Ongoing Efforts: ERN-EYE

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European Reference Network
for rare or low prevalence complex diseases
Network Eye Diseases (ERN-EYE)

PQ-110-003 (Sepofarsen) Phase 2/3 Illuminate Trial

A Story of a Suboptimal Comparison

First year results: Illuminate did not meet primary endpoint of Best-Corrected Visual Acuity (BCVA) at Month 12 compared to sham procedure control group

Traditional analysis approach of TE vs sham is difficult to show Tx effect due to high variability & small N

However, when adjusting TE & sham eyes by subtracting effects of their corresponding CE, a numeric treatment difference between sepofarsen & sham is observed

- Consistent w/ Phase 1b/2 study results
- Individual participants demonstrated improvement from baseline in multiple endpoints
- Responses also seen in year 2 when 2nd eye/sham was treated

Overall good safety profile: no intraocular inflammation, no systemic effects

EMA & FDA recommended setting up another phase 2/3 trial prior to submitting Marketing Authorization Application

ProQR Therapeutics Announces Transaction Completed for Théa to Acquire Sepofarsen and Ultevursen Ophthalmic Assets

https://www.proqr.com/press-releases/proqr-therapeutics-announces-transaction-completed-for-thea-to-acquire-sepofarsen-and-ultevursen-ophthalmic-assets

Divestment of sepofarsen and ultevursen completed – Théa to continue development of sepofarsen and ultevursen for patients with LCA10 and Usher syndrome

Agreement provides ProQR with initial payment of €8M and up to €165M in earn-out payments, as well as potential double-digit royalties based on commercial sales in the US and EU

Transaction supports ProQR's strategic focus on its proprietary Axiomer® RNA editing technology platform and continued advancement of pipeline

LEIDEN, Netherlands & CAMBRIDGE, Mass., Dec. 08, 2023 (GLOBE NEWSWIRE) --
ProQR Therapeutics N.V. (Nasdaq: PRQR) (ProQR), a company dedicated to changing lives through transformative RNA therapies, today announced it has completed a transaction divesting late stage ophthalmic assets, sepofarsen and ultevursen, to Laboratoires Théa (Théa).

08 Dec 2023

Sepul Bio, a Théa Pharma Company
Patient recruitment ongoing
Patients HeZ or HoZ for
frequent c.2991+1655A>G mutation in *CEP290*

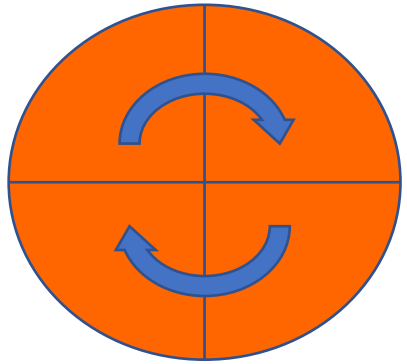
SWOT analysis of the current ecosystem: TRIALS & therapies FOR RED

STRENGTHS

- Ophthalmology **always active field of pioneer scientific and medical research as "…first to… " :** new therapies (ASO, gene replacement, CRISPR & editing, …)
- Strong inter continental / international academic collaborations
- Close interactions: & empowerment: medical & patient
- Previous successes (cf Luxturna)

WEAKNESSES

- Huge heterogeneity of IRDs
- Small trial populations
- Rare diseases judged based on the same criteria as Common Diseases
- Chronic non-life-threatening diseases compared to other RD
- National Regulations vary +++ (EMA, FDA, MHRA, etc.)
- Recent Interruption of trials , need another story than Luxturna getting "old"



THREATS

- Unawareness of investors, about **RED**
- Lack of interest
- Business failure => **choice to invest in more common diseases**
- Global economic situation => decrease of investments in RD
- Lack of continuation of national or international rare diseases plans (exp ERNs) : fragility of systems

OPPORTUNITIES

- Promising pre-clinical research, with ongoing new innovations
- Ongoing trials with more promising results
- Revisiting trial designs (ex. Realized IHI, REDI/RUSH study, …)
- 3rd meeting for ACT4Red, & development of transatlantic action plans

Supporting Clinical Trials - RealiseD

Statistical design and analysis to maximize evidence generation from small samples, while protecting validity and computational performance.

RealiseD
compRehensive mEthodological and operational Approach to cLinical trIalS in ultra-rarE Diseases

RealiseD Clinical Use Cases

=> **Change of paradigm**: with acceptation of stability of disease or slowing down of functional deterioration as relevant goal.

Pressure testing through 4 ERNs

ERN-EYE **ERN BOND** **EpiCARE** **EuroBloodNet**

ERN BOND
EUROPEAN REFERENCE NETWORK ON RARE BONE DISEASES

EpiCARE

ERN | EuroBloodNet

***To address the lack of adapted outcomes and outcome measures reflecting burden of disease ERN-EYE will develop for 3 IRDs (LCA, Stargardt, achromatopsia)*:**

- Validated PROMs accurately reflecting changes in daily life
- Functional and anatomical tests & natural histories

COCIR Advancing Healthcare · efpia · EuropaBio · MedTech Europe from diagnosis to cure · Vaccines Europe · innovative health initiative · Co-funded by the European Union

Multistakeholder Meetings at a Glance

Bringing innovation to the patient in a rapidly changing ecosystem

RAPIDLY CHANGING GLOBAL ECOSYSTEM

Purpose: *To improve clinical trials for **R**are **E**ye **D**iseases (**RED**), by sharing struggles, issues and successes & to* shape the landscape for clinical trials for inherited retinal diseases by illustrating the need for leaner, innovative trial designs with **better outcomes and more realistic endpoints** tailored specifically to rare eye diseases

Stakeholders:

- Patient organisations (Retina International, FFB, others…)
- ERN-EYE (60 HCPs in the EU, awarded by the EC as network)
- Regulators (representives from EMA & FDA)
- Academics & Experts (international)
- Pharmaceutical companies

Reminder

Chatham House Rules Apply

What it means:

Identity and affiliation of speakers and participants must remain confidential.

