed with much less duplication. That is especially relevant for ultra-rare mutation-specific therapies.
Even so, many questions remain open. Participants pointed to uncertainty about where the platform begins and ends, whether it should apply mainly to manufacturing and quality or more broadly, what new clinical and non-clinical evidence would still be needed when the variable part changes, and how evidentiary expectations should work in very small populations. The discussion therefore focused less on immediate implementation and more on where IRDiRC could add value. Suggestions included helping define the concept more clearly, connecting scientific, regulatory, and patient perspectives, linking the topic to N-of-1 development, and helping shape the field while guidance and legislation are still evolving. The session ended with the sense that platform technologies are promising but not yet mature, and that they may justify a future working group or task force if IRDiRC decides to prioritise them.

4. Ethical and regulatory readiness for AI-based tools in rare disease therapy development
This session examined how ready the field is for AI-based tools in rare disease therapy development from ethical, methodological, regulatory, and HTA perspectives. Examples discussed included treatment-response prediction, drug repurposing, adaptive trial design, biomarker discovery, and personalised therapy pathways. AI was seen as promising because rare disease development often involves very small populations and limited conventional evidence, but the discussion remained cautious.
Five main challenges structured the discussion: validation and reproducibility, transparency and explainability, bias and representativeness of training data, data governance and cross-border sharing, and regulatory and HTA acceptance of AI-generated evidence. Participants stressed that technically advanced models are not enough if they cannot be validated in real-world settings and across different centres and populations.
A strong message was that AI is often added to projects because it is fashionable, even when the project was not built around it. The real weakness is not innovation itself, but verification and clinical utility. Models may perform well on training data yet fail in practice. For AI to be credible in regulatory settings, speakers argued that it needs high-quality data, cross-border validation, patient-level testing, and prospective evaluation.
This led to a second major theme: data quality and access. Rare disease datasets are often small, fragmented, and unrepresentative, which limits the usefulness of AI. One promising approach discussed was to let algorithms move to the data rather than moving data into one central system, so

results can be combined without fully centralising sensitive data. At the same time, participants warned that some health systems are becoming more restrictive about sharing data, partly for commercial reasons.
Bias and lack of normative reference data were also highlighted. One example involved vocal biomarkers, where a detectable signal exists but there is not yet enough reference data to know whether it can serve as a meaningful endpoint. AI was seen as more likely to succeed in areas with stronger datasets, such as imaging, and some suggested that validated models from common diseases might be adapted for rare diseases with similar features.
Another recurring theme was trust and organisational readiness. One example described by a funder, was that caution is needed when using AI, even internally, because governance and safeguards are not yet sufficiently defined. From a regulatory perspective, the discussion suggested that AI will only be accepted when its scope is clear, its purpose is well defined, and the resulting evidence can be understood and assessed within existing or adapted frameworks.
The session also recognised the opportunities. AI may help with biomarker discovery, modelling disease progression, predicting treatment response, and designing trials where conventional approaches are difficult. It may also support analysis across related conditions rather than treating each rare disease in complete isolation. Even so, the overall conclusion was careful: the field still needs better data, stronger validation, clearer standards, and more regulatory clarity before AI can be used confidently in rare disease therapy development. The discussion pointed toward a possible future IRDiRC working group or task force on governance, readiness, and methodological standards.

4. Topic session on regulatory science

This session brought together three connected strands of work from the Regulatory Science Committee. It first reviewed two published studies on orphan drug development and global approvals, then introduced the next RSC paper, and finally summarised the ongoing Task Force on regulatory convergence for AAV-based gene therapies. Across all parts, the central message was that rare disease therapy development is shaped not only by scientific merit, but also by company capacity, funding, evidence packages, submission strategy, and the degree of alignment between regulatory systems.

1. Published study on orphan drug development success

The first paper examined non-oncology orphan drugs designated in 2017 by FDA and EMA, using a 7–8 year follow-up window to assess progression through development and approval. The analysis looked at clinical stage transitions, attrition, product type, sponsor size, disease prevalence, and funding sources.

