Pharmacokinetics and Ocular Tolerability of Suprachoroidal CLS-AX (axitinib injectable suspension)

ARVO 2020 Program: #B0130

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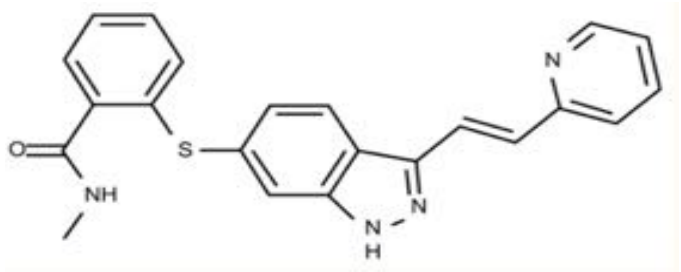

1. Clearside Biomedical, Inc.

Financial Disclosures

- LM: Commercial Relationship(s);Clearside Biomedical, Inc.:Code E (Employment);Clearside Biomedical, Inc.:Code I (Personal Financial Interest)
- VK: Commercial Relationship(s);Clearside Biomedical, Inc.:Code E (Employment);Clearside Biomedical, Inc.:Code I (Personal Financial Interest)
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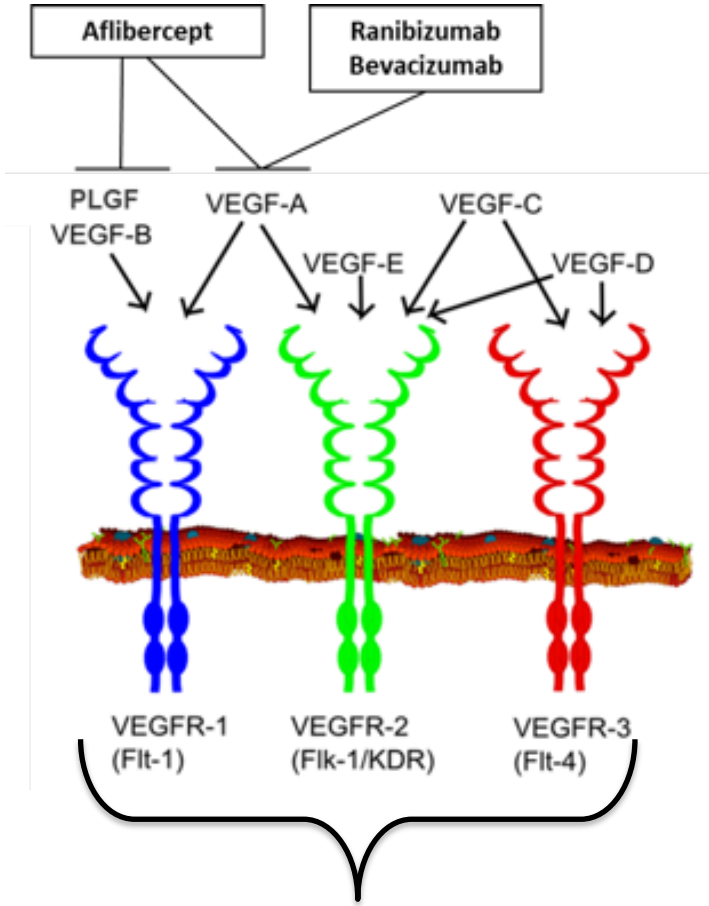
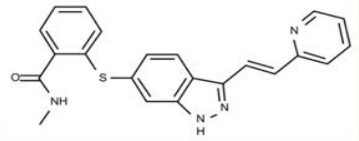
Inhibition of multiple VEGF receptors by CLS-AX may provide more complete blockade of the neo-angiogenesis process associated with nAMD versus currently available monotherapy

- Anti-VEGF-A drugs provide clinically sub-optimal efficacy and create an unmet need to develop new drugs and optimize drug delivery techniques with the goal of improving and maintaining visual acuity[1,3,5]
- Axitinib is a potent and highly selective pan-VEGF receptor inhibitor[2]
- Approved as an oral agent for renal cell carcinoma (Inlyta®)
- A recent Phase 2 study demonstrated that targeting VEGF-A, VEGF-C & VEGF-D may result in improved efficacy compared to targeting VEGF-A alone[6]



