Graybug Pipeline Opportunities in Retina

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Graybug Vision: Saving Sight with Transformative Science

Focused on developing innovative medicines for ocular diseases:

Program	Indication	Research	Preclinical	Phase 1	Phase 2	Phase 3
Retina						
GB-102	Wet Age-Related Macular Degeneration (wet AMD)					
GB-601	Retinitis Pigmentosa (RP)					
GB-701	Geographic Atrophy (GA)					
Glaucoma						
GB-401	Primary Open-Angle Glaucoma (POAG)					
Cornea						
GB-501	Mucopolysaccharidosis Type 1 (MPS1) associated corneal clouding					

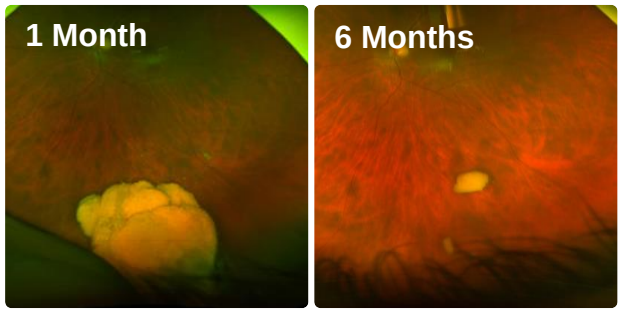
Small molecule delivery platforms

Targeting twice-yearly formulations with sustained-release technologies

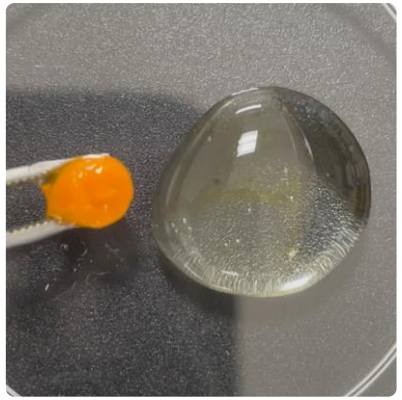
GB-601 and GB-701 formulation development ongoing with versatile delivery technologies

Microparticles

GB-102 v2 depot images from Macular Edema study:



GB-102 v3 remains intact under sheer stress testing:



Implant

GB-401 implant images from rabbit GLP tox study:

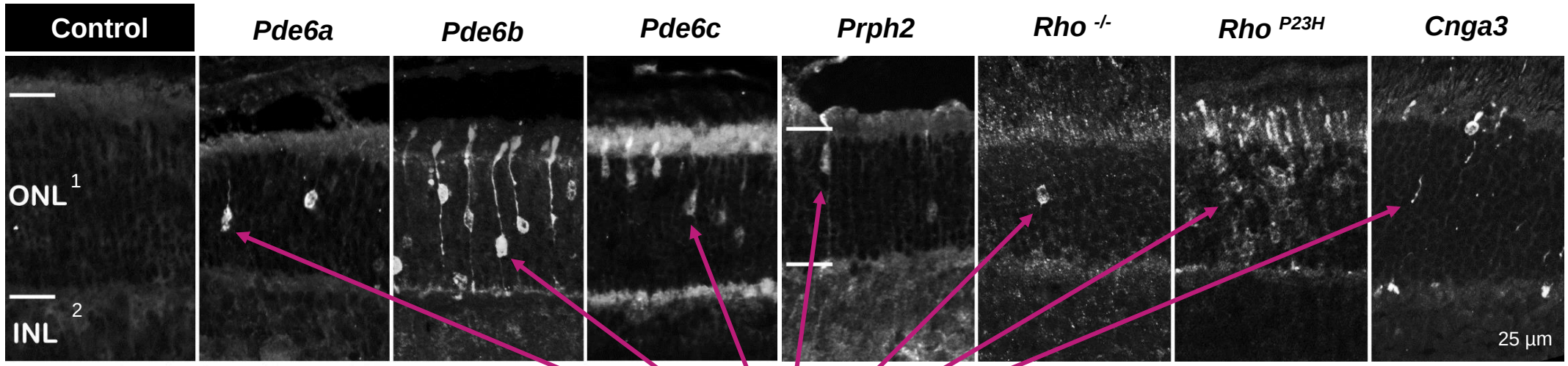
Proprietary applicator:

GB-601 (cGMP Analogs)

For treatment of inherited retinal diseases (IRDs)

High levels of cyclic guanosine monophosphate (cGMP) are known to trigger non-apoptotic photoreceptor cell death in many RD disease models

cGMP appears as white stain in rodent models, which leads to photoreceptor cell death

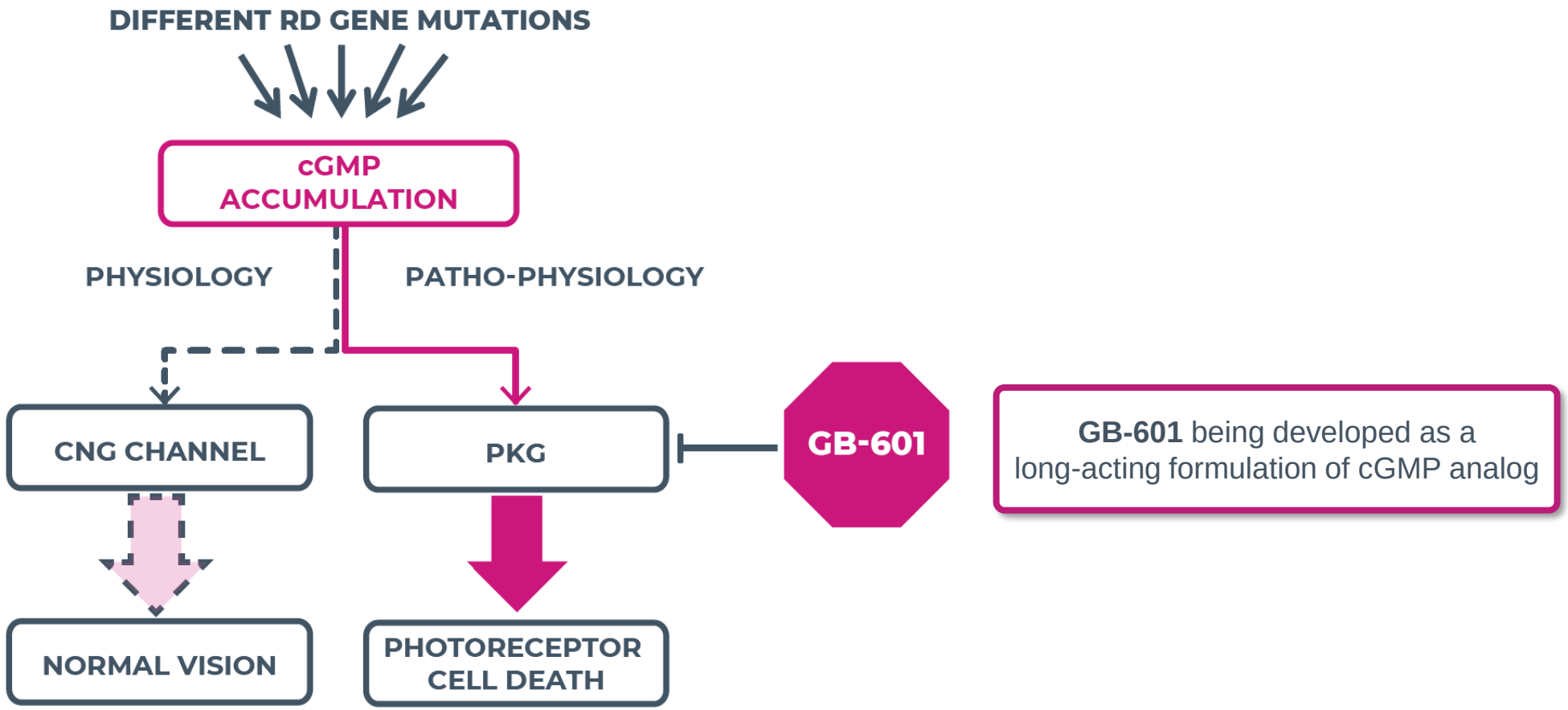


1. Outer nuclear layer
2. Inner nuclear layer

cGMP
(white stains in ONL)

*Terminal deoxynucleotidyl transferase dUTP nick end labeling (TUNEL) assay
RD: retinal degenerative