What is communicated to the outside world is done with the approval of the whole group.

Purpose:

- Encourage **honest, open discussion**
- Support **collaborative problem-solving**
- Protect personal and organizational privacy

In practice:

- You **may not name or quote** anyone directly
- No recording or attribution without consent

Act4REd : Taking action together on what we could not do alone

Multistakeholder Meetings at a Glance

An Ongoing Initiative

1st meeting: Ghent, 30 November 2022 (ERN-EYE scientific workshop)

- Sharing challenges
- Highlighting the need for leaner, innovative trial designs, with better outcomes and more realistic endpoints tailored specifically to rare eye diseases.
- Publication in ***Drug Discovery Today, September 2024*** (https://doi.org/10.1016/j.drudis.2024.104095)

European Reference Networks

2nd meeting: Dublin, 5 June 2024 (Retina International Conference)

- Creation of the ACT4Red initiative
- Determination of three topics of focus
- Organisation of dedicated groups for each topic

Retina International

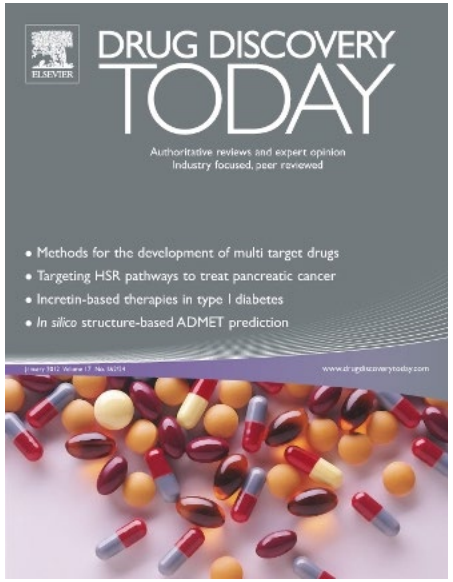
Preparatory meetings for each topic (Online)

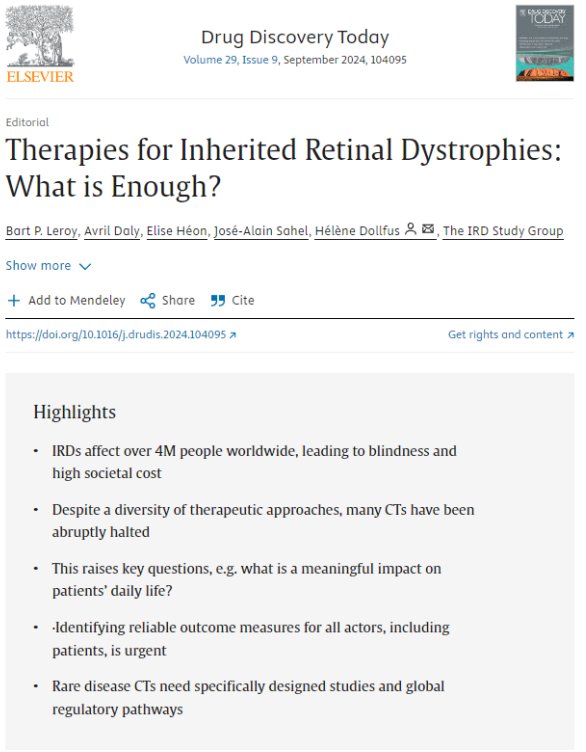
- Determination of priorities & relevant deliverables

3rd meeting: Salt Lake City, 3 May 2025 (ARVO 2025 Annual Meeting)

- Review of the current ecosystem
- Plan of action

ARVO





ELSEVIER

Drug Discovery Today

Volume 29, Issue 9, September 2024, 104095

Editorial

Therapies for Inherited Retinal Dystrophies: What is Enough?

Bart P. Leroy, Avril Daly, Elise Héon, José-Alain Sahel, Hélène Dollfus, The IRD Study Group

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https://doi.org/10.1016/j.drudis.2024.104095 Get rights and content

Highlights

- IRDs affect over 4M people worldwide, leading to blindness and high societal cost
- Despite a diversity of therapeutic approaches, many CTs have been abruptly halted
- This raises key questions, e.g. what is a meaningful impact on patients' daily life?
- Identifying reliable outcome measures for all actors, including patients, is urgent
- Rare disease CTs need specifically designed studies and global regulatory pathways

Act4RED

Act4RED: Advocating for Rare Eye Disease Policy Advancement

Retina International

EUROPEAN REFERENCE NETWORK DEDICATED TO RARE EYE DISEASES ERN-EYE

FOUNDATION FIGHTING BLINDNESS

CORE Committee of Retinal Experts

Current
Legislative Initiatives

Emerging
and Upcoming Policy Actions

Strategic
Vision for Long-Term Influence

Current Legislative Initiatives

- **EU Pharmaceutical Legislation**

  Focus: Orphan drugs, paediatric treatments, innovation pathways

- **HTA Regulation Implementation**

  Patient-relevant evidence in therapy evaluation

- **EU Critical Medicines Act**

  Emphasis on supply chain resilience, diagnostics, newborn screening

- **Life Science Strategy Consultation**

  Input to ensure retinal conditions are included in EU Research & Innovation strategies

