

Starting a career in start-ups (during a global pandemic)

Laura Ensign, Ph.D.

CRS 2022 Annual Meeting & Expo

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada

Advanced Delivery Science

Starting a career in start-ups (pandemic edition)

- Freya Biosciences, March 2020



- NovusBio, LLC, March 2021

NOVUS

- Novus Vision Inc, July 2021

VISION

- Zephyrus Therapeutics, LLC, April 2022



CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



“Growing up” in the right environment

“Mucus-penetrating particle” technology

- Founded at JHU in 2009
- Joint patents filed 2011/2012
- IPO 2017
- First product approved 2018
- Second product approved 2020



CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



“Growing up” in the right environment



kala•
PHARMACEUTICALS



CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

July 11 – 15, 2022 | Montreal, Canada

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



“Growing up” in the right environment



CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



Learning a new skill set

- The key to doing anything new is to learn from people who know what they are doing (apprenticeship)
- In research, we naturally seek to collaborate with those who have complementary skillsets
- The best collaborations are based on trust and mutual respect of skillsets



CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



Many (non-research) competencies needed for successful start-ups

- Legal (formation documents, confidentiality agreements, consulting agreements, board agreements, partnerships, intellectual property, licensing, etc.)
- Fundraising
- Business development
- Administrative (taxes, accounting, ordering)
- Regulatory
- Clinical trial design
- Marketing/brand development



CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



Novus Vision mentors (and co-founders)



Justin Hanes, Ph.D.
Founder, Director, CEO

Founder of Kala Pharmaceuticals (Nasdaq: KALA), GrayBug Vision (Nasdaq: GRAY; former CEO & CSO), Neuraly (acquired), Theraly Fibrosis (acquired), Orpheris, and Ashvattha Therapeutics.

Co-inventor of OcuGel



Jerry Cagle, Ph.D.
Founder, President
Chief Operating Officer

Long time Global Head of Alcon Research and Development.

Experienced in developing topical and intraocular products across broad therapeutic classes.

Brought over 300 ophthalmic products to market



CRS 2022 Annual Meeting & Expo

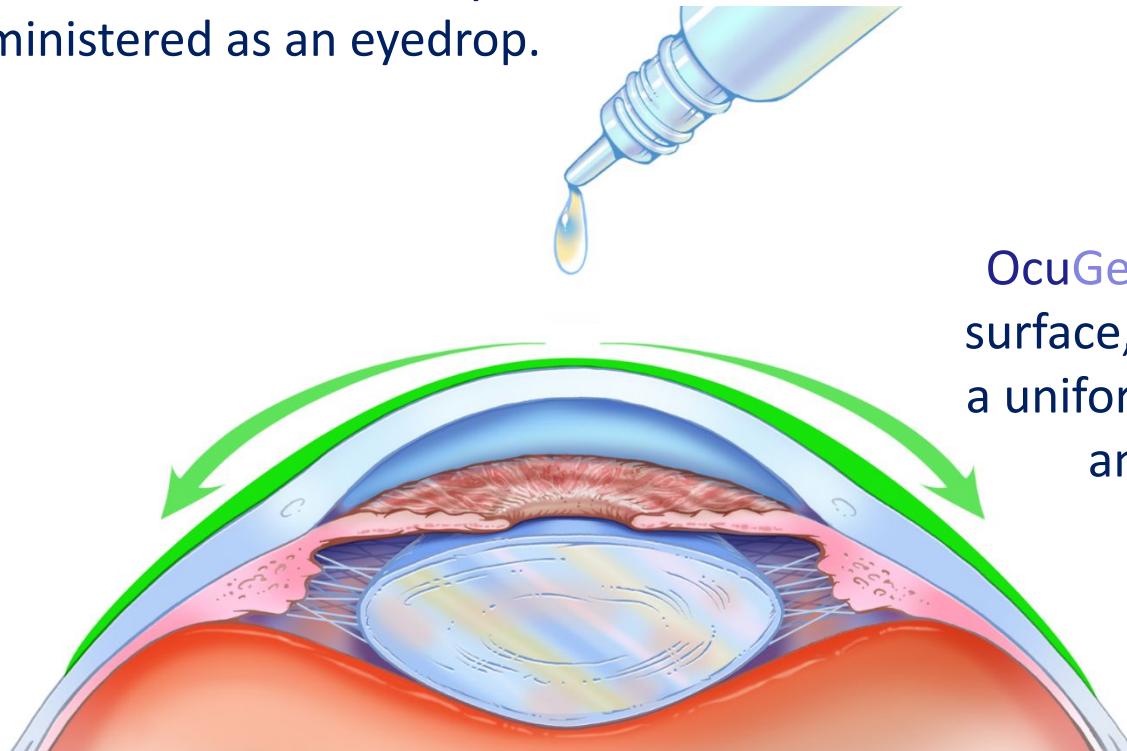
Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



The technology: OcuGel

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.



