Phase 1 Study of an Intracameral Travoprost Hydrogel-based Implant for the Treatment of POAG and Ocular Hypertension

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Financial Disclosures

- Sponsorship of clinical trial: Ocular Therapeutix, Inc.
- Goldberg D (presenting author), Walters TR and Bacharach J are investigators in the clinical trial sponsored by Ocular Therapeutix, Inc.
- Goldstein MH, Cheung M, Braun E & Silva F are employees of Ocular Therapeutix, Inc.

Unmet Need in Glaucoma Therapy

Poor Adherence has been shown to be Associated with Disease Progression and Blindness

- Glaucoma is a chronic condition which cannot be reversed and must be monitored for life[1]
- Lowering intraocular pressure (IOP) is critical for slowing disease progression in glaucoma and ocular hypertension[2]
- Prostaglandin analogues are commonly used as the first line of therapy to effectively lower IOP[3]

Chronic Eye Drop Therapy Issues affecting IOP Control Management

- Poor adherence to regimen[1,4,5]
- Limited bioavailability[6]
- Dissatisfaction with local side effects[7]
  - Hyperemia with topical travoprost eye drops
- Limitations with topical drops application[8]
  - Difficulty with handling the bottle
  - Limited instillation accuracy
  - Potential washout of drops

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2. Noecker RJ. Ther Clin Risk Manag. 2006;2(2):193-206.
3. Quigley HA, Broman AT. Br J Ophthalmol. 2006;90(3):262-267.
4. Olthoff CMG, Schouten JSAG, van de Borne BW, Webers CAB. Ophthalmology. 2005;112(6):953-961.
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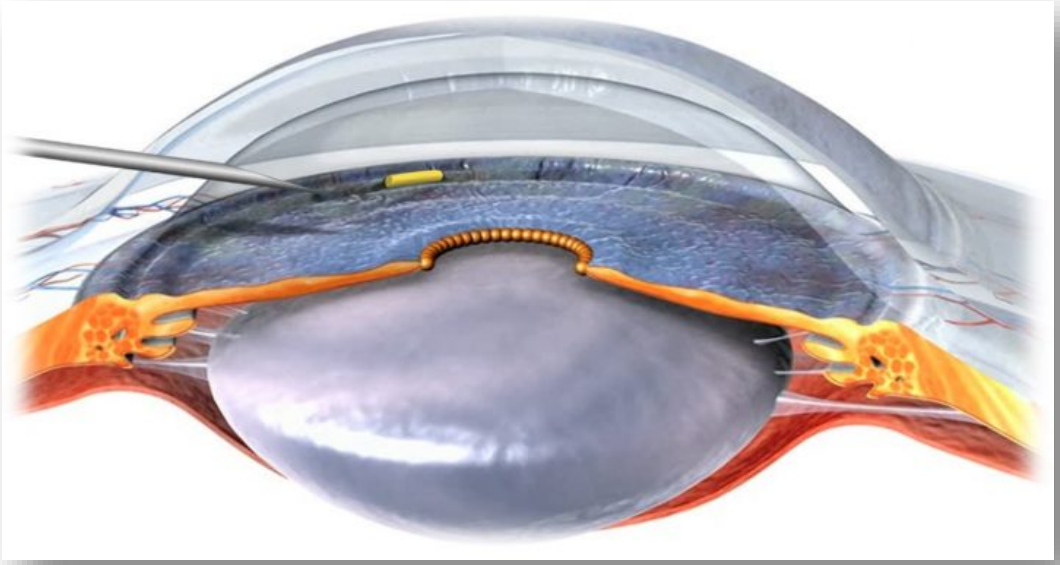
6. Saettone MF. Business Briefing: Pharmatech. 2002;1:167-171.
7. Inoue K. Managing adverse effects of glaucoma medications. Clin Ophthalmol. 2014;8:903-913.
8. An JA, Kasner O, Samek DA, Lévesque V. J Cataract Refract Surg. 2014;40(11):1857-1861.

