OSPREY: First-in-Human Phase 1 Study of the RNA-Based Therapy STK-002 in Autosomal Dominant Optic Atrophy

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Author	Disclosures
Patrick Yu-Wai-Man	Consulting services for Stoke Therapeutics
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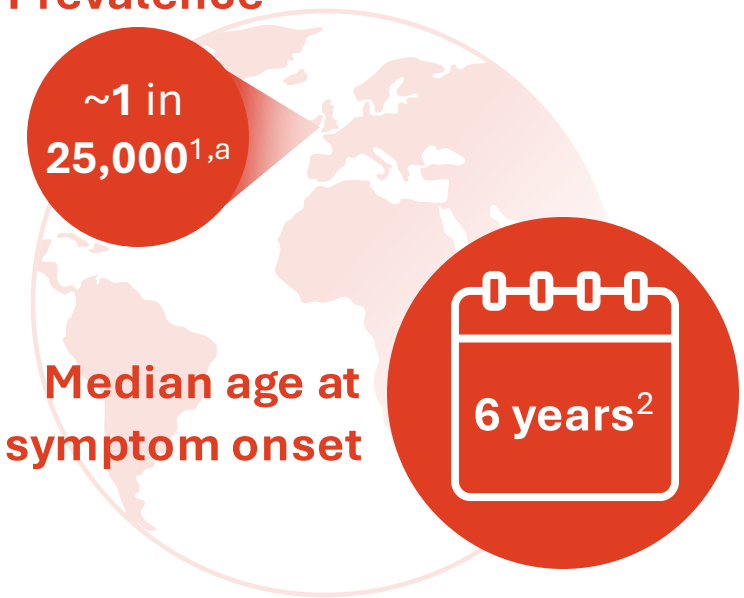
Alice Wyse Jackson	Employee of Stoke Therapeutics
Charles Liu	Employee of Stoke Therapeutics
Kelly Saluti	Employee of Stoke Therapeutics
Barry Ticho	Employee of Stoke Therapeutics
Steven Gross	Employee of Stoke Therapeutics

ADOA is the most common hereditary optic neuropathy, causing vision loss that significantly impacts patient QoL

Epidemiology

Prevalence



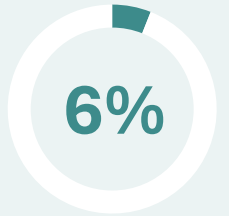
Ocular symptoms

- Bilateral vision loss[3,4]
- Central field deficits[3]
- Color vision defects[3,4]
- Low contrast sensitivity[5]
- Visual acuity loss[4–6]

of patients are symptomatic by **age 10**[7]

Burden

Patients have significantly lower **vision-related QoL**[5,b]



of adult patients have a current driver's license[8]