- **Biotechnology Act Participation**

  Stakeholder in shaping biotech policy

Emerging and Upcoming Policy Actions

- **Joint Action on Pricing & Reimbursement**

  Advocating for fair, transparent access across the EU

- **Revision of Medical Devices Regulation**

  Ensure inclusion of vision-specific diagnostics and technologies

Strategic Vision for Long-Term Influence

- **EU Parliament Special Interest Group**

  Strengthen visibility of retinal health issues in parliamentary debates

- **WHO Resolution**

  Recognition of RD as a global health priority (soft law)

- **Multi-Annual EU Budget Advocacy**

  Secure long-term funding for vision research and innovation

Act4RED Collaboration Goals

We must **reinforce strategic engagement** with EU institutions, foster structured and inclusive **multistakeholder collaboration**, and **drive policy actions** that deliver **measurable** and **impactful outcomes**.

Strengthen ties with:

- European Commission DGs
- European Parliament committees
- National ministries of health and innovation

Promote:

- Clear, measurable outcomes for all **Act4RED** initiatives
- Cross-sectoral policy alignment

Strategic National Engagement - Ireland 2026

The **Irish Presidency of the Council of the EU** (July-Dec 2026) presents a pivotal opportunity to **elevate innovation in rare disease** on the European agenda through national leadership and strategic influence.

Planned actions:

- Engaging with the Irish government and The European Economic and Social Committee (EESC) to prioritise clinical trials and research innovation on the EU agenda
- Through this vocate for visibility of RED within broader health priorities

Key Platforms Advancing Rare Disease Research

ERDERA
European Rare Diseases Research Alliance

Funding is a core element of **ERDERA**'s strategy to transform rare disease research in Europe. Its mission is to bridge gaps in scientific knowledge, foster international collaborations, and deliver tangible benefits to millions of patients affected by rare diseases across Europe and beyond.

imi innovative medicines initiative

IMI is the world's largest public-private partnership in health with a total budget of €5 billion - half from the European Union and half from the pharmaceutical industry, through EFPIA.

ACT4RED MSM

- Introduction
- Topic 1: Endpoints
- Topic 2: PROMS
- Topic 3: Communication
- Wrap -up

2025 Salt Lake City in the context of ARVO

3rd May 2025

Group 1: Endpoints

Chairs: Bart Leroy, Rachel Huckfeldt

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Network Eye Diseases
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European Reference Network dedicated to Rare Eye Diseases

TOPIC 1 Endpoints

Lead & participants: **Bart Leroy, with Rachel Huckfeldt**, Allison Ayala, Marc Pennesi, David Birch, Kenji Fujita, Robert MacLaren (TBC) and the Forum for Ocular Diseases.

General objectives:

- 360° overview of FST Use in research (survey, review of literature)
- EMA and FDA feedbacks/Blockages reviews
- Production of a position paper (publish) – Statement to be sent to agencies

Deliverable: Joint position paper between ACT4Red (ERN-EYE, FFB, RI,…) and the Ocular Disease Forum.

Next steps:

- Formalise co-authorship with industry
- In-depth discussions for the content of the paper to be continued on the 28th of May in Washington

FOUNDATION FIGHTING BLINDNESS

CLINICAL CONSORTIUM

FST Background and Data Review

David Birch

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Review of FST Endpoint Properties from RUSH2A Natural History Study

Building the Case for Clinical Relevance

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CLINICAL CONSORTIUM

FST Minimal Clinically Important Difference

Lee McDaniel

MLMT Results

FOUNDATION FIGHTING BLINDNESS
CLINICAL CONSORTIUM

VFQ Results

Discussion

- Feedback on FST MCID analysis approach
- Totality of evidence supports a 10 dB cutoff – strong enough case?
- Limitations of data, especially MLMT results
- Framing of 10 dB cutoff? Upper limit?
- Kenji Fujita to discuss Atsena strategy regarding IND submission with FST, FDA feedback

TOPIC 1 Endpoints

Talks

FST Background and Data Review – David Birch - 10 min

- Overview of FST Testing
- Review of Endpoint Properties from RUSH2A
- Building the Case for Clinical Relevance

FST MCID – Lee McDaniel – 25 min

- Reminder of Overall Mission of REDI Working Group
- Regulatory View
- MCID/Anchor Methods
- Summarize Anchors Used and Why
- Summarize LCA Datasets Obtained and Planned Approach
- Luxturna Data / Results
- Atsena Data / Results
- Summary of MCID ranges from both datasets/anchors – w/our takeaway (e.g. totality of evidence supports a 10db cutoff for FST)

Discussion Points

- We welcome thoughts about the FST MCID analysis approach/recommendations
- **Kenji Fujita** to discuss Atsena strategy regarding an IND submission with FST – FDA feedback, plans for next steps

TOPIC 1 Endpoints

Position paper

Outline:

1. ***What is FST?***
2. ***What type of conditions could FST be an endpoint for?***
3. ***How FST correlates to daily living?***

Challenges:

Regulatory agencies need a cutoff point linked to a validated endpoint and test (for example MLMT).
Correlating FST to daily living

Suggestions:

Asking industries to share their FST data – sharing initiatives are ongoing, but could be increased
Including quotes from patients and experts in the field, explaining their point of view (using a focus group, like for example Atsena with LCA patients).

