# RESTOR(E)ing VISION across Europe:

## a consortium collaborating to conquer seven rare anterior eye diseases

Rare Eye Diseases (REDs) collectively represent a major cause of visual impairment and blindness for children and young adults in Europe.[1] Importantly, REDs also affect adults and the aging population. The onset and progression of many REDs are characterized by common pathophysiologic mechanisms. Defective wound healing of the cornea and ocular surface, excessive inflammation, nerve degeneration, stem cell dysfunction, and abnormal vessel ingrowth are common denominators in many REDs, representing a critical medical problem and an area of unmet medical need.

The RESTORE VISION Consortium (**Table 1**) proposes, for the first time, a ground-breaking approach to disrupt these atypical mechanisms with the aim of making therapy more effective. Our novel approach, to foster translation into clinical practice, is based on the repurposing of existing drugs and the development of new drugs, totaling 9, all with preliminary data showing remarkable effects in restoring the cell physiology, immune response, avascular conditions, neural function and signaling environment in the cornea in the context of rare diseases from animal models into clinical trials. In Europe, approximately 30 million people suffer from blindness and visual impairment.[2] The prevalence and number of EU cases of the seven REDs addressed in this project are displayed in **Figure 1**. We estimate that there are around 500,000 European patients suffering from the seven REDs that the Restore Vision project addresses. This represents approximately 1.7% of the total European population living with visual impairment and blindness.

The overall conceptual plan for the project comprises three main streams of activity, running in parallel. **Stream 1**: preclinical verification and development; **Stream 2a**: clinical studies for which data exists; **Stream 2b**: clinical studies for which additional data will be collected; and **Stream 3**: ethics, regulatory, exploitation, and management.

**Stream 1** involves preclinical studies to test the efficacy of the drugs in the RED models, verify their mechanisms of action (MoA), confirm drug targets in human samples, and, in a subsequent round, test the newly formulated eye drops in the RED models showing the greatest efficacy.

**Stream 2** involves clinical studies, with ethical, regulatory, and safety/toxicity data on the eye drop formulations made available in the preparatory phase. For those cases in which drugs are already used in the eye or where first-in-human data exists, these activities will proceed directly to clinical investigations (**Stream 2a**). RESTORE VISION drugs already at an advanced stage of development but still in need of additional preclinical data or improved formulation for RED will be grouped in **Stream 2b**. Following the Scientific Advisory Board and consortium reviews, the most therapeutically active compounds with highest probability of being effective in more than one RED will be brought forward for human ethical approval and clinical trial preparation. The RESTORE VISION project will test the presence of the targets in human samples of the disease, mitigating the risk of targeting a process irrelevant in humans. Some data from **Stream 1** will support the second stream (such as eye drop formulation, MoA) but components of **Stream 2** will run parallel,

*Thomas Ritter, PhD (middle left), author of this article and head of the consortium, University of Galway, with the RESTORE VISION investigators at the kickoff meeting*

*Table 1. Public, private, and patient partners of the RESTORE VISION consortium. Nordic partners in bold.*

| Participant organization name | Country | Type |
|---|---|---|
| National University of Ireland Galway (NUIG)* *Coordinator | Ireland | Academic |
| **Linköpings Universitet (LiU)** | **Sweden** | **Academic** |
| Ospedale San Raffaele SRL (OSR) | Italy | Academic |
| Universidad Miguel Hernández de Elche (UMH) | Spain | Academic |
| INSERM UMRS 1138 (INS) | France | Academic |
| Klinikum der Universitaet zu Koeln (UKK) | Germany | Academic |
| **Aniridia Europe (AE)** | **Norway** | **Patient** |
| **Cell2Cure (C2C)** | **Denmark** | **SME** |
| KÔL Laboratories (KÔL) | France | SME |
| Catalyze Group (CAT) | Netherlands | SME |