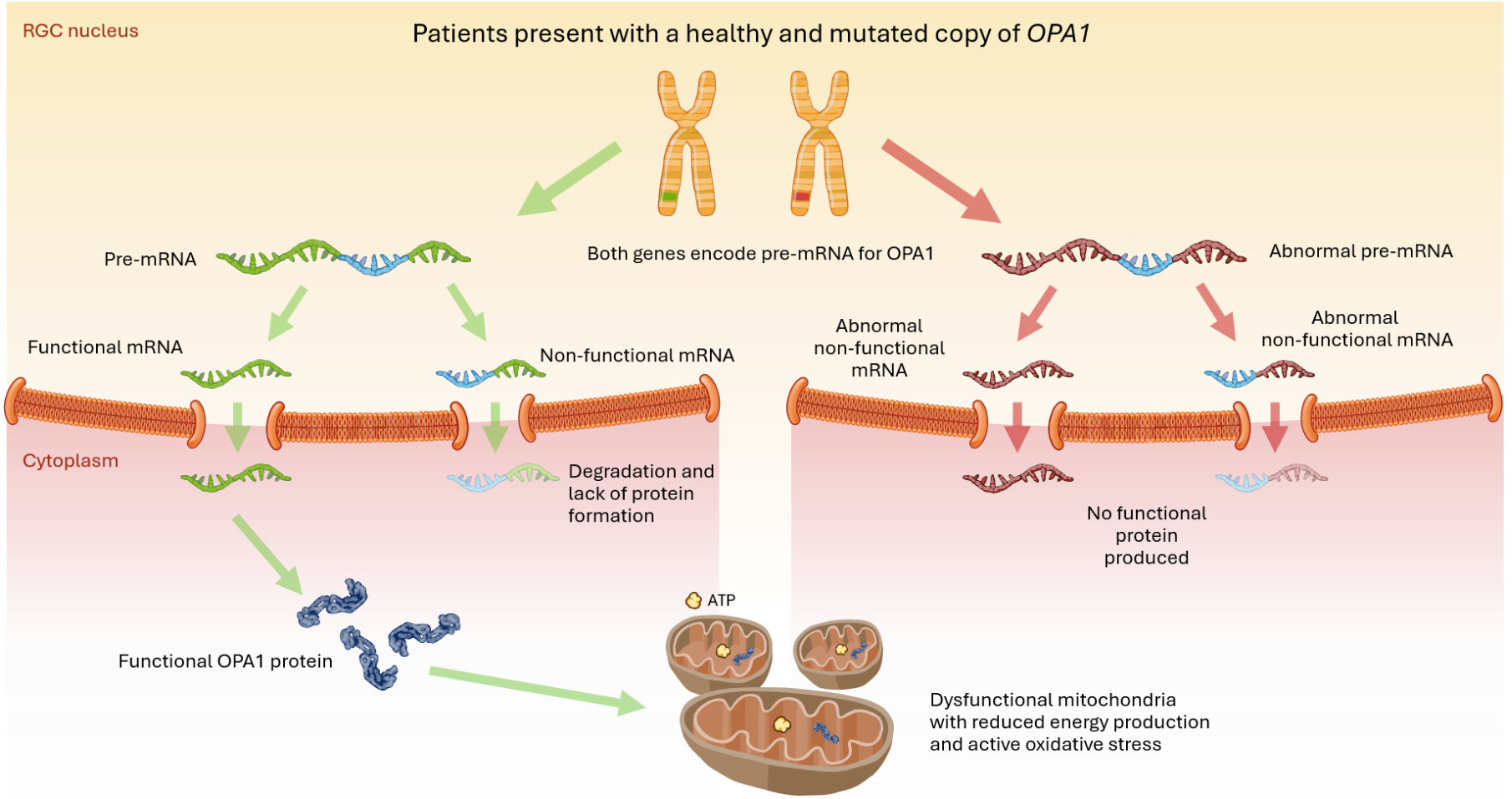
of patients are registered as legally blind[8]

There are no approved treatments for ADOA

[a]UK prevalence data. [b]Compared with health controls.[5]
ADOA, autosomal dominant optic atrophy; QoL, quality of life; UK, United Kingdom.

1. Yu-Wai-Man P *et al. Ophthalmology* 2013; 120 (8): 1712–1712.e1. 2. Han J *et al. BMC Ophthalmol* 2022; 22: 322. 3. Lenaers G *et al. Orphanet J Rare Dis* 2012; 7: 46. 4. Lenaers G *et al. Prog Retin Eye Res* 2021; 83: 100935.
5. Eckmann-Hansen C *et al. Acta Ophthalmol* 2022; 100 (7): 797–804. 6. Autosomal Dominant Optic Atrophy Association. So…What is ADOA? Available at: https://www.adoaa.org/what-is-adoa. Accessed July 2026.
7. Yu-Wai-Man P *et al. Ophthalmology* 2010; 117 (8): 1538–1546.e1. 8. Votruba M *et al. Arch Ophthalmol* 1998; 116 (3): 351–358.

ADOA is primarily caused by *OPA1* gene variants[1–4] that lead to reduced functional OPA1 protein expression[3,4]



ADOA, autosomal dominant optic atrophy; mRNA, messenger ribonucleic acid; OPA1, OPA1 mitochondrial dynamin like GTPase; RGC, retinal ganglion cell.

1. Almind GJ *et al. BMC Med Genet* 2012; 13: 65. 2. Cohn AC *et al. Am J Ophthalmol* 2007; 143 (4): 656–662. 3. Chun BY *et al. Curr Opin Ophthalmol* 2016; 27: 1855–1865. 4. Lim KH *et al. Nat Commun* 2020; 11 (1): 3501.

