Ocular Drug Delivery Companies Spun Out of the Center for Nanomedicine at the Wilmer Eye Institute / Johns Hopkins

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The Wilmer Eye Institute and Johns Hopkins University School of Medicine

THE CENTER FOR NANOMEDICINE AT JOHNS HOPKINS

MEDICAL INNOVATIONS THROUGH ENGINEERING, SCIENCE AND MEDICINE

Training the Next Generation of Leaders

Advancing science & human health

12 companies launched in 12 years

>$800 million USD invested

Multiple FDA Approved Products

Clinical trials for >15 diseases:

- Ocular, CNS, Fibrosis, Obesity, HIV, COVID-19, more

<u>Leadership</u>

Justin Hanes, Founder & Exec. Director
Rangaramanujam Kannan, co-Director
Peter McDonnell, Wilmer Eye Inst. Director & Chair of Ophthalmology
Laura Ensign, Wilmer Eye Inst. Vice Chair for Research

Example CNM Companies / Company Founders

kala PHARMACEUTICALS

Ocular Diseases
(e.g., Dry Eye, Pain & Inflammation)

GRAYBUG VISION

Ocular Diseases
(e.g., AMD, Glaucoma)

NOVUSBIO & NOVUS VISION

Ocular, GI Tract,
Women's Health

Theraly Pharmaceuticals

Diabetes

Neuraly

CNS Diseases
(e.g., Parkinson's, Alzheimer's)

Theraly FIBROSIS

Fibrosis
(skin, liver, lung, pancreas)

Ashvattha Therapeutics

Oncology, COVID, Ocular

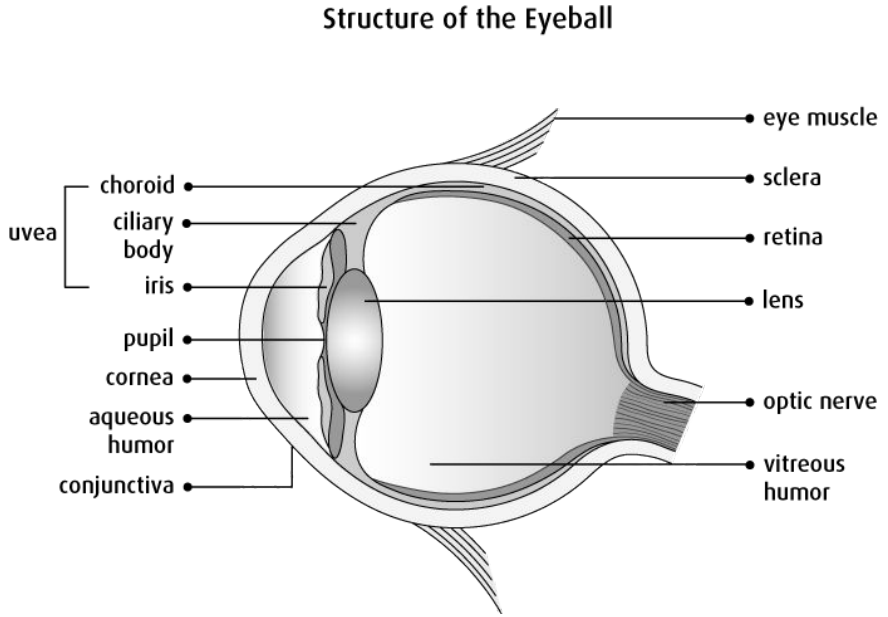
Orpheris

CNS Diseases
(e.g., Autism Spectrum Disorders)

spiral therapeutics
a hearing loss pharmaceutical company

Hearing Loss

Ocular Disease: Front vs. Back of Eye



Front of the Eye Examples	Back of Eye Examples
Glaucoma – IOP Reduction	Glaucoma – Neuroprotection
Dry Eye Disease	Age Related Macular Degeneration
Ocular Pain & Inflammation	Retinal Degenerative Diseases

Typically treated topically (eye drops)

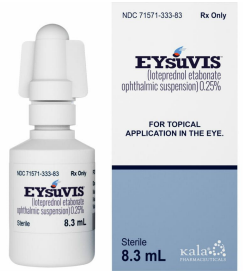
Typically treated by ocular injection

kala PHARMACEUTICALS

- Technology: Mucus Penetrating Particles (“MPP”)
- IPO in 2017
- FDA-approved drugs
  - INVELTYS™ for Ocular Pain & Inflammation
  - EYSUVIS® for Dry Eye Disease

INVELTYS™
(loteprednol etabonate ophthalmic suspension) 1%

EYSUVIS®
(loteprednol etabonate ophthalmic suspension) 0.25%



graybug
vibrant.vision

- Technology: Long-acting injectable non-inflammatory microparticles
- IPO in 2020
- Pipeline Includes:
  - Twice yearly injectable for AMD
    - preclinical work published in ***Nature Comm.*** in 2020
  - Long-acting injectable for Glaucoma
  - Long-acting injectable for Retinitis Pigmentosa
  - Long-acting injectable for Geographic Atrophy
  - Gene therapy for Corneal Disease (MPS1)

Particle aggregation and bioabsorption in humans: GB-102 (Sunitinib; anti-VEGF for wet AMD)

