Breaking the Norm: Showcasing Hydralese™ as a Superior Polymer in Long-acting Drug Delivery

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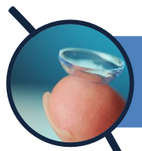
ACS Spring 2022 National Meeting
San Diego, California

PARTNERS FROM INSPIRATION TO REALIZATION

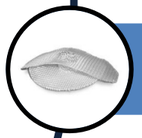
Applications for Polymers in Medicine

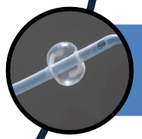
Medical Device

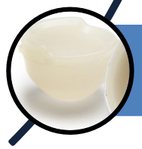

Contact and Intraocular Lens

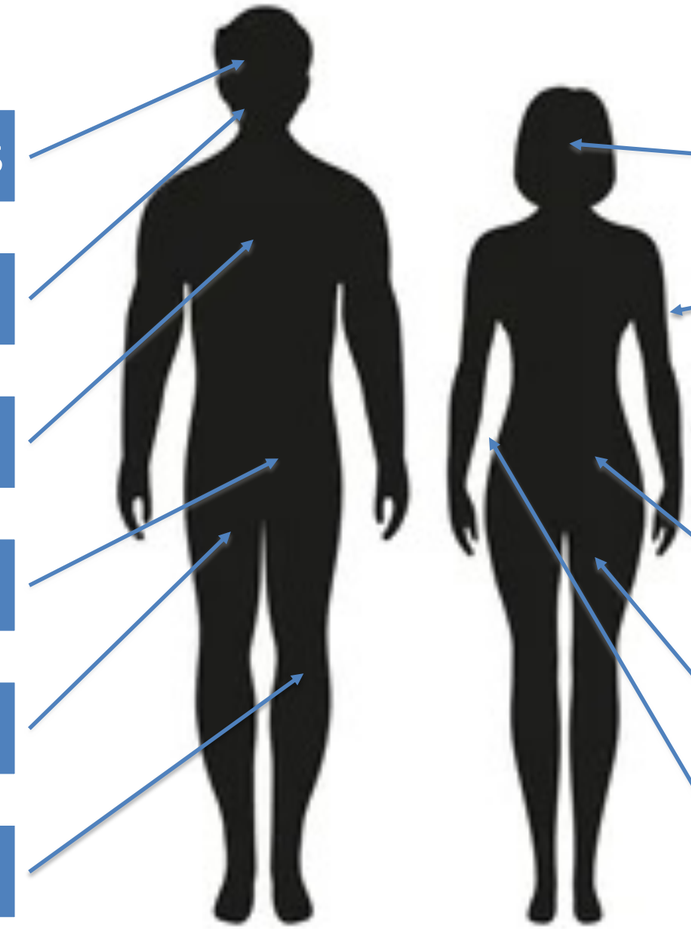

Face Implants


Vascular Grafts

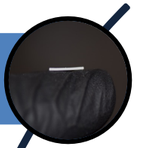

Hernia Patch


Balloon Catheters


Hip/Knee Replacements



Drug Delivery

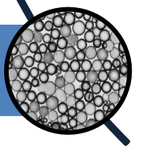
Intraocular Implants


Subcutaneous Implants


Transdermal Patches

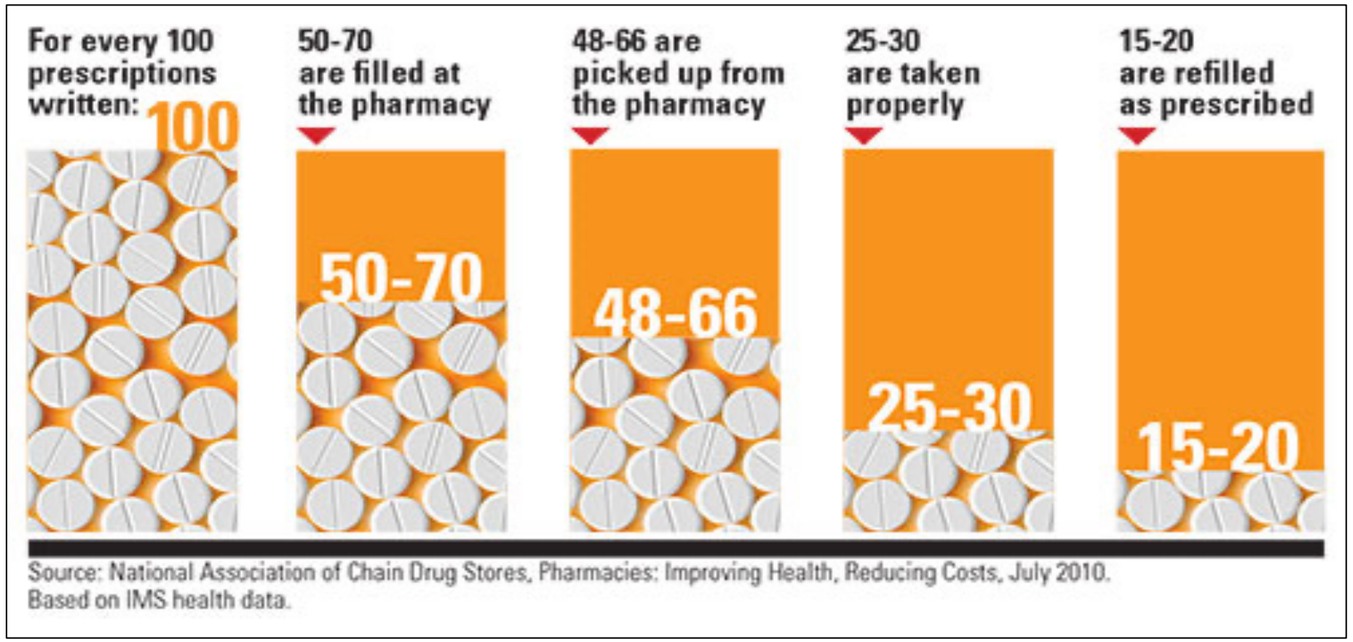

Gastroretentive Devices


Intravaginal Implants

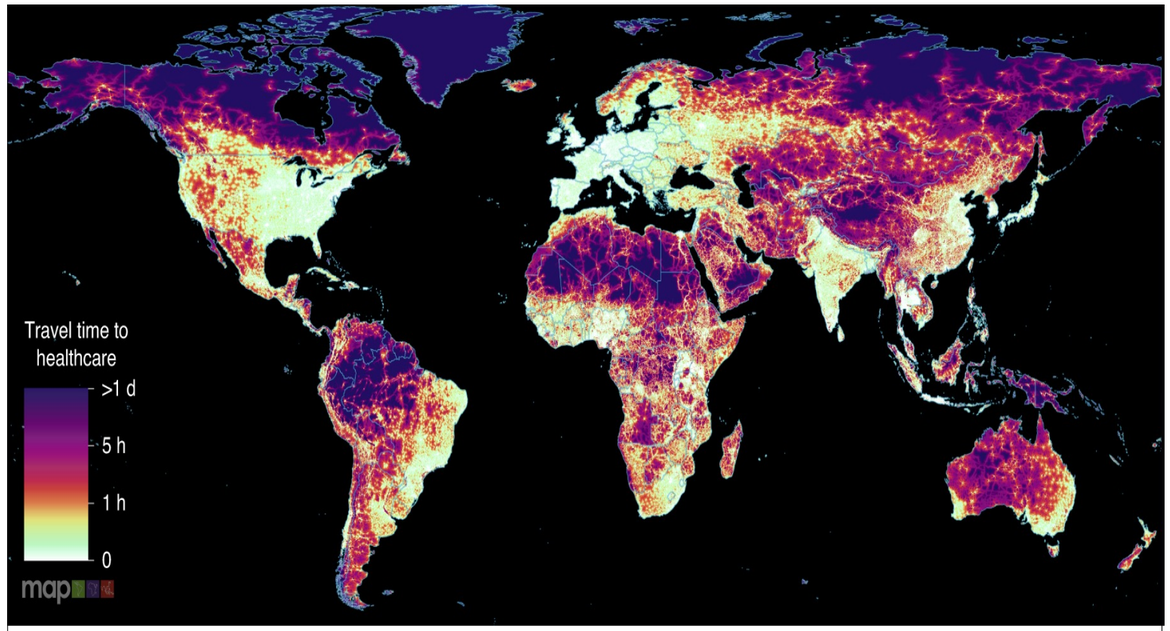

Nano/Microparticles


The Case for Long-acting Drug Delivery Systems (LADDS)

Improved Patient Compliance



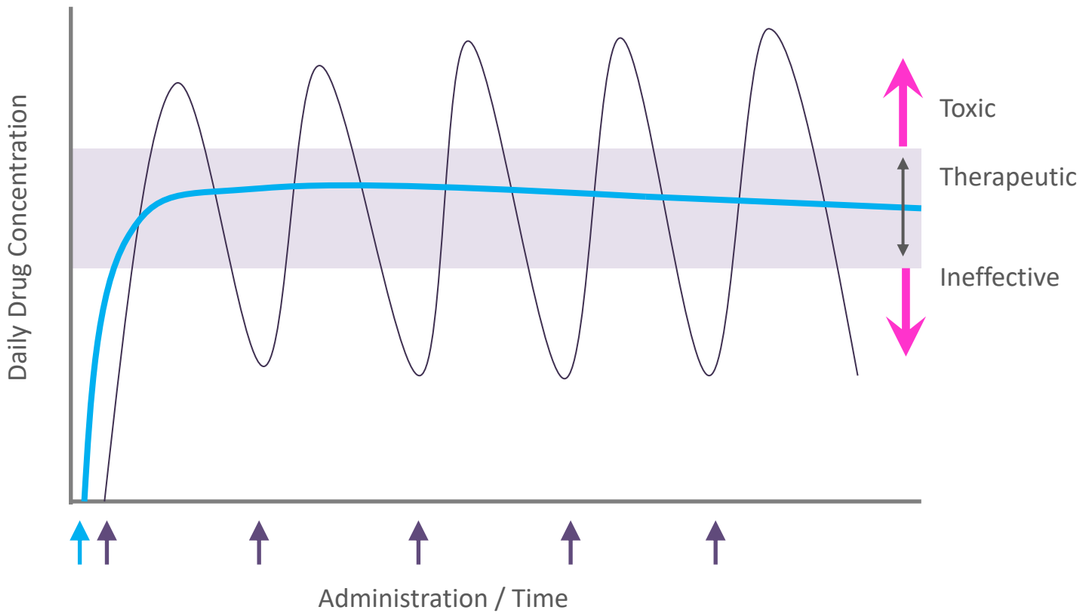
Better Access to Medicine



Weiss, D.J., Nelson, A., Vargas-Ruiz, C.A. *et al. Nat Med* **26,** 1835–1838 (2020). https://doi.org/10.1038/s41591-020-1059-1

