PROGRAM #:
4112 - B0112

TARGETED DELIVERY OF TRIAMCINOLONE ACETONIDE AND CLS011A TO THE POSTERIOR OCULAR TISSUES VIA SUPRACHOROIDAL ADMINISTRATION

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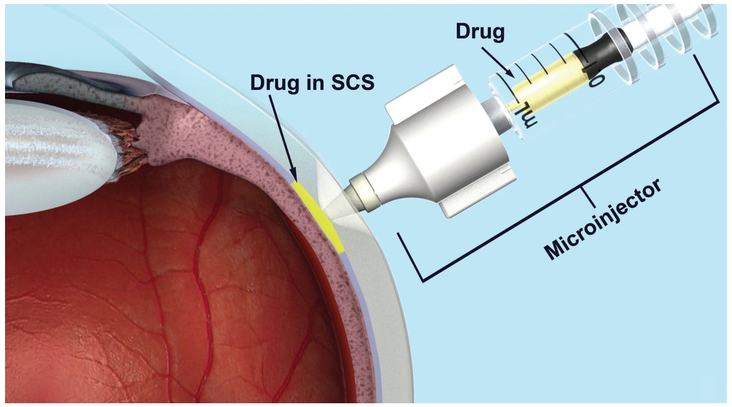
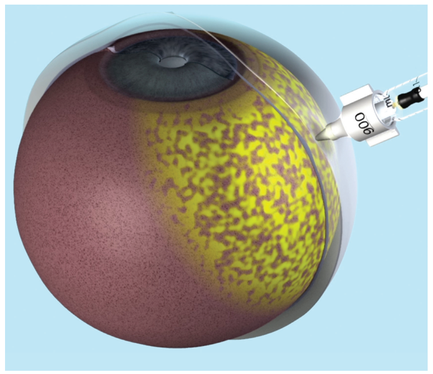
PURPOSE

The ocular pharmacokinetics of two drug candidates, triamcinolone acetonide (TA, corticosteroid) and CLS011A (tyrosine kinase inhibitor) following suprachoroidal injection in rabbit eyes will be presented.

INTRODUCTION

- Clearside Biomedical, Inc., headquartered in Alpharetta, GA, is a clinical-stage biopharmaceutical company developing first-in-class drug therapies to treat blinding diseases of the eye.
- By choosing the appropriate drug or drug combination, potential treatments are being developed using suprachoroidal injection.
- Suprachoroidal dosing for the treatment of eye diseases has several potential advantages including high bioavailability, and differentiating efficacy and safety.
- Clearside currently has 4 development programs: a non-infectious uveitis program currently enrolling a Phase 3 clinical study; an RVO program currently enrolling a Phase 3 clinical study; a DME program that is currently enrolling a Phase 1/2 trial; and a pre-clinical AMD program.





Injected drug formulation spreads around the eye in the suprachoroidal space (SCS).

METHODS

Experiment	Dose	Route	Dose Volume	Endpoints
1	4 mg TA	Suprachoroidal injection	100 µL	Exams; drug level in tissue
2	4 mg CLS011A	Suprachoroidal injection	100 µL	Exams; drug level in tissue