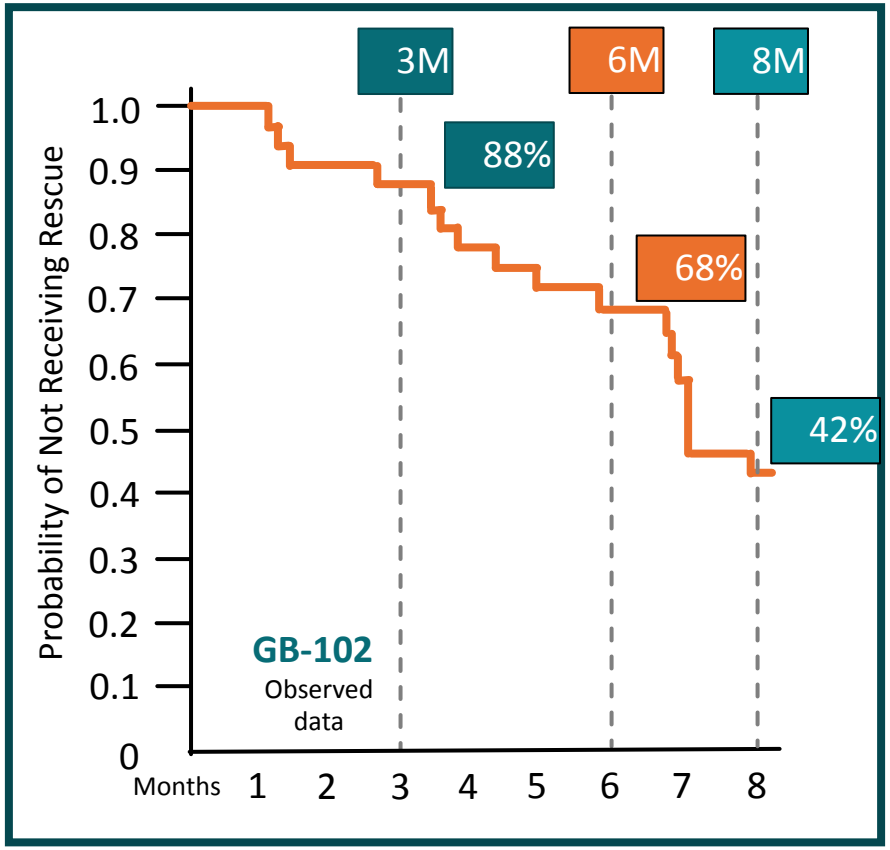
Non-inflammatory & Sustained >6 mo

graybug vibrant.vision

Phase 1/2a in Age Related Macular Degeneration – Rescue Free Survival

	Rescue criteria
BCVA	≥ 10 ETDRS letters from baseline ***with*** intra-/sub-retinal fluid judged to be cause of BCVA loss
CST	> 75 µm from baseline
Hemorrhage	Presence of vision-threatening hemorrhage due to nAMD

LADDER: ≥ 10 letter loss compared to best on-study measurement or ≥ 5 letter loss compared with average of last 2 visits; ≥ 75 um CST with average of last 2 visits or ≥ 100 um compared with lowest on-study average; new macular hemorrhage



GB102 1mg Lasted ≥ 6 Months in 88% of Patients

graybug vibrant.vision

Hanes Lab in 2011 – GrayBug Vision Founded

Grayson
“Gray”

Riley
“Bug”

Graybug IPO
Sept. 25, 2020

New Method to Form Gels that Conform to Mucosal Surfaces

(12) **United States Patent**
Maisel et al.

(10) **Patent No.: US 10,485,757 B2**
(45) **Date of Patent: *Nov. 26, 2019**

(54) **HYPOTONIC HYDROGEL FORMULATIONS FOR ENHANCED TRANSPORT OF ACTIVE AGENTS AT MUCOSAL SURFACES**

(71) Applicant: **The Johns Hopkins University**, Baltimore, MD (US)

(72) Inventors: **Katharina Maisel**, Troy, MI (US); **Laura Ensign**, Towson, MD (US); **Justin Hanes**, Baltimore, MD (US); **Richard Cone**, Baltimore, MD (US)

(73) Assignee: **The Johns Hopkins University**, Baltimore, MD (US)

9/5153 (2013.01); *A61K 31/09* (2013.01); *A61K 31/352* (2013.01); *A61K 31/365* (2013.01); *A61K 31/52* (2013.01); *A61K 31/675* (2013.01); *A61K 47/10* (2013.01)

(58) **Field of Classification Search**
CPC .. A61K 2300/00; A61K 31/09; A61K 31/365; A61K 47/10; A61K 31/352; A61K 31/52; A61K 31/675; A61K 9/0034; A61K 9/5146; A61K 9/5153; A61K 8/90; A61K 9/0031; A61K 9/06
See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,997,652 A 3/1991 Wong

1. An aqueous hypotonic polymeric formulation for use as a barrier and/or in the delivery of a therapeutic, prophylactic, diagnostic or nutraceutical agent to a mucosal or epithelial surface comprising: a gel-forming polymer that is a block copolymer comprising at least one unit that is polyoxyethylene or polyoxypropylene at a concentration which is less than the critical gel concentration of the polymer at the time of application to the mucosal or epithelial surface, which increases in concentration as water is absorbed from the formulation to or above the critical gel concentration of the polymer and a temperature between room temperature and body temperature, thereby forming a gel on the mucosal or epithelial surface, one or more excipients forming a hypotonic formulation of the polymer, and a therapeutic, prophylactic, diagnostic or nutraceutical agent.

6. The formulation of claim **1**, wherein the mucosal or epithelial surface is selected from the group consisting of oral, pharyngeal, esophogeal, pulmonary, ocular, aural, nasal, buccal, lingual, vaginal, cervical, genitourinary, alimentary, anorectal, and skin surfaces.