The Case for Long-acting Drug Delivery Systems (LADDS)

Maintains Therapeutic Dosage



Discrete Dosage Forms

Implants • Microspheres • Coatings
Microneedles • Gastroretentives

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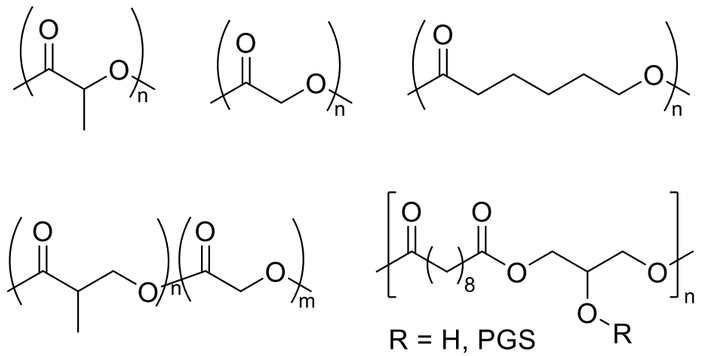
Commonly Used Medical Polymers

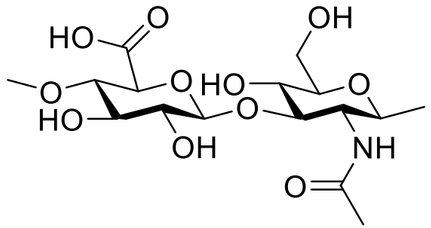
Polyesters



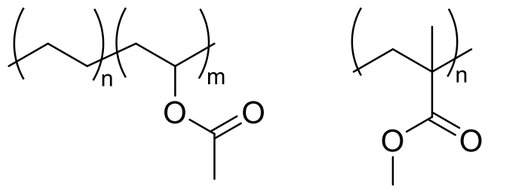
Polyamides

Polyethers

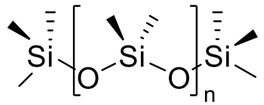
Polysaccharides



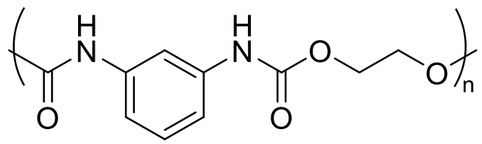
Polyacrylates



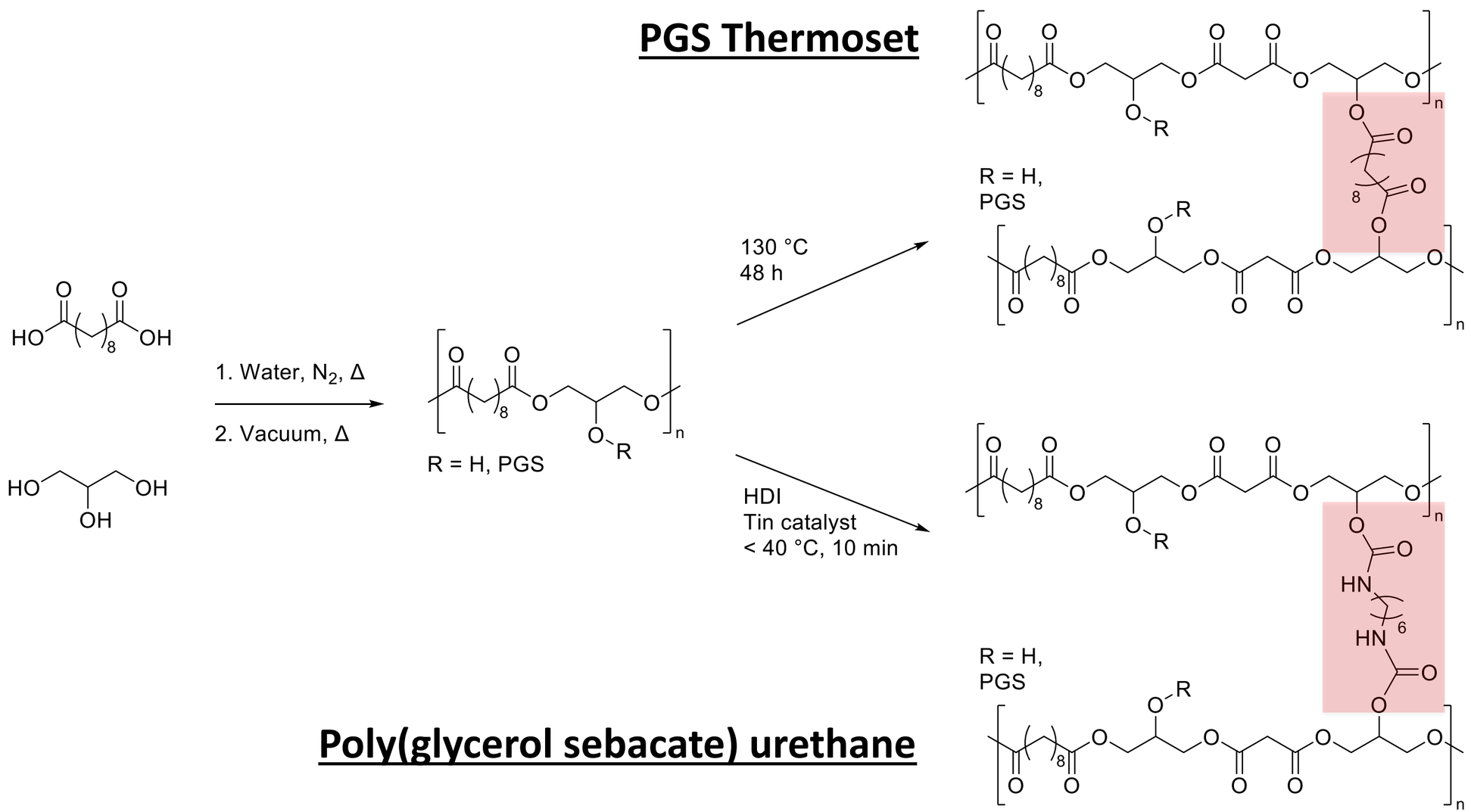
Silicones



Polyurethanes



PGS and PGSU Chemistry



PGSU Stands Above the Rest

		Biodegradables			Biodurables		
Category	Feature	PGSU	PLGA	PCL	EVA	TPU	PDMS
Drug Delivery	Therapeutic duration >6 months	✓		✓	✓	✓	✓
	High drug loading >50% w/w	✓					
	Loading-independent release rate	✓					
	Zero-order release kinetics	✓					
	Rapidly degradable once playload released	✓					
	Reduced burst effect once implanted	✓					
	Reduced tail effect once sub-therapeutic	✓					
	Minimal pH change during implant lifespan	✓		✓	✓	✓	✓
Patient Focus	Minimal fibrous encapsulation	✓		✓	✓	✓	
	All tissues return to normal post treatment	✓			✓	✓	
	Flexible, even at high loading for patient comfort	✓				✓	✓
	Discrete	✓				✓	✓
	Retrievable initially if adverse reaction	✓			✓	✓	✓
	No need for implant retrieval after therapy	✓	✓	✓			
	No chronic inflammatory response	✓			✓	✓	
	Provides patient convenience with reduced dosing	✓			✓	✓	✓
Stability	Polymer stable under sterilization	✓			✓	✓	✓
	Room temp/humidity shelf storage	✓			✓	✓	✓

PGS History and Evolution to PGSU

2002
PGS was popularized in the Robert Langer Lab

2012
Secant licenses PGS Technology from MIT for preliminary investigation

2013
Jeffrey Karp publishes first paper on PGSU

2015
Secant Group develops REGENEREZ®

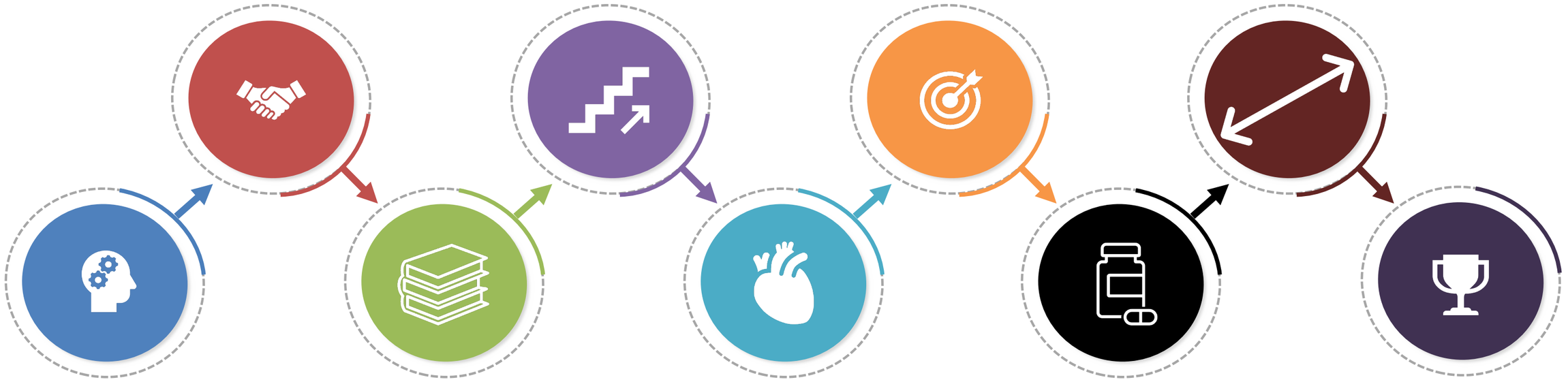
2016
Secant develops PGS cardiovascular grafts

2018
Secant Group develops HYDRALESE™ for controlled release

2019
Small molecule formulations are designed and developed

2021
Expansion of API type (biologics) and device form

2021
Secant group files its first DMF with the FDA for PGSU



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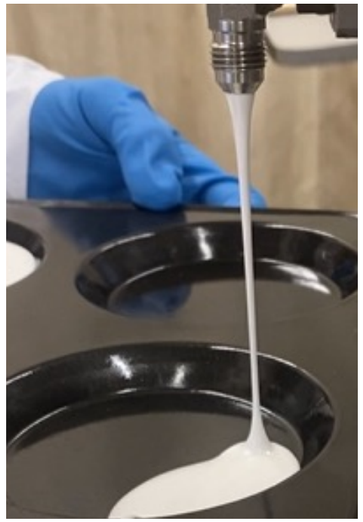
Formulation of API-loaded PGSU Constructs

