OSPREY: An Open-label Study to Investigate Safety, Tolerability, and Exposure of the Antisense Oligonucleotide (ASO) STK-002 in Patients with *OPA1* Autosomal Dominant Optic Atrophy (ADOA)

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Disclosures: *Stoke Therapeutic clinical investigators; [3]Stoke Therapeutic employees

OSPREY

INTRODUCTION

- ADOA is the most common inherited neuro-ophthalmic disorder
- Patients typically present in the 1st decade of life and >1/2 of all patients are registered legally blind by the 5th decade
- Most cases are caused by a heterozygous nuclear gene OPA1 mutation, often leading to OPA1 protein haploinsufficiency
- This is associated with impaired mitochondrial function in retinal ganglion cells leading to apoptosis causing progressive and irreversible vision loss
- STK-002 is an investigational ASO treatment designed to upregulate OPA1 protein expression with the aim of stopping or slowing vision loss in ADOA

OBJECTIVES

Primary Objectives

- To evaluate safety, tolerability, and exposure (serum) of single ascending doses of STK-002 in a first-in-human Phase 1 study (ISRCTN4172562)

Secondary Objectives

- To evaluate changes in visual function, ocular structures, and quality of life after single doses of STK-002

RECRUITMENT CRITERIA

Key Inclusion Criteria

- Clinical ADOA with confirmed heterozygous *OPA1* variant predicted to cause haploinsufficiency
- Ages 6-55y (cohort A: ≥18-<55y, cohort B: ≥6-18y)
- ETDRS letter score 35-70/eye

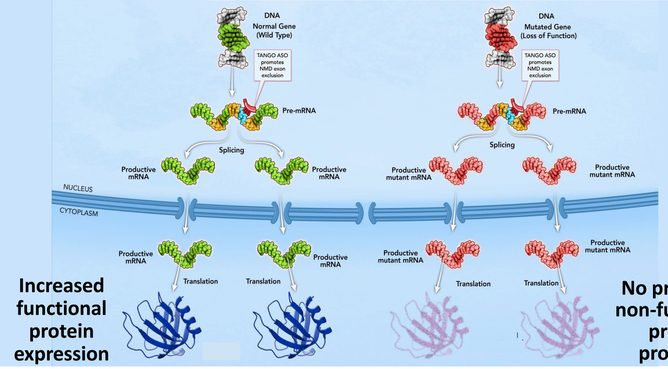
Key Exclusion Criteria

- ADOA plus or Behr syndrome
- Gain-of-function or compound heterozygous *OPA1* variants
- Condition / medications / surgery that could affect optic nerve function
- High myopia (>6D)

