Presentation #: 221-C0032

Sunitinib-Loaded Injectable Polymer Depot Formulation for Potential Once per Year Treatment of Neovascular Age-related Macular Degeneration (wet AMD)

Yu, Yun[1]; Peterson, Ward[1]; Yang, Ming[1]; McKenzie, David[1]; Cardona, Delia[1]; Yu, Connie[1]; Culp, David[2]; Gilger, Brian C.[3]; Zhang, Jin-Zhong[1]; Cleland, Jeffrey[1]
[1]Graybug Vision, Inc., Redwood City, CA, USA; [2]Powered Research, LLC, Research Triangle Park, NC, USA;
[3]Clinical Sciences, North Carolina State University, Raleigh, NC, USA

Current Challenges

Current neovascular AMD (nAMD or wet AMD) therapies are suboptimal due to:

- Need for frequent intravitreal dosing (every 4-8 wks)
- Inability to target more than one disease pathway

Purpose

We previously reported that our clinical-stage product GB-102 delivered pharmacologically active levels of sunitinib in retina/RPE-choroid for 6 months (Yang M, et al. IOVS 2016; 57(12): 5037). The purpose of this study is:

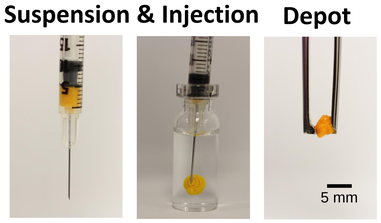
- To develop a longer-lasting microparticle formulation of sunitinib, GB-103, with the goal of delivering sunitinib for up to 12 months following a single intravitreal injection.
- To evaluate the ocular tolerability and pharmacokinetics of the new formulation.

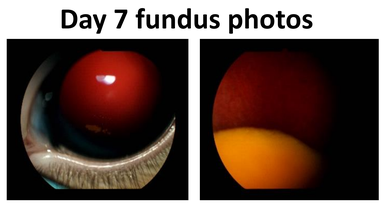
Methods

- A GB-103 formulation was developed and characterized for drug loading (19% by weight), microparticle size (~26 µm) and *in vitro* release kinetics.
- Drug-containing (0.5-1.0 mg sunitinib) microparticles were injected into the vitreous of pigmented rabbits using a 27G needle.
- Ophthalmic examinations were performed at 10 days, and 1, 2, 4, 6 and 8 months.
- Ocular levels of sunitinib were assessed at 10 days, and 1, 2, 4, 6 and 8 months.
- Ongoing *in vivo* study will evaluate the ocular tolerability and pharmacokinetics for up to 12 months.

Results

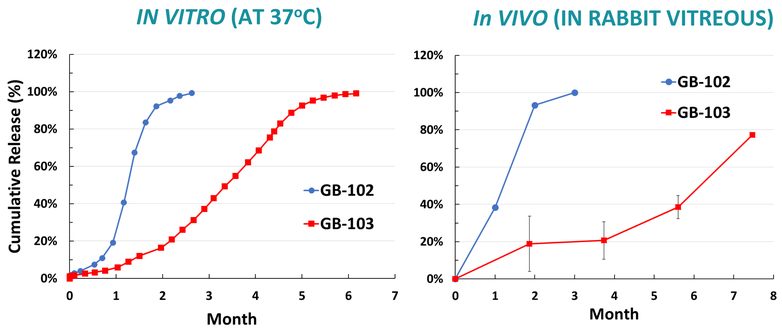
Depot formation





- Our proprietary microparticles coalesce in the inferior vitreous into an immobile, implant-like depot that remains outside of the visual axis.

In Vitro and In Vivo Drug Release Kinetics

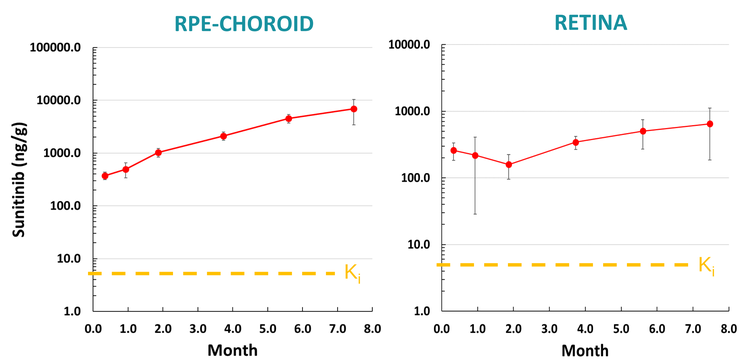


- GB-103 extends the *in vitro* release of sunitinib to 6 months.
- Sunitinib release from GB-103 is further prolonged *in vivo.*

Toxicology

- Slit-lamp and fundus examinations showed no significant ophthalmic exam findings in any of the eyes dosed with the new formulation or with the placebo formulation up to date (8 months post-dose).

Pharmacokinetics (PK)



- GB-103 maintains pharmacologically active levels of sunitinib in retina/RPE-choroid over 8 months in the ongoing study.
- Reversible binding of sunitinib to ocular melanin serves as a secondary drug depot to further extension of drug exposure in retina/RPE-choroid (Peterson W, et al. IOVS 2017; 58(8):1974).

Conclusions

- Intravitreal injection of the GB-103 microparticle formulation is well-tolerated and able to maintain pharmacologically active levels in retina/RPE-choroid for 8 months in the ongoing *in vivo* study.
- *In vivo* study is ongoing to evaluate its ocular tolerability and pharmacokinetics for up to 12 months.
- A single IVT injection of GB-103 microparticles may retain active drug levels in retina/RPE-choroid for 12 months and potentially enable **once-per-year treatment for wet AMD**.