Development of a novel retinal tamponade to replace gas and oil

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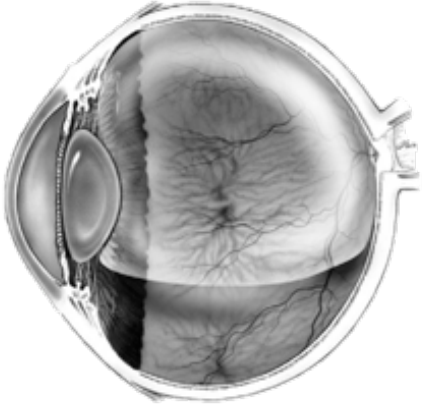
Financial Disclosure

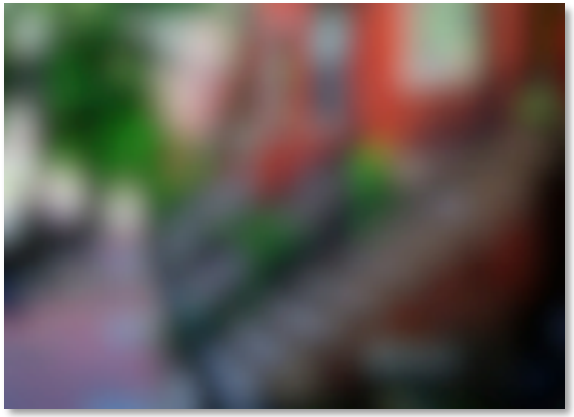
Co-founder and equity co-owner with Tony Stefater MD PhD in a start-up company (Pykus Therapeutics, Inc., Cambridge, MA) which is developing the presented technology for clinical use

Summary

- Gas/oil tamponade is a considerable burden for patients
- Many promising alternatives have not advanced to the clinic
- We have spent the last 5 years developing an *in situ* forming, biodegradable polymer to provide two weeks of continuous retinal tamponade
- No positioning required, no induced refractive shift, no removal surgery
- Human pilot studies to begin Q3 2020

Current tamponade methods are a burden

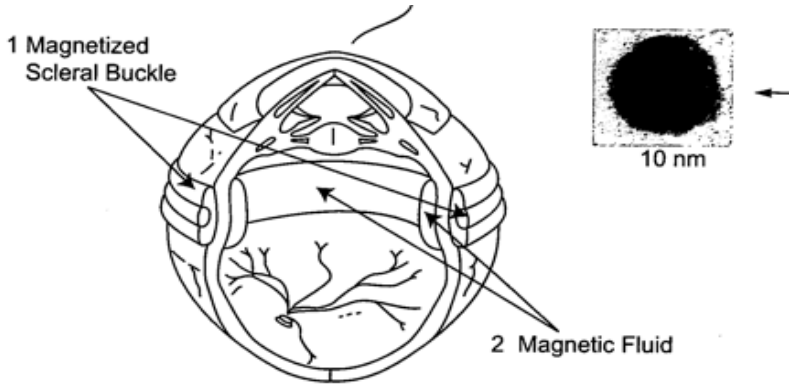


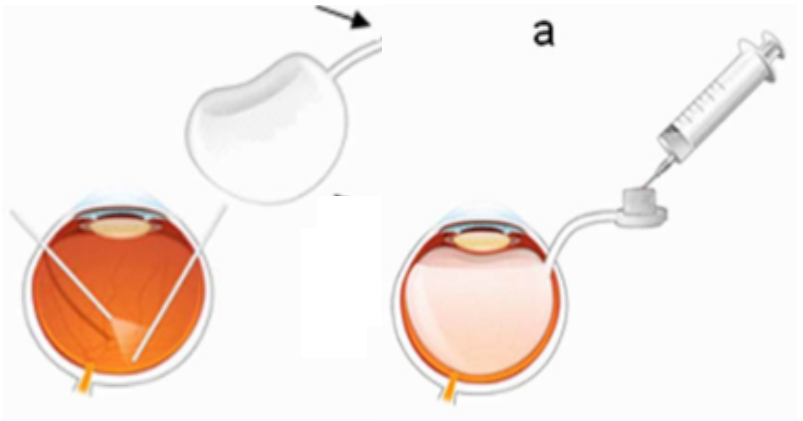


Many promising alternatives have not advanced to the clinic

- Heavy silicone oils
- Magnetic oils
- Combination gas-oils
- Retinal sealants
- Intraocular capsules