CRS 2022 Annual Meeting & Expo

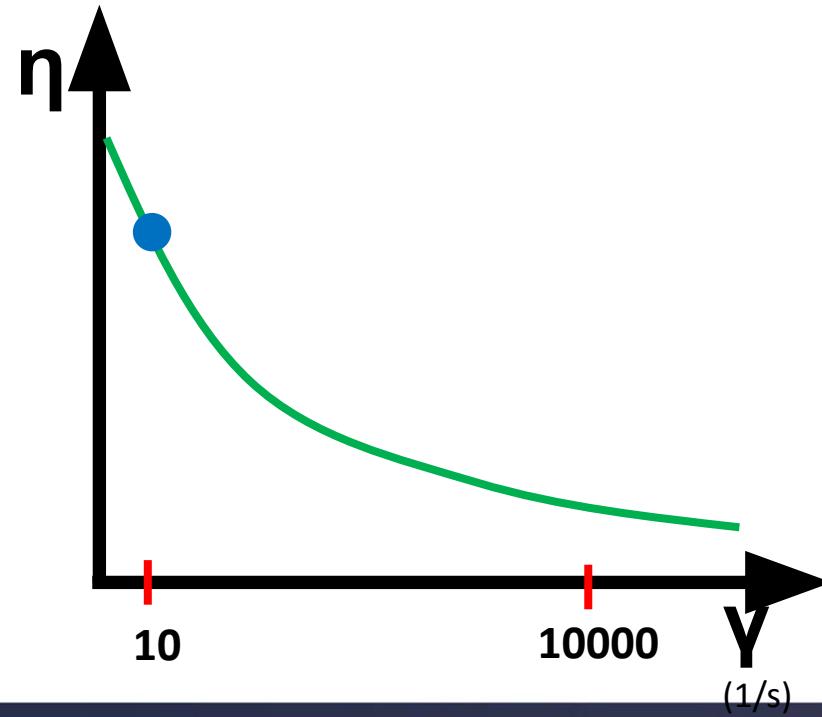
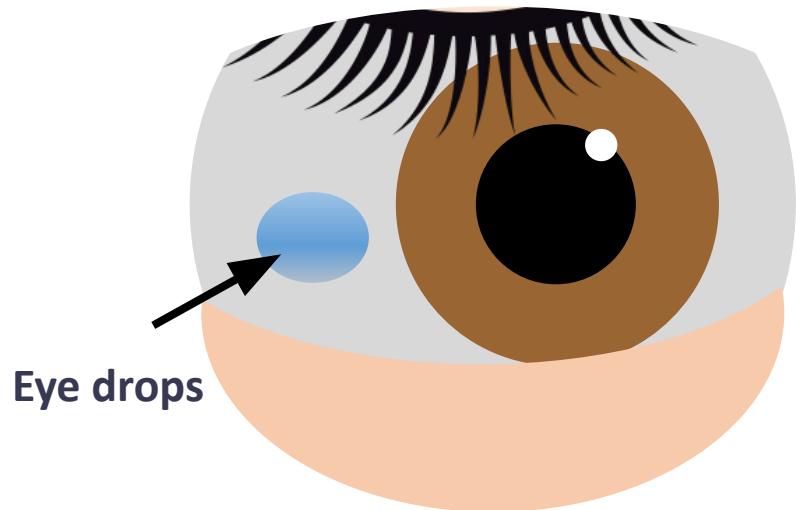
Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



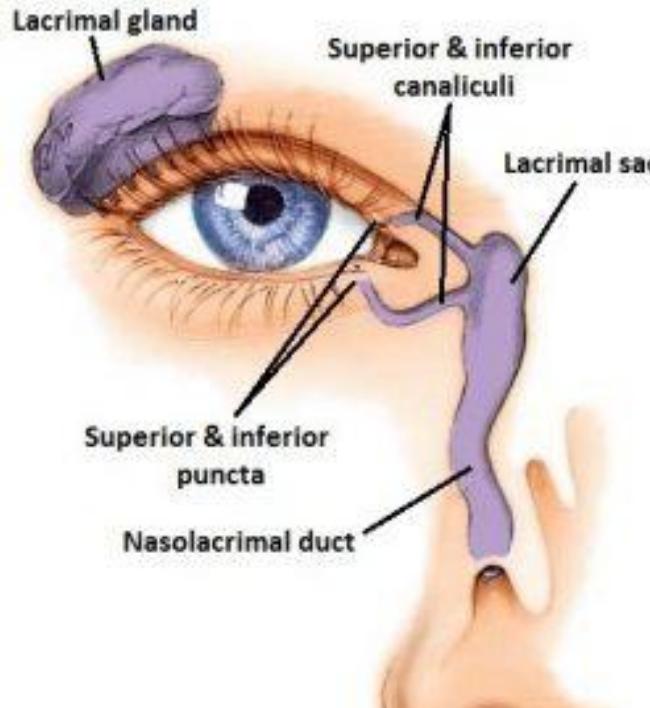
Why do we have to use eye drops so often?

Blinking 12-20 times/min + reflexive blinking and tear production

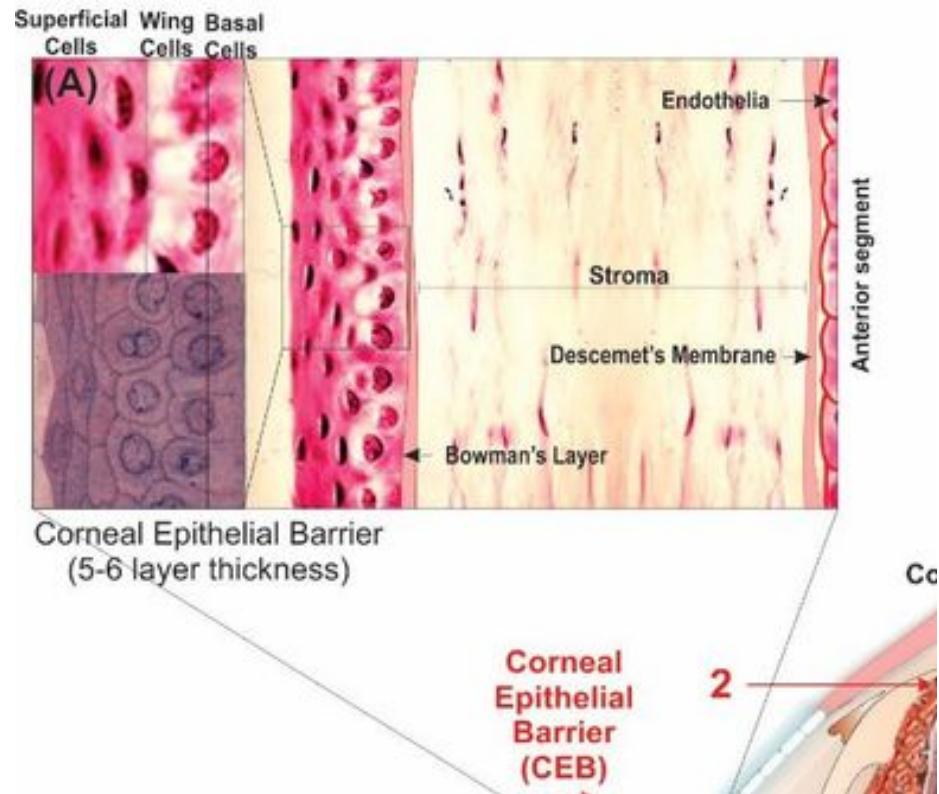


Why do we have to use eye drops so often?