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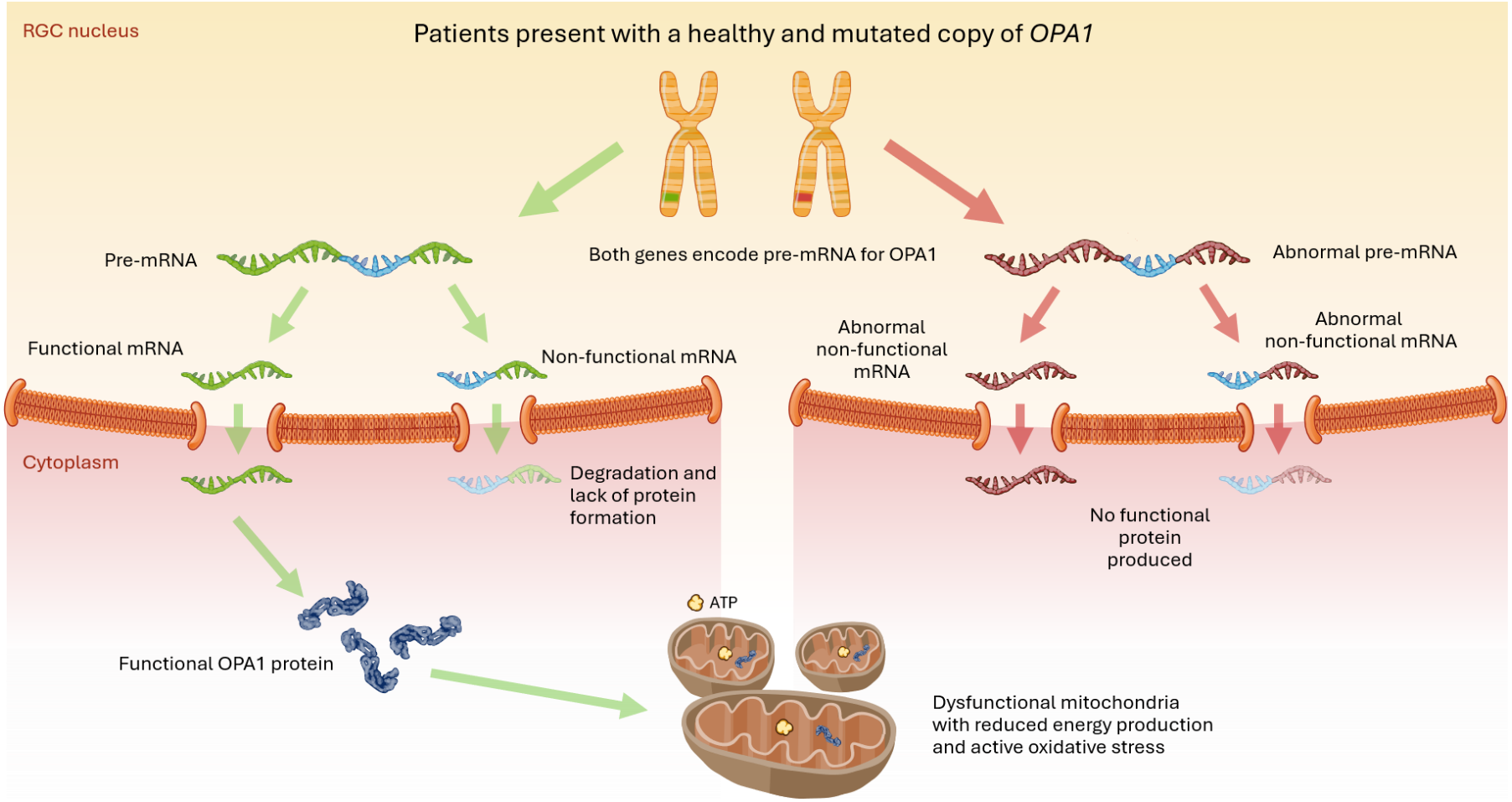
OPA1 deficiency leads to mitochondrial dysfunction, impaired energy production, RGC vulnerability, and vision loss[1]



ATP, adenosine triphosphate; mRNA, messenger ribonucleic acid; OPA1, OPA1 mitochondrial dynamin like GTPase; RGC, retinal ganglion cell.