- Hydrogels



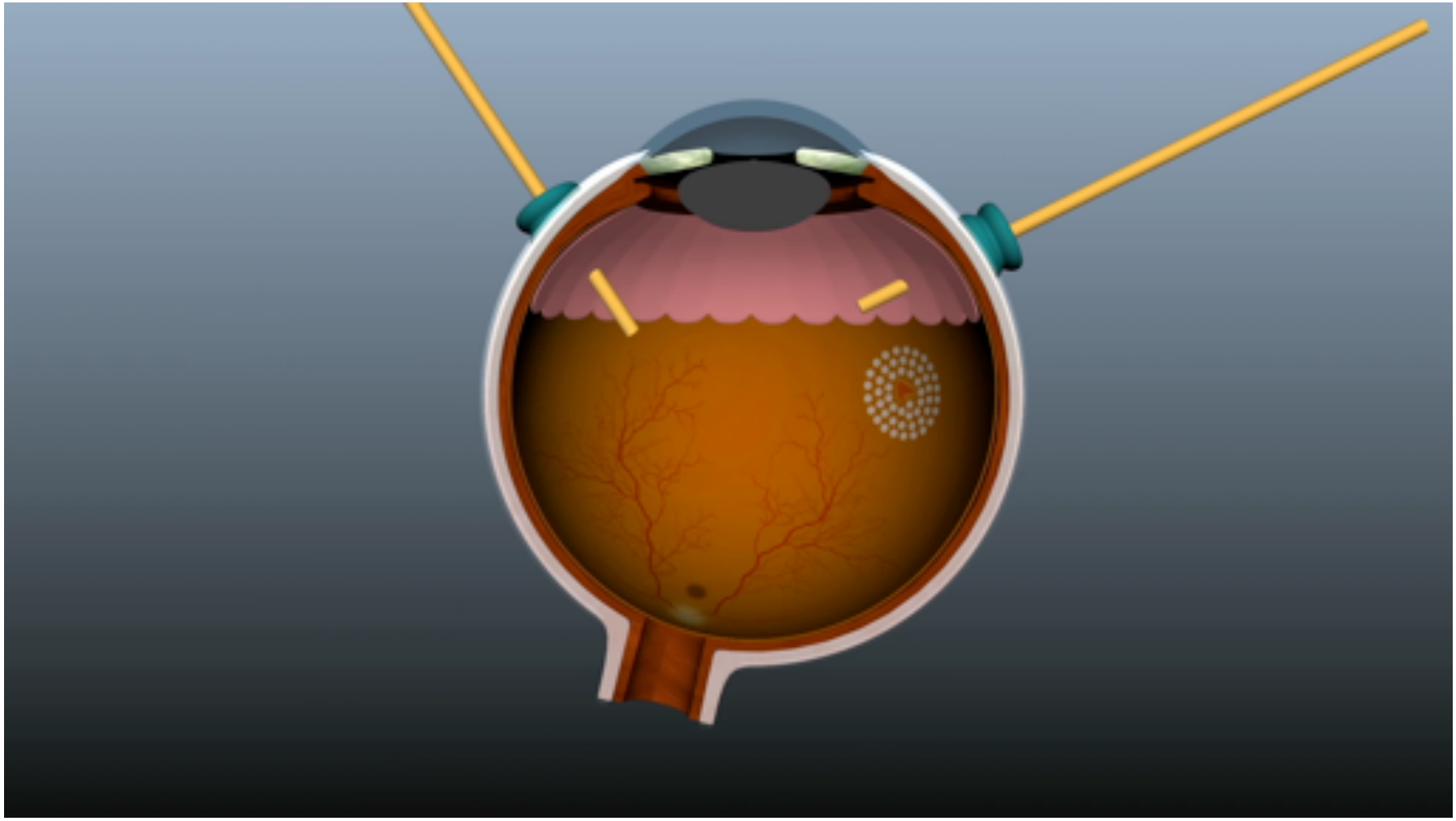


Our Approach

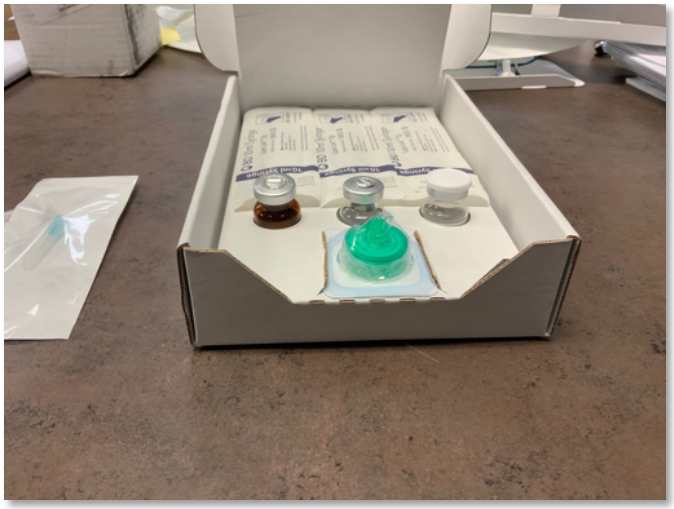
- Find really smart polymer chemists
- Design a tamponade that meets design criteria
- Test it in animals for safety and efficacy
- Manufacture in compliance with Regulatory and Quality standards of the FDA

- Perform clinical trial

Our Approach



PYK-1105 (functionalized PVA-PEG hydrogel)



Physical Characteristics of PYK-1105

Parameter	Result
Time to injection (duration of minimal viscosity after mixing at 25°C)	10 min
Time to gel formation after injection (duration until viscous gel formation at 37 °C)	4 min
Time until degradation	11-14 days
Refractive index	1.3385
Transparency	>90% across visual spectrum

ISO 10993 Biocompatibility Data

- Evaluated in mice and rabbits using standard ISO protocols for evaluating biocompatibility of medical devices

Test	Result
Cytotoxicity	Non-cytotoxic
Intravitreal injection	Non-irritant
Acute systemic toxicity	Non-toxic
Material-mediated pyrogenicity	Non-pyrogenic
Endotoxin	< 0.2 EU/device
Implantation	No macroscopic reaction; minimal to no microscopic reaction
Genotoxicity	Non-mutagenic