Nasolacrimal drainage



Corneal barrier



https://www.researchgate.net/figure/Schematic-demonstration-of-the-anatomy-and-the-biological-membranes-and-barriers-of-the_fig1_304186889

<https://ocvermont.com/tear-duct-surgery/>

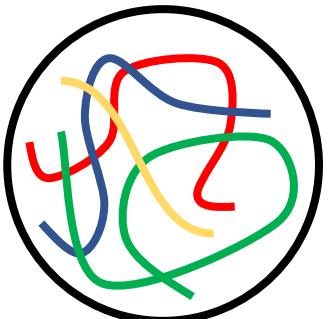
CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



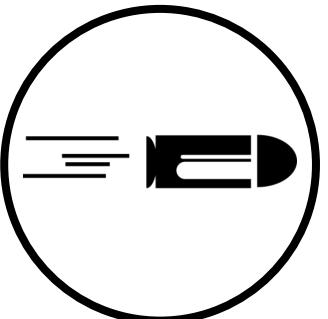
Strategies for improving topical ocular drug delivery



Viscosity Enhancer: Improve corneal residence time and to improve bioavailability

Materials: Polyacrylic acid (polycarbophil), Gellan Gum, Poloxamer.

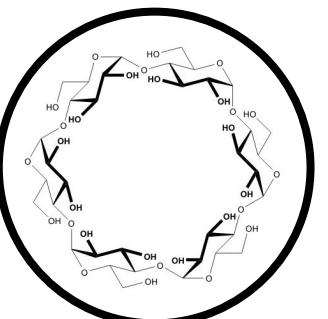
Example: Ocular ointments, creams, and in-situ gel.



Penetration Enhancer: Enhance corneal absorption by modifying corneal integrity

Materials: Chelating agents (EDTA), preservatives (benzalkonium chloride).

Example: Selected in some commercial eye drop formulation as preservatives.



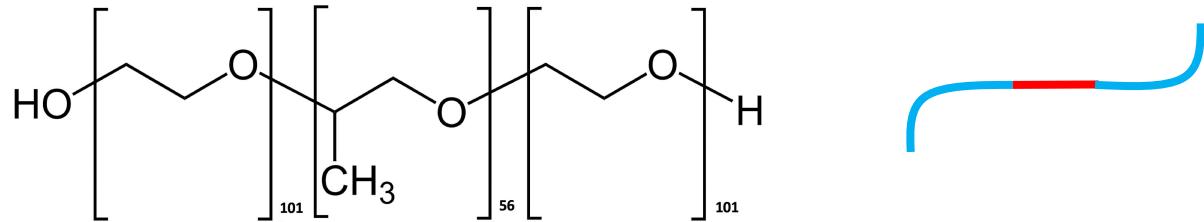
Solubility Enhancer: Increase the hydrophobic drug solubility

Materials: Cyclodextrins (2-hydroxypropyl-cyclodextrin), surfactants

Example: Clorocil ® (Chloramphenicol), Pazeo®

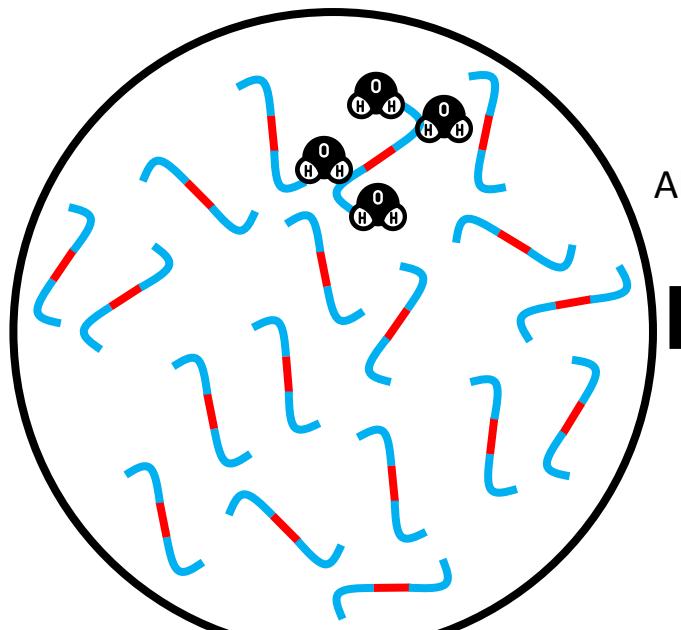


Pluronic/Poloxamer thermogels

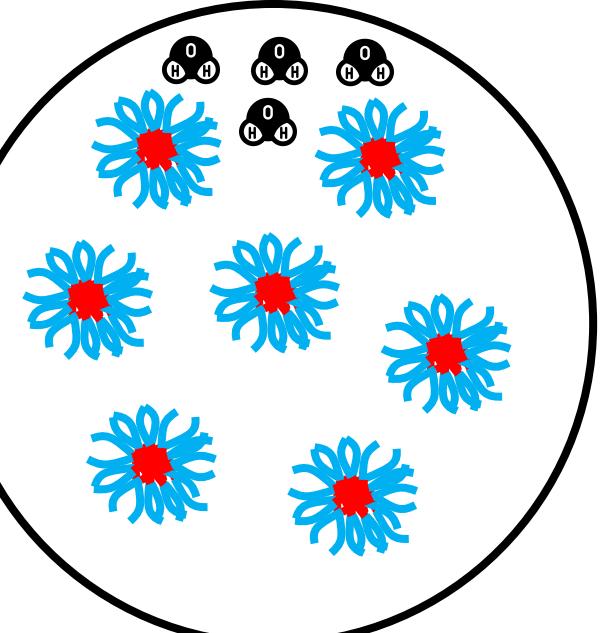
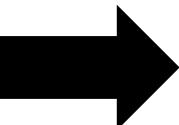


