GB-102 Clinical Update

Is Every 6 Month IVT Dosing in Wet AMD Achievable?

Charles P. Semba, MD, FACC, FACR
Chief Medical Officer

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### Focus on Extended Duration Dosing

**Can 6 Month Dosing Intervals (or Longer) Be Achieved in Wet AMD?**

<table>
<thead>
<tr>
<th>Company</th>
<th>Opportunity</th>
<th>Technology</th>
<th>Lead</th>
<th>Pipeline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical-stage Venture-based Ophthalmology Biotech</td>
<td>Reducing Treatment Burden for Patients and Physicians</td>
<td>Bioabsorbable Microparticle Delivery to Enable Sustained Drug Release For Up to 12 Months</td>
<td>GB-102: Q6 M Dosing in wet AMD with IVT Depot Formulation of Sunitinib</td>
<td>GB-103: Q12 M Dosing in Retina</td>
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<td></td>
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<td>GB-201: Q4 - 6 M Dosing in Glaucoma</td>
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</tbody>
</table>
**GB-102 - Depot Technology**

**Step 1**
Reconstitution

- Buffered Hyaluronate
- GB-102 PLGA/10% sunitinib microparticles
- Surface treated to promote aggregation

**Step 2**
IVT Injection / Bioabsorbable

- Depot
- 27 g needle 50 μL

**Step 3**
Drug Release into RPE/Choroid

- Sunitinib release
- PLGA (poly-(lactic-co-glycolic acid))
- Lactic acid / glycolic acid

- PLGA used in dissolvable sutures
- Biodegrades / bioabsorbs
- Tunable drug delivery
- Depot ~5 mm in size

**Images**

- Day 8
- Day 92
GB-102: Sunitinib is a Potent Anti-Angiogenic

*Inhibits All VEGF Receptors*

- Multiple receptor tyrosine kinase inhibitor
- Approved oral agent for solid tumors (SUTENT)
- First proposed for nAMD in 2006

A Novel Vascular Endothelial Growth Factor Receptor 2 Inhibitor, SU11248, Suppresses Choroidal Neovascularization *In Vivo*

(Takahashi 2006)
Rabbit Tissue Drug Level of Sunitinib
Single Injection 1 mg IVT GB-102

- RPE/Choroid
- Retina
- Vitreous

Sunitinib has high affinity for melanin binding

No detectable plasma drug levels in GLP studies

Sunitinib (ng/mg)

<table>
<thead>
<tr>
<th>Months</th>
<th>RPE/Choroid</th>
<th>Retina</th>
<th>Vitreous</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>10^6</td>
<td>10^4</td>
<td>10^2</td>
</tr>
<tr>
<td>2</td>
<td>10^5</td>
<td>10^3</td>
<td>10^2</td>
</tr>
<tr>
<td>3</td>
<td>10^5</td>
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<tr>
<td>7</td>
<td>10^5</td>
<td>10^3</td>
<td>10^2</td>
</tr>
</tbody>
</table>

Months

Mouse Laser CNV Model
Aflibercept vs. GB-102

- No Effect Range (Placebo)
- aflibercept
- GB-102

Day 0:
- Aflibercept x 1 dose IVT
- GB-102 x 1 dose IVT

Mean CNV Area (mm^2)

- * p<0.05 (GB-102 or aflibercept vs. fellow eye control)

(Campochiaro 2018)
GB-102 - Target Product Profile

*Decrease injection frequency to twice per year*

<table>
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<tr>
<th>Category</th>
<th>Description</th>
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<tr>
<td>Unmet Need</td>
<td>Reduce treatment burden in wet AMD</td>
</tr>
<tr>
<td>Efficacy</td>
<td>Non-inferior to aflibercept Q 8 wks</td>
</tr>
<tr>
<td>Dosing/Schedule</td>
<td>IVT Q 6 months using 27 g needle</td>
</tr>
<tr>
<td>Safety</td>
<td>Similar to approved agents</td>
</tr>
<tr>
<td>Depot</td>
<td>Bioabsorbable / no inflammation</td>
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(Rapid Rise in IVT Injections (2000 - 2016))

(Williams 2014)
Phase 1 (ADAGIO Study) - First-in-Human Trial of GB-102
Wet AMD Subjects Who Have at Least 3 Prior Injections of Anti-VEGF

GOALS

- Safety
- Durability Profile
- Pharmacodynamics
  - Visual acuity (eyechart)
  - Retinal thickness (OCT)
- Systemic Exposure

Topline (6 to 8 Month) Data Will Be Presented at Hawaiian Eye / Retina 2019
January 21, 2019 - Dr. David Boyer, MD
Clinical stage company - completing first-in-human, Phase 1 GB-102 safety/durability study (ADAGIO)

GB-102 topline data presentation - Hawaiian Eye/ Retina January 2019 - Can 6 Month Dosing Be Achieved?

Phase 2 study (PRELUDE) in development - commencing 2H 2019

Pipeline programs for GB-103 (once per year) and GB-201 (glaucoma) in progress
Thank You!