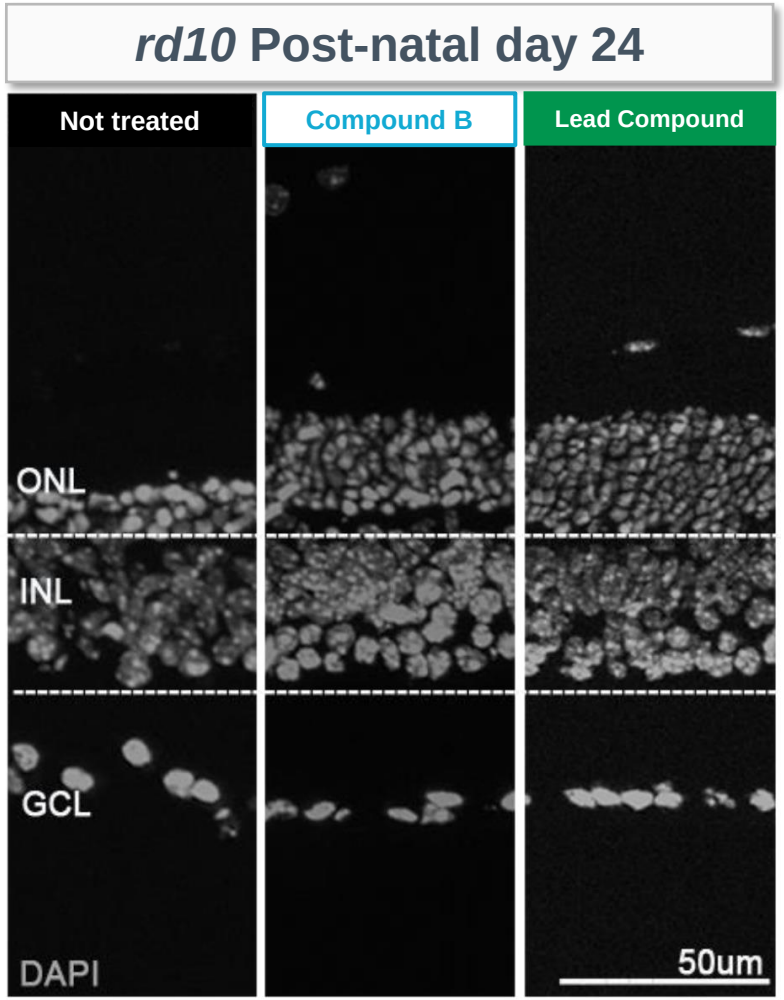
cGMP inhibition allows cell protection, regardless of genetic mutation