OcuGel^{TM}: Breakthrough in Topical Ocular Drug Delivery


nature biomedical engineering

ARTICLES

Gelling hypotonic polymer solution for extended topical drug delivery to the eye

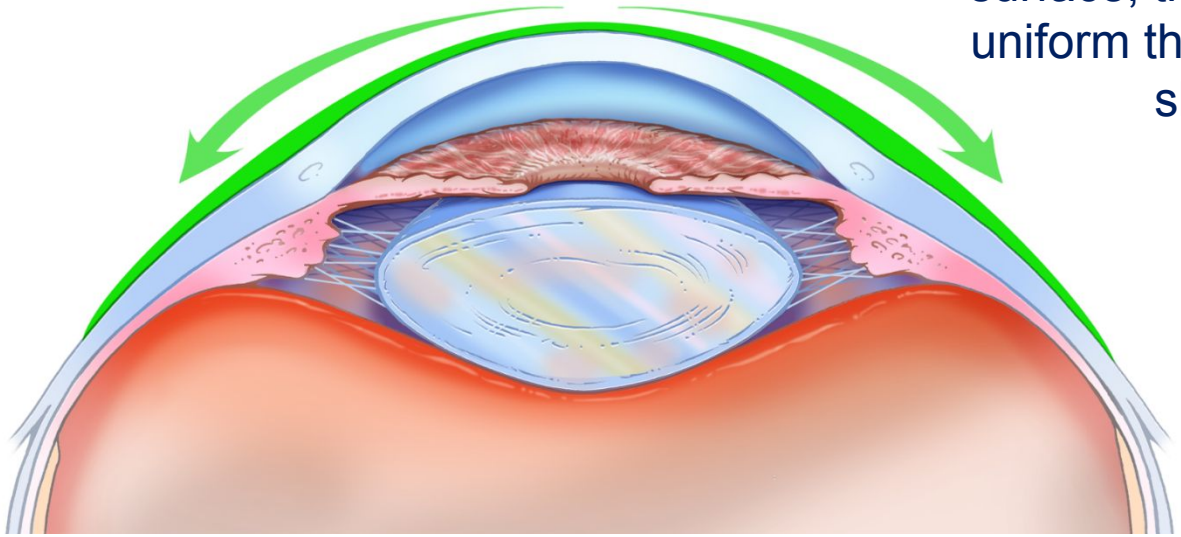
Prof. Laura Ensign

NOVUS VISION

Kim et al, *Nature BME,* 2020

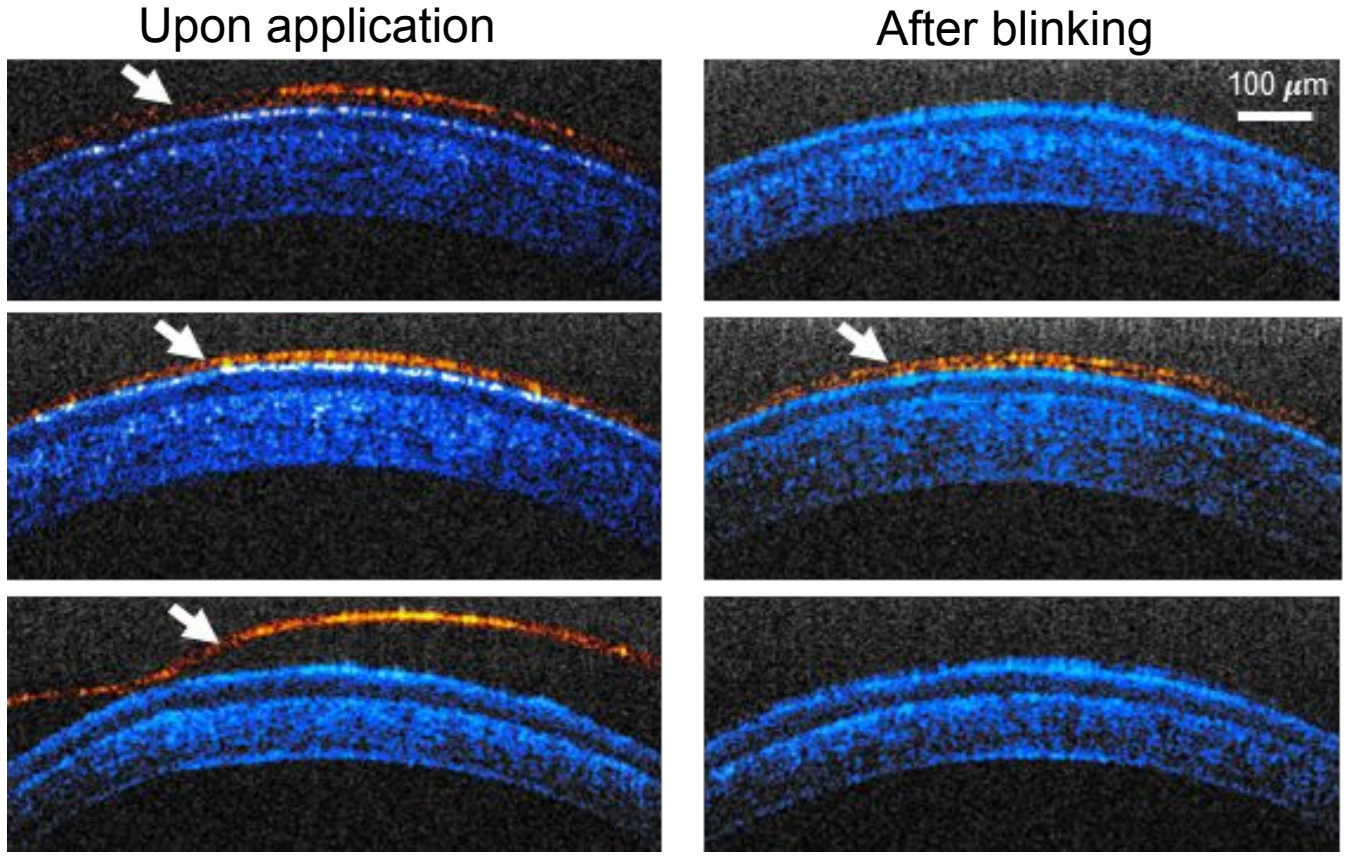
OcuGel™: soothing, solubilizing, controlled release vehicle

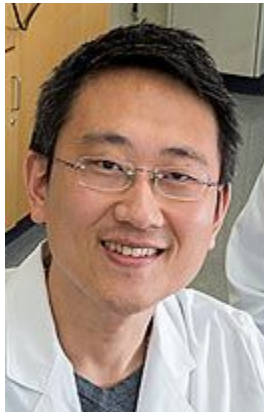
OcuGel™ can be paired with a wide variety of drugs into water-based solutions that are easily administered as an eyedrop.