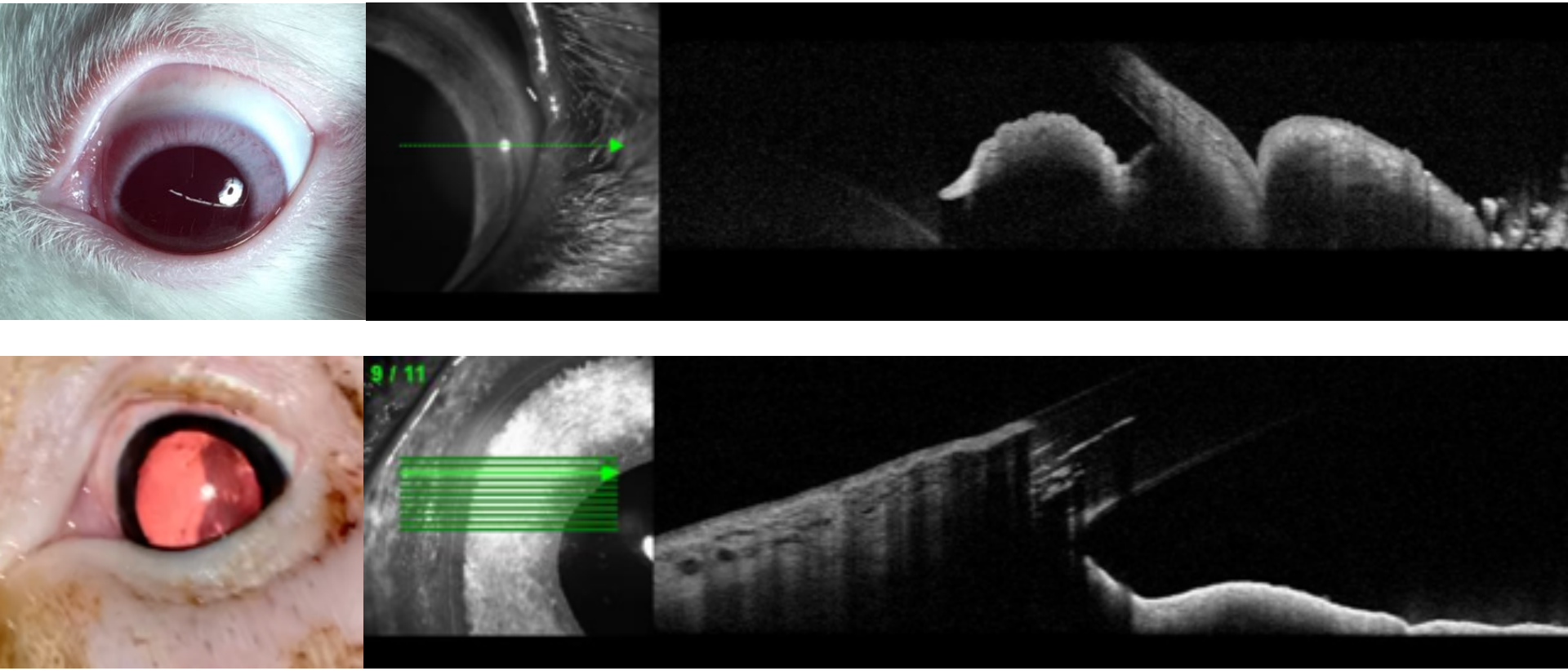
Preclinical studies

- PYK-1105 formulation is well tolerated in a rabbit & mini-pig vitrectomy model
  - 25g vitrectomy/fluid-air exchange/PYK-1105 implantation

- Pre-GLP study in rabbit (4) & mini-pig (5)
  - One pig removed from study on POD3 due to post-op VH

- Manuscript accepted for publication in *JVRD*

Preclinical studies



Representative animals from
post-operative week 4

Preclinical studies

Rabbits

ID	Inflammation Score (conj redness/chemosis + AC reaction + iris)				Notes
	POD7	POD14	POD21	POD28	
PYK-35	3	3	0	0	POD7/14 score for conj injection
PYK-36	2.5	0	0	0	POD7 score for conj injection
PYK-37	1	0	0	0	POD7 score for conj injection
PYK-38	0	0	0	0	

	Vitreous Haze Score				
	POD7	POD15	POD22	POD28	
PYK-35	0	0	0	0	
PYK-36	0.5	0	0	0	
PYK-37	0.5	0.5	0	0	
PYK-38	0	0	0	0	

	Retina score (optic nerve + vasculature + retina + choroid)				
	POD7	POD15	POD22	POD28	
PYK-35	0	0	0	0	
PYK-36	0	0	0	0	
PYK-37	0	0	0	0	
PYK-38	0	0	0	0	