1. Chun BY *et al*. *Curr Opin Ophthalmol* 2016; 27: 1855–1865.

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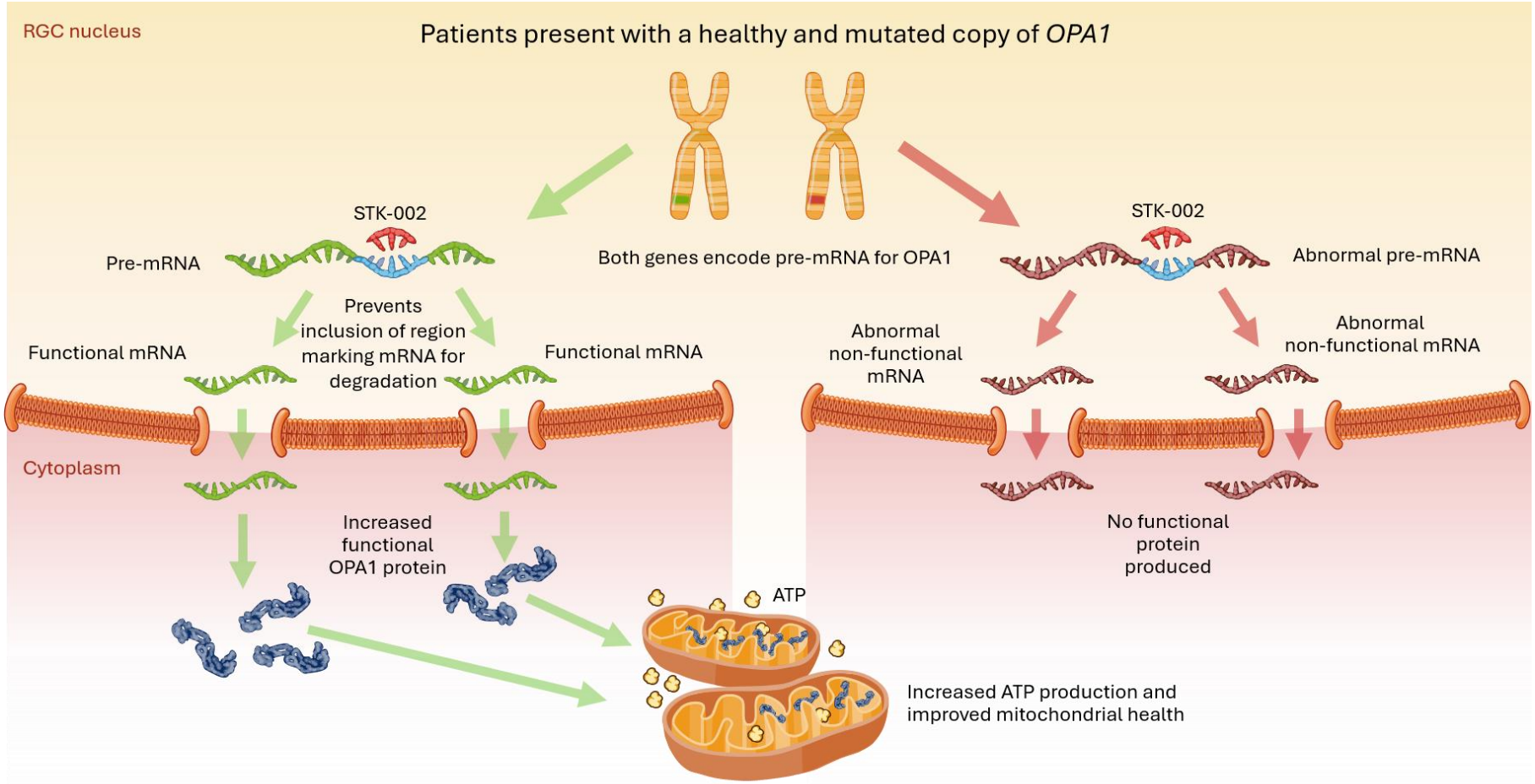
STK-002 is designed to increase OPA1 protein expression in ADOA by enabling the healthy copy of the *OPA1* gene produce more functional mRNA