TOPIC 1 Endpoints

Discussion

Outline:

1. ***What is FST?***
2. ***What type of conditions could FST be an endpoint for?***
3. ***How FST correlates to daily living?***

Moving forward:

- Does this outline serve the goals we want to achieve?
- Are there additional challenges to consider?
- What should be the timeline?
- Patient focus group were suggested – does anyone would like to share their experience with such groups?

Proposed Outline of FST Presentations for ERN-EYE Meeting at ARVO, May 3

1. **FST Background and Data Review** – David Birch - 10 min
   a. **Overview of FST Testing**
      i. What it tests
      ii. Methods of measurement
      iii. Quality
      iv. Baseline Examples
   b. **Review of Endpoint Properties from RUSH2A**
      i. Minimal floor effect
      ii. Sensitive measure of disease progression
      iii. Low test-retest variability
   c. **Building the Case for Clinical Relevance**
      i. Correlation with disease duration
      ii. Delineation of rod vs cone function
      iii. Correlation with PROs

2. **FST MCID** – Lee McDaniel – 25 min
   a. **Reminder of Overall Mission of REDI Working Group**
      i. Primary endpoint comparisons from Consortium NHSs
      ii. Larger Scope
         1. Exploratory endpoints (using NHS and company trial data)
         2. Lessons learned from completed trials
         3. Mock trial design scenarios
   b. **Regulatory View**
      i. Correlation is not enough, need to know how much change is meaningful
      ii. CoR is not enough, need patient experience
      iii. Anchor approach is recommended (discussions at ODF; FDA guidance document)
   c. **MCID/Anchor Methods**
      i. Basic approach
      ii. Mock example
   d. **Proposed Strategy**
      i. Focus on MCID for **improvement**
      ii. Focus on **LCA**
      iii. Rationale - start with one disease, large changes - then expand
   e. **Summarize Anchors Used and Why**
      i. MLMT – 2 unit change
         1. Straightforward, we know it is acceptable to FDA
      ii. NEI-VFQ – 10 point change
         1. FDA has suggested PROs could be useful in these cases (totality of evidence)
         2. Combined with MLMT, will provide supportive/ totality of evidence argument
   f. **Summarize LCA Datasets Obtained and Planned Approach**
      i. Atsena and Luxturna Datasets: Calculate MCID independently via each dataset using MLMT anchor, to see if we get same ballpark on two independent datasets
      ii. Bonus: Opus dataset, not directly comparable, but perhaps supportive – use as an MCID validation approach
   g. **Luxturna Data / Results**
      i. Summary of dataset, what is included (# pts, what visits, trt grps, etc)
      ii. FST MCID ROC and Results Plot from MLMT anchor
   h. **Atsena Data / Results**
      i. Summary of dataset, what is included (# pts, what visits, trt grps, including all pts not just high dose, IOD, etc)
      ii. FST MCID ROC and Results Plot from MLMT anchor
      iii. FST MCID ROC and Results Plot from VFQ anchor (one slide per EACH of the subscales)
      iv. Summary Table of all MCIDs (sorted by AUC)
   i. **Summary of MCID ranges from both datasets/anchors – w/our takeaway (e.g. totality of evidence supports a 10db cutoff for FST)**

3. **Discussion Points**
   a. We welcome thoughts about the FST MCID analysis approach/recommendations
   b. Kenji Fujita to discuss Atsena strategy regarding an IND submission with FST – FDA feedback, plans for next steps

2025 Salt Lake City in the context of ARVO

3rd May 2025

Group 2: PROMS

Chairs: David Keegan, Elise Héon

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TOPIC 2 PROMs

Lead & participants: **David Keegan, with Elise Héon**, Thiran Jayasundera, Benedicte Lescrauwaet, Isabelle Audo, Silvia Cerolini (and the following participant, though unfortunately unable to attend the ARVO meeting: Jennifer Pluim).

General objectives:

- GAP analysis and Pros & Cons of current PROMS => Survey and review of literature
- Deliver position paper and see how to recommend best PROMS to trials & convince agencies on their value as future endpoints

Deliverable: Editorial

Next steps:

- Gap analysis of existing PROMS
- Development of position statements for education
- Possible development of a repository

TOPIC 2 PROMS

Topics :

Introduction: David Keegan

Hélène Dollfus: SeeMyLife: Co-creating paediatric PROMS

Elise Héon: Creating and validating Patient-Reported Outcomes for Children: Process and Challenges

Isabelle Audo: Translation of PROMS questionnaires: the examples of ViSIO-PRO and MRDQ in France

Act4RED Working Group 2 Overview

- What is important to patients (that is directly linked to FDA / EMA / MHRA etc)
  - Children vs Adult
- Essential Properties of a PRO
  - Reliability
  - Validity
  - Ability to detect change
- Linking PROMs to vision function (metric)
- Nuance in determining impact of disease (early vs late onset; Central vs Peripheral vs Global Retinal Disease; syndromic vs non-syndromic)
- Measuring Independence
  - Qualifying and Quantifying what we know is important and true
- Barriers to adoption of PROMs
- Solution to Barriers
  - Gaps

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Approval at Regulatory Agencies

- Safety
- Efficacy
  - Metrics
  - Vision
  - Function
  - QoL
- Value
  - Determined by economists
  - Linking efficacy and cost