OTX-TIC (Travoprost Intracameral Implant)

For Intracameral Injection

Product Attributes

- Travoprost loaded microparticles in hydrogel with a goal of sustained drug delivery of 4-6 months
- Administered via a single injection with proprietary injector (26G-27G)
- Implant resides in the iridocorneal angle, hydrates in less than 2 minutes
- Preservative-free
- Fully biodegradable



Hydrogel implant incorporates travoprost delivered via an intracameral injection

In preclinical models (beagle dogs):

- Steady state *in vitro* and *in vivo* release through 4 months, which correlates to a duration of 4-6 months in humans
- Demonstrated IOP lowering effect of approximately 25-30% through 4 months

OTX-TIC PHASE 1 STUDY

OBJECTIVE: To evaluate the safety, tolerability and efficacy of a single OTX-TIC implant, in subjects with primary open-angle glaucoma or ocular hypertension in a Phase 1 study

DESIGN

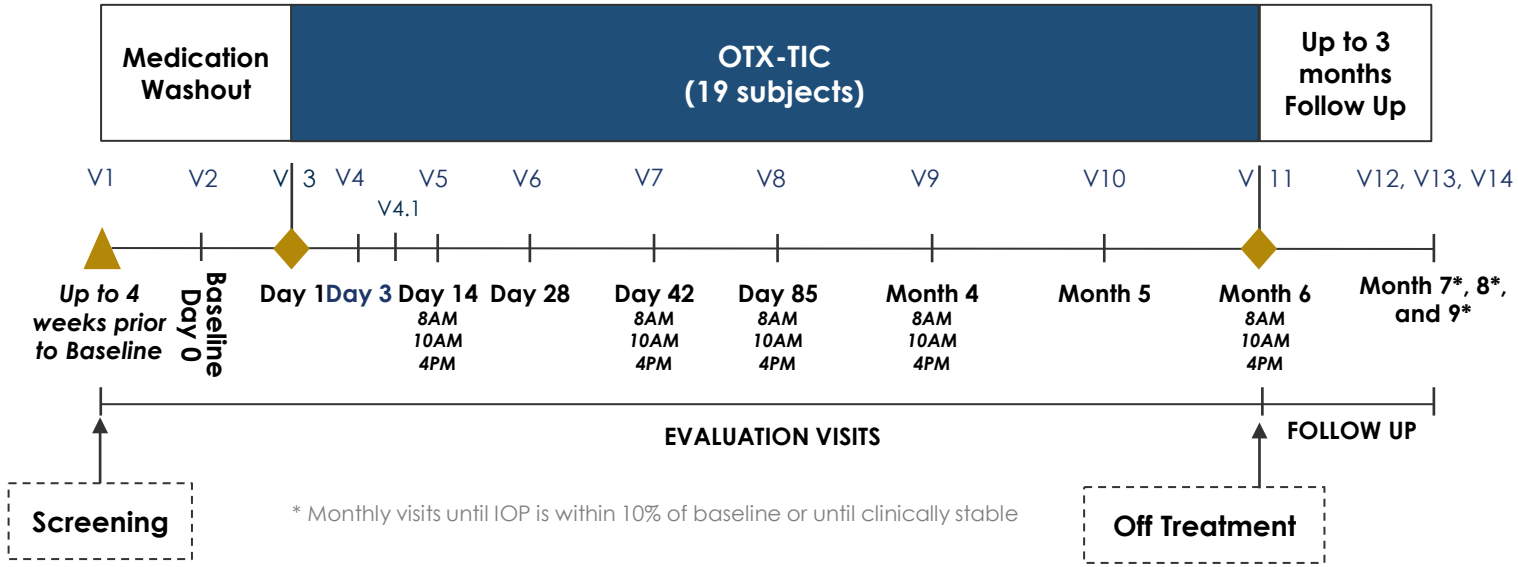
- Open-label, proof-of-concept study
- US study, 19 subjects at 5 sites
- One eye per patient will be treated
- Key Inclusion criteria:
  - Controlled ocular HTN or POAG
  - Open, normal anterior chamber angles on gonioscopy

EVALUATIONS

- Safety, tolerability, and biological activity
- Diurnal IOP at Baseline, 2 weeks, 6 weeks, 12 weeks, Month 4, and Month 6 (8 AM, 10 AM, 4 PM)