Pigs

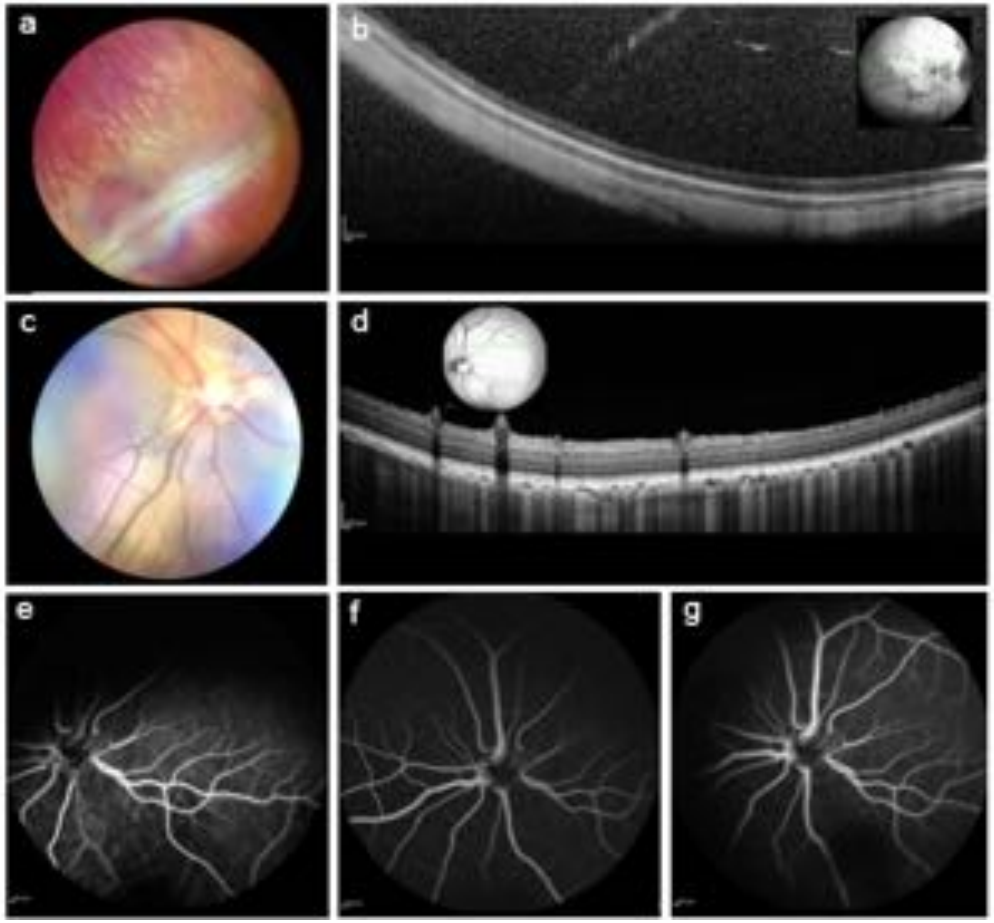
ID	Inflammation Score (conj redness/chemosis + AC reaction + iris)				Notes
	POD7	POD14	POD21	POD28	
6-2	0	0	0	0	
9-2	0	0	0	0	
9-11	0	0	0	0	
4-2	0		0	0	no POD14 exam
89-1	0		0	0	no POD14 exam

	Vitreous Haze Score				
	POD7	POD14	POD21	POD28	
6-2	0	0.5	0	0	
9-2	0.5	0	0.5	0	
9-11	2	1	0.5	0.5	
4-2	0.5		0	0	no POD14 exam
89-1	1		1	1	no POD14 exam