- In Essence
- Patients Declare What is Important
- Experts agree a metric
- Agree best tool to measure
- Industry agree that tool
- Tool becomes the endpoint
- Trial meets that end-point
- Higher chance of approval

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FDA Guidance 2019

- FDA - Patient-Reported Outcome Measures: Use in Medical Product Development to Support Labeling Claims (2019)
  - findings measured by a well-defined and reliable PRO instrument in appropriately designed investigations can be used to support a claim in medical product labeling **if the claim is consistent with the instrument's documented measurement capability**
  - Must consider
    - The population enrolled in the clinical trial
    - The clinical trial objectives and design
    - The PRO instrument's conceptual framework
    - The PRO instrument's measurement properties
    - **Documented evidence of patient input** during instrument development and of the instrument's performance

Guidance

Guidance

Hover Pro Guidance 2021

- Psychometric testing
- Massof Activity Inventory
- Target population large enough to perform an initial Rasch analysis (> 50)
- Validity of the VFQ for use in a given population requires that the items span a difficulty range corresponding to the visual ability range of the population.
- The VFQ must be calibrated separately for new populations with different visual characteristics.

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Hover Pro Guidance

Any publication or presentation reporting the results of PRO using a VFQ should include enough information to allow replication, including:

- The name of the VFQ and, if applicable, the version
- If the VFQ has not been previously validated: Any relevant validation procedure and population information
- If the VFQ has not been previously released: An item list and response scale, including any “not applicable” category
- Method of administration and, if not standardized, the verbal instructions provided to the respondents
- Scoring rules and algorithms
- Provided the instrument has been validated in an appropriate population: Results of the Rasch analysis, especially item measures, item and person error estimates, and item infit statistics

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SeeMyLife

ERN's Mission: « Leaving no one behind with a rare disease in Europe »

Hélène Dollfus on behalf of the ERN-EYE SeeMyLife Consortium
European Joint Programm Rare Diseases project EJPRD SHS

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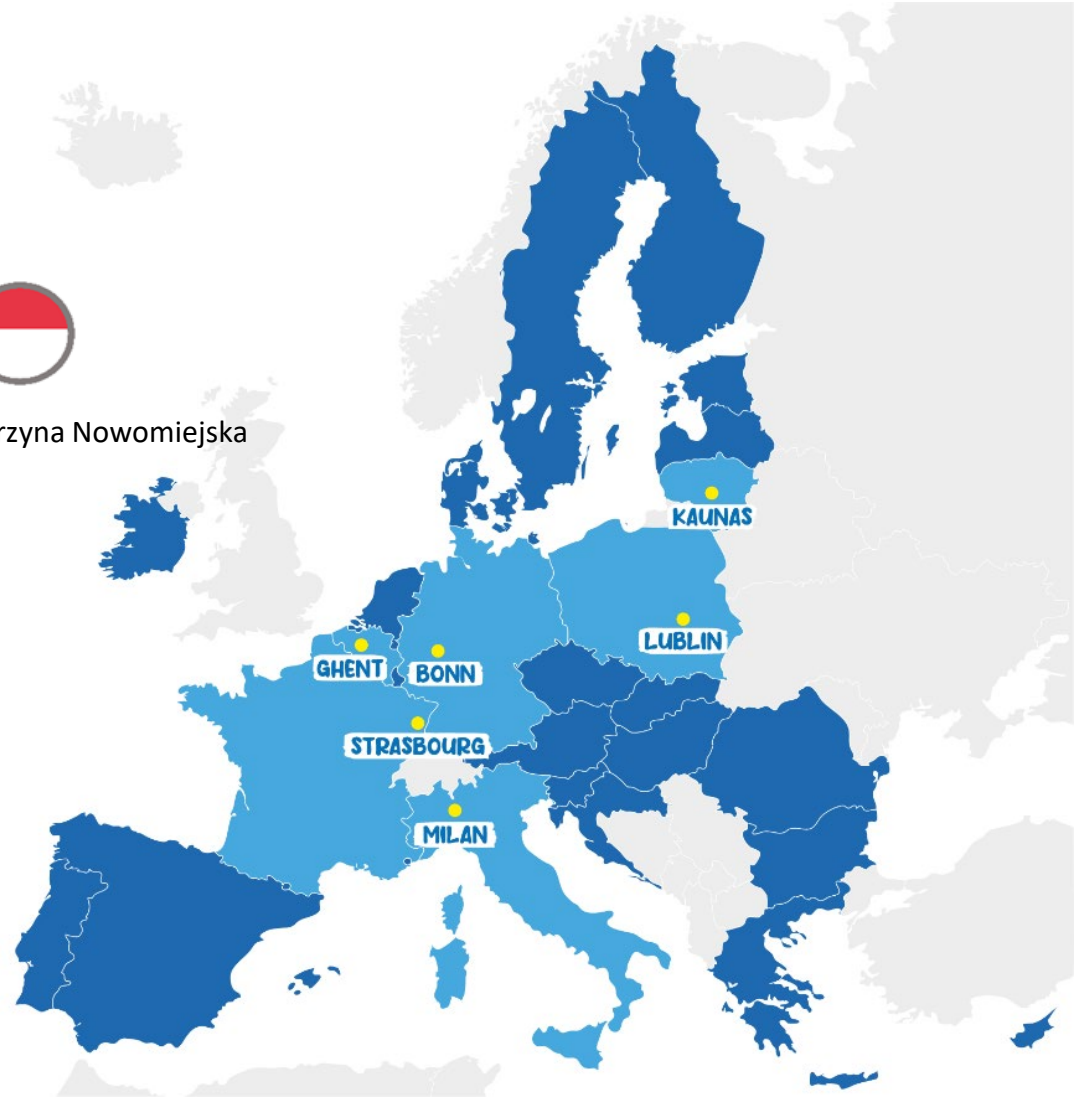
Network Eye Diseases (ERN-EYE)

