# Ligand-conjugated coAAV-SCS-01 capsid outperforms benchmarks in RPE-choroid and retina after suprachoroidal administration in NHPs

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coave THERAPEUTICS

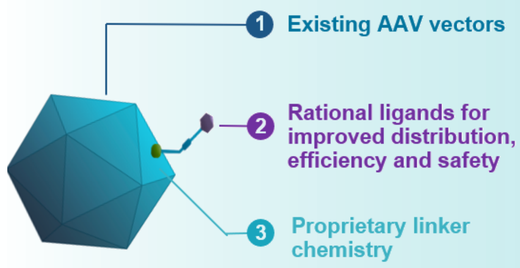
#0336

**Introduction:** AAV gene therapy is promising for ocular diseases, but current vectors have limited distribution and safety. We are developing next-generation capsids using our **ALIGATER™ platform**. Our lead capsid **coAAV-SCS-01** enables safe, broad posterior segment transduction via suprachoroidal (SCS) delivery for inherited and prevalent retinal diseases.

## Barriers to ocular gene therapy

- **Delivery limitations**: restricted posterior segment coverage with current vectors or invasive subretinal surgery
- **Dose-limiting inflammation** requires high steroids and reduced doses
- **Pre-existing immunity** limits re-dosing & second-eye treatment

## Building next-generation AAV vectors using ALIGATER™

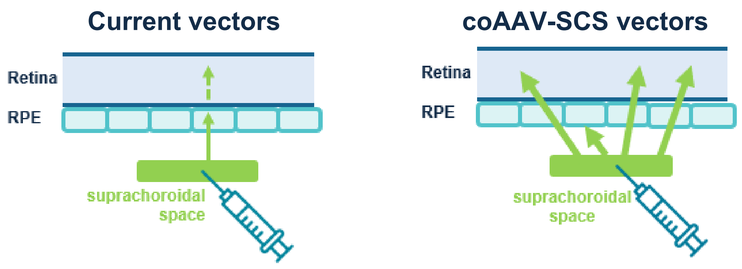



- **One step** chemical conjugation
- **No additional purification step** required
- Compatible with **any AAV vectors**


## Our solution: coAAV-SCS-01 a novel suprachoroidal capsid validated in NHPs

### Why suprachoroidal?

- **Non-invasive**, **clinically-validated** procedure
- **Broad posterior coverage** vs subretinal
- **Low inflammation**, no steroids needed at >10x intravitreal dose
- Potential for safe and effective **second-eye treatment**

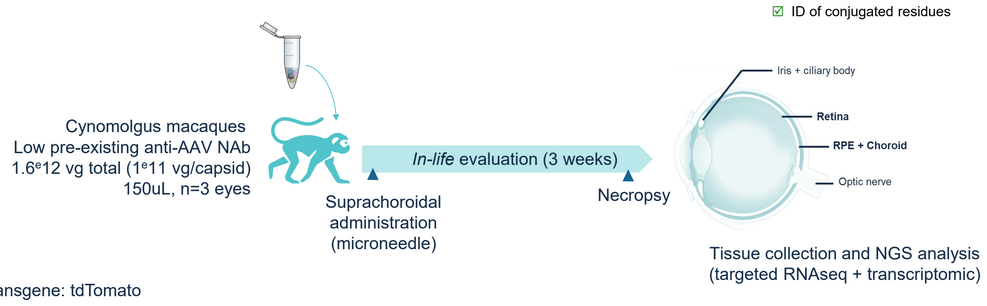



## STUDY 1 (MULTIPLEX): coAAV-SCS-01 and coAAV-SCS-02 outperform 1st and 2nd generation capsids in NHPs

### Study design:

| Library | Capsids |
|---|---|
| **SCS coAAV library (barcoded)** | coAAV-SCS-01, coAAV-SCS-02, A69, A84, A119, A77, A82, A85, A97<br>**Benchmarks**: AAV2, AAV3B, AAV.7m8, AAV8, AAV.v128 |

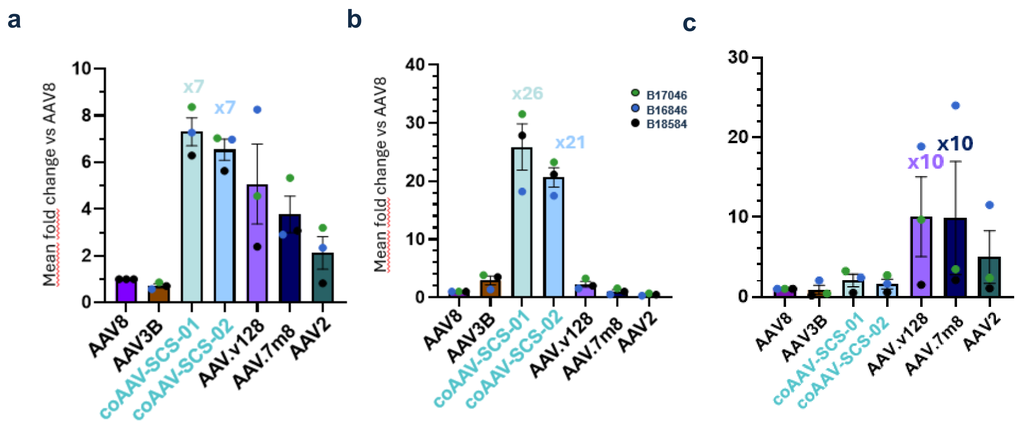
- ☑ Library composition ok
- ☑ E/F capsid ratio <20%
- ☑ Infectivity confirmed *in vitro*
- ☑ Conjugation confirmed by mass shift
- ☑ Number of ligands per capsid
- ☑ ID of conjugated residues




