COMPETITIVE LANDSCAPE OF RETINITIS PIGMENTOSA (RP)

The only approved therapy for RP that covers only **0.3–1% of total RP** cases is Roche's Luxturna® (voretigene neparvovec) for patients that have the RPE65 mutation. Luxturna is a one-time gene therapy based on AAV technology that provides a working RPE65 gene to act in place of the mutated version of the same gene. It was proved to improve vision, particularly night vision, and halt progressive vision loss. It was approved by the FDA in 2017, and it costs on average $850k.

RP patients with a diagnosis other than RPE65 mutation are limited to the best **supportive care**, including reliance on vitamin supplements, protection from sunlight, and visual aids. Vitamin A was shown to be effective for patients with early-stage disease in a high daily dose for slowing disease progression. For late-stage disease, acetazolamide may be effective in patients with autosomal dominant RP complicated by retinal edema.

The different therapeutic approaches and assets in development

There are currently **over 100 drugs in development for RP worldwide** with assets that can be separated into five therapeutic approaches: gene therapy, cell therapy, optogenetics, small molecules, and ocular prosthetic devices. **Few of those approaches are being developed for the late stages of RP** (see Figure 1).

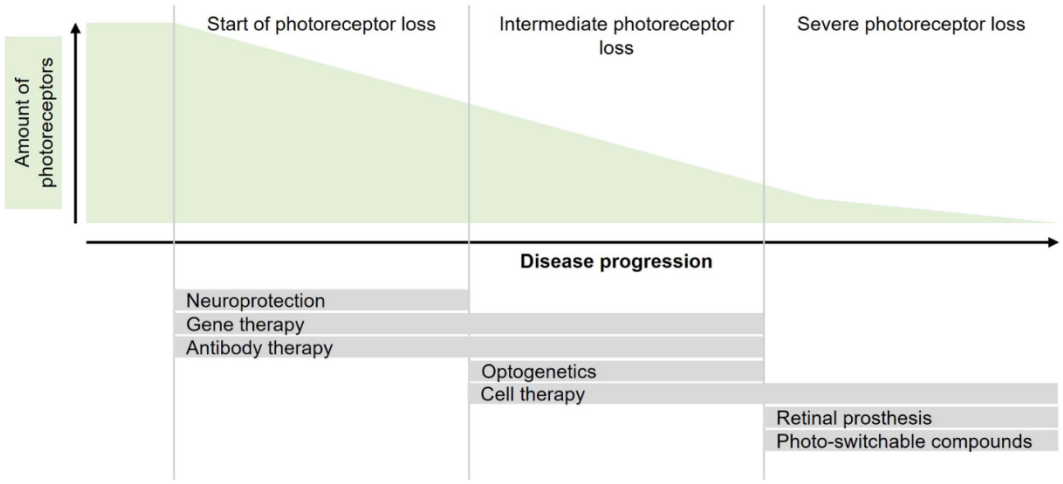

Figure 1 _Image source: Clinical Ophthalmology. 16 2909–2921 (2022)

Kiora Therapeutics' KIO-301 is a molecular photoswitch that has the potential **to restore vision** in patients with inherited and/or age-related retinal degeneration. There are very few direct competitors for KIO-301, as most of the other therapies in development target earlier stages of RP or specific genes that cause the development of RP. Potentially, KIO-301 could be used in combination with gene therapies to improve RP treatment. See Table 1 for a brief on therapies and their progress.

Company	Treatment	Progress
AGTC	Gene therapy	Phase 2/3
4D Molecular Therapeutics	Gene therapy	Phase 1/2
MeiraGTx	Gene therapy	Phase 1/2
Coave Therapeutics	Gene therapy	Phase 1/2
ProQR	Gene therapy	Phase 2/3, on hold
Jcyte	Cell therapy	Phase 2b
ReNeuron	Cell therapy	Abandoned
GenSight Biologics	Optogenetics	Phase 1/2a
Nanoscope Therapeutics	Optogenetics	Phase 2b/3
Bionic Sight	Optogenetics	Phase 1/2
Allergan	Optogenetics	Phase 1/2a
Endogena Therapeutics	Small molecule	Phase 1/2a
Aldeyra Therapeutics	Small molecule	Phase 2
Kiora Phasmaceuticals	Small molecule	Phase 1b

Table 1_ Companies developing RP therapies

Gene therapy. These therapeutics are based on the delivery of a healthy gene to replace the malfunction of a protein that results from a gene mutation. Besides Luxturna, other products in development target mutations in the RPGR genes responsible for X-linked RP; AGTC's AGTC-50 is in phase 2/3 trial; 4D Molecular Therapeutics' 4D-125 is in a phase 1/2 trial; and MeiraGTx's MGT009 is being evaluated in a phase 1/2 trial. Other companies are developing gene therapies targeting other gene mutations: Coave Therapeutics' CTx-PDE6b targets the PDE6B gene mutation and is in a phase 1/2 trial; ProQR's ultevursen is an RNA therapy that targets the mutations in the USH2A gene and is in a phase 2/3 trial currently on hold.

Cell therapy. These therapeutics mainly consist of the use of pluripotent stem cells that differentiate into cells of the retinal tissue to replace those cells that were lost in the course of the disease. JCyte's JCell therapy just completed a Phase 2b trial. ReNeuron had a similar cell therapy program phase 2a clinical trial but it was terminated due to inconclusive data.

Optogenetics. These therapies are based on the delivery of a light-sensitive protein, opsins, via gene therapy and are applied in combination with an optical device such as goggles. Contrary to other gene therapies for RP, these are gene agnostic. GenSight Biologics' GS030 in conjunction with goggles (GS030-MD), is being evaluated in a Phase 1/2a study. Nanoscope Therapeutics' MCO-010 (Phase 2b/3), Bionic Sight's BS01 (Phase 1/2), RetroSense's RST-001 (Phase 1/2a, acquired by Allergan), and Vedere Bio (acquired by Novartis) have similar approaches based on optogenetics.

Small molecules. The drug candidates classified as small molecules normally target enzymes or receptors involved in signaling pathways that contribute to sight or improve eye conditions with the goal to restore vision, such as reducing inflammation or oxidative stress. Another class of small molecules consists of photoswitching molecules that activate in the presence of light to send a signal to the brain, bypassing the photoreceptors. Kiora's KIO-301 is a photoswitch molecule being evaluated in a Phase 1b clinical trial; Endogena Therapeutics' EA-2353 is in a Phase1/2a study; Aldeyra Therapeutics' ADX-2191 is being evaluated in Phase 2 clinical trial.

Ocular prosthetic devices. These devices are implanted into the eye to help patients improve their vision. The Argus II is a prosthetic device that was previously on the market for late-stage RP. This device sends signals of light to the brain via the optic nerve bypassing the photoreceptors. This product was recently discontinued, and the company is testing a similar although newer technology named Orion Visual Cortical Prosthesis System.