OcuGel™ spreads over the ocular surface, then subsequently forms a uniform thin gel that traps drug and slowly releases it.

OcuGel™ Forms Uniform Thin Layer on the Eye and is Not Easily Blinked Away





Yoo Chun Kim, PhD

False colored OCT images
Blue = eye
Red = eye drop

Kim et al., Nature BME 2020

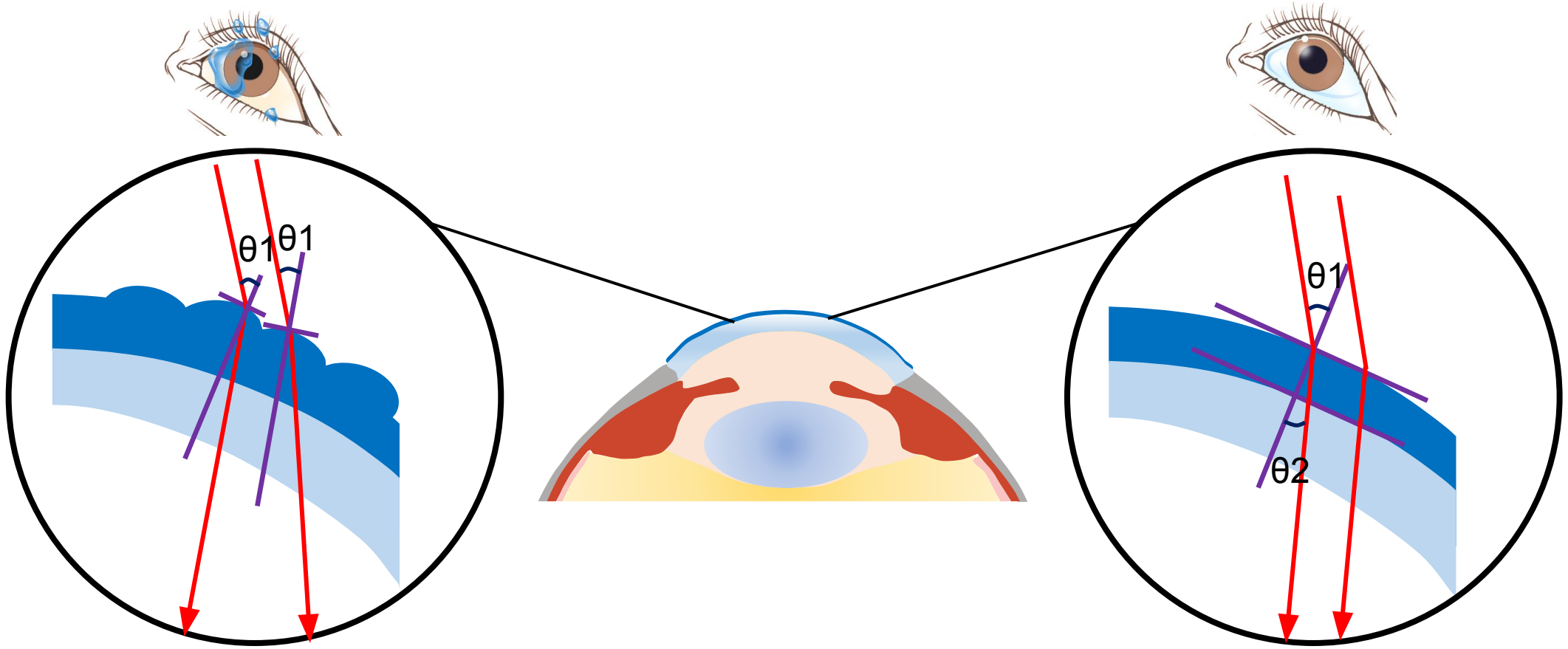
OcuGel™ – Benefits of a Gel without the Drawbacks

Traditional Gels (uneven)