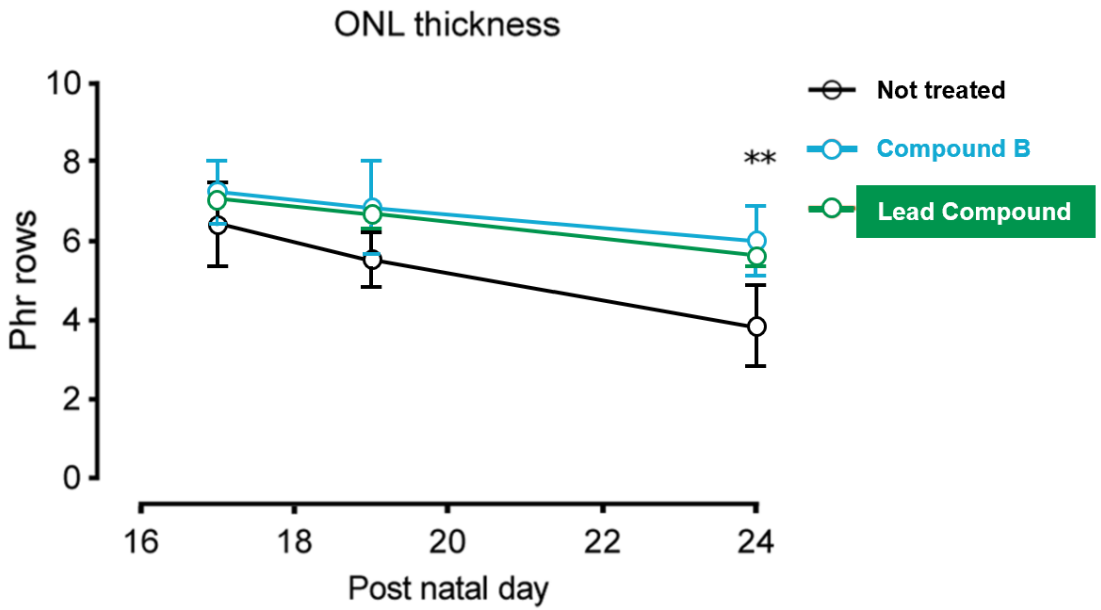


GB-601 being developed as a long-acting formulation of cGMP analog

RD: retinal degenerative; CNG: Cyclic nucleotide-gated; PKG: protein kinase G

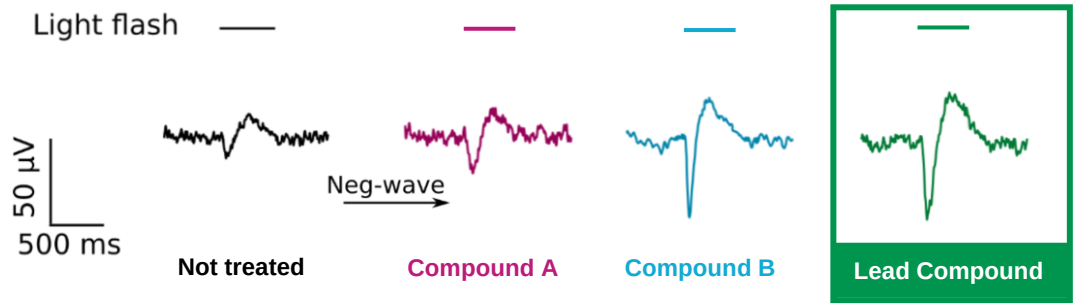
cGMP analogs preserve long-term photoreceptor viability in *rd10* mouse model for retinitis pigmentosa



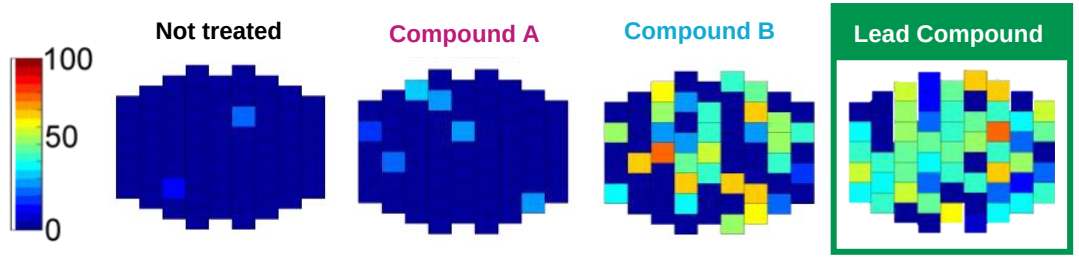


cGMP analogs preserve photoreceptor function in *rd10* mouse model for retinitis pigmentosa

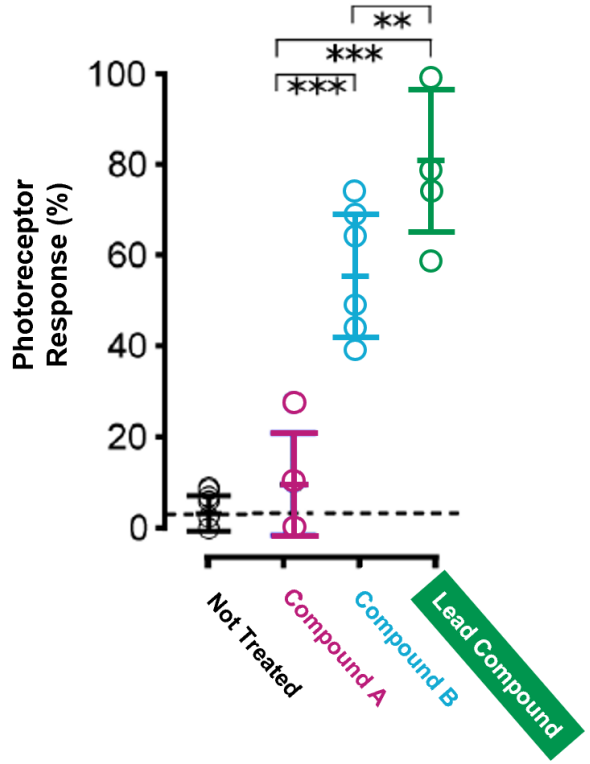
Representative µERG traces measure strength of light-provoked photoreceptor-responses