ACTIVE COMPARATOR

- Non-study eye receives **topical travoprost** daily



Cohort 1: 15µg
(n=5)

Cohort 2: 26µg
(n=4)

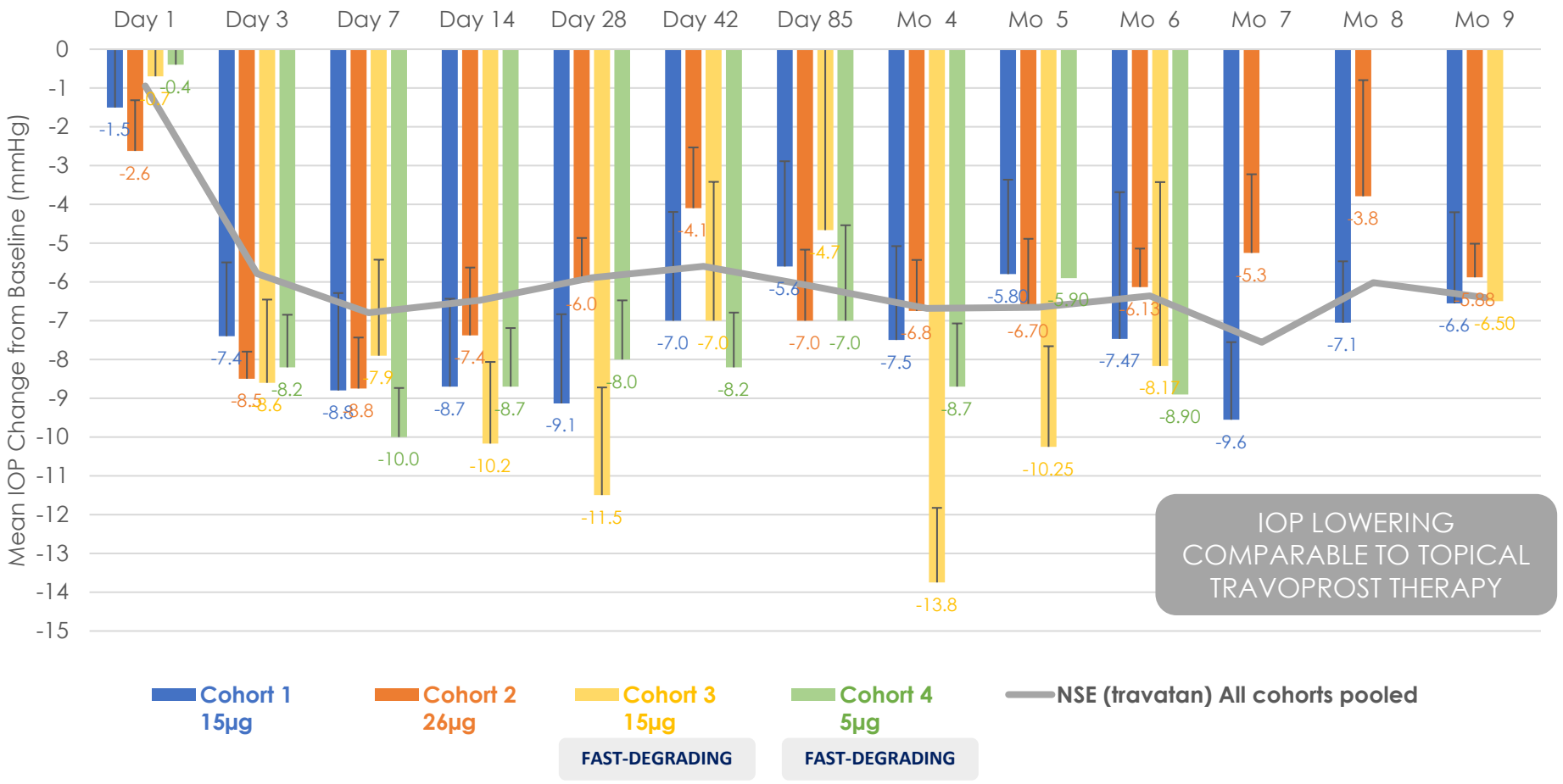
Cohort 3: 15µg
[Fast Degrading Hydrogel]
(n=5)