Blur Vision, Uncomfortable, Cleared Faster

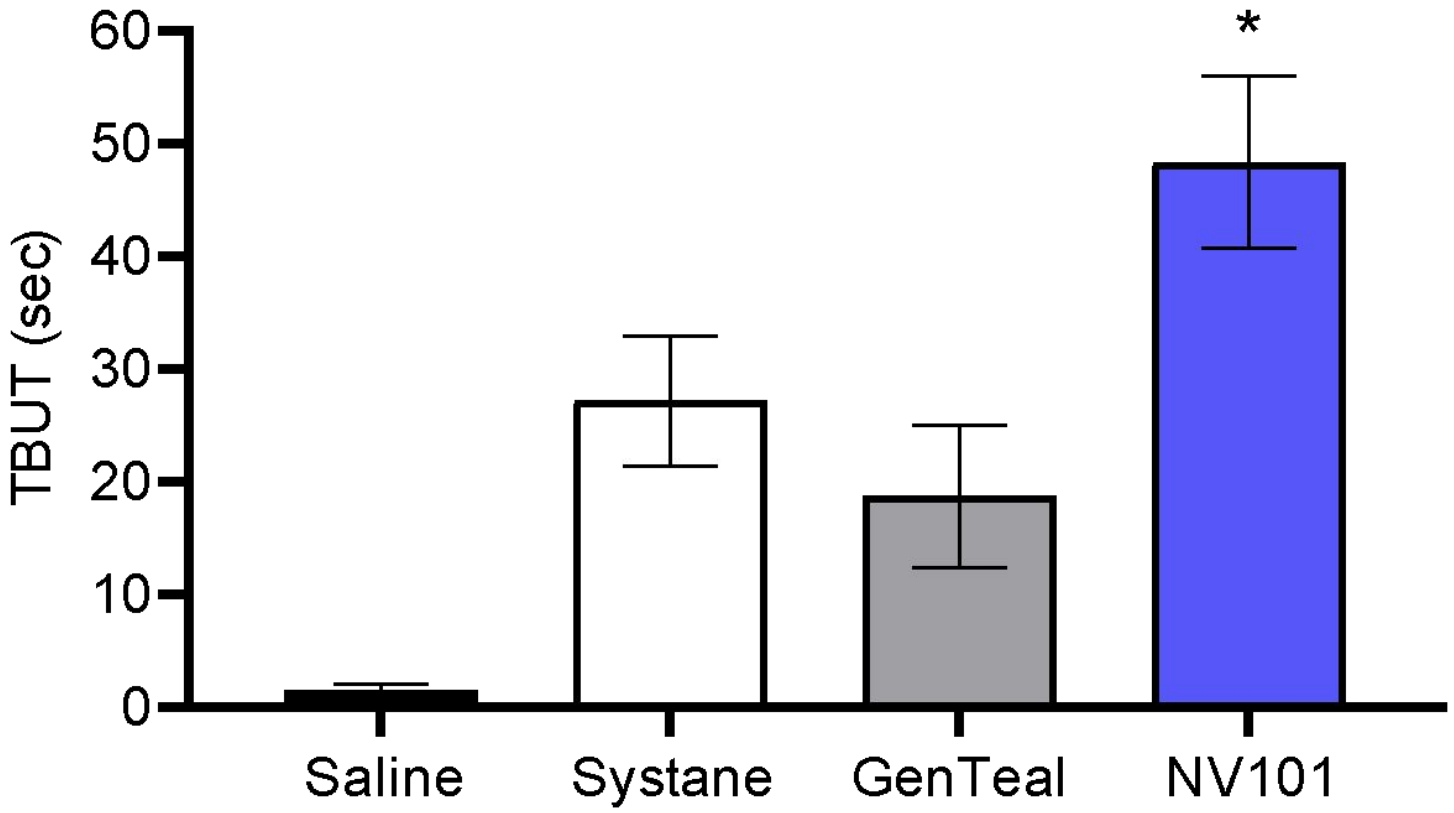
OcuGel™ (Uniform)

Optically Clear, Comfortable, More Durable



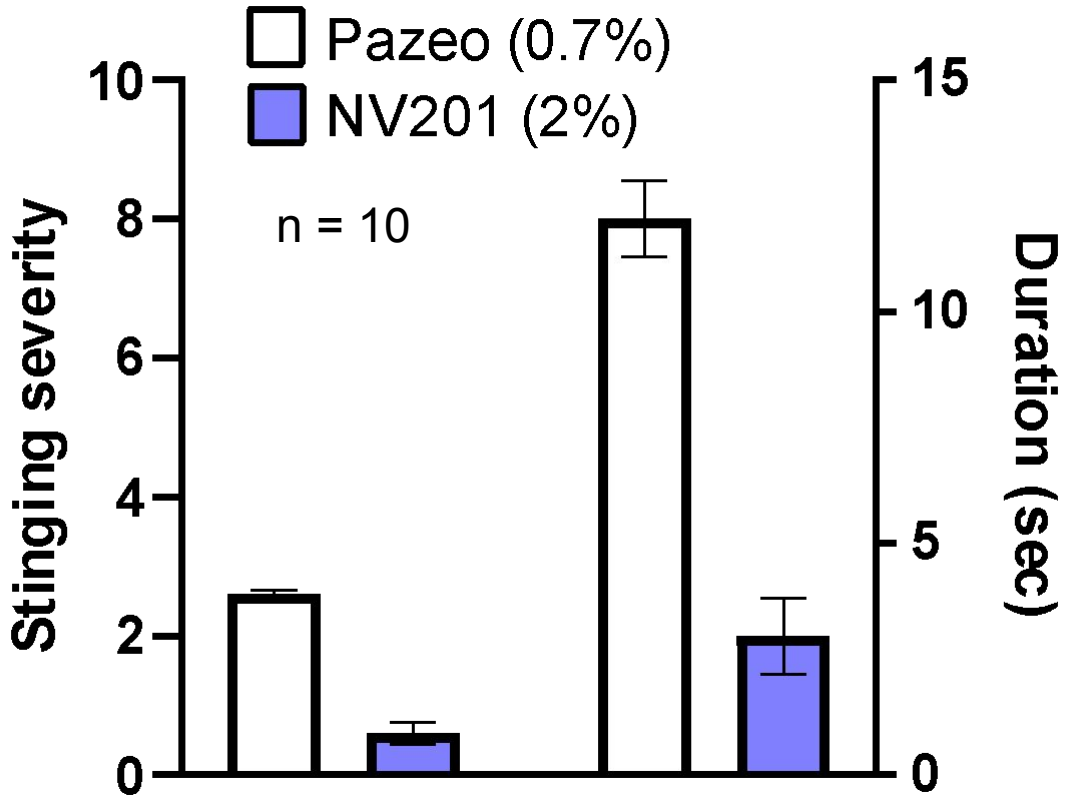
OcuGel™ provides long-lasting surface lubrication

NV101 – OcuGel™ Vehicle is a Superior Artificial Tear Product Candidate in Rabbits