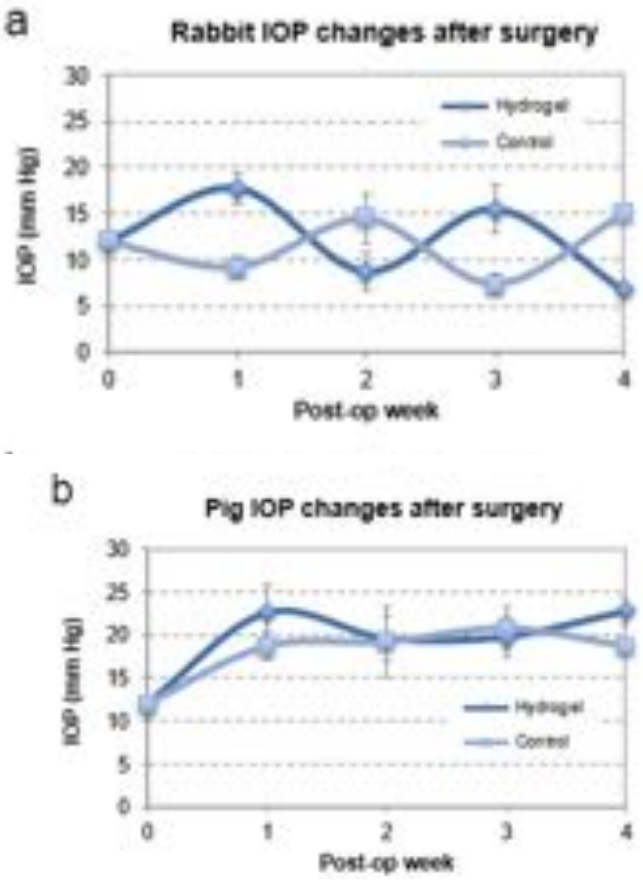
	Retina score (optic nerve + vasculature + retina + choroid)				
	POD7	POD14	POD21	POD28	
6-2	0	0	0	0	
9-2	0	0	0	0	
9-11	1	0	0	0	
4-2	0		0	0	no POD14 exam
89-1	0		0	0	no POD14 exam

Clinical exam scores over first month
(Modified Draize/ McDonald-Shadduck scoring systems)