Transgene: tdTomato

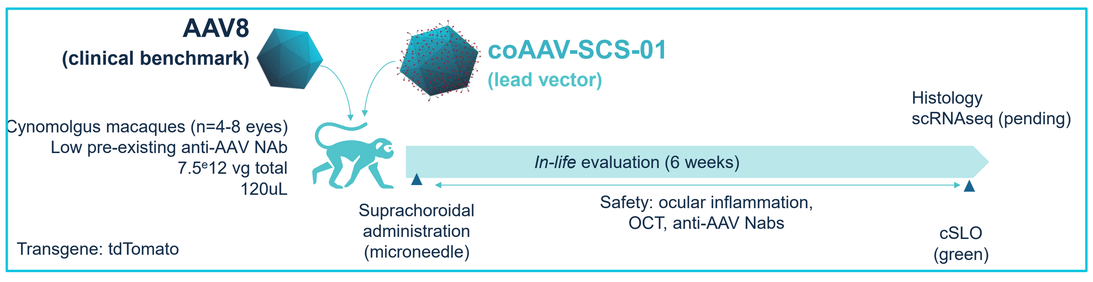
### Vector ranking:

**On-targets: RPE-choroid (a) and retina (b) ; Off-targets: Iris-ciliary body (c)**

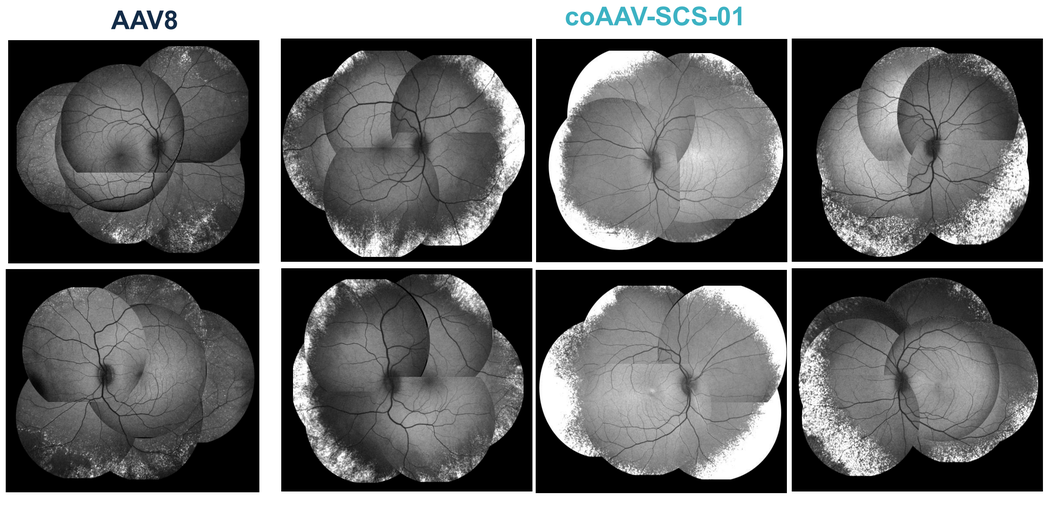



## STUDY 2: Superiority of coAAV-SCS-01 versus AAV8 is confirmed in a 2nd NHP validation study

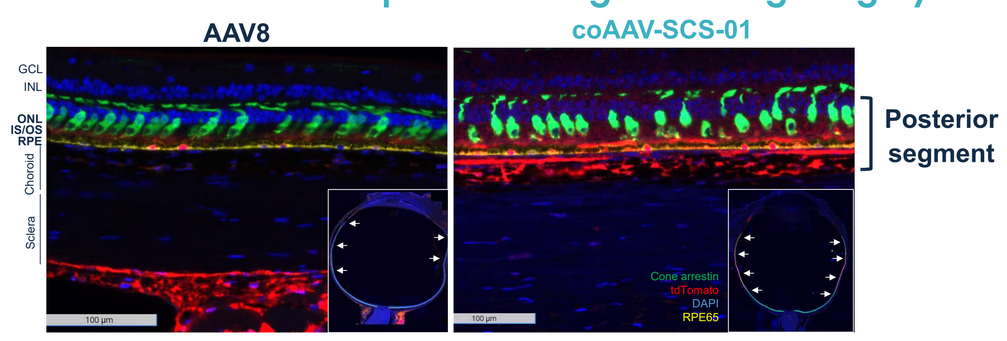
### Study design:



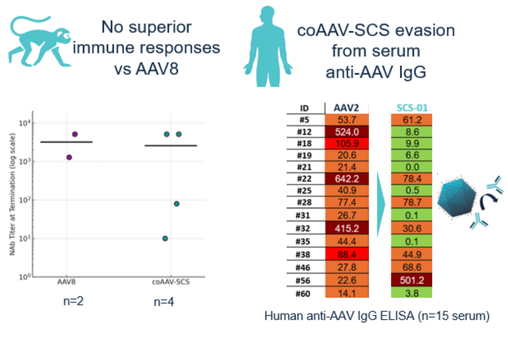

### *In vivo* transgene expression:




### Confirmation of increased posterior segment targeting by IHC




### Safety profile




## KEY CAPSID PROPERTIES

**Up to 26x posterior coverage vs AAV8 with improved RPE-choroid and retina transduction**
**De-targeted from anterior segment = improved safety**
**Immune evasion = potential for 2nd eye treatment**