STK-002 is an RNA-based investigational ASO that upregulates OPA1 expression[1]



ADOA, autosomal dominant optic atrophy; ASO, antisense oligonucleotide; ATP, adenosine triphosphate; mRNA, messenger ribonucleic acid; OPA1, OPA1 mitochondrial dynamin like GTPase; RGC, retinal ganglion cell; RNA, ribonucleic acid.

1. Venkatesh A *et al*. *Nucleic Acid Ther* 2024; 34(5): 221–233.

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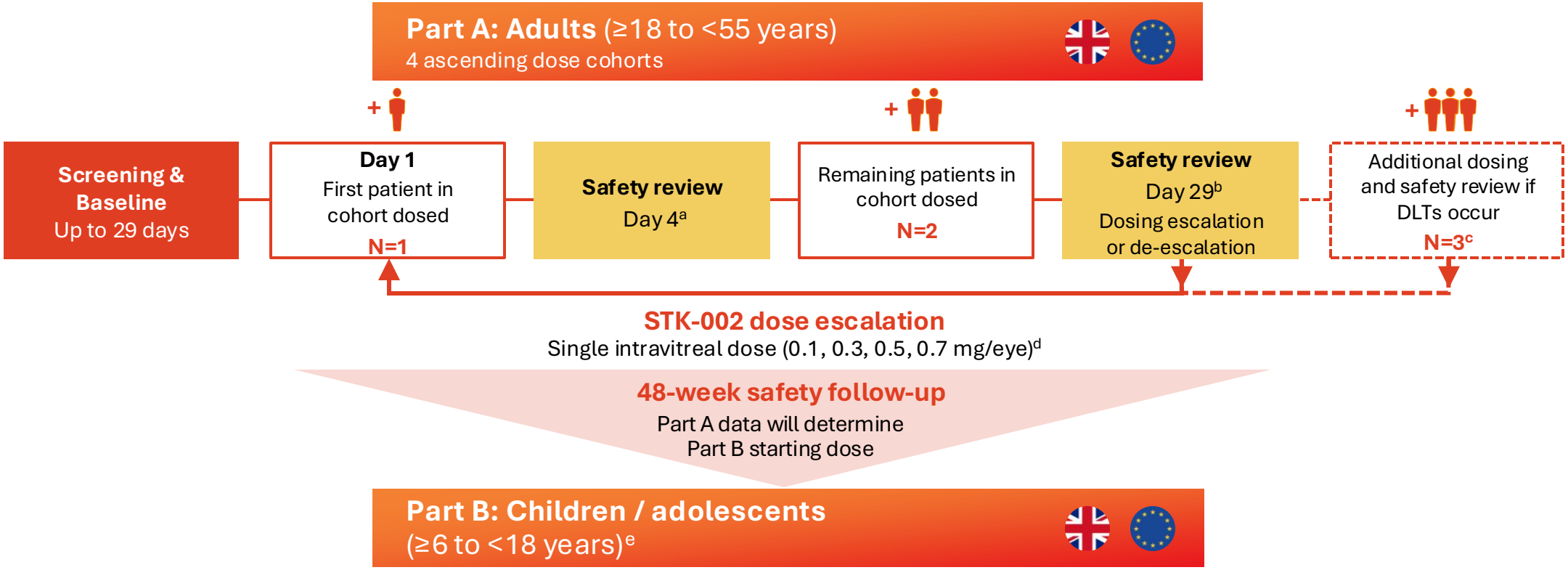
OSPREY is a Phase 1 first-in-human study of STK-002

Evaluating the safety and tolerability of a single intravitreal injection of STK-002 in patients with *OPA1*-associated ADOA



Recruitment ongoing[1]

Eight clinical trial sites are active in the UK, Germany, Denmark, Italy, and Austria

[a]On Day 4, safety data from the first patient will be reviewed by the SMC and a recommendation made prior to dosing the two remaining patients in the cohort. [b]On Day 29, dosing will escalate/de-escalate based on SMC recommendation, with dose escalation only if no DLTs occur in any of the three patients. [c]If one DLT has occurred in the original three patients, three additional patients will be treated at the current dose level. [d]Patients will receive a single intravitreal injection of STK-002 to the most affected or, if both eyes are of equal severity, the non-dominant eye. [e]The first pediatric patient to receive the drug must be ≥12 and <18 years of age.