$$\Delta G = \Delta H - T \Delta S$$

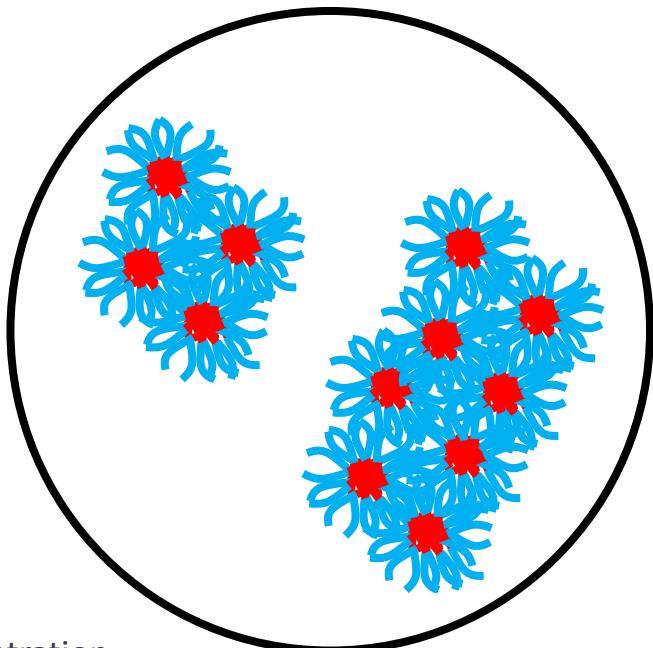
$$\Delta G = \Delta H - T \Delta S$$



Above CMC



Above CGC



CMC = Critical Micelle Concentration

CGC = Critical Gel Concentration

Bodratti, A., (2018). *J functional biomat*, 9(1), 11.



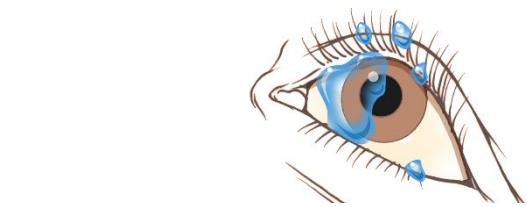
CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

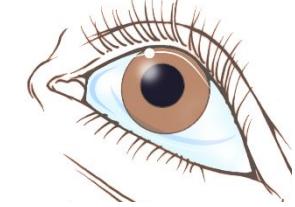
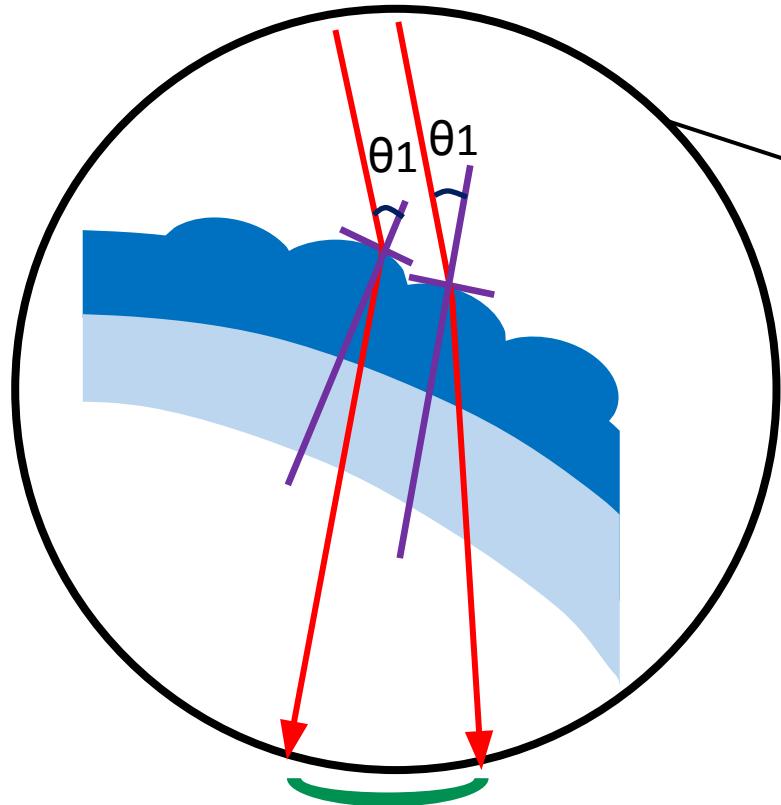
July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