API powder dispersed into liquid PGS resin

+

Crosslinker

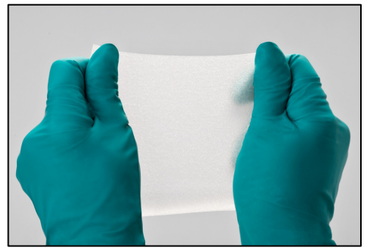
<40 °C



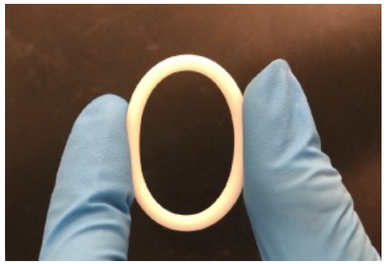
Blend flowed into mold

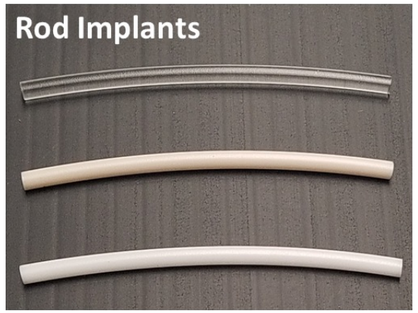
Curing

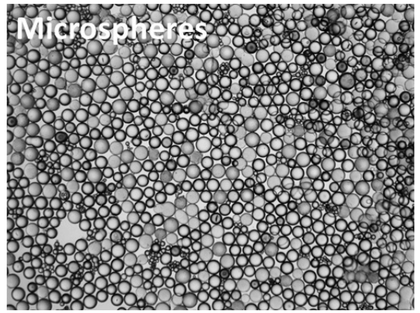
rt, 10 min

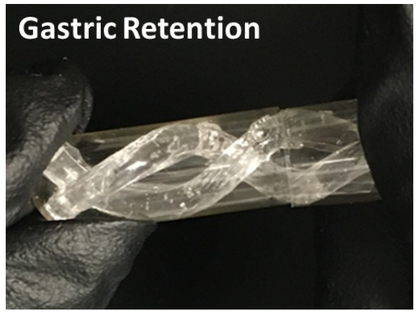


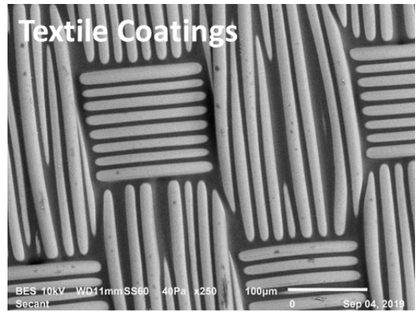
Drug-loaded elastomer removed from mold

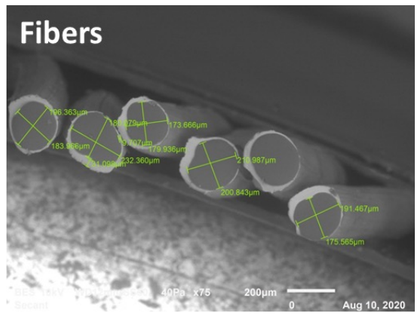


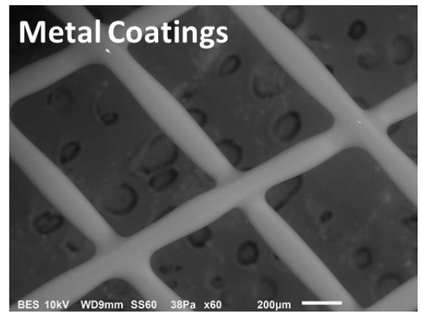












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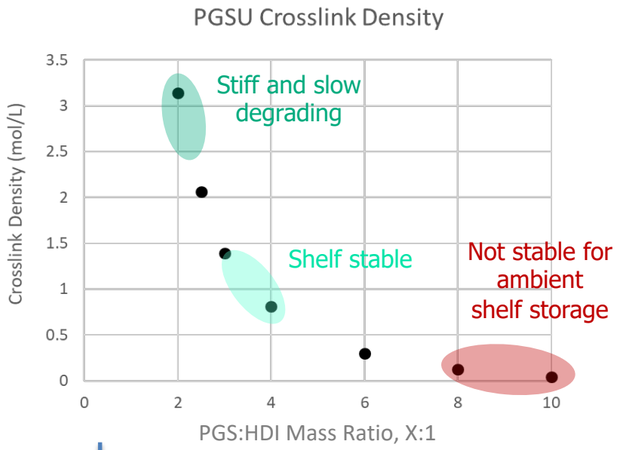
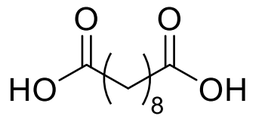
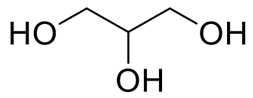
PGSU Properties







Tunable

Surface-eroding

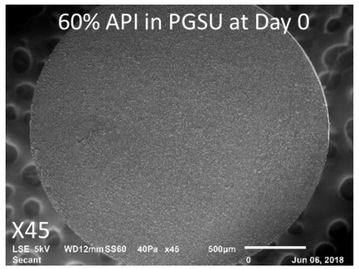
Water impermeable

Bio-based degradants

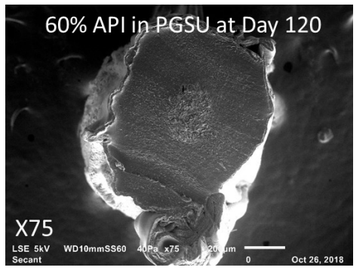
Optically translucent

Elastomeric

Biocompatible



Surface Erosion

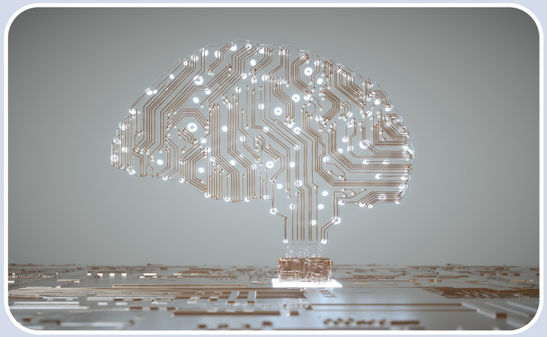


ISO 10993

Applications of LADDS

Sexual and Reproductive Health

- Anti HIV
- Contraception
- STI Prevention



Neurodegenerative Diseases

- Schizophrenia
- Alzheimer’s
- Parkinson’s

Ophthalmic

- Macular Degeneration
- Dry Eye Syndrome
- Glaucoma

Animal Health

- Parasite Prevention
- Antimicrobials
- Antivirals

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Sexual and Reproductive Health

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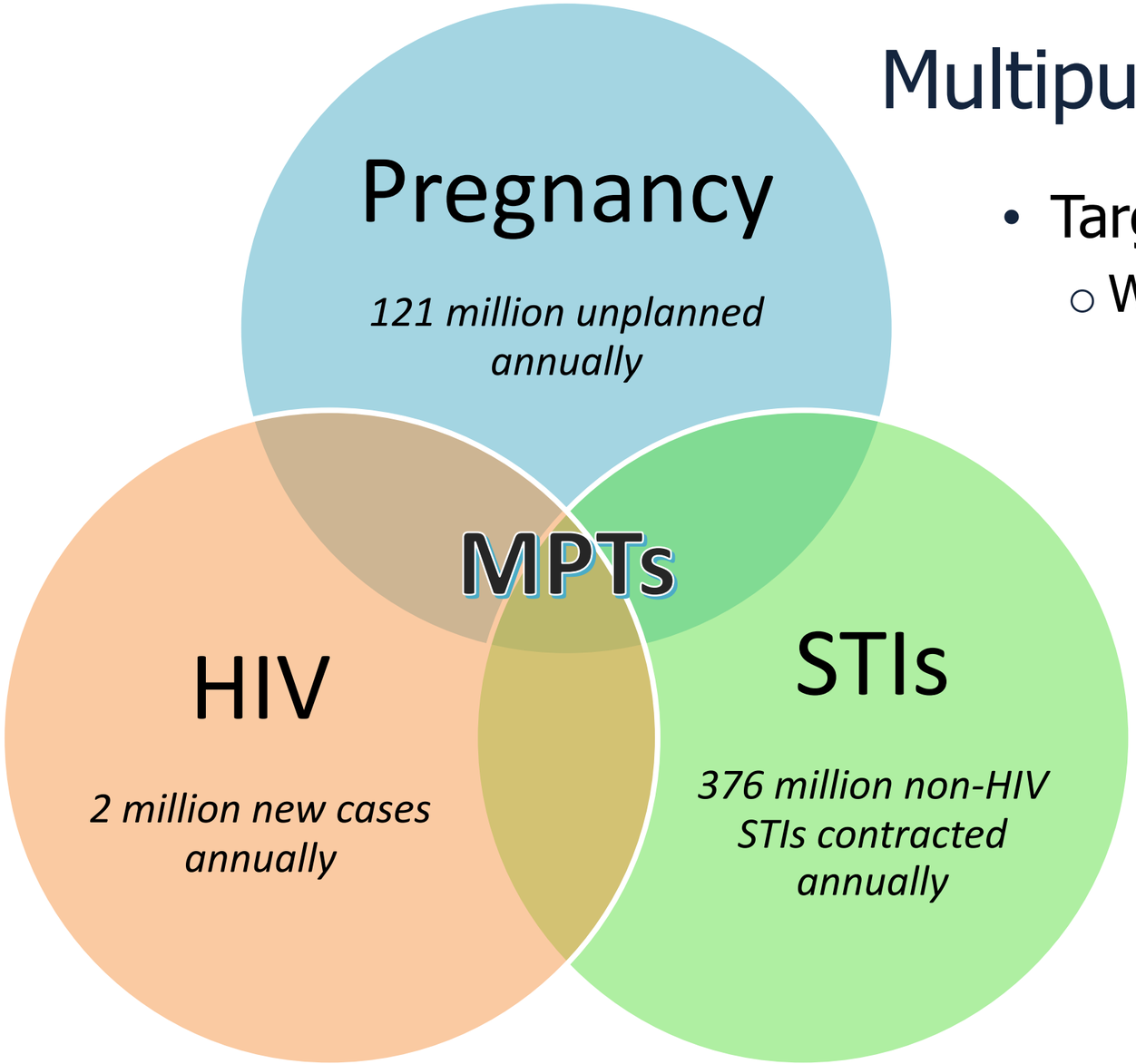
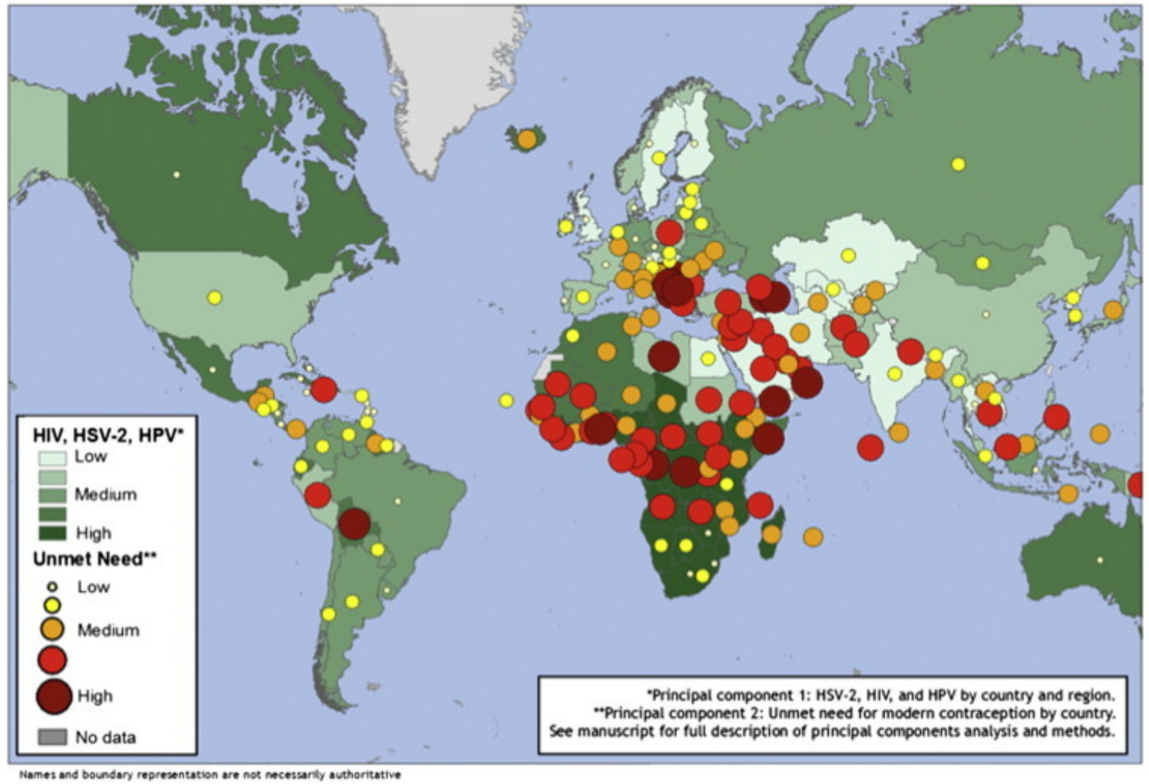
Multipurpose Prevention Technologies