EUROPEAN JOINT PROGRAMME RARE DISEASES

https://www.google.com/search?client=safari&rls=en&q=seemylife+youtube+ern+eye&ie=UTF-8&oe=UTF-8

STUDY
COORDINATION

Hélène DOLLFUS Bart Leroy Agnese Suppeij Robert Finger Reda Zemaitie Katarzyna Nowomiejska



Background

Holistic mixed approaches to capture the real life of children with Rare Eye Diseases

- Rare Eye Diseases (RED) in Europe: leading cause of severe visual impairment/blindness in children.
- Sensory disability with psychological distress → huge impact on patients' lives and families'
- Understanding this impact is key
  - in care
  - shared decision making
  - developing therapies
  - improving social integration

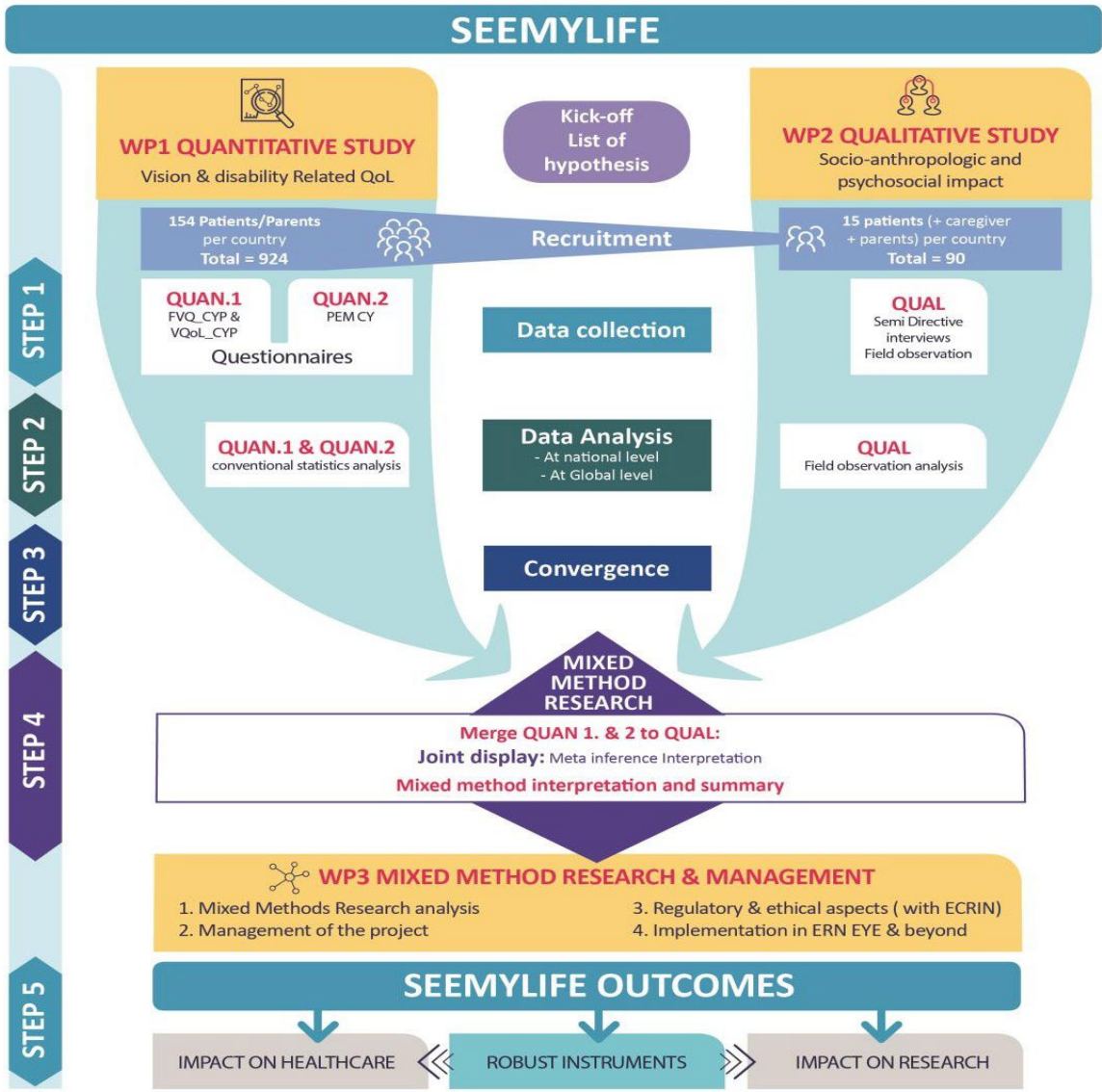
- Current tools to evaluate vision related quality of life (VR-QoL) disregard:
  - age
  - cultural differences
- Lack of knowledge on what aspects of this impact are important at the individual child's level
- Instruments capable of yielding high-quality data, with broad applicability and regulatory compliance, remain to be developed.

