Hydrogel-based, Sustained-release Intracameral Travoprost Implant for Glaucoma Therapy: A Phase 1 Clinical Trial

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Financial Disclosures

- Damien Goldberg (presenting author), Thomas R. Walters and Jason Bacharach were investigators in this clinical trial
- Elizabeth Braun, Matthew Cheung and Michael H. Goldstein are employees and Fabiana Q. Silva is a former employee of Ocular Therapeutix, Inc.
- Clinical Trial Sponsor: Ocular Therapeutix, Inc.

Unmet Need in Glaucoma Therapy

Poor Adherence May 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]

Topical Glaucoma Treatment Issues

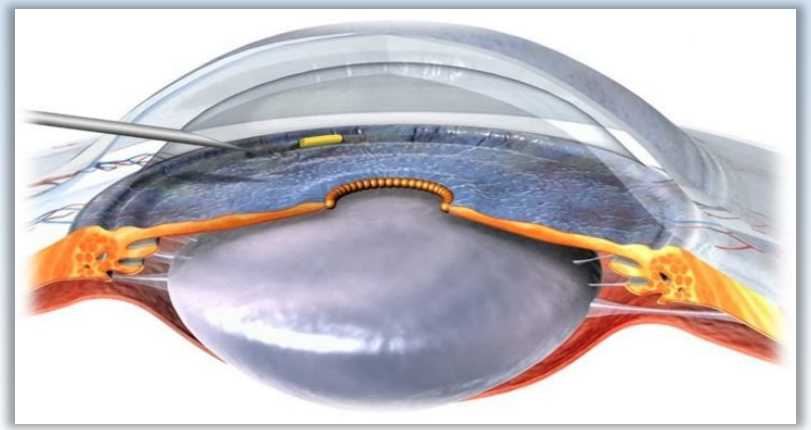
- Poor adherence to regimen[1,4,5]
- Limited bioavailability[6]
- Dissatisfaction with local side effects[7]
  - Hyperemia with topical travoprost eye drops
- Limitations with topical drops application[8]
  - Difficulty with handling the bottle
  - Limited instillation accuracy
  - Potential washout of drops
- Use of preservatives which can aggravate ocular surface disease[9]

References: 1. Nordstrom BL, Friedman DS, Mozaffari E, Quigley HA, Walker AM. *Am J Ophthalmol*. 2005;140(4):598-606. 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. 5. Schwartz GF, Quigley HA. *Surv Ophthalmol*. 2008;53 Suppl1:S57-68. 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. 9. Rasmussen CA, Kaufman PL, Kiland JA. Benzalkonium Chloride and Glaucoma. *J Ocul Pharmacol Ther*. 2014;30(2-3):163-169.