The study showed that orphan drug programmes had higher stage-transition success rates than general drug development benchmarks, with an overall probability of success from IND to approval of 18.6%, compared with lower comparator estimates from broader industry datasets. Biological products showed the highest probability of success, small molecules remained the dominant modality numerically, and gene therapies had lower success in moving beyond early phases. A particularly notable finding was that novel active substances pursued in multiple indications performed better than either single-indication novel products or repurposed marketed drugs.
The study also highlighted the importance of company size and financial strength. Smaller organisations had lower overall probabilities of success, and financial reasons accounted for a large share of programme attrition, especially among academic, foundation-led, and SME programmes. At the same time, most orphan programmes drew on mixed funding, and foundations, charities, and patient organisations supported a large proportion during preclinical development. Disease prevalence did not appear to correlate with success or failure.

2. Published study on global orphan approvals

The second published study examined 53 novel orphan products approved in 2021–2022 across up to six jurisdictions. Its goal was to compare approval timing and the types of evidence relied upon by different regulators.
The main finding was that the same evidence is often used globally, yet approvals still occur far apart in time. According to the slide summary, 69% of products relied on the same evidence across regions, and the most common evidence package was one adequate and well-controlled trial plus confirmatory evidence. Even so, there was an average lag of around three years between approvals across jurisdictions. Most products received their first or second approval in the US or EU, and relatively few were submitted everywhere.
The session used these findings to underline a key regulatory science problem: divergence in access is not necessarily driven by radically different science, but often by timing, sequencing, submission strategy, and jurisdictional requirements. The recommendations on the slides therefore focused on reducing international approval gaps through collaborative programmes, simplified common submission packages, reciprocity models for rare diseases, early regulatory dialogue, and better use of multi-agency pathways.

3. Second RSC paper
The next RSC paper was presented as a deep dive into the subset of products approved in five or six jurisdictions. This substudy includes 18 products and aims to identify the common factors associated with broad multi-regional approval and the factors that reduce divergence in approval timelines.
The factors being examined include:

- product type
- company size
- regulatory requirements
- use of regulatory incentives
- evidence package characteristics
- submission strategies.

The slides suggest that this next step is intended to move from description to explanation: not just showing that approval timelines differ, but identifying what helps products succeed globally and what drives delay. A specific comparison highlighted in the deck is between SMEs and non-SMEs, as well as between biologics and small molecules, the use of global trials or local patient inclusion, and whether agencies accept evaluations conducted in other jurisdictions.

4. Task Force on regulatory convergence
The final part of the session covered the ongoing Task Force: “Advancing AAV-Based Gene Therapies for Rare Diseases: Addressing Early-Development Barriers Through Regulatory Convergence.” Its focus is on the earliest development stages, where misaligned requirements across jurisdictions can create cost, delay, uncertainty, and in ultra-rare diseases, major barriers to viable global development.
The Task Force is examining three main technical areas where cross-jurisdictional differences arise most consistently:

- Chemistry, Manufacturing and Controls (CMC)
- Preclinical evidence generation
- First-in-human clinical trials.

The slides listed specific areas of divergence, including raw material qualification, potency assays, release criteria, comparability and bridging studies, biodistribution, toxicology, immunogenicity, inclusion criteria, dosing, endpoints, GMP requirements, and review frameworks. An important nuance in the presentation was the distinction between difference and divergence. The point was that different requirements do not always amount to problematic divergence; divergence is what developers experience when differences are unanticipated, poorly explained, or difficult to manage.

Some apparent divergences also come from rules outside agencies' direct remit, such as GMO frameworks, diagnostic regulation, ethics review, or GMP audit processes.
The recommendations were grouped for three audiences. For developers, the emphasis was on planning globally from the outset: mapping procedural requirements early, engaging regulators in parallel, adopting scalable manufacturing standards, designing comparability strategies prospectively, and documenting decisions with global submissions in mind. For regulators, the priorities were greater transparency, more public sharing of non-confidential learnings, and stronger multi-agency dialogue. For funders and policymakers, the call was for efficient and innovative pathways, including incentives for early development, pre-competitive research, and shared policies that reflect the realities of ultra-rare disease development.