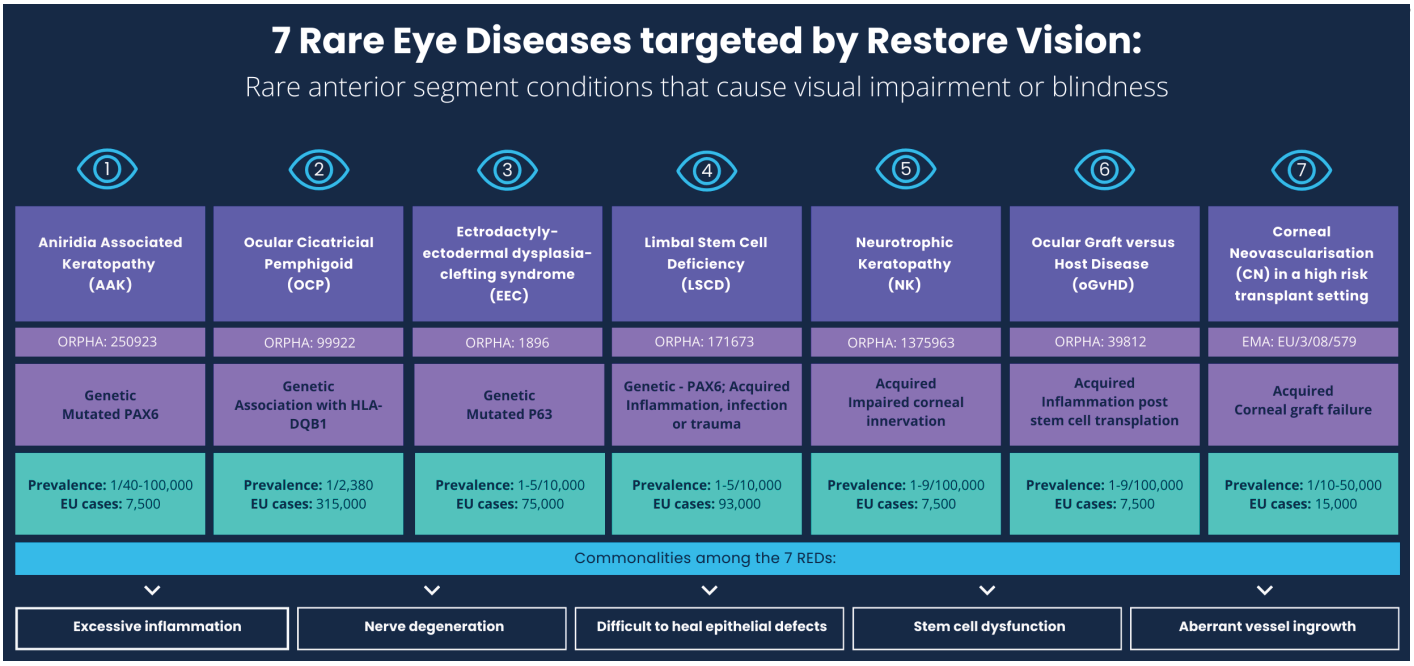


*Figure 1. The family of REDs targeted in this project, their respective Orpha codes, and their pathogenic commonalities.*

with both streams commencing in the first year of the project.

**Stream 3** provides for the non-scientific components including ethics, regulatory, management, dissemination, and exploitation. In addition, trial design for future trials based on results obtained herein is established to speed up the translation. This third stream will feed into the key activities within the first two streams, as shown in **Figure 2**.

We adopt the approach shown in **Figure 2** as a streamlined way to evaluate promising new and repurposed drug candidates for translation into the first clinical studies. Many rare diseases of the cornea and ocular surface do not have effective treatment options today, with patients and doctors struggling to find appropriate treatment. At the same time, academic research is not generally equipped to bring new drug candidates into clinical use, lacking the resources and knowledge present in pharmaceutical companies and regulatory bodies. In RESTORE VISION, a unique team of project partners will work towards moving several drug candidates further along the pipeline to clinical use. Importantly, although rare diseases are, by definition, not often seen in ophthalmology clinics, the common denominator of these diseases in terms of corneal inflammation, neurotrophic deficit, dry eye, wound healing problems, vascularization and stem cell dysfunction affect many more patients with different ocular conditions. The knowledge generated within the project is thus expected to have wide implications for the treatment of corneal disease.