- Target demographic:
  - Women in early to middle adulthood

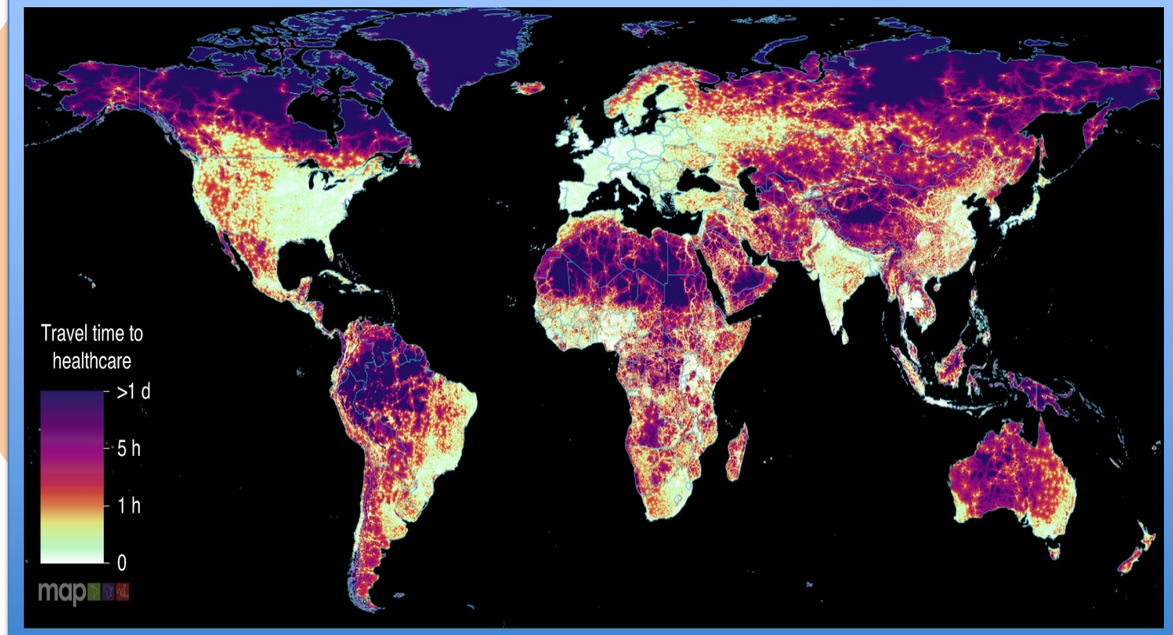


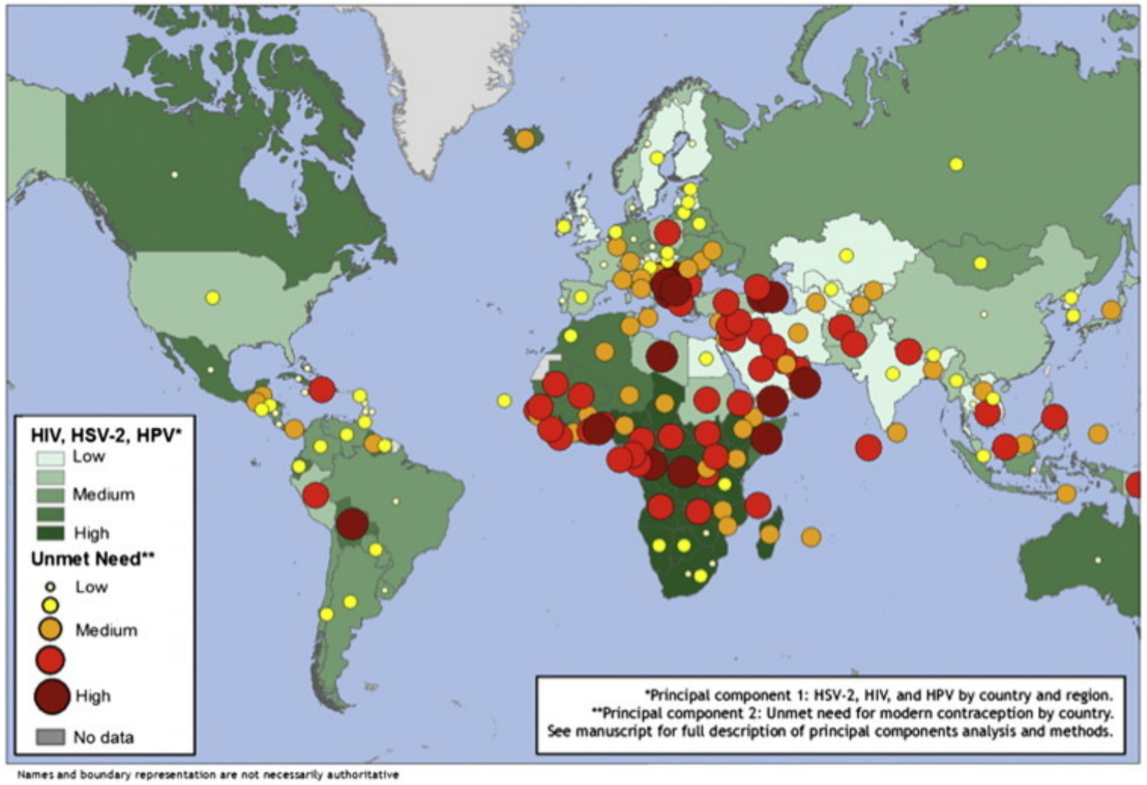
Multipurpose Prevention Technologies

Pregnancy

- Target demographic:
  - Women in early to middle adulthood

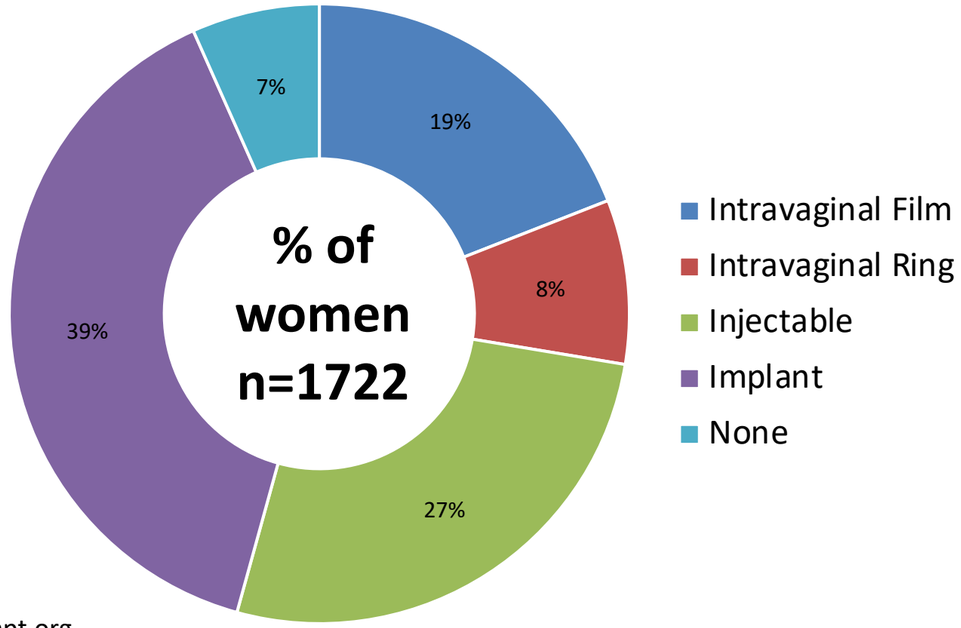
- Better Access to Medicine

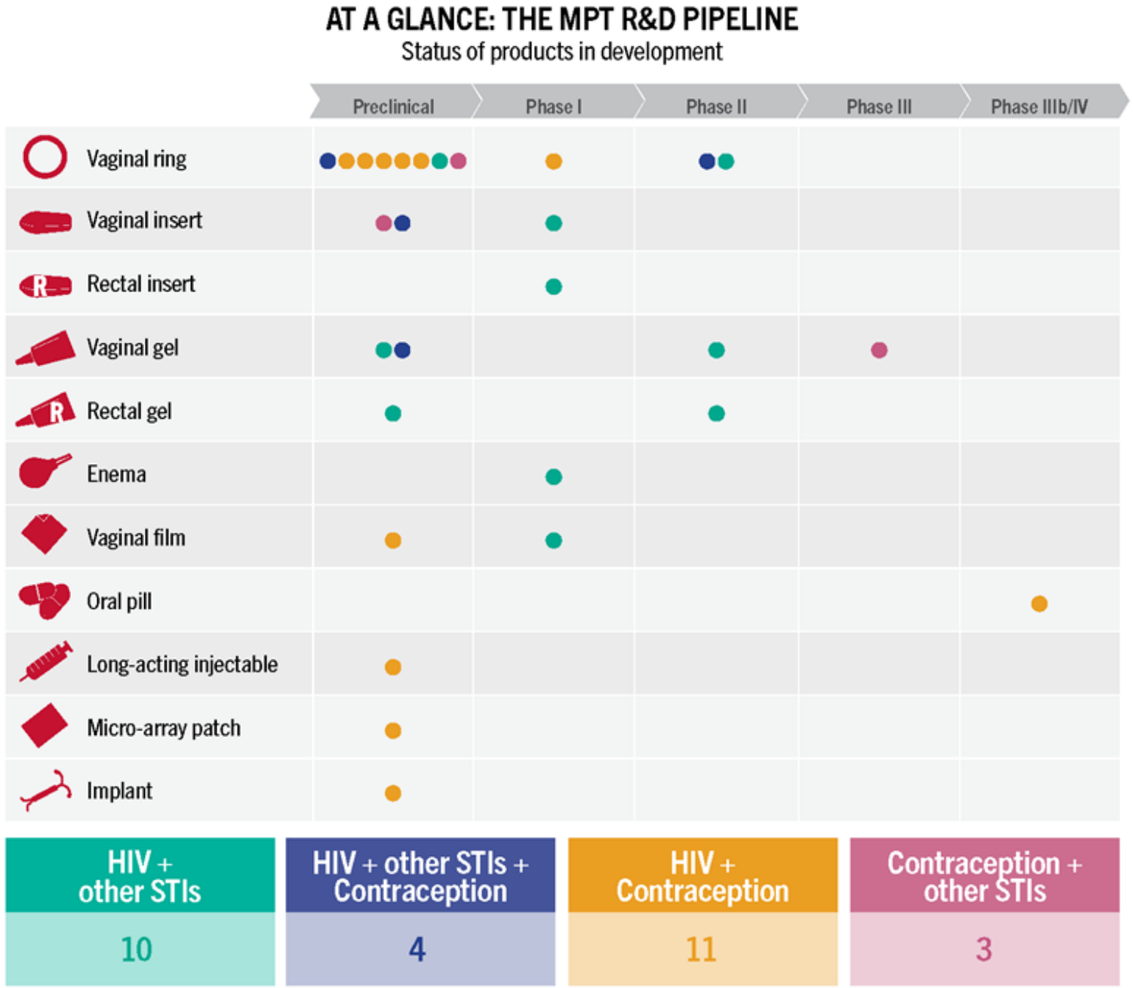




The MPT Pipeline

- Requirements:
  - Affordable
  - Long-lasting