OTX-TIC: Travoprost Intracameral Implant

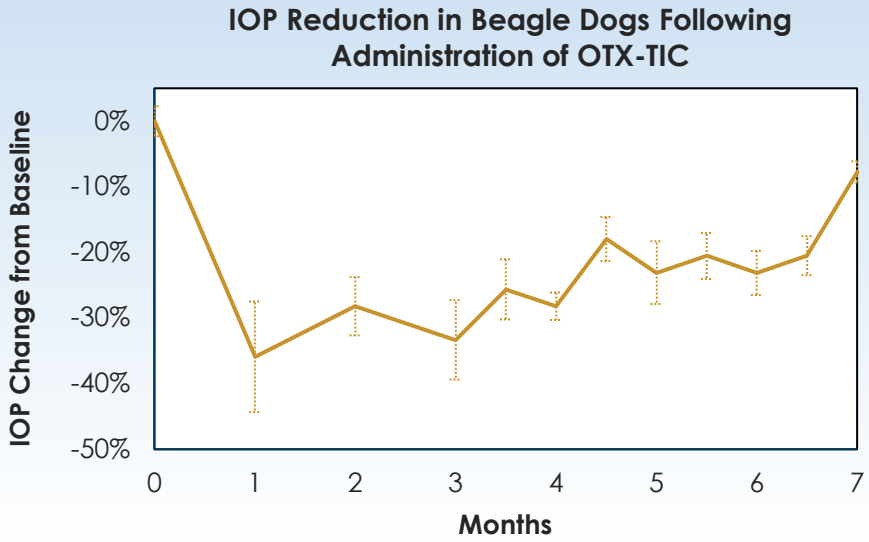
Travoprost Intracameral Implant

- Sustained-release, biodegradable, preservative-free implant with travoprost-loaded microparticles in hydrogel
- Administered by a single injection (26-27G) and resides in the iridocorneal angle



Preclinical Studies in Beagle Dogs

- IOP lowering effect of approximately 25-30% through 4-6 months[1]
- No statistically significant changes in central corneal thickness over the course of 7 months[2]



References: 1. Blizzard C, Desai A, Gelormini A, et al. Preclinical Assessment of OTX-TIC (travoprost) Biodegradable Hydrogel Intracameral Implant for the Treatment of Glaucoma. Presented at the ASCRS Annual Meeting, April 15, 2018. Washington DC. 2. Driscoll A, Blizzard C, Desai A, et al. Effect of OTX-TIC, a Sustained Release Travoprost Intracameral Implant on Central Corneal Thickness in Beagles. Presented at the Association for Research in Vision and Ophthalmology Annual Meeting. April 28 – May 2, 2019. Vancouver, Canada.

Study Design: Open-label Phase 1 Clinical Trial

Objective

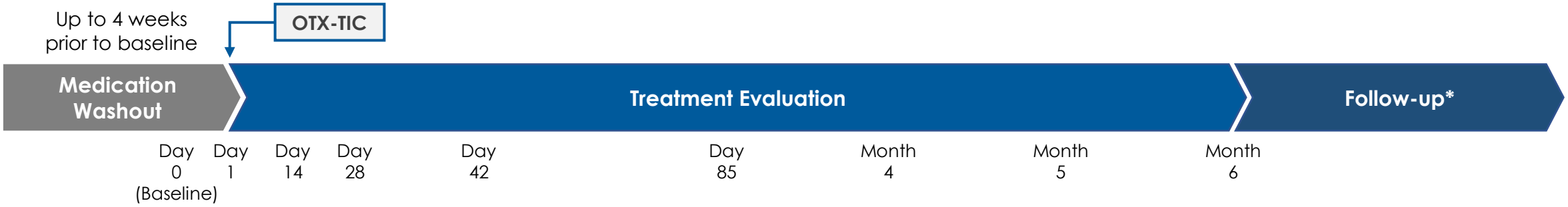
- To evaluate the safety, tolerability and efficacy of a single OTX-TIC implant, in subjects with POAG or OHT

Treatment

- OTX-TIC in the Study Eye
- Topical travoprost in the Non-study Eye

Evaluations

- Safety, tolerability, and biological activity
- Diurnal IOP (8AM, 10AM, 4 PM) at Baseline, Day 14, Day 42, Day 85, Month 4, and Month 6



Key Inclusion Criteria

1. Controlled ocular POAG or OHT
2. Open, normal anterior chamber angles on gonioscopy

	OTX-TIC Dose
Cohort 1 (n=5)	15 µg
Cohort 2 (n=4)	26 µg
Cohort 3 (n=5)	15 µg (fast-degrading hydrogel)
Cohort 4 (n=5)	5 µg (fast-degrading hydrogel)