More information at www.restorevision-project.eu.

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*References*

1. European Commission, *ERN-EYE: a European Reference Network dedicated to Rare Eye Diseases.*
2. European Blind Union, *About Blindness and Partial Sight: Facts and Figures.*

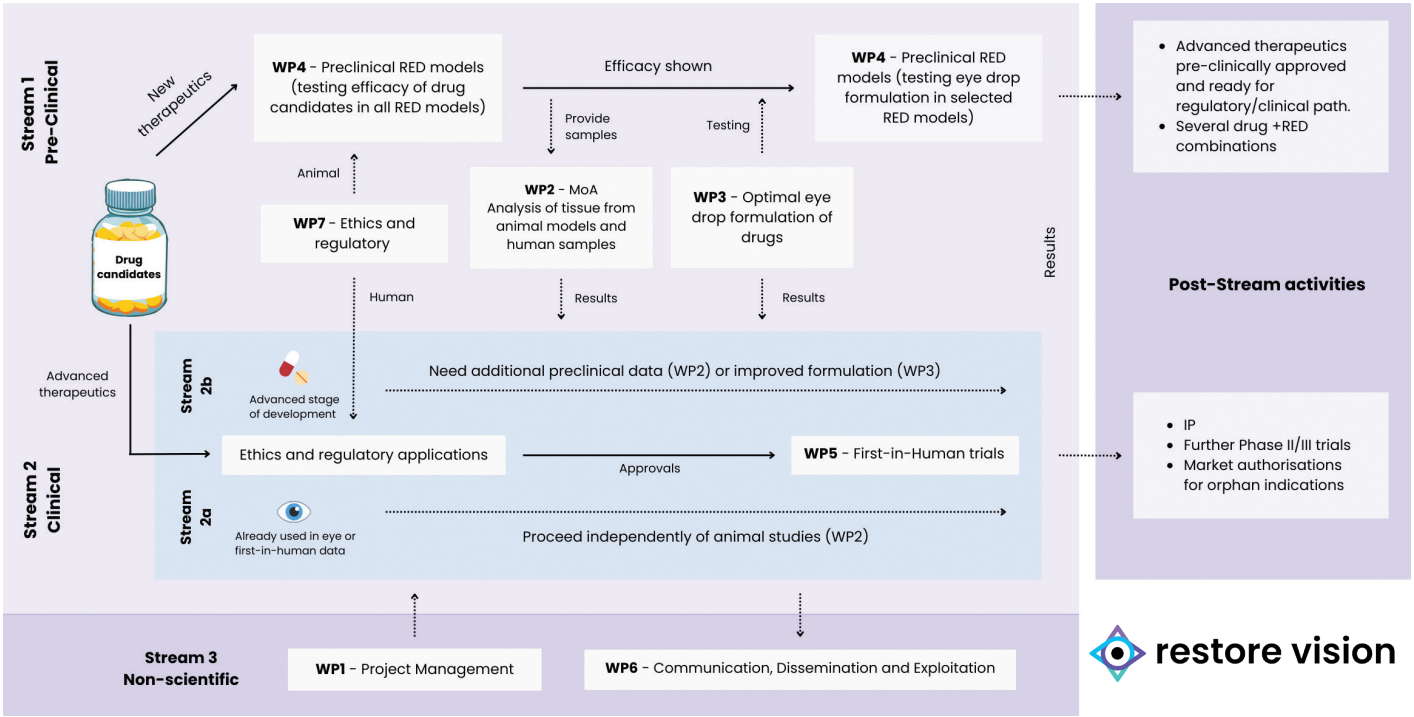


*Figure 2. The overall RESTORE VISION conceptual plan.*