ADOA, autosomal dominant optic atrophy; DLT, dose-limiting toxicity; SMC, Safety Monitoring Committee.

1. ISRCTN.com. ISRCTN41725621. Available at: https://www.isrctn.com/ISRCTN41725621. Accessed July 2026.

The principal aim of OSPREY is to assess safety and tolerability of STK-002

Objectives

Primary	Safety and tolerability
	Exposure
Key secondary	Visual function
	Patient-reported outcomes
Exploratory	Retinal mitochondrial dysfunction

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The principal aim of OSPREY is to assess safety and tolerability of STK-002

	Objectives	Endpoints
Primary	Safety and tolerability	Incidence, type, and severity of AEs, ocular safety[a]
	Exposure	Exposure of STK-002 in serum
Key secondary	Visual function	Contrast sensitivity (low contrast BCVA)
	Patient-reported outcomes	QoL (NEI-VFQ-25, IVI-C, and EQ-5D/EQ-5D-Y)
Exploratory	Retinal mitochondrial dysfunction	OcuMet Beacon™ imaging

[a]Other safety parameters include changes in vital signs, AREDS scores, assessment of inflammation, corneal epithelial grading, immunogenicity parameters, retinal toxicity / retinal thinning, physical examination, and laboratory parameters.
AE, adverse event; AREDS, Age-Related Eye Disease Study Clinical Lens Grading System; BCVA, best-corrected visual acuity; EQ-5D/EQ-5D-Y, EuroQol 5-dimension / EuroQol 5-dimension (Youth); IVI-C, Impact of Vision Impairment for Children; NEI-VFQ-25, National Eye Institute Visual Function Questionnaire-25; QoL, quality of life.
ISRCTN.com. ISRCTN41725621. Available at: https://www.isrctn.com/ISRCTN41725621. Accessed July 2026.

OSPREY is evaluating STK-002 in patients with *OPA1*-associated ADOA

INCLUSION CRITERIA

- Genetically confirmed *OPA1*-associated ADOA
- Aged ≥18 to <55 years (Part A) or ≥6 to <18 years (Part B)
- Best corrected vision score between 35 and 70 letters in the intended treated eye
- Acceptable full field ERG and OCT

EXCLUSION CRITERIA

- Specific *OPA1* variants[a]
- Diagnosis of ADOA-plus or Behr syndrome
- Current or previous eye conditions that might affect the study
- At risk of uveitis or ocular infection
- Current or previous treatments that might cause or potentially treat optic neuropathy

[a]A gain-of-function variant, or compound heterozygous or homozygous pathogenic or likely pathogenic variant in the *OPA1* gene.
ADOA, autosomal dominant optic atrophy; ERG, electroretinogram; OCT, optical coherence tomography.

OSPREY: Clinical significance

Significance	Status	Future
Represents an important translational step	Dosing complete in first and second cohorts	Will inform dose selection and future clinical development of this novel RNA-based potentially disease-modifying approach
Will demonstrate the potential of upregulating OPA1 expression by leveraging the healthy copy of the gene	Dose escalation continuing	
	Initial data expected in H1 2027	

ADOA, autosomal dominant optic atrophy; OPA1, OPA1 mitochondrial dynamin like GTPase; RNA, ribonucleic acid.

Conclusion

STK-002 is among the first RNA-based therapies in ophthalmology and has the potential to be the first disease-modifying therapy for ADOA

ADOA, autosomal dominant optic atrophy; RNA, ribonucleic acid.

References

- Almind GJ *et al*. *BMC Med Genet* 2012; 13: 65.
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- Eckmann-Hansen C *et al*. *Acta Ophthalmol* 2022; 100 (7): 797–804.
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Thank you

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