Axitinib



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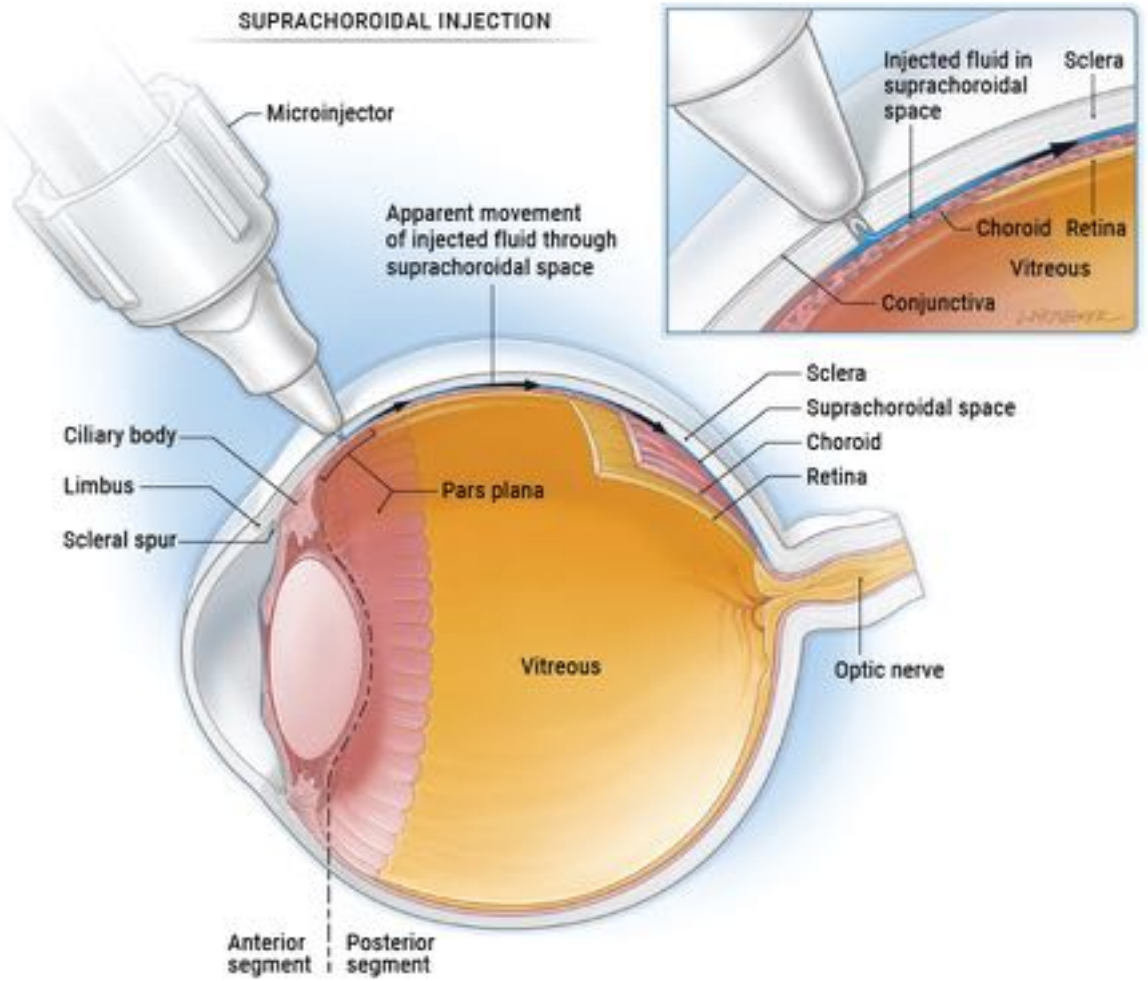
CLS-AX, administered suprachoroidally, has the potential to be a longer-acting therapy for nAMD Treatment



Reference: Clearside Biomedical Inc.

- Directly targets drug delivery to the back of the eye at high doses
- Potentially lower drug concentrations are needed at dosing compared to other routes of administration
- Minimizes drug exposure to non-diseased tissues
- Less invasive, in-office procedure

Suprachoroidal injection results in posterior and circumferential drug delivery

- Administered drug flows **posteriorly and circumferentially** in the suprachoroidal space within the posterior segment
- Suprachoroidal injections are administered **4 – 4.5 mm from the limbus**, in the superior temporal quadrant.
- Each injection utilizes a proprietary **SCS Microinjector®** device

Reference: Clearside Biomedical Inc.