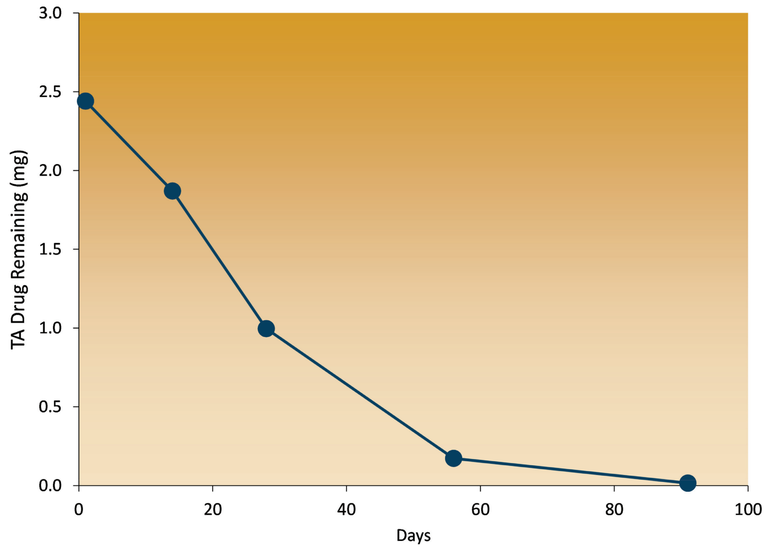
- On Day 0, male rabbits were administered a single bilateral suprachoroidal injection of TA in Experiment 1 and of CLS011A in Experiment 2.
- Clinical observations, body weights, and intraocular pressure (IOP) were assessed up to 13 weeks post-dose.
- Plasma and ocular matrixes (sclera/choroid/retinal pigment epithelium: SCR, retina, vitreous, iris-ciliary body: ICB, aqueous, and lens) were collected for quantification of drug concentrations. Analyses were performed using HPLC/MS/MS at defined time points throughout the 13 week study.

RESULTS

Triamcinolone Acetonide Administration

- TA was detectable throughout the 91 day period in eyes after dosed by suprachoroidal administration as noted in Figure 1.
- Based on area under the curve analysis, 96% of the drug was exposed to SCR and retina after SCS administration.
- Exposure to TA was very low in the anterior chamber including: aqueous humor, iris, lens, and vitreous humor following Suprachoroidal injection.

Figure 1. TA Drug Remaining in Sclera/Choroid/RPE

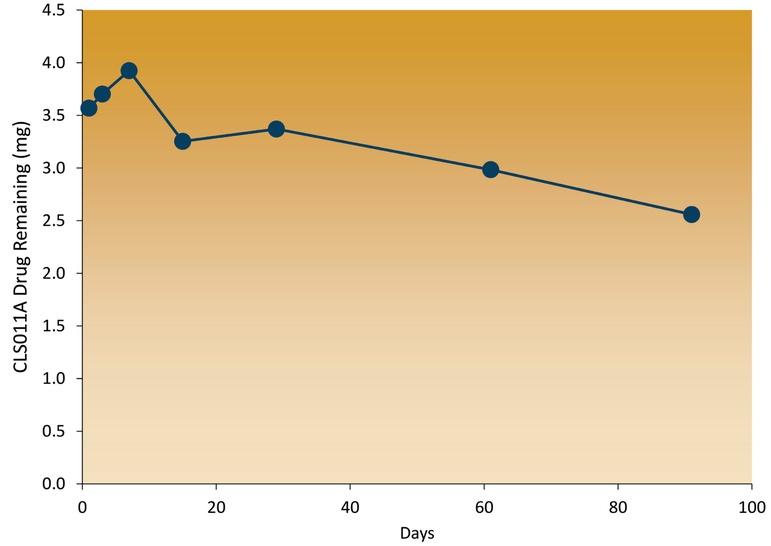


RESULTS

CLS011A Administration

- Results from suprachoroidally injected CLS011A showed drug levels in the SCR that were at least 3 orders of magnitude higher than vitreous and drug was below limits of detection (1 ng/mL) in the aqueous.
- Exposure to CLS011A was very low in the anterior chamber including: aqueous humor, iris, lens, and vitreous humor following Suprachoroidal injection.

Figure 2. CLS011A Drug Remaining in Sclera/Choroid/RPE



CONCLUSIONS

- Suprachoroidal administration of 4 mg/eye of TA and 4mg/eye CLS011A were well tolerated in each study. There were no observed adverse effects related to treatment or method of administration.
- Systemic exposure to each drug was minimal.
- Absorption into the posterior segment of the eye was observed in each case with drug remaining in substantial amount over the 13 weeks observation period.
- There was minimal exposure of drug candidate to the anterior segment of the eye in each case; Data not shown in this poster.
- These data suggest that suprachoroidal injections of TA and CLS011A result in favorable distribution of drug candidate to the posterior segment for an extended duration.
- The potential for extended duration of drug exposure to the posterior segment tissues (retina and choroid) might lend itself to efficacy for an extended period of time.

Website: www.clearsidebio.com