  - Easy to use/administer
  - Safe
- Improve patient compliance
- Make preventative treatment available





www.theimpt.org

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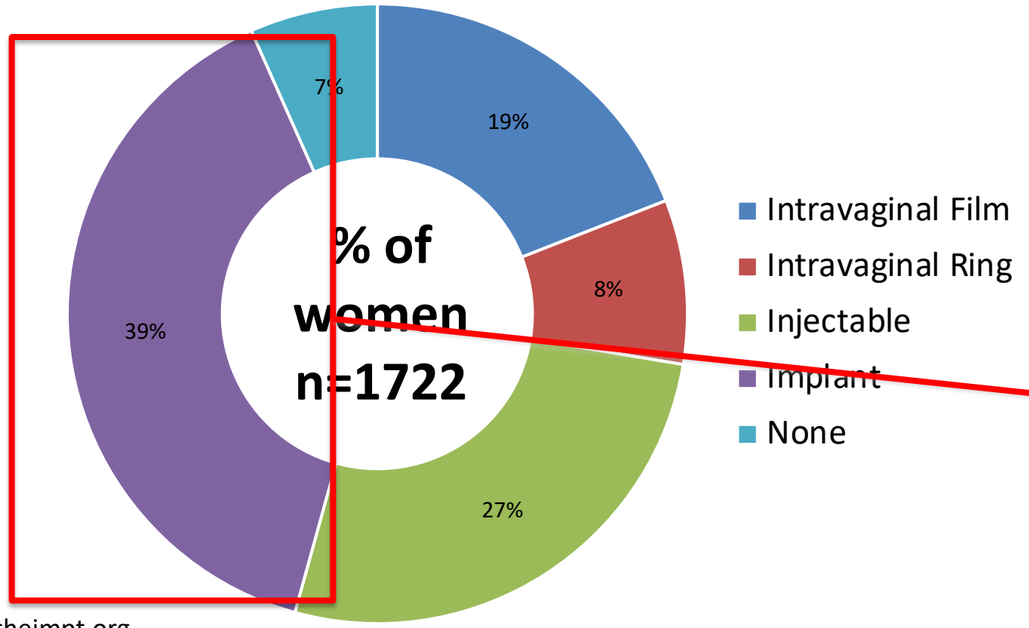

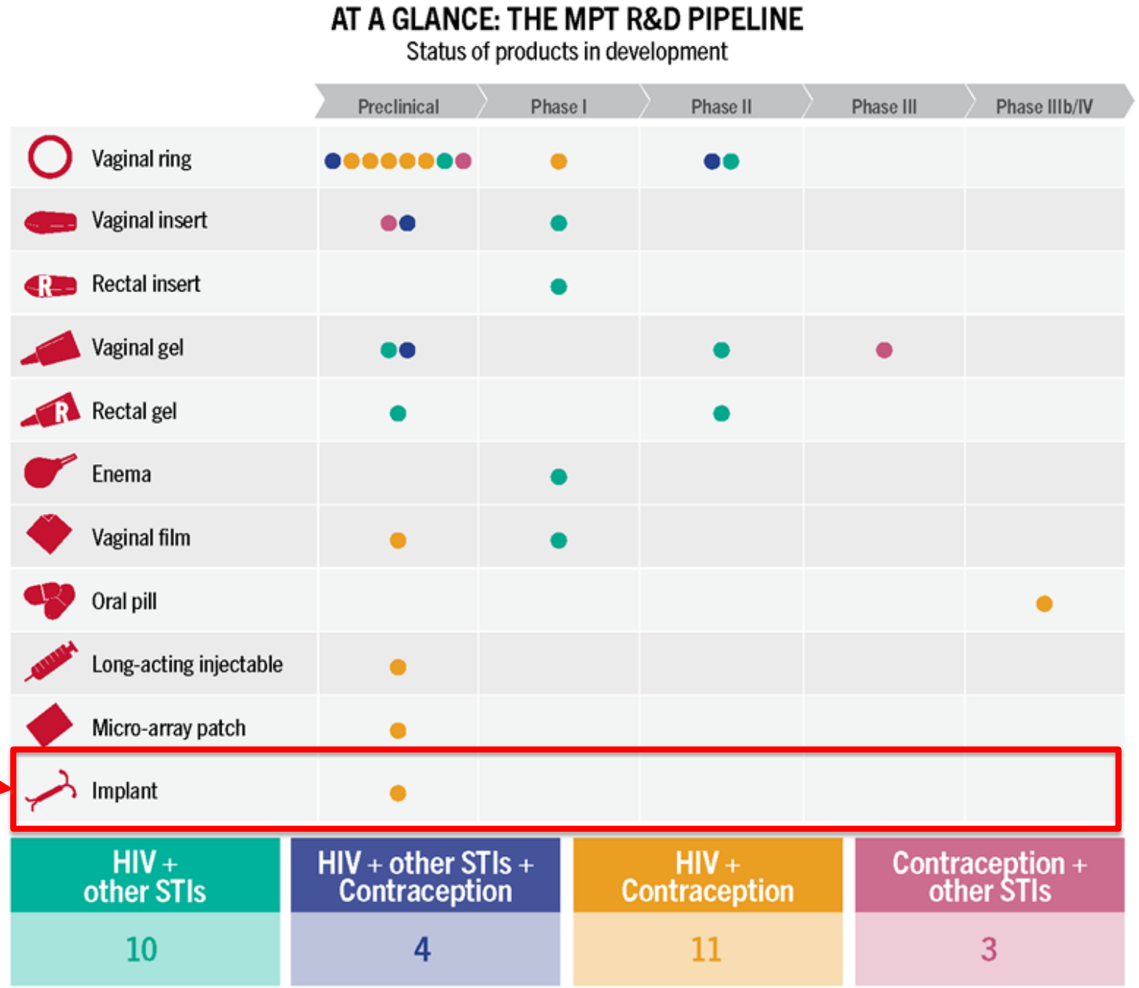

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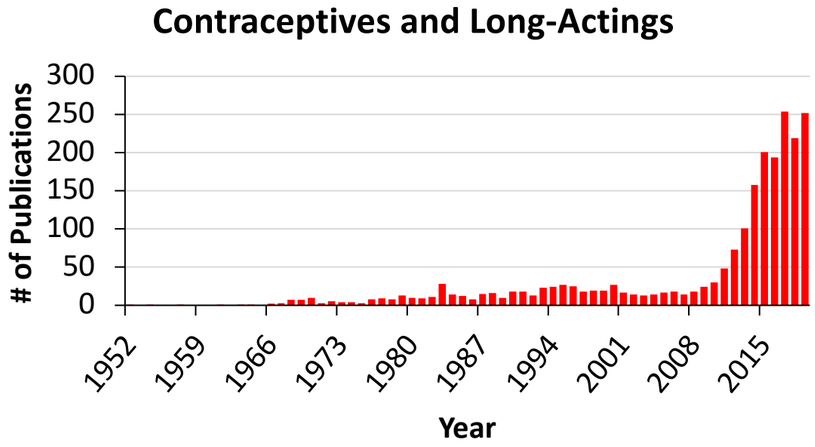
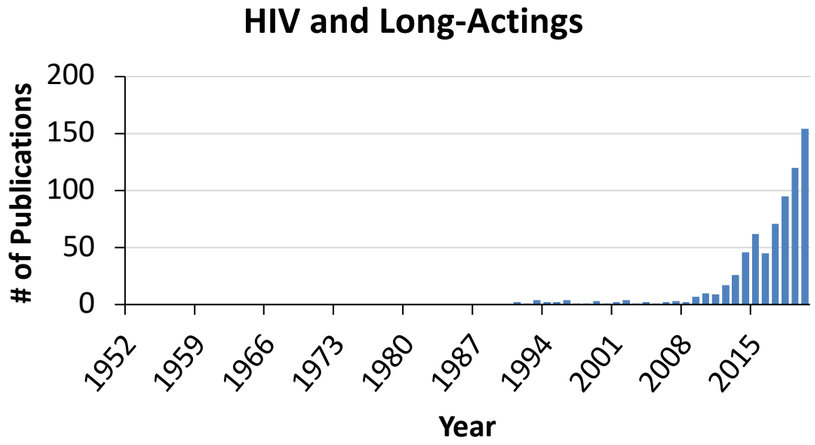
Publication rates indicate a market opportunity