Preclinical studies

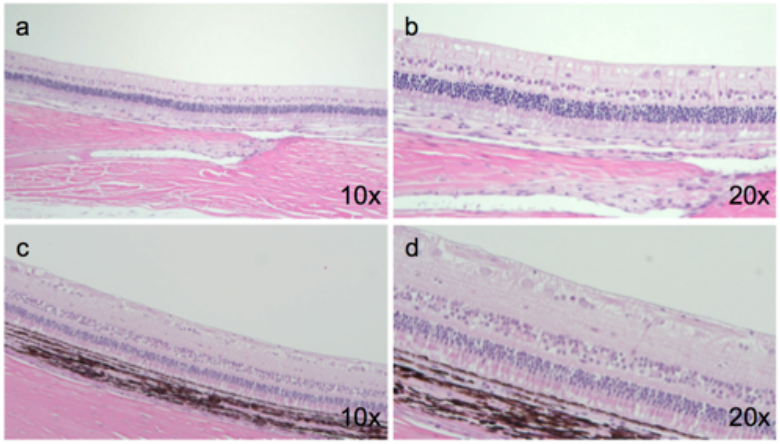


Representative animals from
Post-operative week 4



IOP remains normal
post-operatively

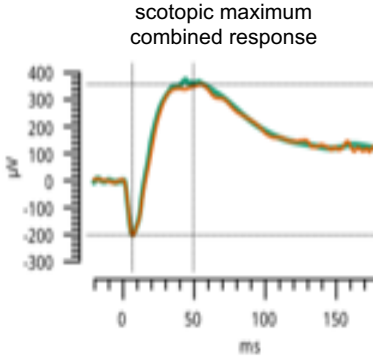
Normal histopath; normal ffERG

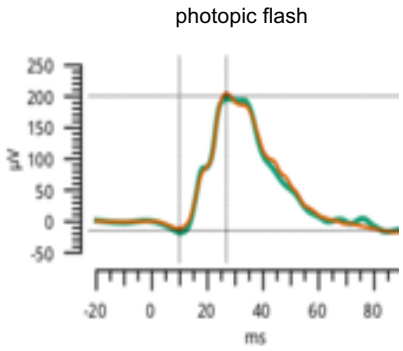


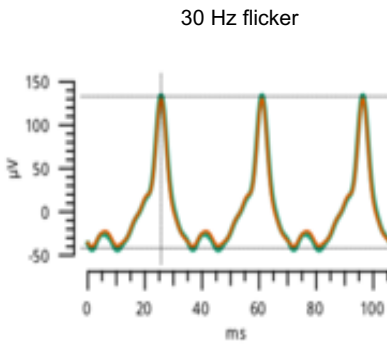
Rabbit H&E, post-operative week 4

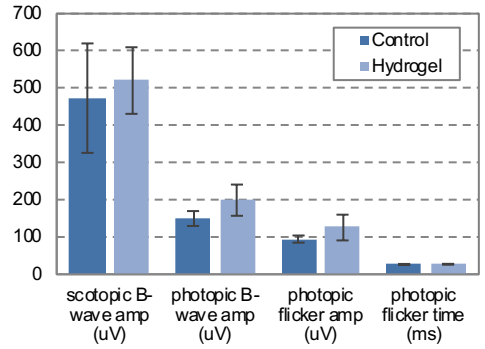
Mini-pig H&E, post-operative week 4

Rabbit, pow4

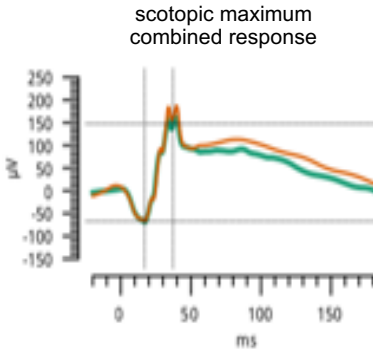


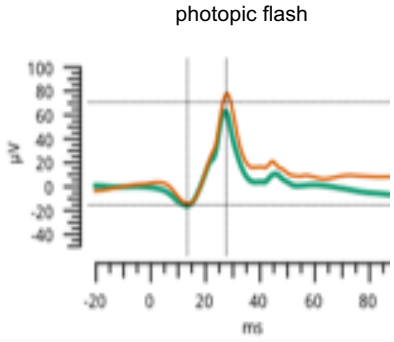


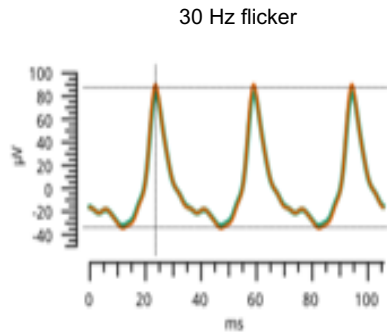


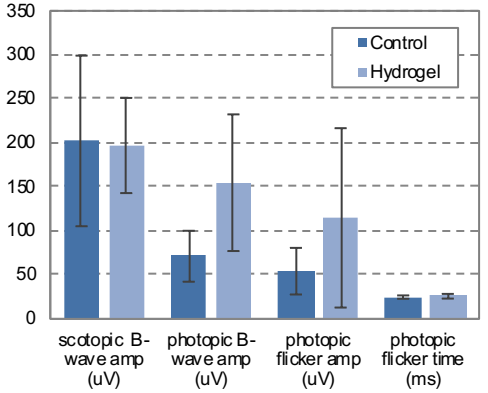


Mini-Pig, pow4









Pilot human study

- 10 patient, first-in-human study to begin Q3 2020
- Multicenter, single cohort, open label study
- Enrollment restricted to patients with RRD who have limited visual potential
- Primary outcome is safety and tolerability
- Patients will be followed for 6 months post-operatively
- Interim study results expected Q1 2021

Team

Leadership Team

James A. Stefater, MD, PhD
President & Cofounder
Vitreoretinal surgeon; Eye Heath Services

Tomasz P. Stryjewski, MD
Chief Scientific Officer & Cofounder
Vitreoretinal surgeon; Tallman Eye
Co-Founder, Helio Vision Inc.

Sameer Sabir
Executive Chairman
Founder & CEO, Brixton
Founder & CEO, Seven Oaks
Founder & CEO, MoMelon

Larry Roth
Product Development
20+ years experience in medical device devopment

Gordon Roberts
Quality
20+ years in medical device quality and regulatory

Maureen O'Connell
Regulatory
20+ years in ophthalmic device regulatory

Olivier Kagan
Project Management
Previously Director of Quality Systems at NSF

Lori Gilmartin, RN
Clinical Operations
20+ years in clinical study mana

Advisors

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