Superior tear break up time (TBUT) compared to #1 tear on US market

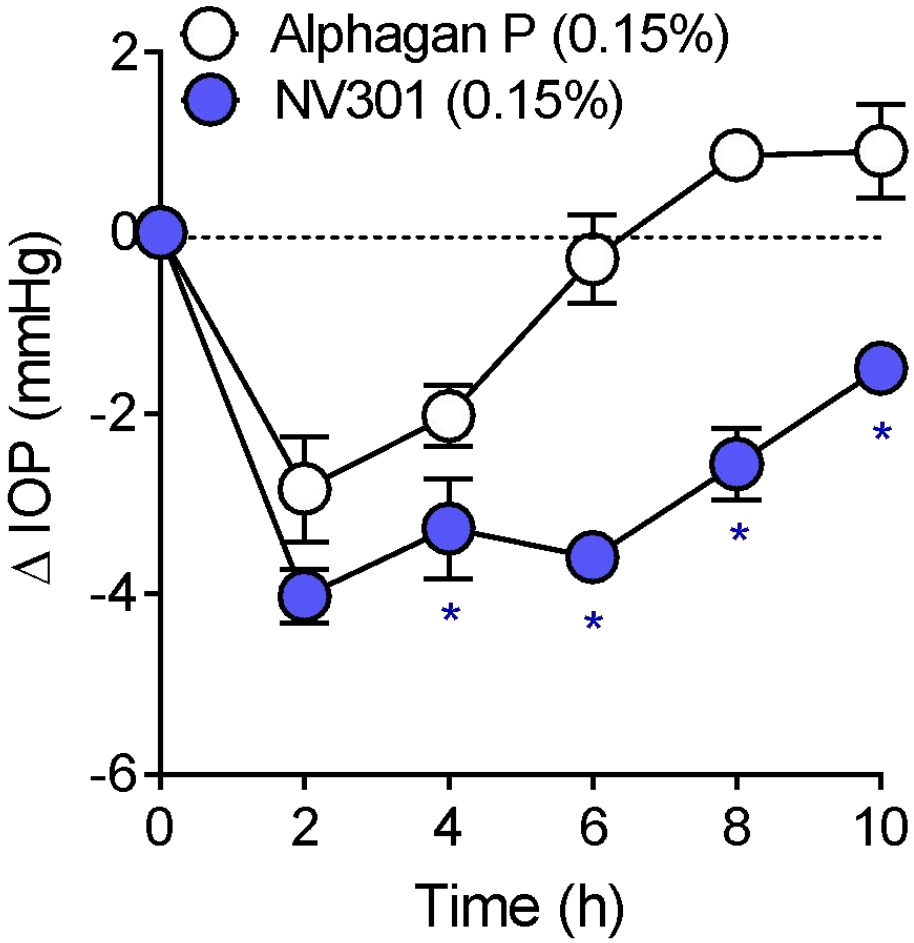
Superior comfort in human subjects



Stinging severity
0-1 = No stinging/burning to trace (e.g. tap water)
10 = Severe stinging and burning (e.g. jalapeno pepper sauce)

OcuGel™ improves efficacy of brimonidine

Brimonidine 0.15% for Glaucoma



NV301 shows superior IOP lowering in this study in normotensive NZW rabbits

Alphagan P 0.15%, IOP lowering effect is lost by t=6 h (TID product)