5. Future events

IRDiRC meetings (internal)

- Online Consortium Assembly Meeting: 17 June 2026
- Fall Consortium Assembly Meeting: 13-14 October 2026
- RE(ACT) Rare Disease Congress: 10-12 March 2027, Budapest, Hungary (in partnership with ERDERA and BlackSwan Foundation)

External meetings

- DIA Europe 2026 Annual Meeting: 24-26 March, Rotterdam, Netherlands
- 2026 Clinical Outcome Assessment Meeting: 16-17 April, Washington DC, USA
- Undiagnosed Disease Day 2026: 29-30 April, Gdansk, Poland
- Health and Business Growth Summitt: 19-21 May, Zagreb, Croatia
- European Conference on Rare Diseases (ECRD) 2026: 3-4 June, Prague, Czech Republic
- World Orphan Drug Congress USA: 9-11 June, Boston, USA
- World Orphan Drug Congress Europe: 26-28 October, Amsterdam, Netherlands

6. Publications

Non-oncology orphan drug development: Productivity and probability of success. Samantha Parker, Jida El Hajjar, Anneliene H. Jonker, Susan R. Kahn, Persefoni Kritikou, Christina Kyriakopoulou, Anthony Haight. *Drug Discovery Today*.
Access the publication: here.

Challenges and Opportunities for the Use of Telehealth in Rare Disease Diagnosis, Treatment, Research, and Education: Key Opinion Leader Interviews by the IRDiRC Telehealth Task Force. Melissa Parisi, Adam Hartman, Mary Catherine Letinturier, Elena-Alexandra Tataru, Gareth Baynam, Lara Bloom, Marco Crimi, Giuseppe Didato, Sofia Douzgou, Anneliene Jonker, Martina Kawome, Frederike Muller, Ratna Puri, Birute Tumiene, Maria Della Rocca, James O'Brien, Nuala Ryan, Thong Meow-Keong, Faye Chen. *Therapeutic Advances in Rare Disease*.
Access the publication: here.

Rare disease preparedness: The time is now. Gareth Baynam; Ruxandra Draghia Akli; Anne R. Pariser; Chun-Hung Chan; Elena-Alexandra Tataru; Daniel Scherman; David A. Pearce. *Rare Disease and Orphan Drugs Journal*.
Accepted for publication.

Translating multi-omics into healthcare: requisites for scalable and equitable implementation. Birute Tumiene, David R Adams, Robert Allaway, Maria J Barrero, Chun-Hung Chan, Victor Faundes, Vanessa S Fear, Polina Glezer, Claudia Fuchs, Tudor Groza, Elisa Houwink, Saumya Jamuar, Mary Letinturier,

Richa Midan Lomash, Ratna Puri, Juergen Reichardt, Ruty Mehrian-Shai, Francois van der Westuizen, Gaurav Varshney, Shinya Yamamoto, Gareth Baynam. *Human Genomics.*
Access the publication: here.

Stigma in Rare Diseases: An Unmet Global Health Need. Gareth Baynam; Elena-Alexandra Tataru; Ahmed-Sherrif Kanvela Yussif; Angus Clarke; Catherine Coveney; Claudio Carta; Diana Kwast-Hoekstra; Gregory Fagan; Helen Malherbe; Helene Cederroth; Hilmi Bolat; Marc Dooms; Martina Mwabva Kawome; Matt Bolz-Johnson; Samuel Agyei Wiafe; Shirlene Badger; Sophie H Turner; Rayner Kay Jin Tan; Ritu Jain. *The Lancet Global Health.*
Submitted to journal.

The roadmap for the development of the Human Variome -Development of functional multi-omics analyses for the understanding of human biology. Birute Tumiene, David R. Adams, Robert Allaway, Maria J. Barrero, Chun-Hung Chan, Víctor Faundes, Vanessa S. Fear, Polina Glezer, Claudia Fuchs, Tudor Groza, Elisa J.F. Houwink, Saumya Shekhar Jamuar, Mary Catherine V. Letinturier, Richa Madan Lomash, Ratna Dua Puri, Juergen K. V. Reichardt, Ruty Shai, Francois van der Westhuizen, Gaurav K. Varshney, Shinya Yamamoto, Elena-Alexandra Tataru, Gareth Baynam. *Orphanet Journal***.**
Submitted to journal.

7. Task Force composition

Following the open call for nominations conducted in January-February 2026, the selected members of the three Task Forces and one Working Group were presented. The activities planned for 2026 are:

- Digital Twins in Rare Disease Research and Care *(task force)*
- Models of Care for Care Coordination *(task force)*
- Optimizing the Use of Data Sources and Registries *(task force)*
- Digital Biomarkers *(working group)*

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Disclaimer

Certain elements of the meeting discussion have been intentionally omitted from this report, as the details relate to sensitive or confidential matters. This document is intended for public dissemination. The opinions presented in the report do not reflect the position of the member organisations.