THE UNMET NEED: Understanding the impact of vision loss on daily lives as perceived by the children and teenagers

Context & Methodologies used to achieve objectives

SeeMyLife

- **ERN-EYE** based project, with other expert non-ERN stakeholders
- 8 to 18 years old
- **Multinational:** 6 EU MS : FR, DE, IT, BE, LT, and PL
- **Multilevel** (functional vision & social anthropology & patients & care givers)
- **Mixed Methods Research (MMR), using simultaneously QUAN & QUAL tools:**
  - Quantitative (**QUAN**) Vision Related-QoL (**VR-QoL** = **FVQ_CYP** and **VQol_CY**) tools & psychosocial **PEM_CY** => **J RAHI collaboration**
  - Qualitative (**QUAL**) socio-anthropologic investigations can capture reliably children's and teenagers' **PRO**s.
  - The rigorously translated **FVQ_CYP** and **VQol_CY** can capture self-reported **VR-QoL** in each of 6 EU member states (MS) and transnationally with cross-cultural validation.



Impact of SeeMyLife

- **Holistic approach** to child-centered evaluation of QoL in the European **RED** population, delivering validated cross-cultural tools:
  - **European standards for VR-QoL and PROMS in children**
  - **Evaluate the socio-anthropological consequences of poor vision and blindness** in European children and this young population with **RED**

- Better understanding of young patients' own experience – will enable the implementation of **holistic interventions** for children with **RED**.
  - Robust, standardized, and culturally sensitive instruments to assess VR_QoL

  => **patient-focused approach in the development of clinical trials**
  - **Children and teenagers with a voice** in the *curing, caring, and healing* of their **RED & remove barriers to their social participation**.
  - **Improvements for the current situation of caregivers** of children/teenagers affected by **SVI/B** in 6 EU countries

I) **Validated tools that will enable shared decision-making in both clinical and research settings and across disciplines and enable follow-up of progression or interventions** of **RED** in children and young patients
II) **Boosted clinical research (trials with industry)**
III) **Patient centric interventions in children and teenagers**

" Creating and validating PROMs for Children: Process and Challenges"

ERN-EYE

ACT4Red

May 3, 2025

Elise Heon MD FRCSC

The Hospital for Sick Children

Toronto, Canada

Where we are at

1) Partnered with 10 international English-speaking sites
   - Canada, Australia, New Zealand, USA (2), Ireland, Singapore, England (2)

   - Contracts and Ethics for each site
   - Finalizing questionnaire for children and caregivers
   - Set up questionnaire in RedCAP
   - Cognitive interviews
     - Refine questionnaire
   - Validation phase
     - Then opportunity to translate and validate in different cohorts

orphanet
human phenotype ontology
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Translation of PROMS questionnaires: the examples of ViSIO-PRO and MRDQ in France

Isabelle Audo, Côme Le Gall, Benoit Blanchard, Colas Authié, Philippe Chaumet-Riffaud, José-Alain Sahel

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Ophthalmol Ther (2023) 12:1359–1386
https://doi.org/10.1007/s40123-023-00670-8

ORIGINAL RESEARCH

Psychometric Validation of the ViSIO-PRO and ViSIO-ObsRO in Retinitis Pigmentosa and Leber Congenital Amaurosis

M. Dominik Fischer · Francesco Patalano · Christel Naujoks · Judit Banhazi · Christine Bouchet · Paul O'Brien · Christine Kay · Jane Green · Todd Durham · Helena Bradley · Nicola Williamson · Melissa Barclay · Joel Sims · Isabelle Audo

Received: December 14, 2022 / Accepted: January 31, 2023 / Published online: February 27, 2023

Kay et al.
Journal of Patient-Reported Outcomes (2023) 7:74
https://doi.org/10.1186/s41687-023-00610-x

Journal of Patient-Reported Outcomes

RESEARCH Open Access

Qualitative exploration of the visual function impairments and impacts on vision-dependent activities of daily living in Retinitis Pigmentosa and Leber Congenital Amaurosis: content validation of the ViSIO-PRO and ViSIO-ObsRO measures

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The MRDQ also focuses on capturing visual functional symptoms only.

Michigan Retinal Degeneration Questionnaire (MRDQ)

Thank you for your willingness to participate in this research study. The purpose of this interview is for us to gather more information about your vision condition. If any of the questions make you feel uncomfortable, or if you do not wish to answer, please let me know and we will skip the question.

The following questions are about changes in your vision or symptoms you may have experienced specifically due to your vision condition. Please answer these questions as if you are doing the tasks alone and without the assistance of another person, unless otherwise specified. Additionally, if you wear glasses or contact lenses, please answer all of the following questions as though you are using them.

If you do not perform any of the tasks or if that task is not relevant to your life for reasons other than vision, please select "not applicable."

Start time of interview: _____

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Michigan Vision-related Anxiety Questionnaire (MVAQ)

Thank you for your willingness to participate in this research study. The purpose of this interview is for us to gather more information about your vision-related anxiety. If any of the questions make you feel uncomfortable, or if you do not wish to answer, please let me know and we will skip the question.

The following questions are about your vision-related anxiety that you may have experienced specifically due to your vision condition. Please answer these questions as if you are doing the tasks alone and without the assistance of another person, unless otherwise specified. Additionally, if you wear glasses or contact lenses, please answer all of the following questions as though you are using them.

If you do not perform any of the tasks or if that task is not relevant to your life for reasons other than vision, please select "not applicable."

