Presentation Number: 2909-A0096

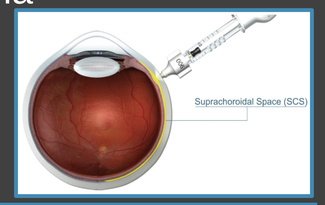
# Suprachoroidally delivered non-viral DNA nanoparticles transfect chorioretinal cells in non-human primates and rabbits

Viral Kansara[1,E, I], Jesse Yoo[1, E, F, P], Mark J. Cooper[2, P], Ozge S Laird[2], Donna Taraborelli[1, E, F, P], Robert Moen[2, P], Glenn Noronha[1, E, F, P]

E-mail: viral.Kansara@clearsidebio.com

1. Clearside Biomedical, Georgia, United States 2. Copernicus Therapeutics, Inc., Ohio, United States

Disclosures: F (Financial Support); I (Personal Financial Interest); E (Employment); C (Consultant); P (Patent); R (Recipient)




## Purpose

- Suprachoroidal (SC) delivery offers the potential to more precisely target chorioretinal tissues while avoiding surgical risks associated with a subretinal injection and may offer a novel alternative for gene-based therapies for the treatment of ocular diseases.
- The purpose of this effort was to evaluate ocular tolerability and chorioretinal cell transfectability of suprachoroidally injected non-viral DNA nanoparticles (DNPs) in non-human primates (NHPs) and rabbits.

## Methods

- Two separate studies evaluated chorioretinal cell transfectability and ocular tolerability of suprachoroidally injected non-viral DNPs in NHPs and in rabbits. The DNPs consisted of a single copy of plasmid DNA with a polyubiquitin C/luciferase transcriptional cassette.
- Cynomolgus monkeys (N=4 per group) received a single bilateral suprachoridal injection (0.1 mL) of either saline (negative control), ellipsoid-shaped DNPs or rod-shaped DNPs.
- New Zealand White (NZW) rabbits (N = 4 per group) received a single suprachoroidal injection (0.1 mL) of either saline (negative control), ellipsoid-shaped DNPs, or rod-shaped DNPs. A cohort of rabbits also received a single unilateral (left eye) subretinal injection of rod-shaped DNPs.
- Animals were assessed for anterior segment inflammation, for intraocular pressure (IOP) changes, and electroretinographic changes at baseline, day 1, and day 7 post-dose in the rabbit study and at baseline, day 1, day 8, and day 22 post-dose in the NHPs.
- Luciferase activity was measured in NHP ocular tissues at week 1 and 3-weeks post-injection in the NHPs and at week 1 in rabbit ocular tissues by bioluminescence assay.

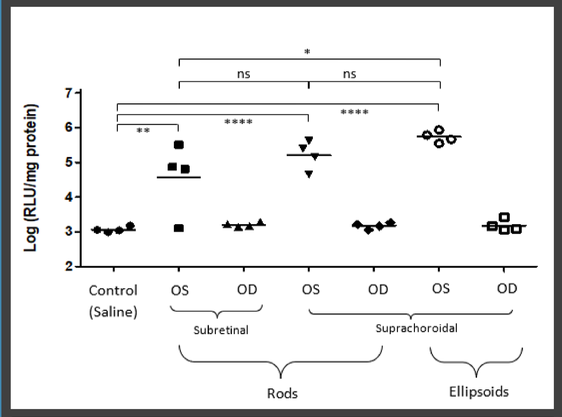
## Study Design

| Study | Group | Test article | Route of Administration | Volume |
|---|---|---|---|---|
| Rabbit & NHP | 1 | Vehicle | Suprachoroidal Injection | 100 µL |
| Rabbit & NHP | 2 | Ellipsoid DNPs Luciferase | Suprachoroidal Injection | 100 µL |
| Rabbit & NHP | 3 | Rod DNPs Luciferase | Suprachoroidal Injection | 100 µL |
| Rabbit | 4 | Rod DNPs Luciferase | Sub-retinal injection | 50 µL |