Cohort 4: 5µg
[Fast Degrading Hydrogel]
(n=5)‡

NB: Interim look as of 04/12/2021; Unmonitored data.
‡Ongoing follow-up

All Cohorts: Mean IOP Change From Baseline

IOP Decreased After 2 Days Following OTX-TIC Implantation & Lowering to 7-11 mmHg Recorded



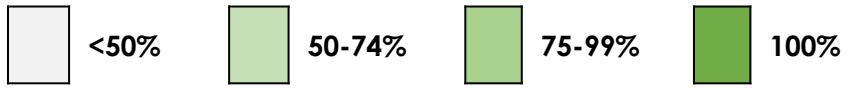
NB: Interim look as of 04/12/2021. Unmonitored data (8AM measurements). If the study eye was given other IOP lowering medication, the IOP value was removed from the analysis

All Cohorts: Duration Of Effect With One Implant

Cohort 2 Showed the Most Consistent Durable Response in all Subjects up to Month 6 & 50% of Subjects up to Month 9

	Day 42 % (n/N)	Day 85 % (n/N)	Month 4 % (n/N)	Month 5 % (n/N)	Month 6 % (n/N)	Month 7 % (n/N)	Month 8 % (n/N)	Month 9 % (n/N)	Month 10-22 % (n/N)
Cohort 1 (15 µg) N=5	**100**(5/5)	**100**(5/5)	**80**(4/5)	**80**(4/5)	**60**(3/5)	40 (2/5)	40 (2/5)	40 (2/4)	20 (1/5)
Cohort 2 (26 µg) N=4	**100**(4/4)	**100**(4/4)	**100**(4/4)	**100**(4/4)	**100**(4/4)	**100**(4/4)	**75**(3/4)	**50**(2/4)	NA
Cohort 3 (15 µg) (Fast-degrading) N=5	**100**(5/5)	**60**(3/5)	40 (2/5)	40 (2/5)	40 (2/5)	20 (1/5)	20 (1/5)	20 (1/5)	NA
Cohort 4 (5 µg) (Fast-degrading) N=5‡	**100**(5/5)	**100**(5/5)	**80**(4/5)	**75**(3/4) ‡	**75**(3/4) ‡	NA	NA	NA	NA
Total‡	**100 (19/19)**	**89 (17/19)**	**74 (14/19)**	**72‡ (13/18)**	**67‡ (12/18)**	**50 (7/14)**	**43 (6/14)**	**39 (5/13)**	**20 (1/5)**

‡Last subject in Cohort 4 past Month 4 timepoint so far and follow-up is ongoing



NB: Interim look as of 04/12/2021. Unmonitored data (8AM measurements)

All Cohorts: Safety Overview

Ocular Adverse Events in the Study Eye

			Fast-degrading		
Number of subjects with ocular AEs:	**Cohort 1 (15µg) N=5**	**Cohort 2 (26µg) N=4**	**Cohort 3 (15µg) N=5**	**Cohort 4* (5µg) N=5**	**OTX-TIC N=19**
Iritis (low grade)	2	2	1	1	6
Peripheral anterior synechiae	3	0	0	0	3
Corneal Edema	0	1	0	0	1
Subconjunctival Hemorrhage	0	0	1	0	1
Elevated IOP	0	0	2	0	2
Transient BCVA decrease	0	1	1	0	2
Total AEs per cohort	**5**	**4**	**5**	**1**	**15**