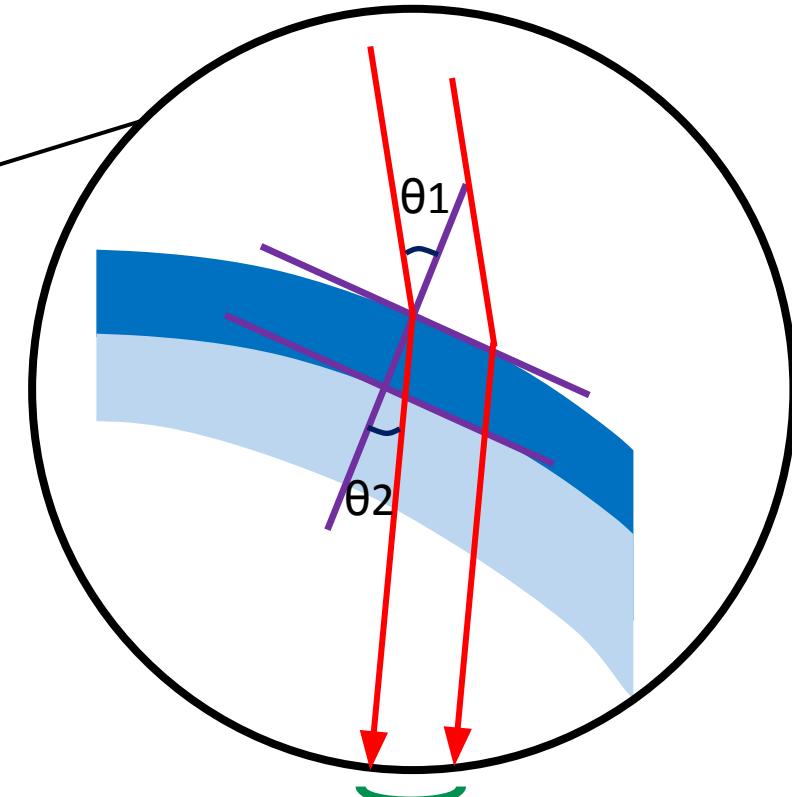
Gels and vision



Uneven gel/ointment layer

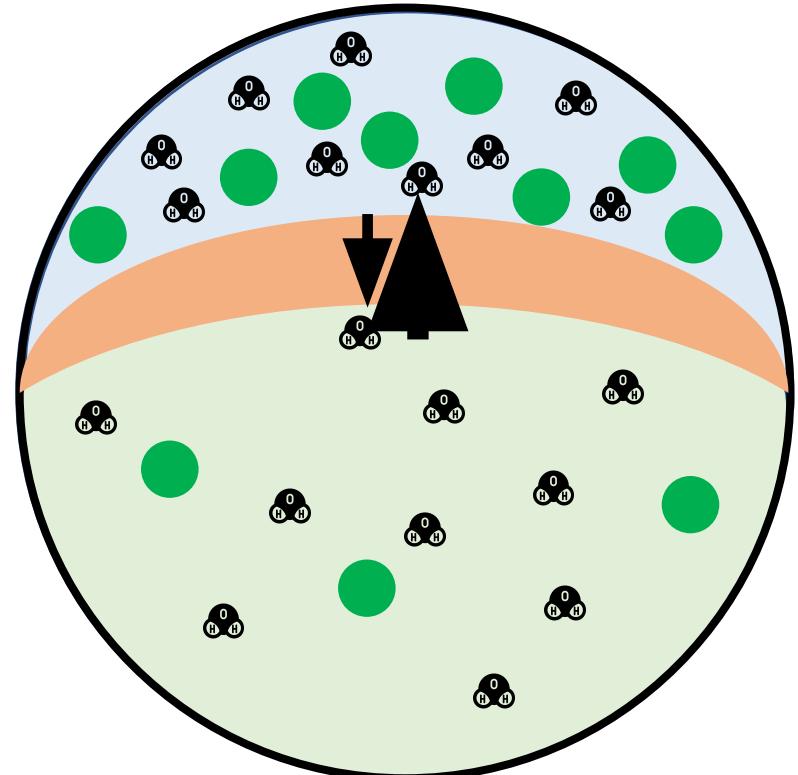


Uniform layer

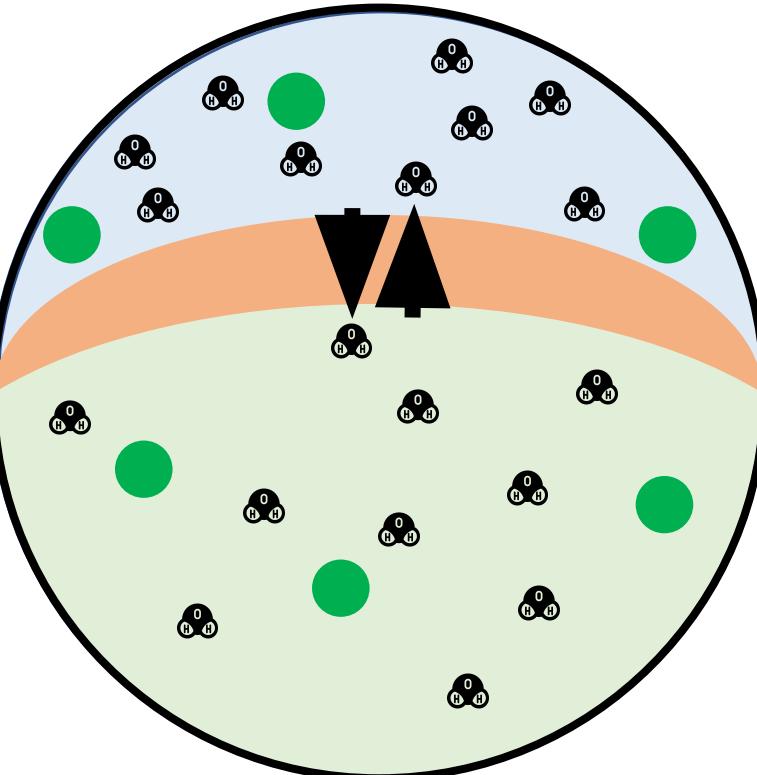


Osmotic pressure regulates ion balance

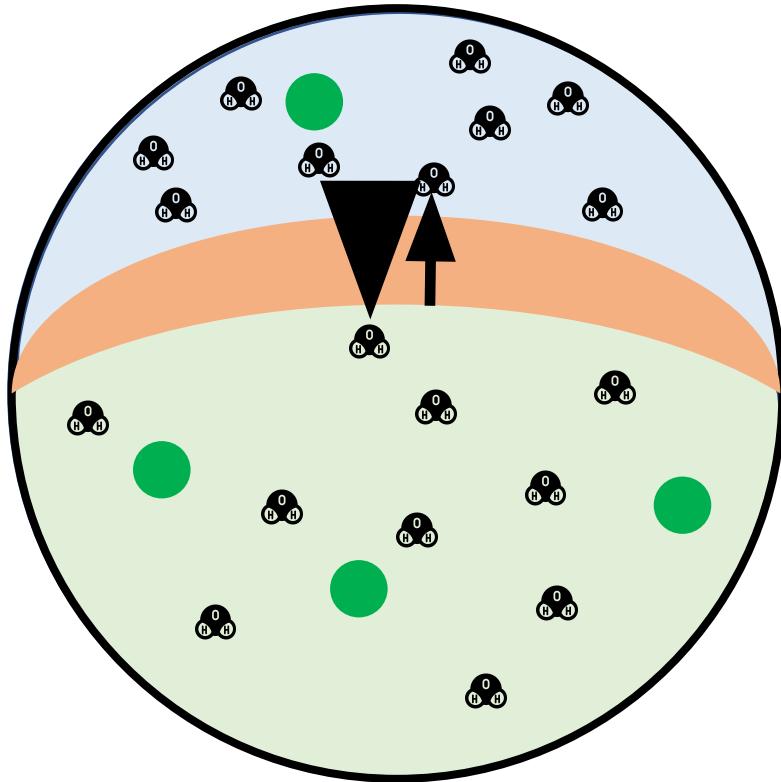
Hypertonic formulation



Isotonic formulation



Hypotonic formulation



● Solute/ion

● Water molecule



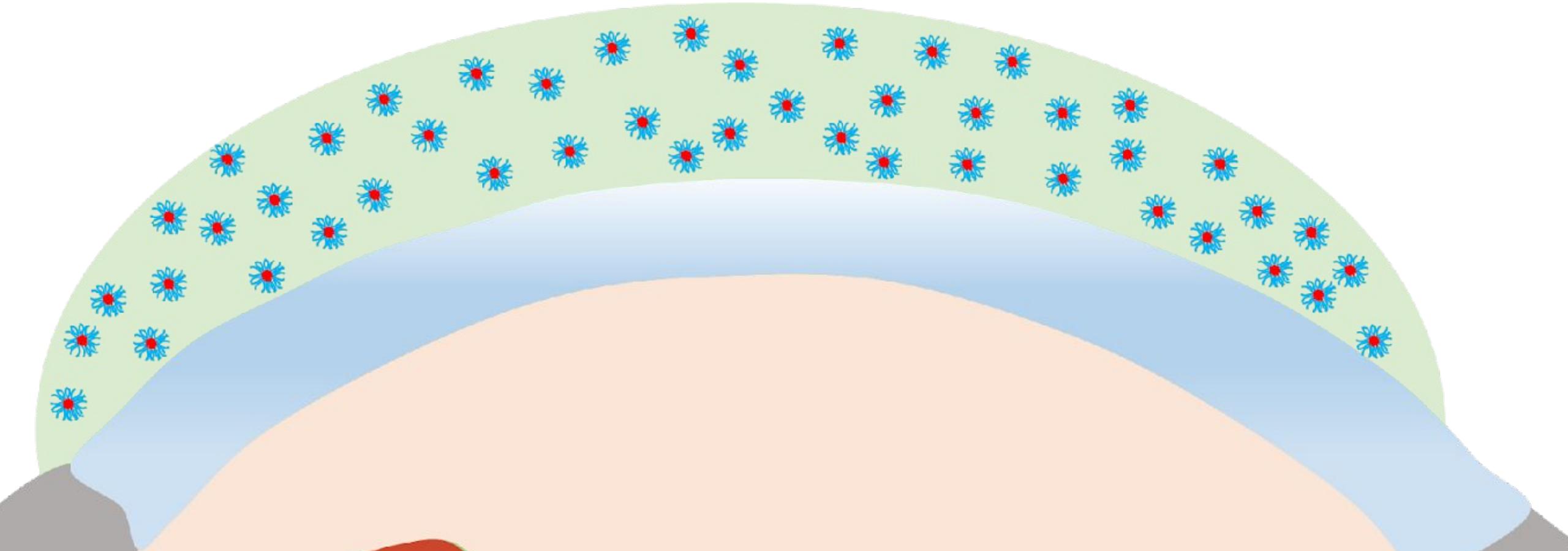
CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



Pluronics in a hypotonic vehicle, below the CGC



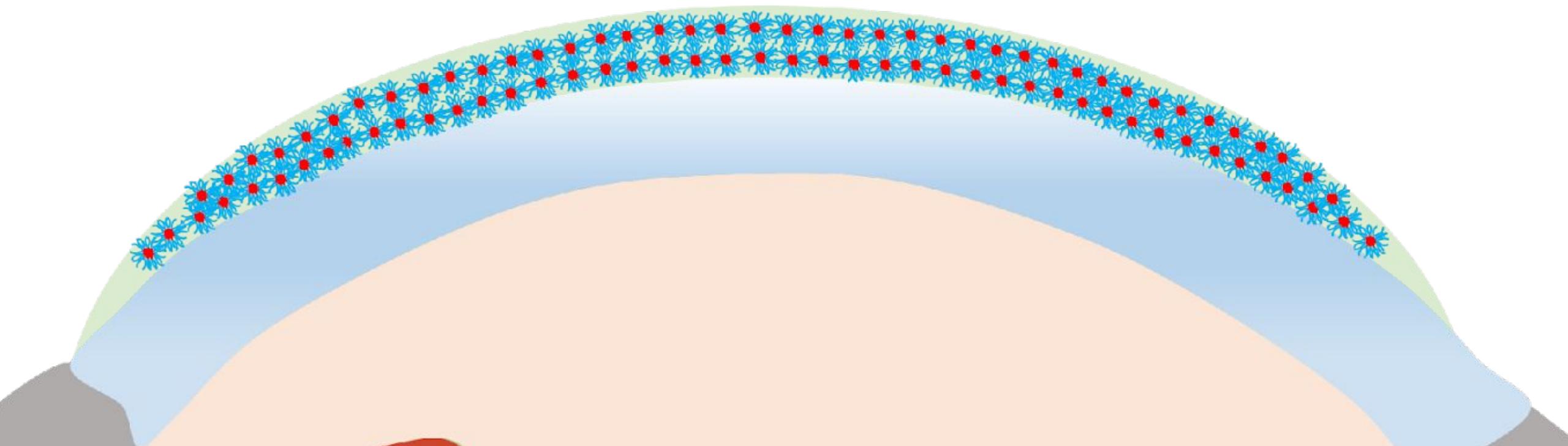
CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



Pluronics in a hypotonic vehicle, below the CGC



CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

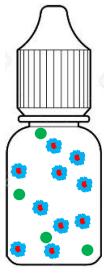
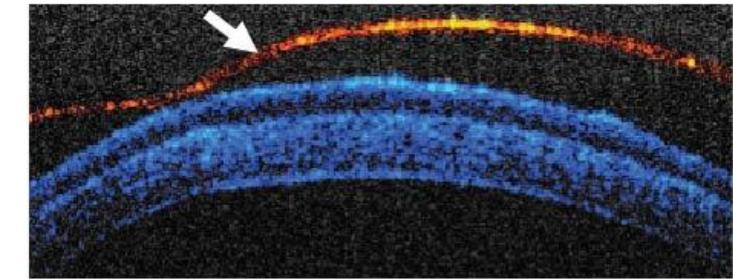
July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