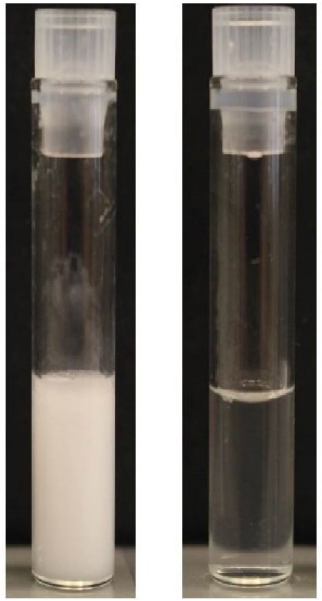
NV301 IOP reduction lasts >10h

NV301 potential for QD product, or BID with superior IOP lowering

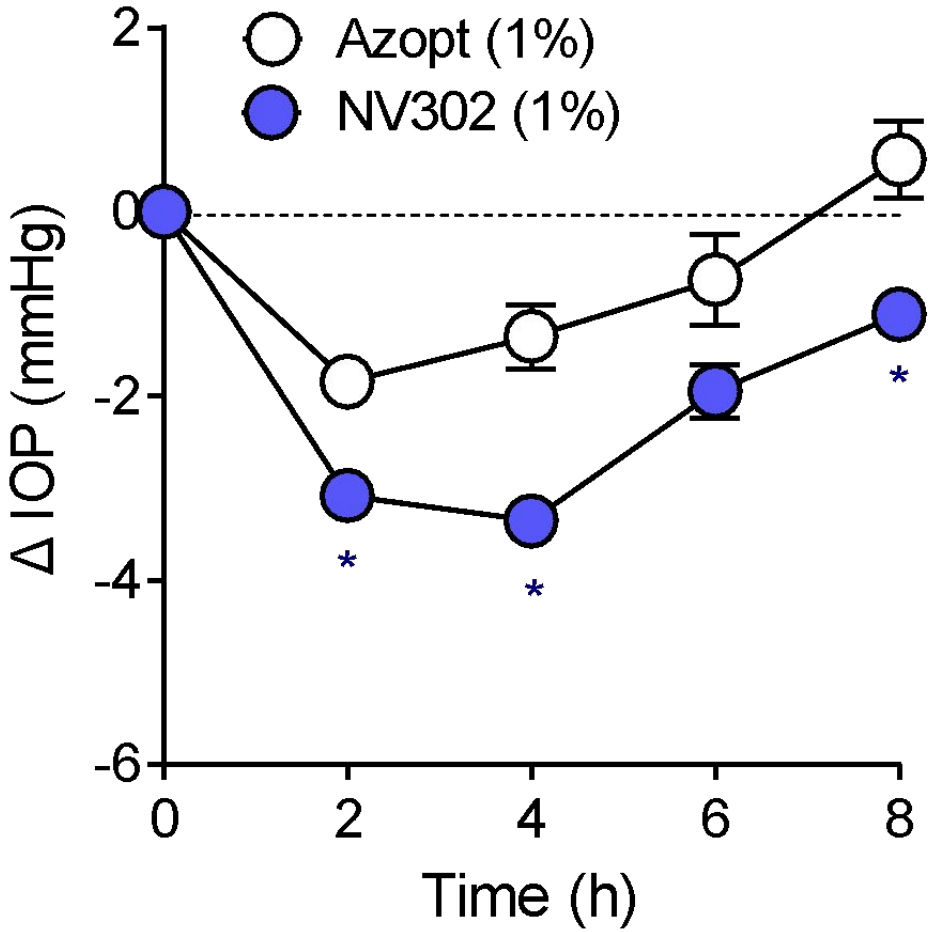
Kim et al, *Nature BME,* 2020

OcuGel™ improves efficacy of brinzolamide

Brinzolamide 1% for Glaucoma



Azopt NV302



NV302 shows superior IOP lowering in this study in normotensive NZW rabbits

Market leader, Azopt 1%, is a TID product

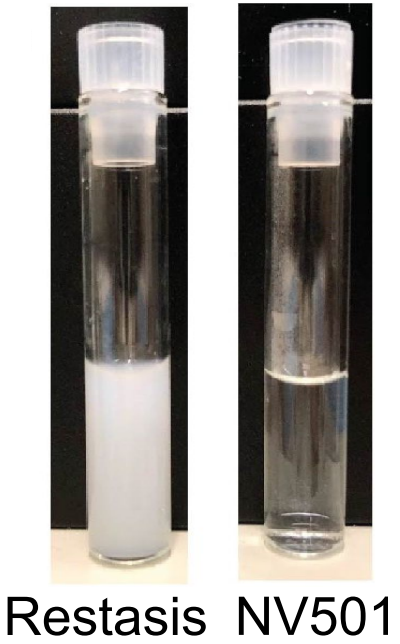
NV302 has potential for QD or BID dosing and superior IOP lowering

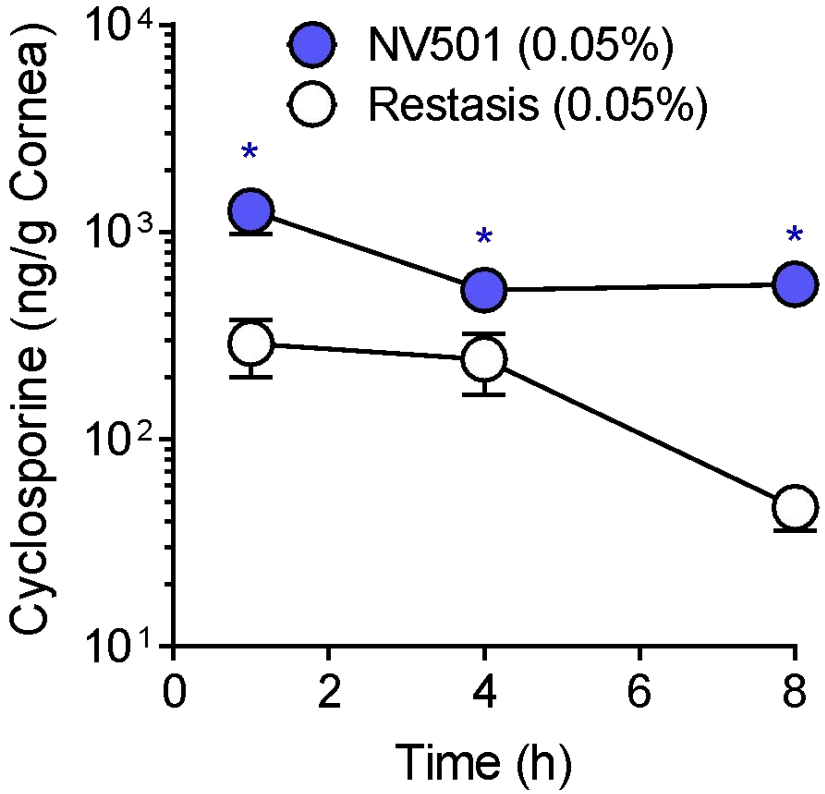
QD prostaglandin + CAI product would be significant