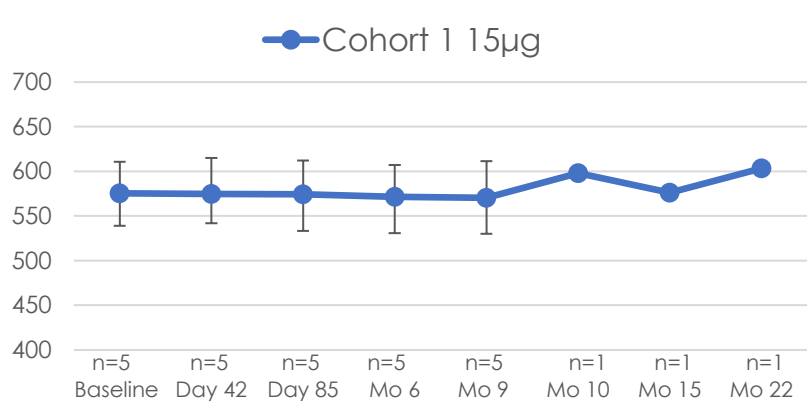
NB: In Cohort 1, two same subjects had low grade iritis and peripheral anterior synechiae

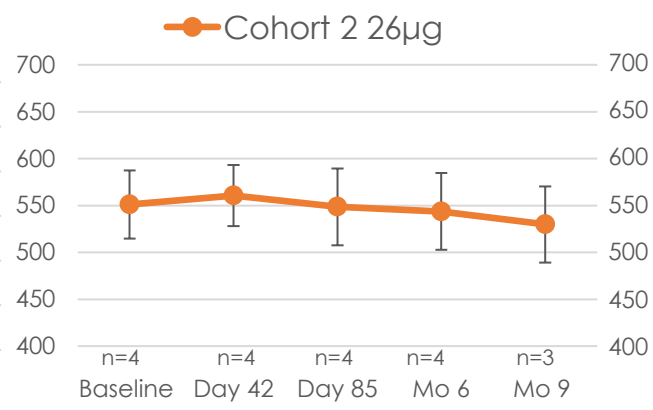
NB: Interim look as of 04/12/2021; Unmonitored data; .*Cohort 4: Ongoing follow-up

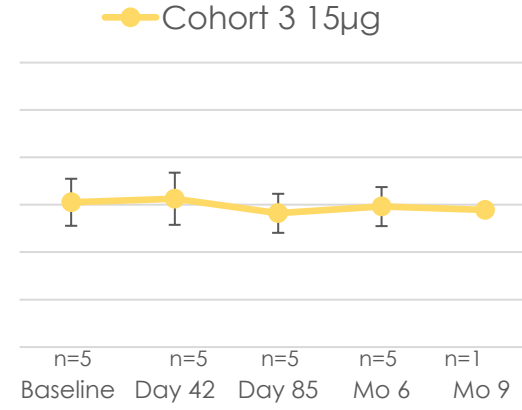
All Cohorts: No Effect Observed On Corneal Health

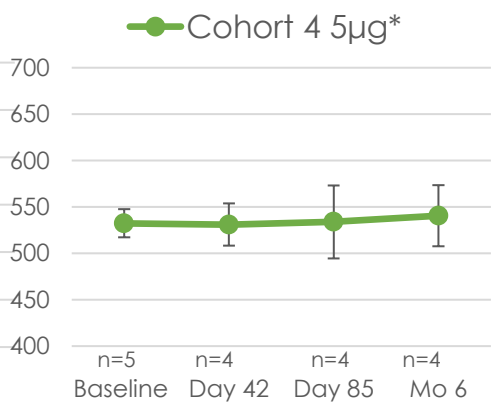
Pachymetry & Endothelial Cell Counts Indicate No Clinically-Meaningful Change from Baseline

Pachymetry (µm)