## Results

**Rabbit Experiment**

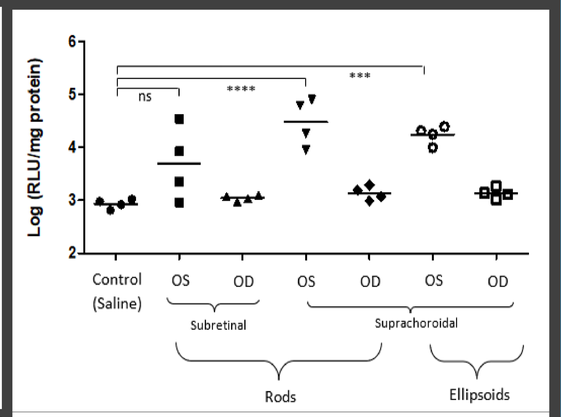
RPE-CHOROID-Sclera




OS: Dosed
OD: Undosed

Bonferroni's multiple comparison test: ** p<0.01, *** p<0.001, **** p<0.0001
ns, non-significant

RETINA

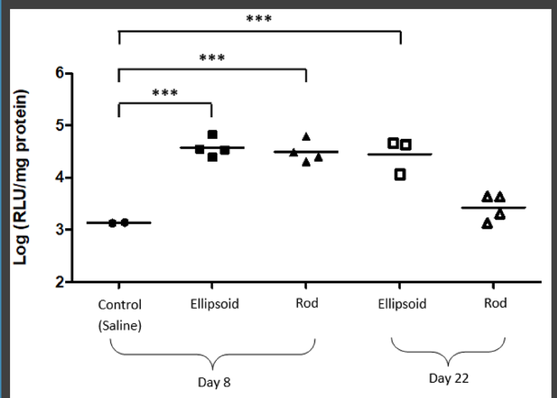



OS: Dosed
OD: Undosed

Bonferroni's multiple comparison test: ** p<0.01, *** p<0.001, **** p<0.0001
ns, non-significant

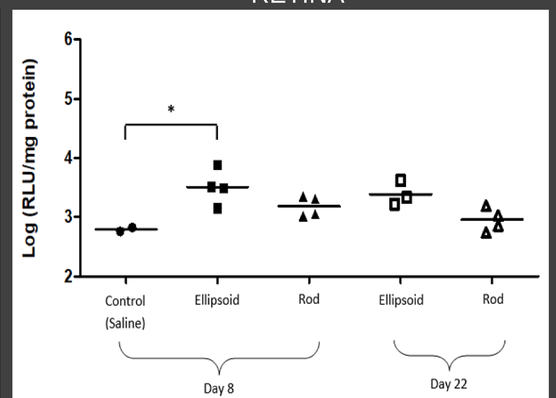
**Non-human Primate Experiment**

RPE-CHOROID-Sclera




1-way ANOVA, p<0.0001.
Bonferroni's multiple comparison test: * p<0.05, ** p<0.01, ***p<0.001

RETINA




1-way ANOVA, p<0.0001.
Bonferroni's multiple comparison test: * p<0.05, ** p<0.01, ***p<0.001

## Results

- ✓ Suprachoroidally injected non-viral DNPs were generally well-tolerated in NHPs and rabbits.
- ✓ Luciferase activity was observed in the retina and choroid of eyes that received suprachoroidal injections in NHPs and rabbits.
- ✓ In NHPs, the persistence of luciferase activity was observed through day 22 (last study timepoint) with ellipsoid-shaped DNPs, while a decline (32% and 90% in retina and choroid/RPE, respectively) was observed with rod-shaped DNPs at day 22.
- ✓ In rabbits, suprachoroidally injected DNPs (both rod and ellipsoid) and subretinal DNPs (rod-shaped) resulted in comparable luciferase activity at week 1 (last study timepoint).

## Conclusions

- ❖ Suprachoroidal administration of non-viral DNPs resulted in efficient chorioretinal transfection in NHPs and rabbit. Suprachoroidally injected DNPs were well-tolerated and will be further evaluated for their safety and efficacy.
- ❖ These data provide evidence that suprachoroidal injection of DNPs is well-tolerated with high levels of luciferase activity and should be further evaluated for ocular gene delivery.
- ❖ SC and SR administration achieved comparable expression in rabbits indicating that in the future, gene therapy could potentially be administered in the office via SC delivery instead of by pars plana vitrectomy.

## References

1. Acta Ophthalmol. 2019 Jan 31.Suprachoroidally injected pharmacological agents for the treatment of chorio-retinal diseases: a targeted approach.