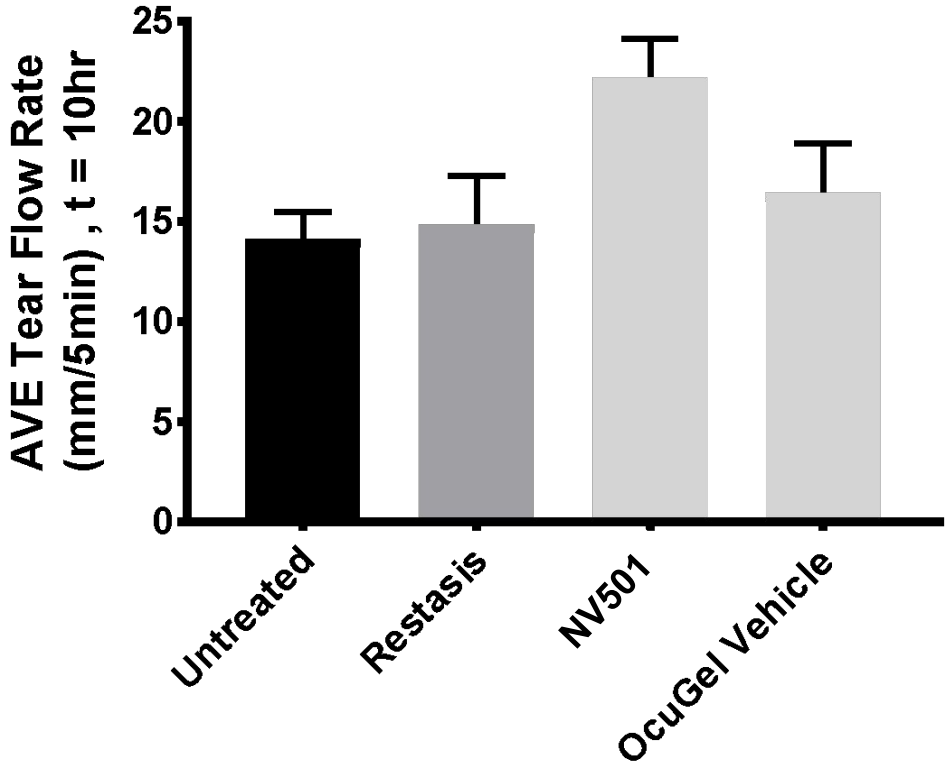
Kim et al, *Nature BME,* 2020

OcuGel™ improves delivery of cyclosporine

CsA 0.05% for Dry Eye Disease







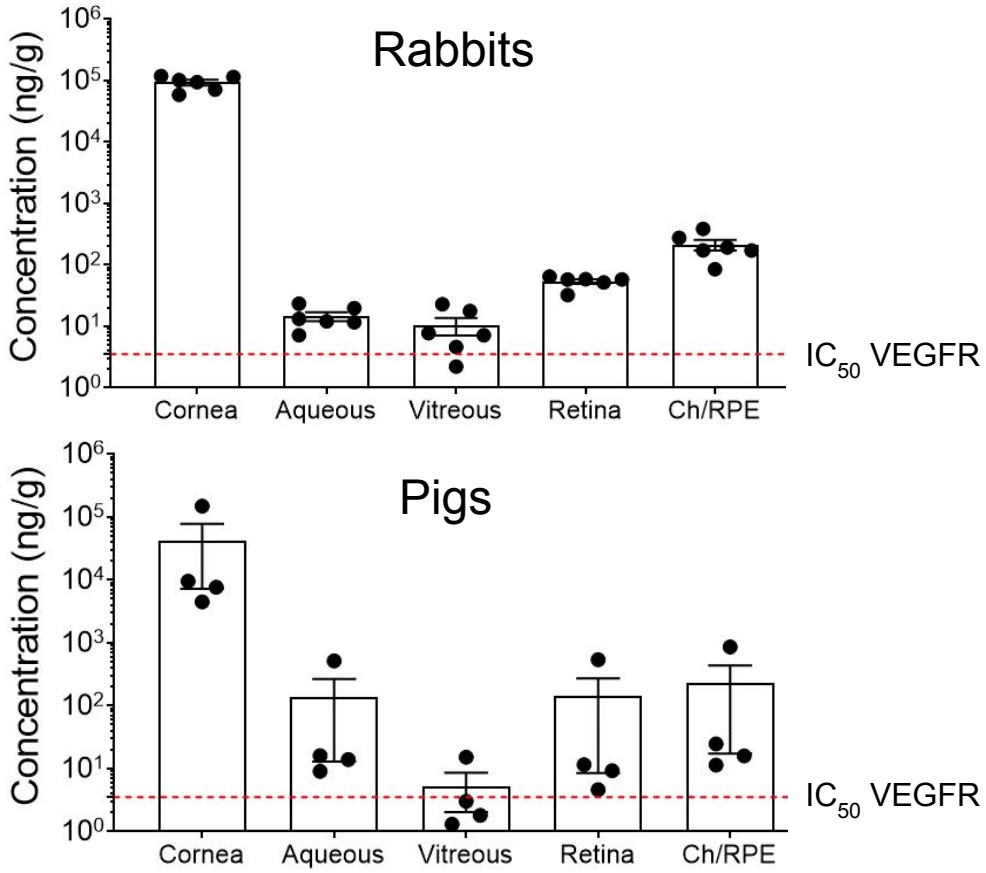
Potential for QD Dosing & Faster Onset of Action

Kim et al, *Nature BME,* 2020

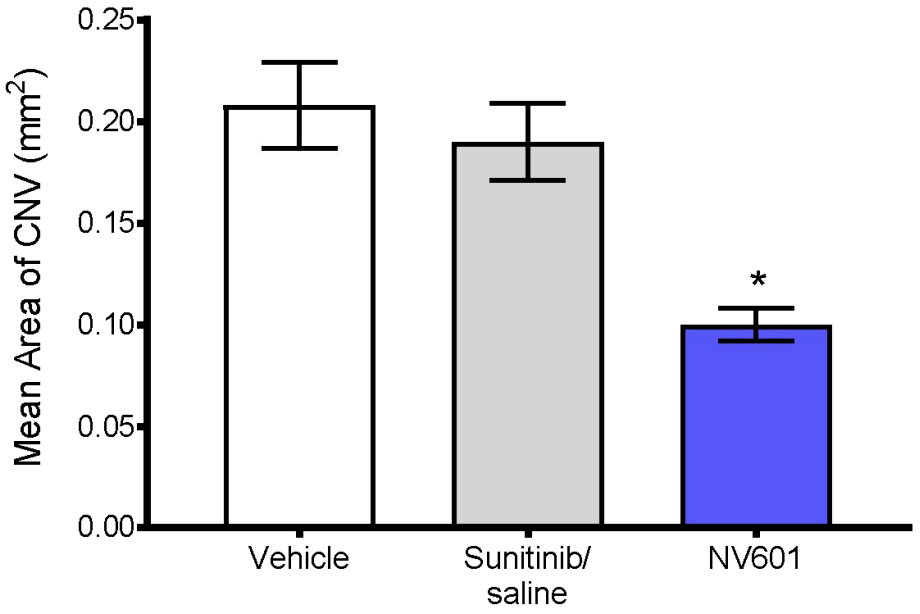
Effective Eye Drop for AMD – POC in Large Animals (QD Dosing)

Sunitinib 0.4% for Neovascular AMD

Sunitinib Drug Levels
NV601



Efficacy in Pigs – wAMD Model
NV601



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Kim et al, *Nature BME,* 2020

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