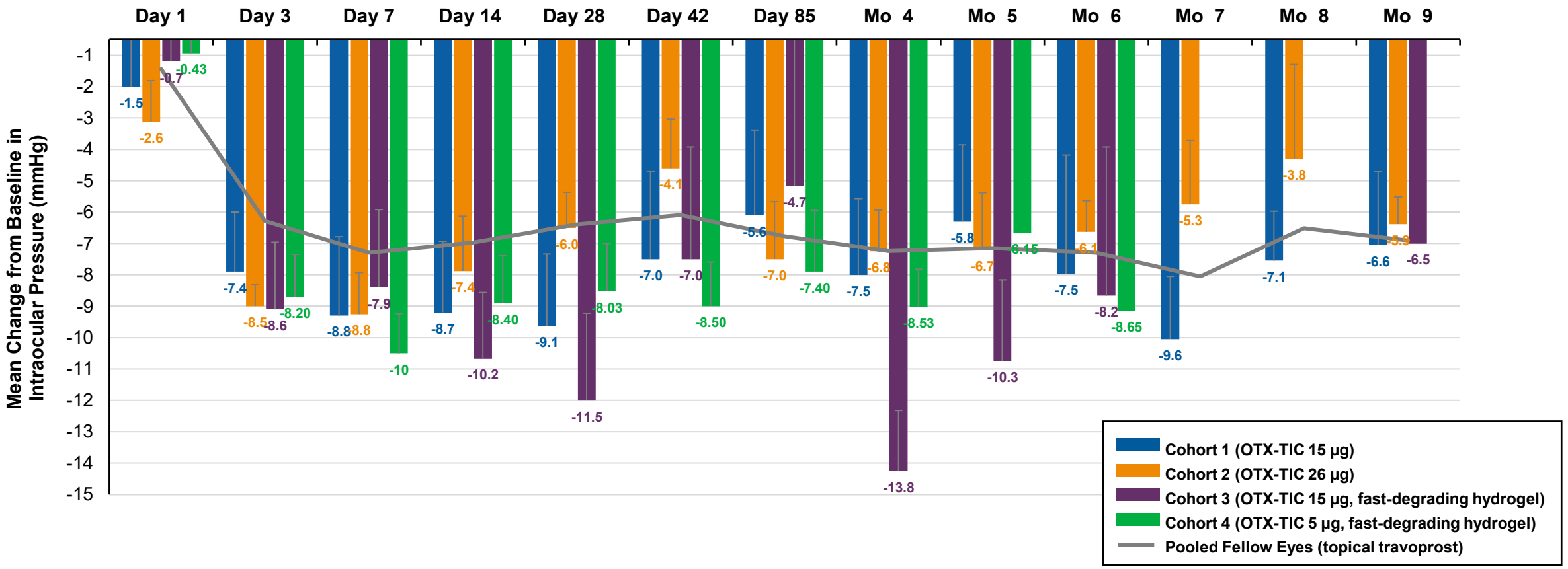
*Monthly visits until IOP is within 10% of baseline or until clinically stable

Baseline Demographics

	Cohort 1 (n=5)	Cohort 2 (n=4)	Cohort 3 (n=5)	Cohort 4 (n=5)
Mean age (SD), years	72.8 (5.6)	74.3 (7.1)	65.8 (7.9)	66.0 (14.4)
Range	65-80	63-82	53-76	47-84
Female, n (%)	3 (60%)	4 (100%)	4 (80%)	4 (80%)
Race, n (%)				
White	5 (100%)	2 (50%)	2 (40%)	5 (100%)
Black	0	2 (50%)	3 (60%)	0
Mean Baseline IOP (SD) After Washout, mmHg				
Study eye (OTX-TIC)	26.8 (3.5)	26.1 (0.9)	26.5 (4.3)	24.9 (0.8)
Non-study eye (Topical travoprost)	25.8 (2.5)	25.1 (0.9)	25.2 (4.0)	22.9 (1.9)
IOP Lowering Treatments Prior to Washout, n (%)				
Naïve	1 (20%)	0	0	3 (60%)
1 Medication	2 (40%)	3 (75%)	5 (100%)	2 (40%)
2 Medications	1 (20%)	1 (25%)	0	0
≥3 Medications	1 (20%)	0	0	0

Mean IOP Change from Baseline

- IOP reduction began 2 days following implantation of OTX-TIC and was comparable to topical travoprost



* Subjects who received rescue therapy (ie, IOP lowering medication other than OTX-TIC) were excluded from analysis