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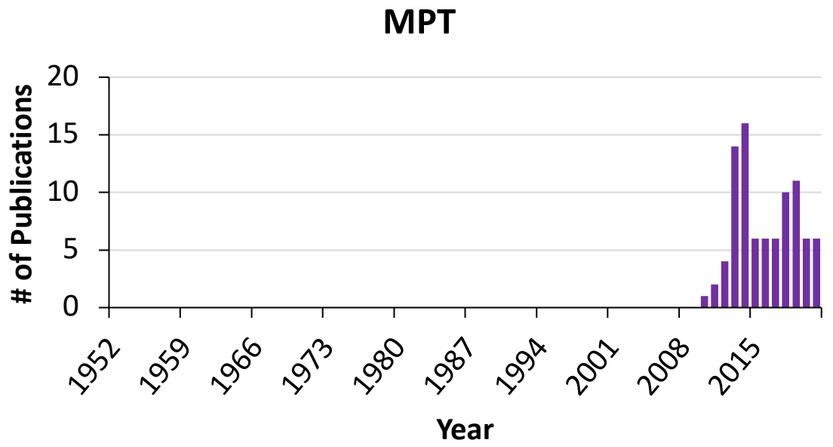


A Constant Changing Landscape

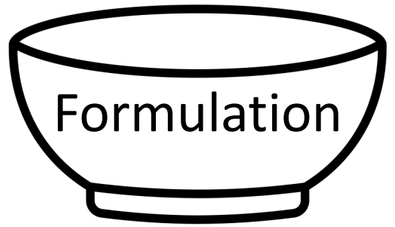
2/3 of pipeline are rings but evidence shows need for implantables and injectables

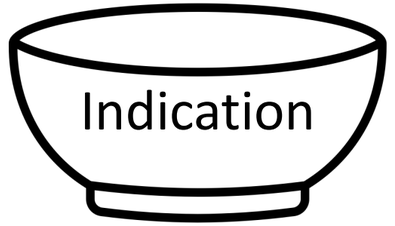
New APIs including biologics are starting to be developed

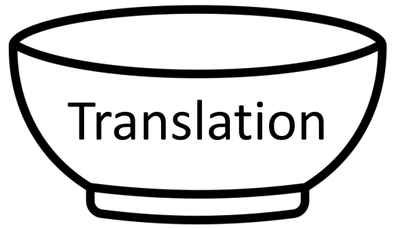
Non-HIV indications are growing, including rapid increase in STI prevention

Co-formulation requirements for hydrophobic AND hydrophilic APIs

Too many academics and not enough industrial researchers



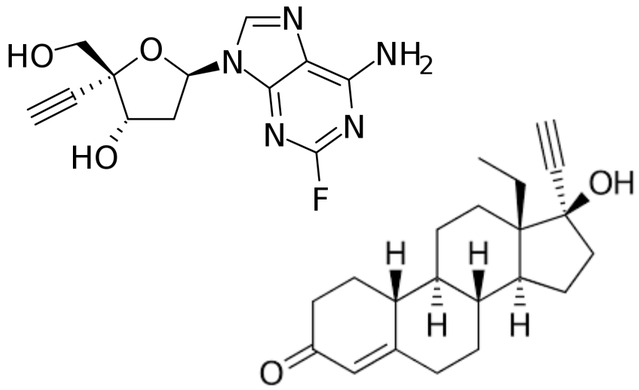




https://unitaid.org/assets/Multipurpose-Prevention-Technologies-Technology-Landscape-and-Potential-for-Low-and-Middle-Income-Countries.pdf

Formulating MPT LAIs

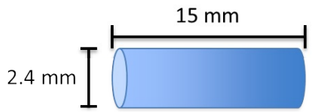
- Goal: Dual delivery of an antiretroviral and contraceptive
  - Antiretroviral: EFdA
  - Contraceptive: Levonorgestrel
- Preliminary IVE Study Formulations:

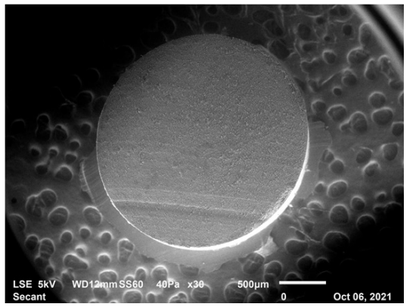


EFdA only (SG149-101)

Loading: 40 % EFdA

Size: 2.4 mm x 15 mm

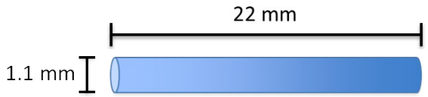


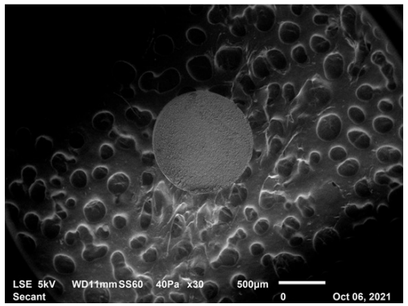


LNG only (SG149-99)

Loading: 55 % LNG

Size: 1.1 mm x 22 mm

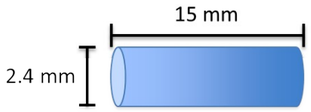


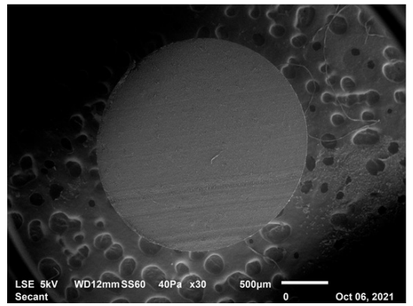


Combo (SG149-100)

Loading: 40% EFdA, 15% LNG

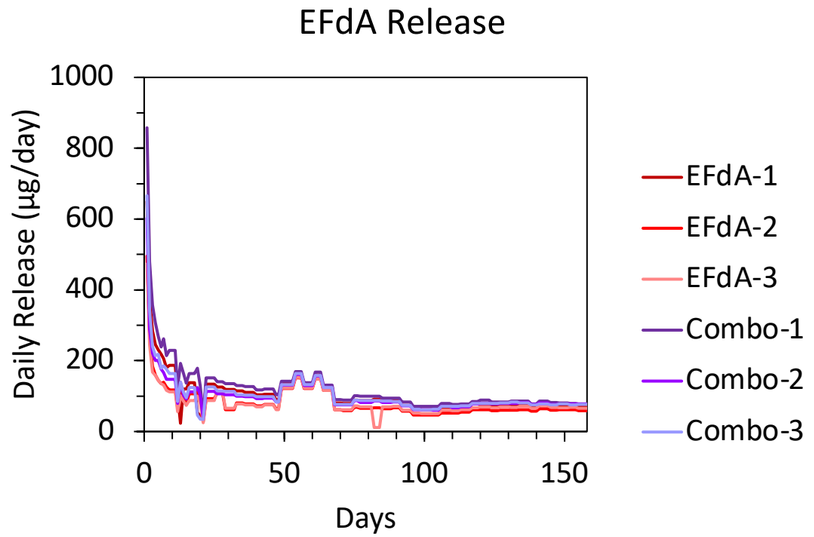
Size: 2.4 mm x 15 mm

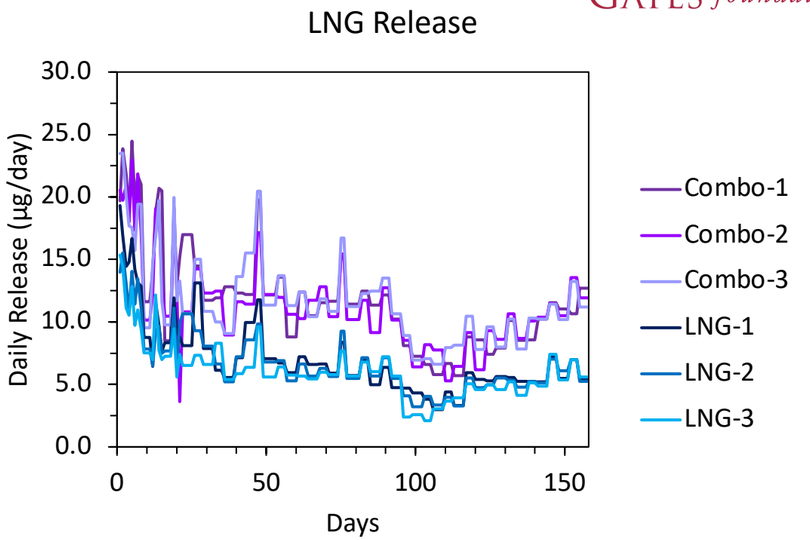


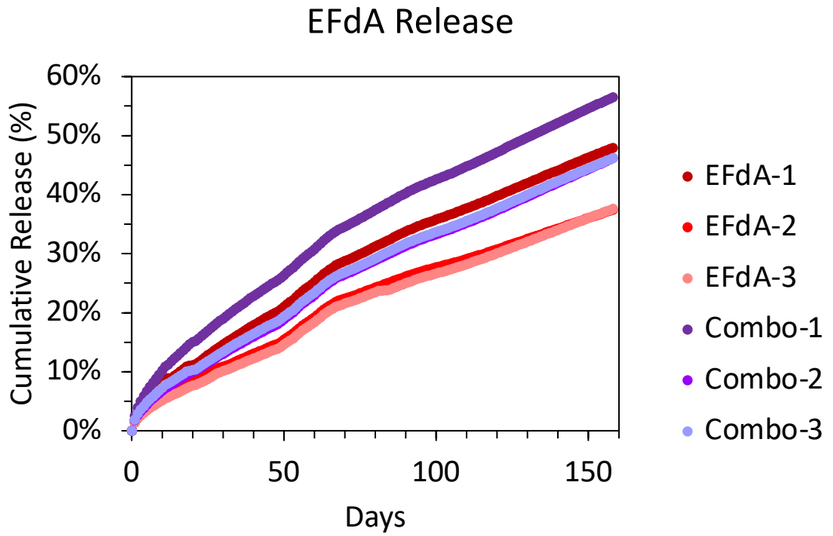


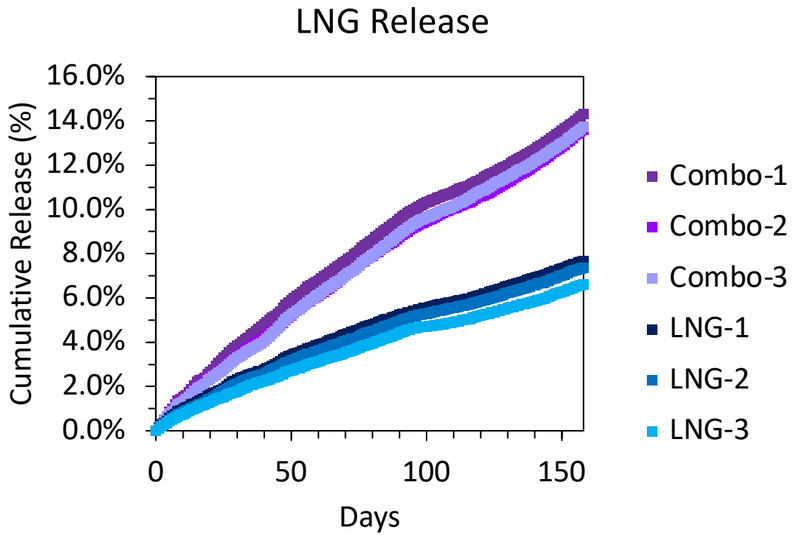
In Vitro Elution Studies

- Release after 158 days
  - Negligible burst release observed in all three formulations
  - Linear release profile
  - Complete release expected by:
    - EFdA in 1 year
    - LNG in 6 years
    - Combo in 1-3 years