Study Sites

- Cambridge, UK; Cardiff, UK; London, UK; EU sites to be determined

Haploinsufficiency with STK-002



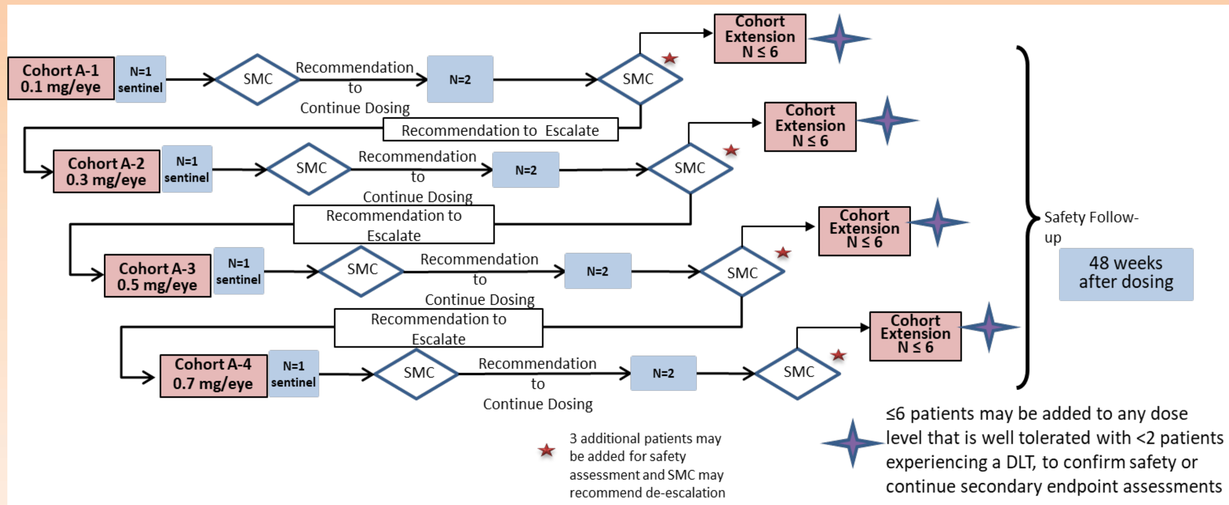
Increased functional protein expression

No protein or non-functional protein produced

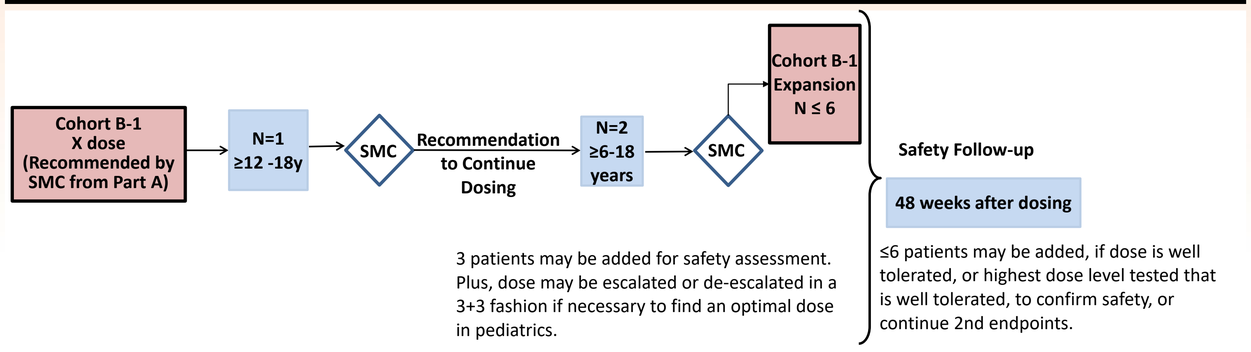
STUDY DESIGN

- **Intravitreal 50uL dose at pars plana in one eye - eye with more severe disease**
- **3+3 ascending dose design / 48-week duration**
- N=up to 60 (48 in Part A, 12 in Part B)
- Part A, 4 dose levels (0.1, 0.3, 0.5, & 0.7 mg) with an option to add 2 dose levels – maximum dose 1.2 mg per Safety Monitoring Committee
- Ophthalmic assessments:
  - BCVA, low contrast BCVA (Sloan), MnREAD, slit lamp examination, static automated perimetry (24-2), ff-ERG, PhNR (phototopic negative response), sd-OCT, OcuMet Beacon flavoprotein fluorescence (exploratory)
- Other assessments:
  - QOL*, blood /urine for safety and exposure pharmacokinetics (PK), biomarkers (serum, plasma, whole blood), adverse events

Part A – Progression (≥18 to <55y)



Part B – Progression (≥6 to <18y)



*EQ-5D=European Quality of Life-5 Dimensions; EQ-5D-Y=European Quality of Life-5 Dimensions (Youth); ISCEV=International Society for Clinical Electrophysiology of Vision; IVI-C=Impact of Vision Impairment for Children; NEI=National Eye Institute; NEI-VFQ-25=National Eye Institute Visual Function Questionnaire-25; SMC=Safety Monitoring Committee; DLT=Dose-limiting toxicity