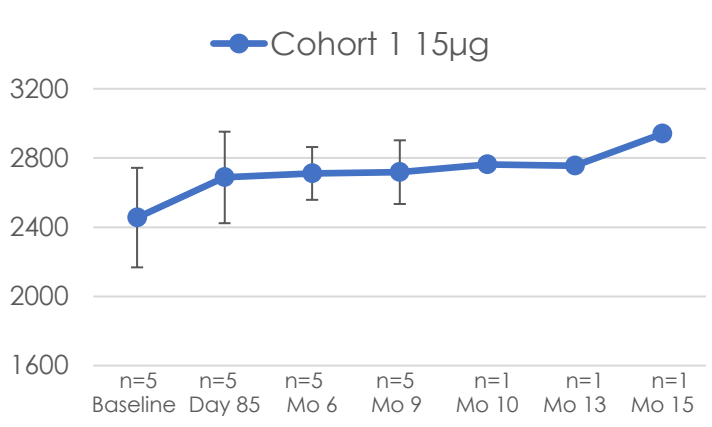


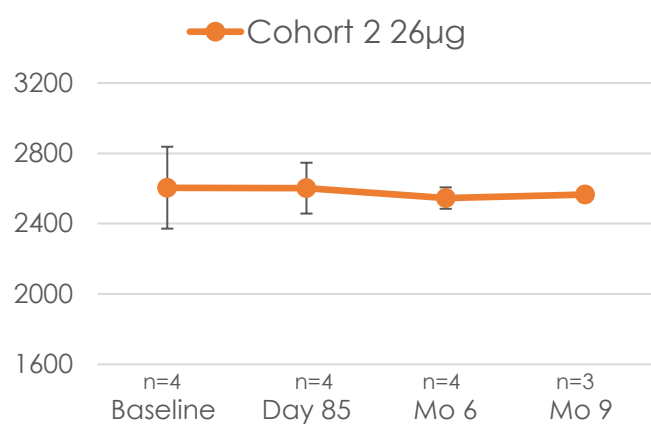


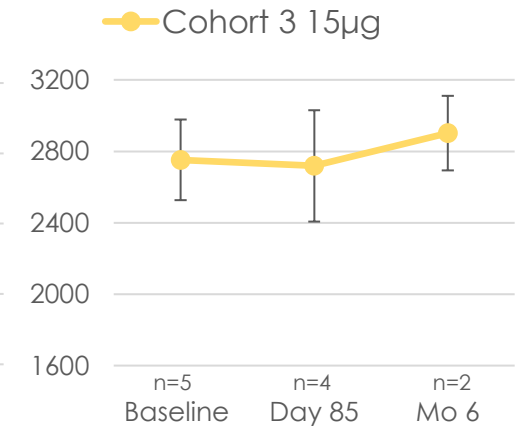


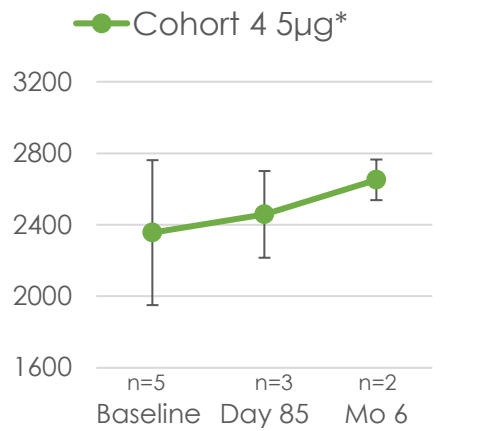


Endothelial Cell Counts (Automated)









NB: Interim look as of 04/12/2021; Unmonitored data.*Cohort 4: Ongoing follow-up

Conclusions

OTX-TIC shows Promise as a Sustained-Release Therapy with a Long Duration of Action

☑**Clinically-meaningful decrease in IOP**

Mean IOP values were decreased in patients receiving both OTX-TIC as early as two days following administration, and mean IOP decrease was comparable to topical travoprost therapy

☑**Duration of therapy**

Many subjects exhibited duration of IOP-lowering effect of 6+ months in Cohorts 1 and 2, and between 3-6 months in Cohorts 3 and 4 (fast degrading implant) with a single implant: Longest and most consistent IOP lowering in Cohort 2

☑**Bioresorbable**

Implant biodegraded in 5- 7 months (Cohorts 1 & 2); Fast degrading implants biodegraded in 3-5 months (Cohorts 3 & 4)

☑**Implant location and movement**

Implant was not observed to move at slit lamp and was visible at all exams in all patients using gonioscopy

☑**Corneal health**

Endothelial cell counts, pachymetry assessments, and slit lamp examinations indicate no changes from baseline

NB: Interim look as of 04/12/2021; Unmonitored data.

NEXT STEPS:

- **Ongoing Study; Continued long-term evaluation in 1 subject in Cohort 4**
- **Phase II Trial Planning Initiated; Planned start-up later this year**