Ophthalmic Therapies

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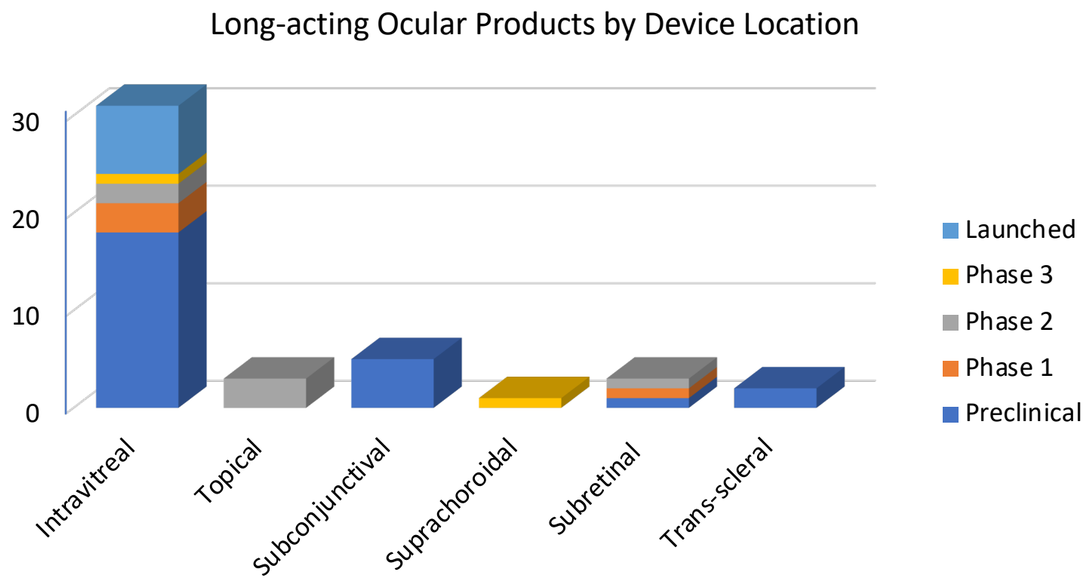
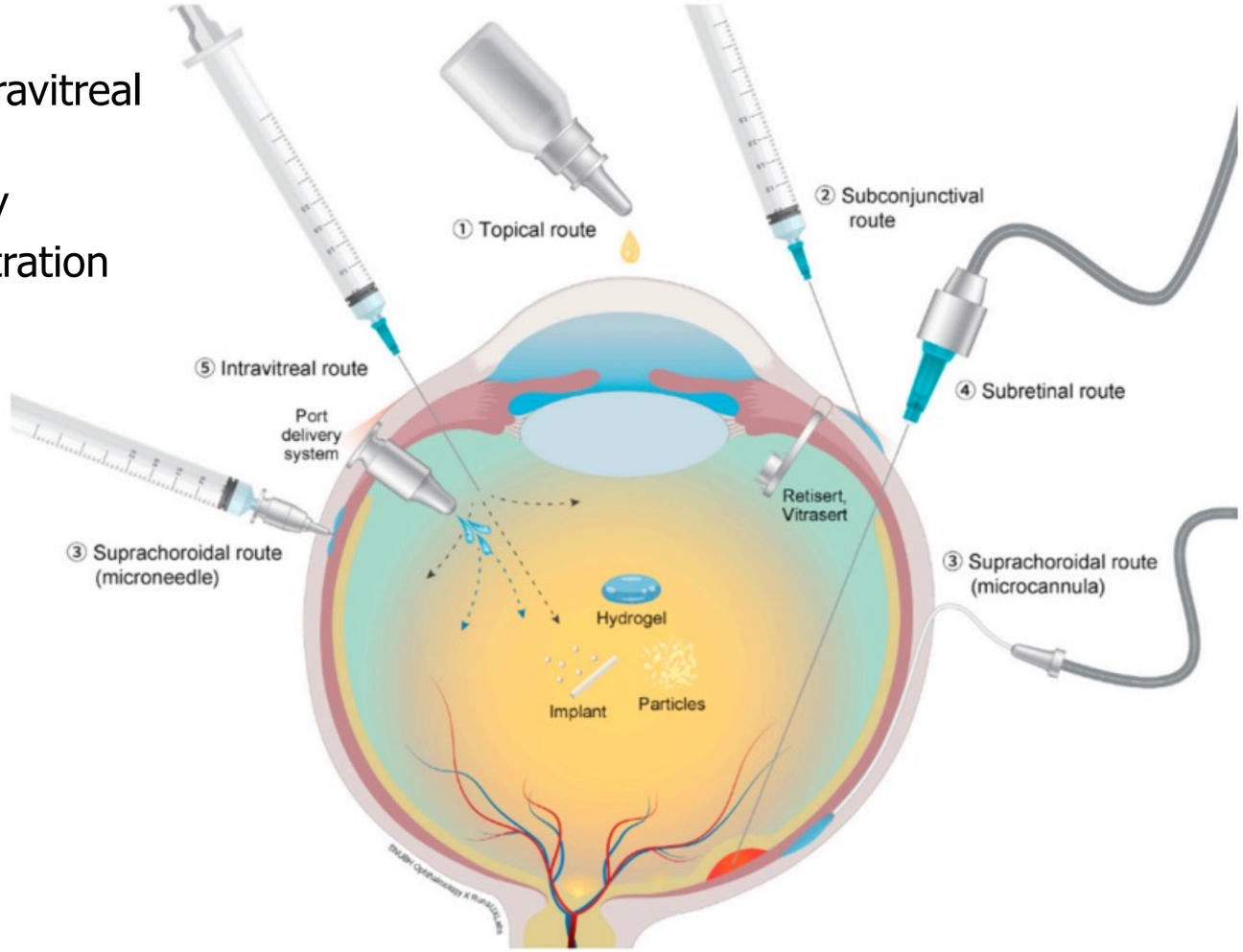
Ocular Drug Delivery Pipeline

- Increased patient compliance
- Reduced risk of retinal detachment from repetitive intravitreal injections
- Low bioavailability of APIs when administered topically
- Difficult to achieve daily dose through topical administration
- Biodegradability a requirement





Kim, H.M.; Woo, S.J. Pharmaceutics 2021, 13, 108. https:// doi.org/10.3390/pharmaceutics13010108

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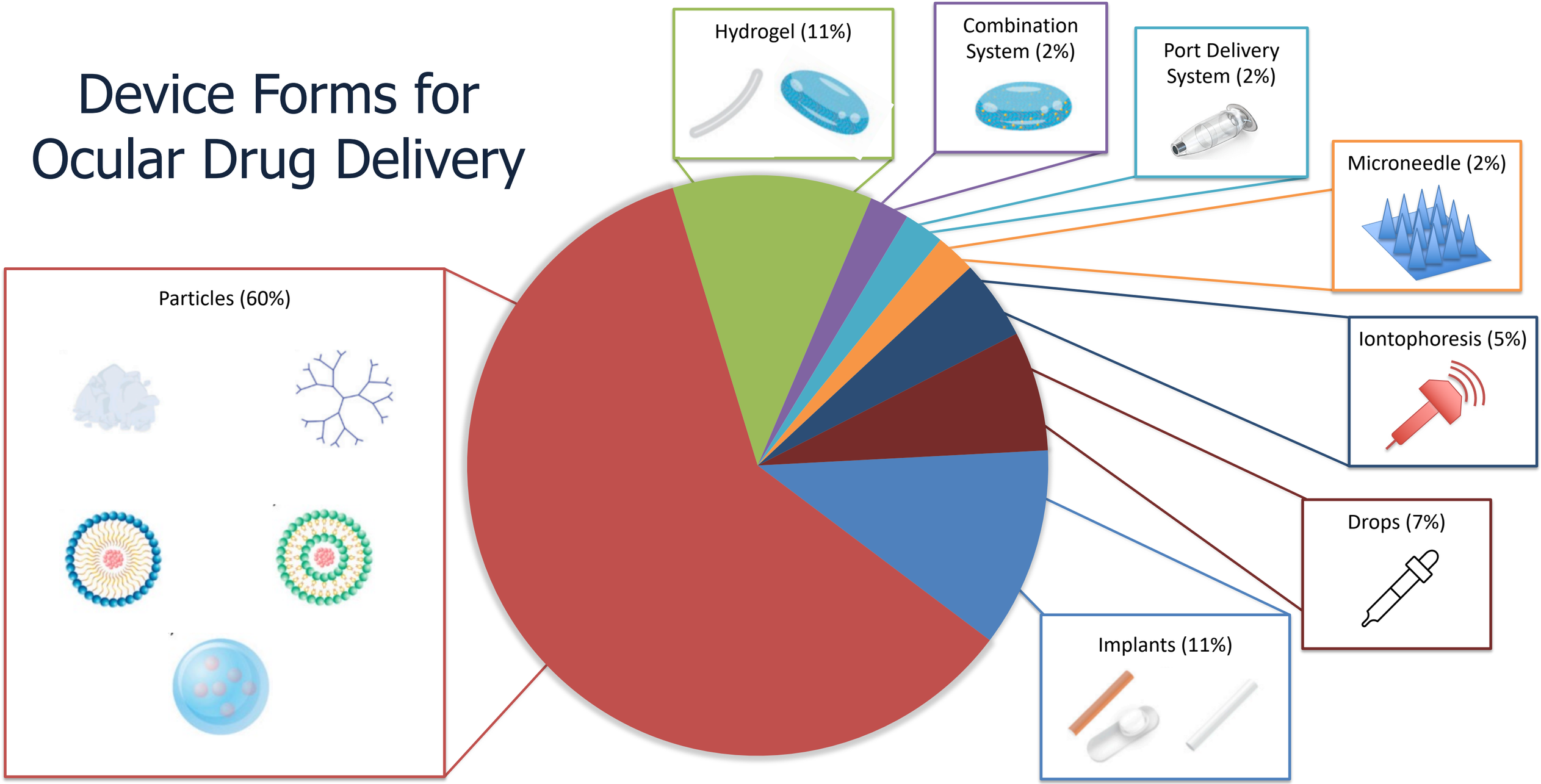
Device Forms for Ocular Drug Delivery



