Health Technology Briefing
August 2025

OCU400 for treating retinitis pigmentosa in children and adults

Company/Developer	Ocugen Inc

☒ New Active Substance ☐ Significant Licence Extension (SLE)

NIHRIO ID: 34660	NICE ID: Not available	UKPS ID: Not available

Licensing and Market Availability Plans

Currently in phase III clinical development.

Summary

OCU400 is in development for the treatment of retinitis pigmentosa (RP). RP is an inherited eye condition that affects the cells that line the back of the eye in the region known as the retina (the light-sensitive layer at the back of the eye). RP is one of the most complicated genetic conditions, and over 80 causative genes have been identified. Symptoms initially include difficulty seeing in dim light, including transitioning from light to dark and vice versa. Peripheral vision will also decline, resulting in a narrowing of the visual field and, in some cases, resulting in complete blindness. There are currently no approved treatments that can effectively slow or stop the progression of RP.

OCU400 works by targeting special proteins called nuclear hormone receptors (proteins that help control how genes are turned on or off) to adjust how genes behave in the retina. OCU400 may help restore balance in the retina, which could protect and possibly save the cells that help in vision (called photoreceptors). OCU400 has been shown to be safe and effective in early-stage clinical trials and is administered by sub-retinal injection (under the thin layer at the back of the eye that helps you see). If licensed, OCU400 will provide a treatment option for patients with RP.

This briefing reflects the evidence available at the time of writing and a limited literature search. It is not intended to be a definitive statement on the safety, efficacy or effectiveness of the health technology covered and should not be used for commercial purposes or commissioning without additional information. A version of the briefing was sent to the company for a factual accuracy check. The company was unavailable to comment.
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Proposed Indication

Treatment of retinitis pigmentosa (RP) in children and adults.[1,2]

Technology

Description

OCU400 (AAV-hNR2E3) is a novel gene-agnostic modifier gene therapy product based on nuclear hormone receptor gene, NR2E3.[3] OCU400 targets nuclear hormone receptors to modulate gene expression within the retina and may help reset retinal homeostasis, potentially stabilising cells and rescuing photoreceptor degeneration. OCU400 has the potential to be a gene-agnostic therapeutic for RP patients with inherited retinal degeneration.[4]

OCU400 is in clinical development for the treatment of RP subjects aged 5 years and older[1,2]. In the phase III clinical trial (liMeliGhT, NCT06388200), OCU400 is administered via subretinal injection at a concentration of 2.5 x 10^{10}vg/eye.[1]

Key Innovation

For the vast majority of people with RP, there are no treatments that can effectively slow or stop the progression of the condition, representing an unmet clinical need.[5,6] OCU400 is a therapy designed to reset the dysfunctional gene network in patients with RP, regardless of their specific mutation, and reestablish a healthy cellular homeostasis via NR2E3's regulation of photoreceptor development and maintenance, metabolism, phototransduction, inflammation, cell survival, and other physiological functions.[7]

OCU400 is classified as an advanced therapy medicinal product (ATMP) within the definition of a gene therapy medicine. The scientific recommendation for an ATMP classification is issued by the EMA's Committee for Advanced Therapies.[3] If licensed, OCU400 would offer an additional treatment option for patients with RP.

Regulatory & Development Status

OCU400 does not currently have Marketing Authorisation in the EU/UK for any indication.

OCU400 is not in phase II or III clinical development for any other indication.

OCU400 has the following regulatory designations/awards:

- an orphan drug in the EU in 2021 for the treatment of both retinitis RP and Leber Congenital Amaurosis.[8-10]
- Regenerative Medicine Advanced Therapy (RMAT) designation by the US FDA in 2023 for treatment of RP associated with RHO Mutations.[11]

Patient Group

Disease Area and Clinical Need

RP is an inherited eye condition that affects the photoreceptor cells responsible for capturing images from the visual field. These cells line the back of the eye in the region known as the retina. RP is one of the most complicated genetic conditions, and over 80 causative genes have been identified.[5] Mutations in the

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rhodopsin-encoding gene RHO are the leading cause of autosomal dominant RP. Mechanisms underlying rhodopsin-related retinal dystrophy, include but are not limited to endoplasmic reticulum stress and calcium ion dysregulation resulting from protein misfolding, mis-trafficking, and malfunction.[12] A recurrent missense mutation in NR2E3, specifically c.166G>A (p.Gly56Arg), has been identified as a cause of autosomal dominant RP.[13] Rod cells are usually initially involved, and difficulty seeing in dim light, including transitioning from light to dark and vice versa, is one of the earliest symptoms.[5] Peripheral vision will also decline, resulting in a narrowing of the visual field. Central vision is often maintained until much later.[5] Symptoms usually start in childhood, and most people eventually lose most of their sight.[14] The initial symptoms of RP most commonly appear in young adulthood, with over three-quarters of patients developing symptoms by 30 years of age. However, due to delays in referral and diagnosis, diagnosis can often be delayed, with the average age of RP diagnosis reported to be 35.1 years.[6]