Activity map of µERG recordings indicates reactivity to light in spatial context



Quantification of retinal light responsiveness



GB-601 being developed as a long-acting formulation of cGMP analog

Potential Benefits:

1. cGMP inhibition allows cell protection, **regardless of genetic mutation**
2. cGMP analogs have the **potential to treat >30% of IRD patients**
3. cGMP analogs demonstrated **improved photoreceptor viability and function** in pre-clinical models of disease
4. **Long-acting formulation needed** to make cGMP analogs a clinically relevant treatment option

GB-701 (Factor B Inhibitor)

For treatment of geographic atrophy (GA)

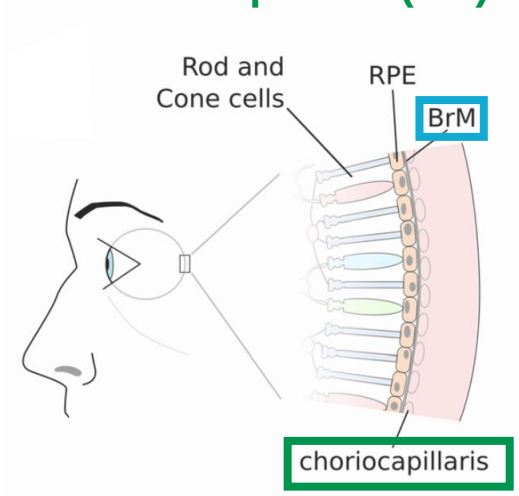
Opportunity for a sustained-release small molecule targeting factor B inhibition

- **Complement inhibition is a clinically validated approach to delay progression of the disease**
  - Recent readout of Apellis' and Iveric Bio's pivotal trials confirms evidence with C3 or C5 inhibition
- **Geographic Atrophy is a chronic disease that will require few injections per year to be commercially viable**
  - Targeting a twice per year injection frequency would be ideal for patients and commercial viability
- **Graybug developing a sustained-release therapeutic targeting human Factor B**
  - Leverage existing formulation expertise
  - Partnering with Insilico Medicine for A.I. drug discovery
  - Insilico existing collaborations include Johnson & Johnson, Pfizer, Teva

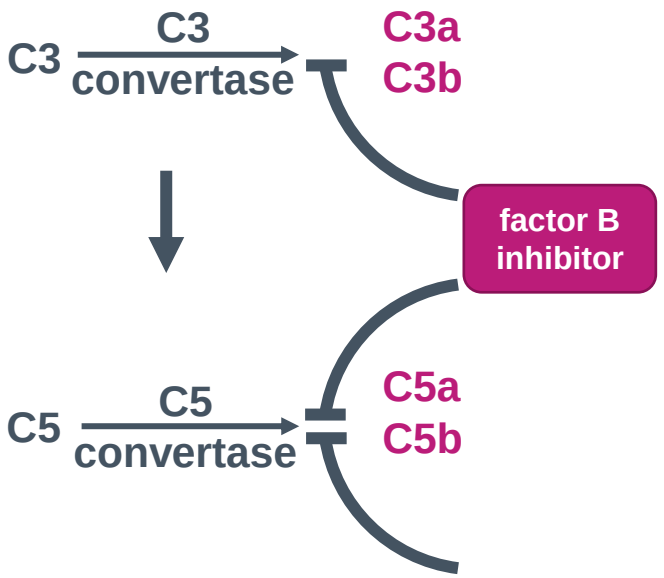
GB-701 being developed as a long-acting formulation of factor B inhibitor