Study Objective

Assess the durability (PK) and ocular tolerability of suprachoroidally administered CLS-AX (axitinib injectable suspension) in Dutch Belted (pigmented) rabbits during a 10-week study

Methods

- CLS-AX was administered as a single bilateral injection to the suprachoroidal space at a dose of **0.03 mg/eye** or **0.1 mg/eye** (n=2 animals per group/ time-point)
- Clinical ocular exams were performed via **indirect ophthalmoscopy** and **slit-lamp biomicroscopy** at pre-dose and at wks. 1, 2 and 4. **OCT** was performed at pre-dose, wk. 6 and wk. 9 or 10
- **Plasma** samples were collected at predose and on days 2, 8, 15, 31, 45, 61, 66 and 68. **RPE-choroid-sclera (RCS)**, **retina**, **aqueous humor** and **vitreous humor** samples were collected at terminal end-points
- Bioanalytical assays were performed via an LC-MS/MS method. Pharmacokinetic parameters were calculated using Phoenix WinNonlin (Version 6.4)

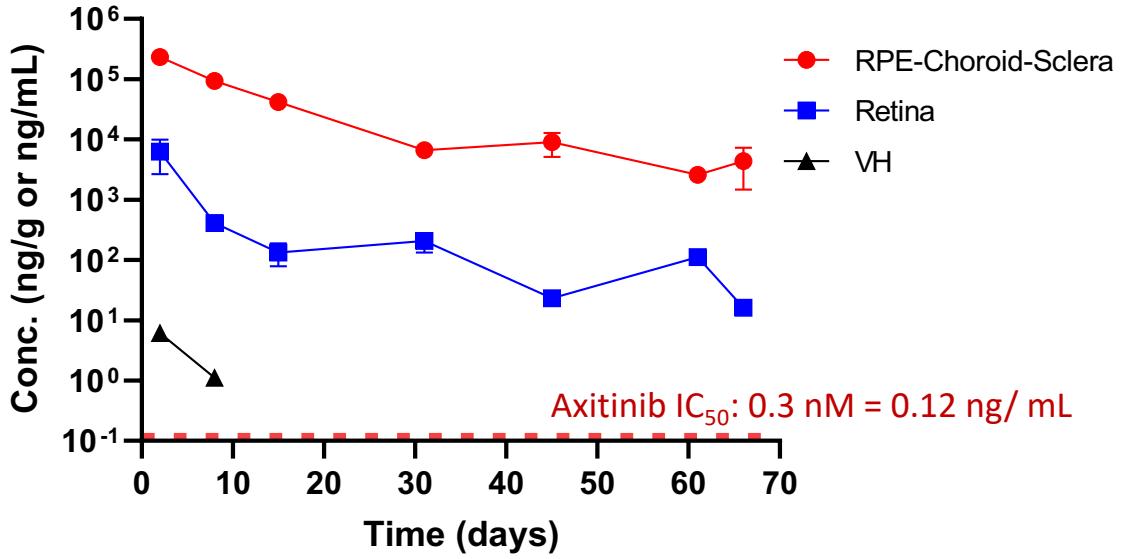
Generally, CLS-AX was well tolerated in DB rabbits

- ✓ No ophthalmic abnormalities were observed in any of the animals beyond wk. 1
  - On study day 3, there was an observation of moderately severe (+3) aqueous flare in one animal and mild (+1) conjunctival hyperemia in 5 animals

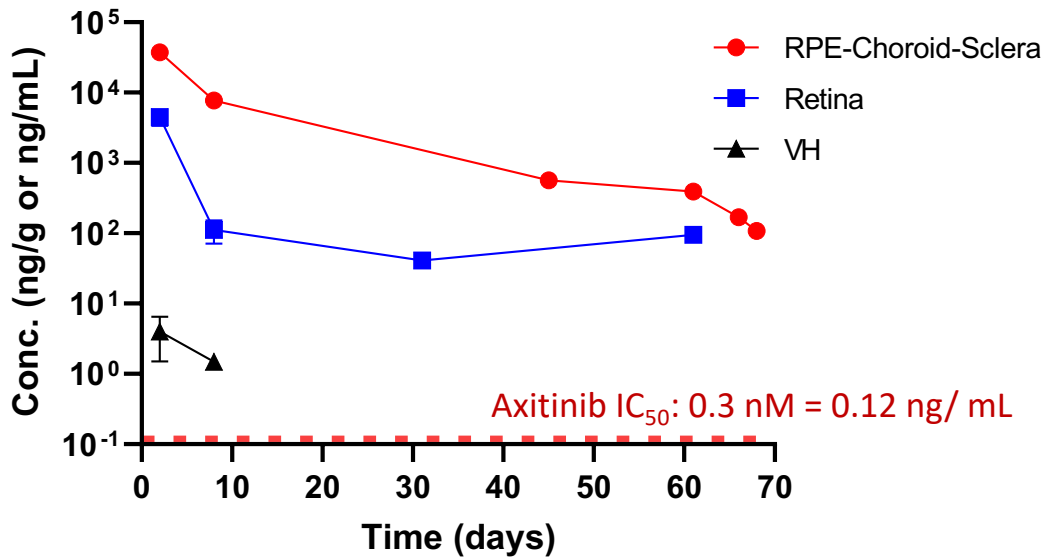
- ✓ OCT showed no evidence of abnormalities and choroidal or retinal degeneration for the duration of the study