Eye drop distribution in vivo

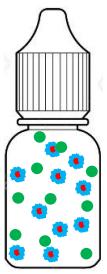
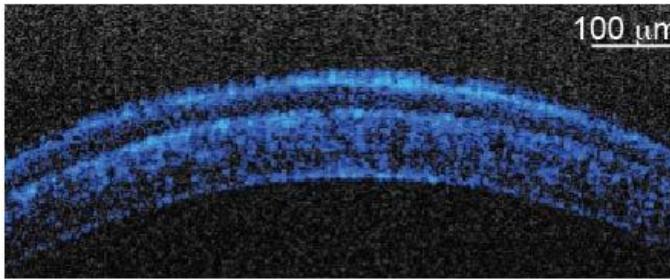


Topical administration

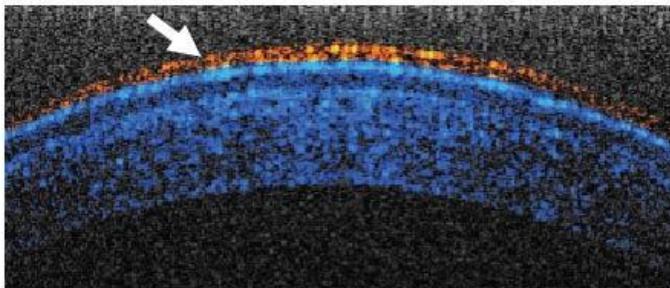
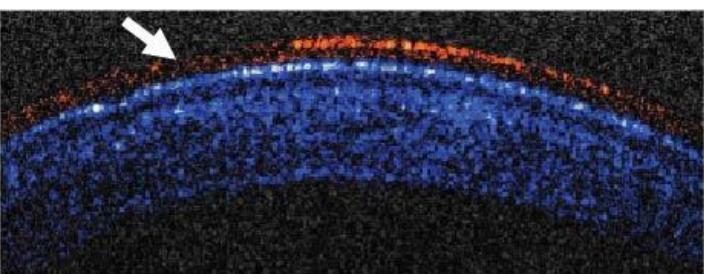


18% Iso

After blinking



12% Hypo



12% Iso

Kim et al, *Nature BME*, 2020



CRS 2022 Annual Meeting & Expo

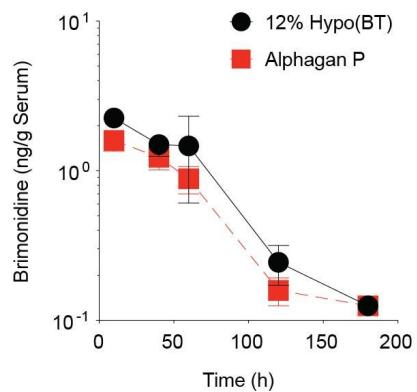
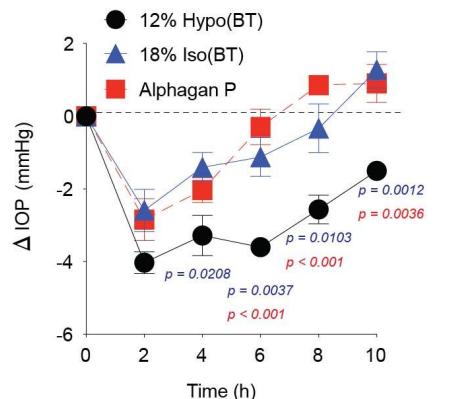
Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada

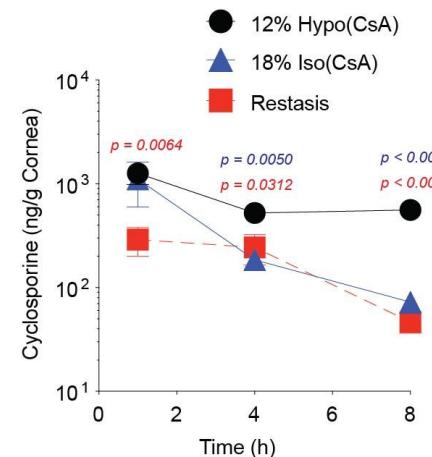
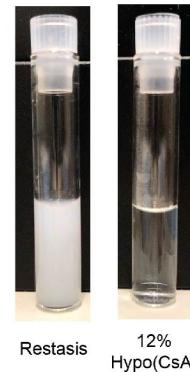
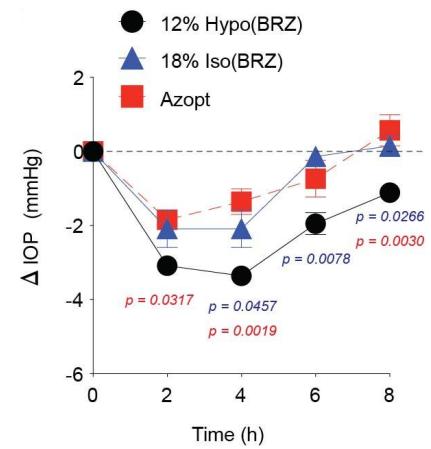


Broad impacts on eye drop performance

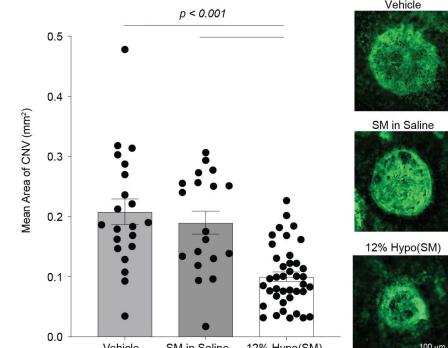
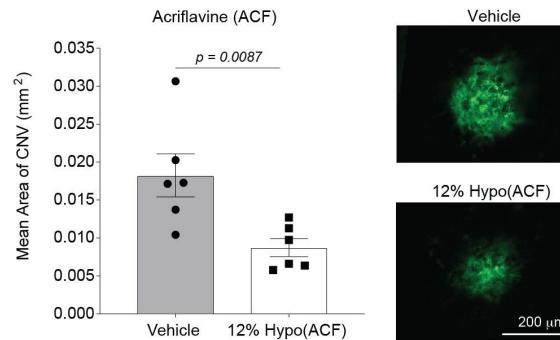
Improved delivery of water soluble drugs without increasing systemic exposure