1 Better penetration to:

1. **Bruch's Membrane (BrM)**
2. **Choriocapillaris (CC)**



2 Block *all* effector molecules



3 Sustained-release

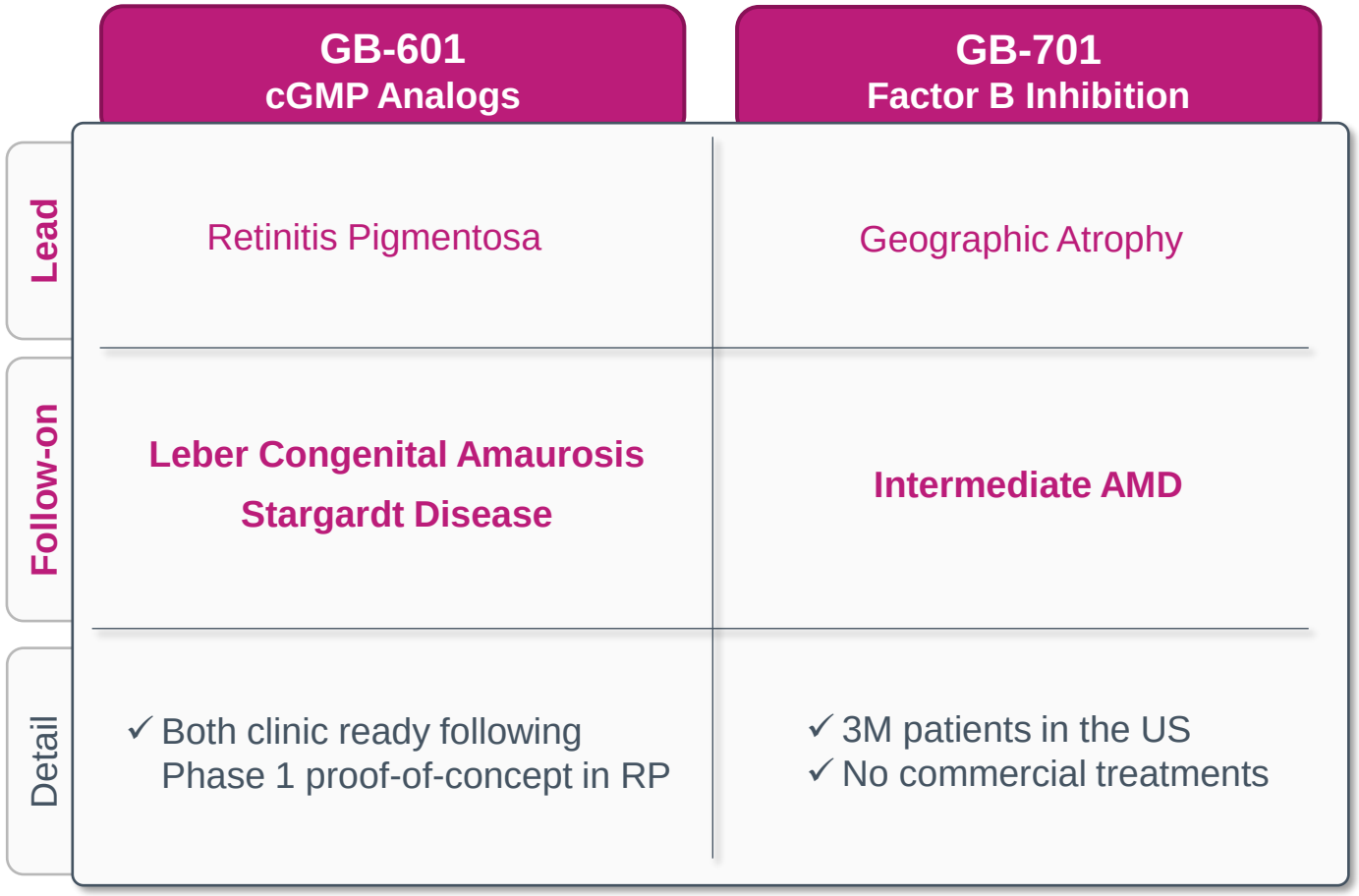
Commercially viable product profile

- GA is a **chronic disease**
- Targeting **twice-per-year** treatment regimen

[1]Halawa et al., J.Clin. Med., 2021
[2]Risitano et al., Lancet Hematol., 2021

Platform Opportunity

Upside potential in indications beyond lead programs



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