In the UK, RP affects approximately 1 in 3,000 individuals, equating to about 19,816 diagnosed cases in 2021. In England, 2023-24, there were 123 finished consultant episodes (FCEs) and 112 admissions for hereditary retinal dystrophy (ICD-10 code H35.5) which resulted in 84 FCE bed days and 95 day cases.[15]

Recommended Treatment Options
There are currently no pharmacological treatment options recommended by the National Institute for Health and Care Excellence (NICE) for RP. However, for patients with biallelic RPE65 mutation-associated retinal dystrophy (a subset of RP), NICE recommends voretigene neparvovec when vision loss is progressive and there are sufficient viable retinal cells for therapy.[16]

Clinical Trial Information

Trial	**liMeliGhT, NCT06388200;** A Phase 3, Multi-Center, Randomized Study to Assess The Efficacy, Safety and Tolerability of Subretinal OCU400 Gene Therapy for the Treatment of Retinitis Pigmentosa **Phase III –** Recruiting **Location(s):** USA and Canada **Primary completion date:** June 2025
Trial Design	Randomised, parallel assignment, single masked
Population	N=150 (estimated); subjects with RP associated with RHO mutations and patients with any other RP associated mutation; aged 5 years and older; all sexes
Intervention(s)	Sub-retinal administration of OCU400 with a concentration of 2.5 x 10^{10} vg/eye
Comparator(s)	No comparator
Outcome(s)	Primary outcome measures: • Number of participants with change in functional vision in the study eye of RP subjects as assessed by Luminance Dependent Navigation Assessment (LDNA) [Time Frame: 52 weeks] • Number of participants with change in functional vision in the study eye in Gene Agnostic group as assessed by LDNA [Time Frame: 52 weeks] See trial record for full list of other outcomes
Results (efficacy)	-

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Results (safety)	-

Trial	NCT05203939; A Phase 1/2 Study to Assess the Safety and Efficacy of OCU400 for Retinitis Pigmentosa Associated with NR2E3 and RHO Mutations and Leber Congenital Amaurosis with Mutation(s) in CEP290 Gene **Phase I/II –** Active, not recruiting **Locations:** USA **Primary completion date:** March 2027
Trial Design	Non-randomised, sequential assignment, open label
Population	N=22 (actual); subjects with RP associated with NR2E3 and RHO mutations and in patients with Leber Congenital Amaurosis due to mutation(s) in CEP290 gene; aged 6 years and older
Intervention(s)	Phase I: Sub-retinal injection of OCU400: • Low dose cohort – up to 1.66×10^{10} vg/mL • Medium dose cohort – up to 3.33×10^{10} vg/mL • High dose cohort – up to 1.66×10^{11} vg/mL • Paediatric arm – up to 3.33×10^{10} vg/mL (medium dose) Phase II: • High dose – sub-retinal injection of OCU400 up to 1.66×10^{11} vg/mL • Adult arm – sub-retinal injection of OCU400 up to 3.33×10^{10} vg/mL (medium dose)
Comparator(s)	No intervention
Outcome(s)	Primary outcome measures: • Study Drug-related adverse events [Time Frame: 1 year] • Treatment-Emergent adverse events [Time Frame: 1 year] • Serious adverse events [Time Frame: 1 year] See trial record for full list of other outcomes
Results (efficacy)	100% (9/9) of treated evaluable subjects demonstrated improvement or preservation in visual function compared to untreated eyes at both one and two years. 100% (9/9) of treated evaluable subjects demonstrated improvement or stabilisation in mobility testing, which was only performed up to one year. OCU400 demonstrated meaningful improvement of 2-line gain (10 letters on ETDRS chart) in low-luminance visual acuity (LLVA) in treated eyes when compared to untreated fellow eyes. This treatment effect was statistically significant (p=0.01) in all subjects, regardless of mutation at two years, validating the gene-agnostic mechanism of action for OCU400.[17]
Results (safety)	Favourable long-term safety and tolerability profile with no serious adverse events related to OCU400.[17]

Estimated Cost

The cost of OCU400 is not yet known.

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Relevant Guidance

NICE Guidance

- NICE Highly specialised technologies guidance. Voretigene neparvovec for treating inherited retinal dystrophies caused by RPE65 gene mutations (HST11). October 2019.
- NICE interventional procedures guidance. Insertion of a subretinal prosthesis system for retinitis pigmentosa (IPG537). December 2015.
- NICE interventional procedures guidance. Insertion of an epiretinal prosthesis for retinitis pigmentosa (IPG519). June 2015.

NHS England (Policy/Commissioning) Guidance

- NHS England. Clinical Commissioning Policy: Argus II retinal prosthesis for retinitis pigmentosa. 16027/P. July 2016.
- NHS England. Manual for prescribed specialised services 2016-2017 (published 2016): chapters 12 (adult specialist ophthalmology services) and 120 (specialist ophthalmology services for children).

Other Guidance

- British Medical Journal Best Practice. Retinitis Pigmentosa. 2025.[18]

Additional Information

Ocugen Inc did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development.

As a result, the NIHR Innovation Observatory has had to obtain data from other sources.

UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit.

We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

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