CLS-AX injected suprachoroidally exhibited high, efficacious and sustaine levels of axitinib to posterior ocular tissues

Mean Concentrations of Suprachoroidally Administered CLS-AX in Ocular Tissues (0.1 mg/eye)

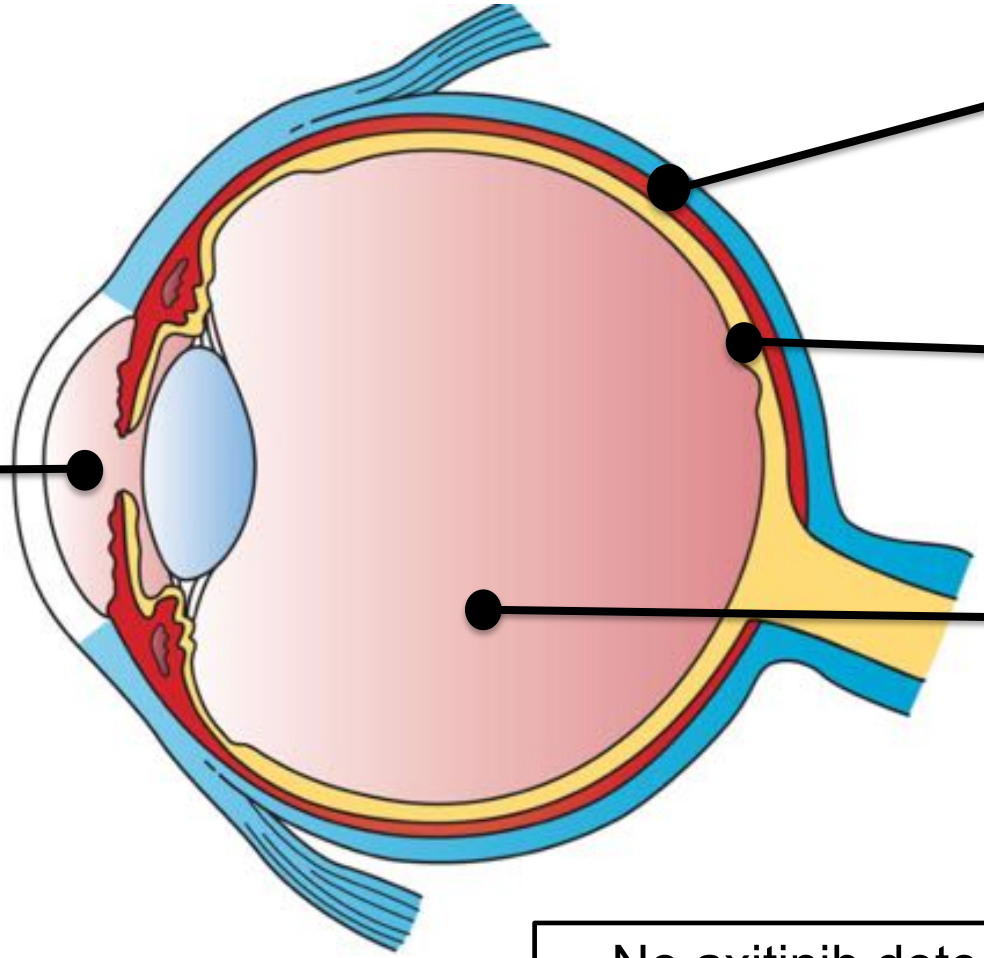


Mean Concentrations of Suprachoroidally Administered CLS-AX in Ocular Tissues (0.03 mg/eye)



- Axitinib concentrations within the **RCS (drug depot)** and **retina** were maintained 3-5 log orders **above IC_{50}** over the study duration
- **Plasma** and **aqueous humor levels** of axitinib were **below the limit of quantitation**

Area Under the Curve (AUC) values for CLS-AX were maintained at high levels in the Retina and RCS for the duration of the study



No axitinib detected in the aqueous humor*

RCS (drug depot)

0.1 mg dose: 55,600 µg.hr/g
0.03 mg dose: 8,120 µg.hr/g

Retina

0.1 mg dose: 674 µg.hr/g
0.03 mg dose: 414 µg.hr/g

Vitreous Humor

No quantifiable axitinib beyond day 7 post-dose

No axitinib detected in plasma*

*LLOQ = 1 ng/mL

Conclusion

CLS-AX administered via **suprachoroidal injection**, provided **sustained, targeted, high levels** of axitinib to the back of the eye and was **well-tolerated**. Given this durability, intrinsic high potency and pan-VEGF inhibition, CLS-AX administered suprachoroidally has the potential to be a bi-annual therapy for nAMD

THANK YOU!