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TOPIC 2 PROMS

Deliverables and challenges

Editorial: To demonstrate the crucial impact of PROMS, by

1. Giving a place for patients to speak about their needs and expectations
2. Giving anecdotes (+/- videos) to demonstrate independence
3. Highlighting the consequences of not using PROMS in CT, using the example of Luxturna.

Challenges:

- What is important for patients can vary according to disease or age. *(Ex: children will value independance, parents will value progress.)*
- Patients do not express their needs as PROMS questions => need to develop a reliable and valid tool that has an ability to detect change
- PROM should be tailored to diseases, populations, acuity level and expectations.
- Many PROMs exist, but are underused due to lack of knowledge to choose the right one, patience to conduct and lack of expertise to perform the analysis
- Incorporating into registries

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Network Eye Diseases (ERN-EYE)

TOPIC 2 PROMS

Discussion

Suggestions:

- Development of questionnaires with specific modules (ex: cone function, rod function, mobility, …) to better tailor the PROMS to the population
- Assess existing PROMS to highlight existing gaps
- Educate on existing PROMS' uses and limitations.

Editorial: To demonstrate the crucial impact of PROMS, by

1. Giving a place for patients to speak about their needs and expectations
2. Giving anecdotes to highlight the consequences of not using PROMS in CT, using the example of Luxturna.

Moving forwards:

- What are the current barriers to the use of PROMS?
- What solutions could be implemented to overcome those barriers?
- Does this proposal and outline serve the goals we want to achieve?
- Are there additional challenges to consider?
- What should be the timeline?
- How could patient testimonials be gathered?

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3rd May 2025

Group 3: Communication

Chairs: Avril Daly , Todd Durham, Hélène Dollfus

Retina International
FOUNDATION FIGHTING BLINDNESS
European Reference Network
Network Eye Diseases
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ERN-EYE
European Reference Network dedicated to Rare Eye Diseases

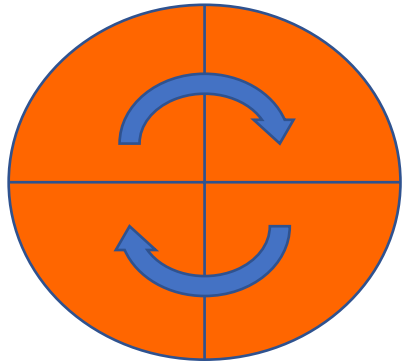
SWOT analysis of the current ecosystem: TRIALS & therapies FOR RED

STRENGTHS

- Ophthalmology **always active field of pioneer scientific and medical research as "…first to… " :** new therapies (ASO, gene replacement, CRISPR & editing, …)
- Strong inter continental / international academic collaborations
- Close interactions: & empowerment: medical & patient
- Previous successes (cf Luxturna)

WEAKNESSES

- Huge heterogeneity of IRDs
- Small trial populations
- Rare diseases judged based on the same criteria as Common Diseases
- Chronic non-life-threatening diseases compared to other RD
- National Regulations vary +++ (EMA, FDA, MHRA, etc.)
- Recent Interruption of trials , need another story than Luxturna getting "old"



THREATS

- Unawareness of investors, about **RED**
- Lack of interest
- Business failure => **choice to invest in more common diseases**
- Global economic situation => decrease of investments in RD
- Lack of continuation of national or international rare diseases plans (exp ERNs) : fragility of systems

OPPORTUNITIES

- Promising pre-clinical research, with ongoing new innovations
- Ongoing trials with more promising results
- Revisiting trial designs (ex. Realized IHI, REDI/RUSH study, …)
- 3rd meeting for ACT4Red, & development of transatlantic action plans

TOPIC 3 Communication

Lead & participants: **Avril Daly*, Todd Durham** and Hélène Dollfus*****, with Mike Schwartz, Russell Wheeler, Zuhal Butuner, Abayomi Ogundele (representing Katalin Pungor), and the following participants, though not attending ARVO: Catherine Mathis, Magali Taiel.

**Retina International* . ***Foundation Fighting Blindness* ****ERN-EYE*

General objectives:

- Generation of **Communication material** of **ACT4Red**
- Development of a **Communication plan:** about "*What are IRDs?*"; "*What is meaningful*?") that would be useful for regulators and would raise awareness with investors, pharma companies, etc.
- **Communicate inside ACT4Red** about breaking news in the scope of **ACT4Red**

Proposed contributions to date :

ERN-EYE: communication team of ERN-EYE (Caroline and Fred)

ACT4RED@chru-strasbourg.fr

TOPIC 3 Communication tools

Objectives

Delivering a clear message on:

- ENDPOINTS CHALLENGES
- Acceptable FDA & EMA Design of TRIALS
- Preclinical to clinical trial facilitations

Gathering and sharing information within the group => Suggestion:

1) Send information to ERN-EYE email address: ACT4RED@chru-strasbourg.fr
2) ERN-EYE share to the rest of the group using short newsletters or bullet point format with links

Next steps:

- Elaborate a communication plan on “What is meaningful?” to regulators (speaking with the “same voice”), repeated messages
- Raising awareness with Investors, Pharma, General public, … “Who are RED patients & their challenges?”

Suggestions:

- Webinars (ERN platform)
- LOGO (ACT4Red)
- Common Statement (on all our websites) with co-signatures
- Short Videos in a few languages (English, French, Spanish, Italian, German …?)
- Diffusion by each party

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Wrap-up Conclusion

All Chairs: general discussion and next steps

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THANK YOU !

- Contact

ACT4RED@chru-strasbourg.fr