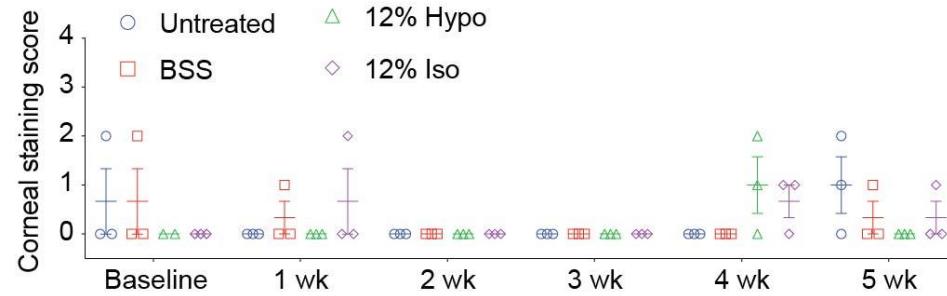
Solubilization and improved delivery of low solubility drugs



Improvement in posterior drug delivery



Biocompatible in sensitive model with repeated dosing



Kim et al, *Nature BME*, 2020



CRS 2022 Annual Meeting & Expo
Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



Why was this technology well-suited for clinical development?

- Patents!
 - Surprising, unexpected, not obvious
 - Broad (awarded) claims that are not easy to circumvent
- Addresses a range of unmet needs
 - Current therapies with significant drawbacks and/or diseases that are unaddressed
 - Room in the market/differentiation from competitors
 - Materials with a history of safety/extensive preclinical safety data
 - Initial development pathways that are relatively fast/inexpensive



CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada



Learnings based on my limited experience

- Do not be intimidated by working outside your comfort zone
- Find and work closely with people who are experienced and know what they are doing
- Figure out what roles you do and do not want to fill
- Find the right people to fulfill vacant roles and trust them to do their job
- Be prepared to incentivize people appropriately
- Do not let your attachment to your invention impede progress (align your priorities with your end goal)



CRS 2022 Annual Meeting & Expo

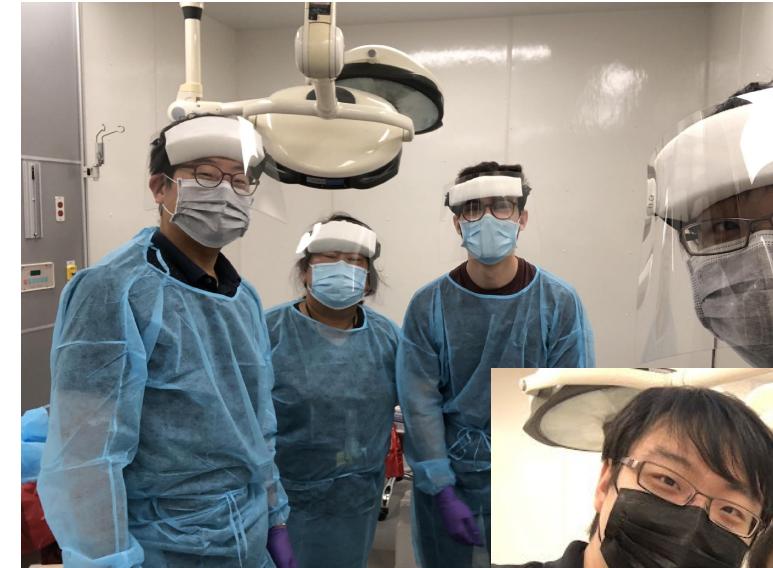
Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada

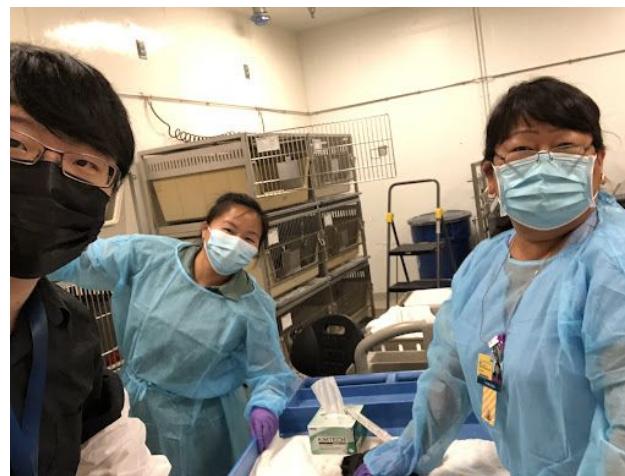


Acknowledgments

Justin Hanes, Ph.D.
Jerry Cagle, Ph.D.
Tung-Heng (Henry) Hsueh, Ph.D.
Yoo Chun Kim, Ph.D.
Nicole Anders, Ph.D.
Matthew Appell
Cynthia Berlinicke, Ph.D.
Peter Campochiaro, M.D.
Abhijit Date, Ph.D.
Charles Eberhart, M.D., Ph.D.
Hyounkoo Han, Ph.D.
Sean Hackett
Ping He
Avelina Hemingway
Albert Jun, M.D., Ph.D.
Byoung-Jin Kim
Youngwook Kim
Raquel Lima e Silva, M.D.
Peter J. McDonnell, M.D.
Ian Pitha, M.D., Ph.D.
Usha Rai
Matthew Shin
Amy Xiao
Donald J. Zack, M.D., Ph.D



Stay tuned!



**NOVUS
VISION**

CRS 2022 Annual Meeting & Expo

Advanced Delivery Science

July 11 – 15, 2022 | Montreal Congress Center, Montreal Canada