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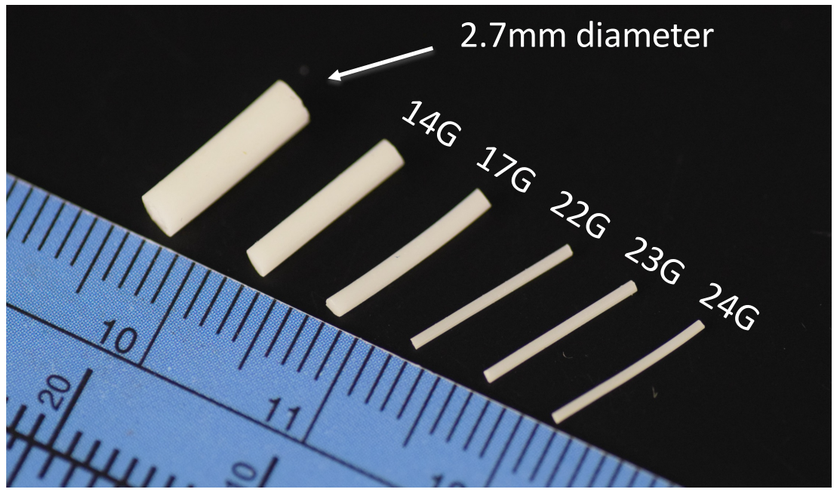
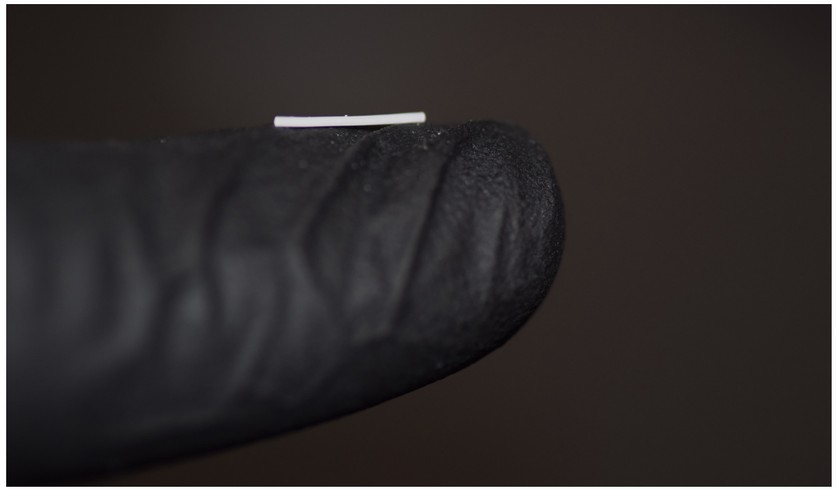
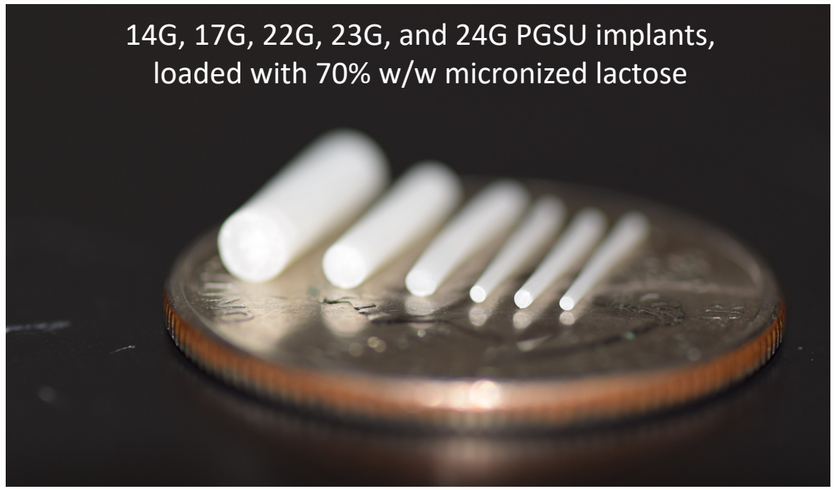
Smaller Devices Means Smaller Needles



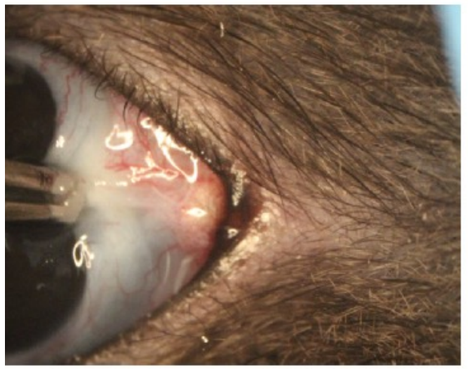




14G, 17G, 22G, 23G, and 24G PGSU implants, loaded with 70% w/w micronized lactose

- Drug loading up to 80%
- Diameter as small as 200um
- Low material requirements for formulation process
- Smaller devices are better tolerated in the eye

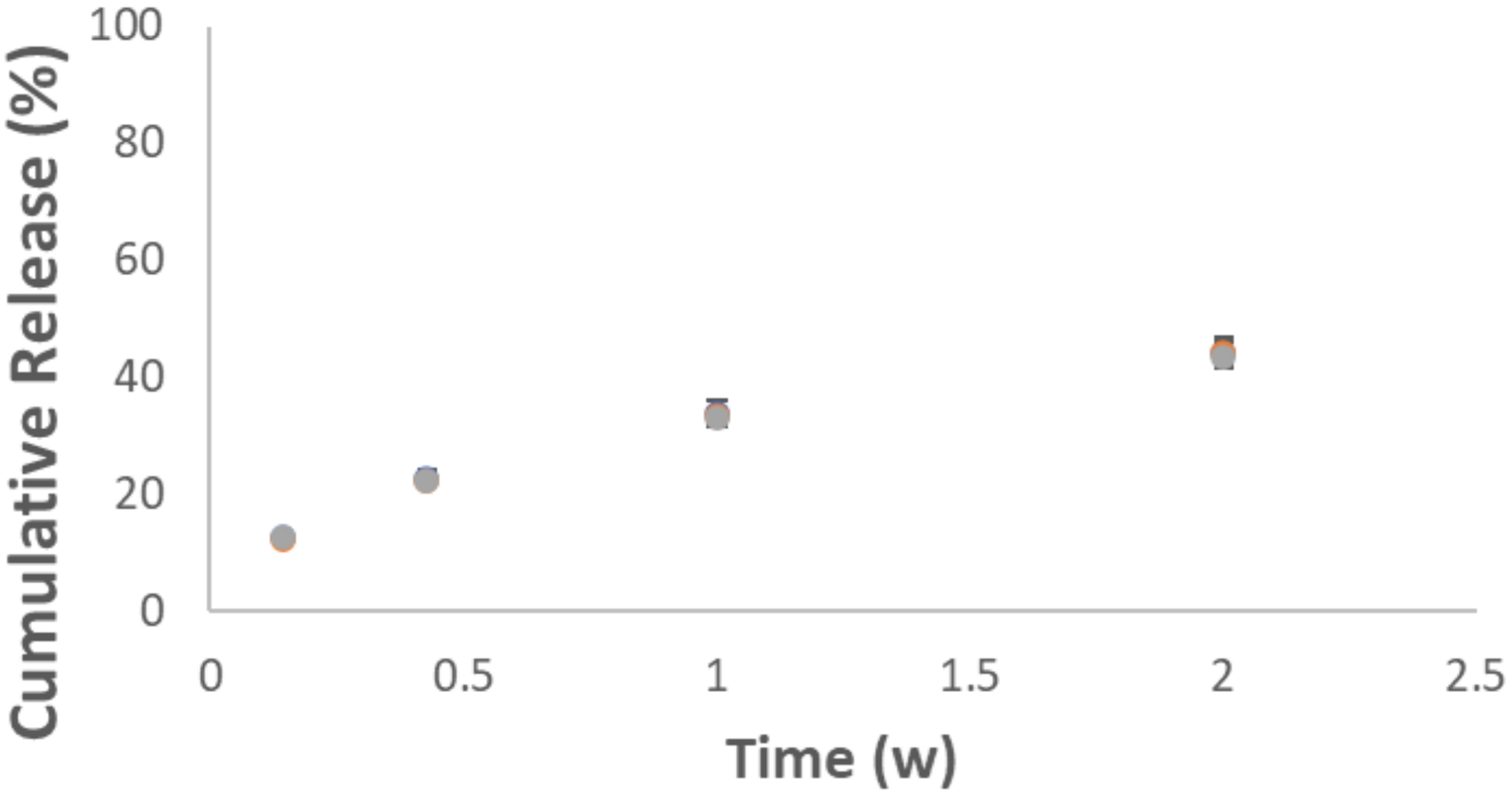
Rat model, episcleral implantation, 2 weeks



No conjunctival or corneal inflammation or changes

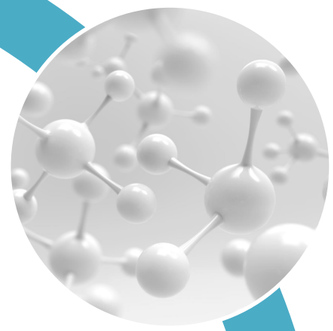
Proof of Concept Studies for Microimplants

- Devices:
  - 10 % w/w loaded with a hydrophobic corticosteroid
  - 300 µm diameter
  - 20 mm length
- Minimal bust release, even in high surface area devices.
- Tight reproducible release rates across devices.
- Not true zero-order release but pretty close.



From polymers to partnerships, Secant helps companies realize their long-acting drug delivery needs.

Hydralese™



New Device Forms

- Smaller microdevices
- Gastroretentive shapes
- Microparticles

New APIs

- Peptides
- Proteins
- Antibodies

New Partnerships

- Secant continues to partner with new customers and collaborators

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- Stephanie Reed, Ph.D.
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- Dennis Carney

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