Duration of Effect with a Single Implant

- Cohort 2 showed the most consistent durable response in all subjects up to Month 6 and in 50% of subjects up to Month 9

Percentage of Study Eyes Not Requiring Rescue Therapy After a Single Implant Administration

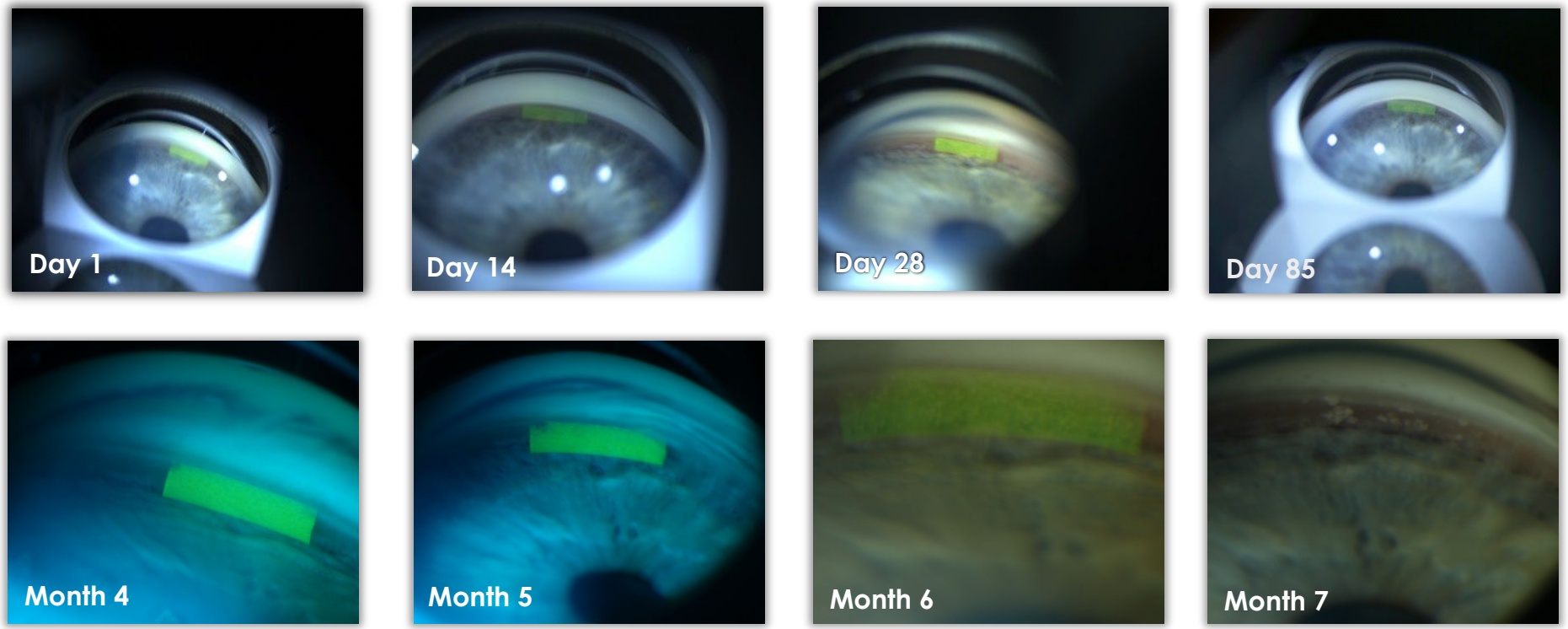
	Day 42 % (n/N)	Day 85 % (n/N)	Month 4 % (n/N)	Month 5 % (n/N)	Month 6 % (n/N)	Month 7 % (n/N)	Month 8 % (n/N)	Month 9 % (n/N)	Month 10-22 % (n/N)
Cohort 1 (15 µg) N=5	**100**(5/5)	**100**(5/5)	**80**(4/5)	**80**(4/5)	**60**(3/5)	40 (2/5)	40 (2/5)	40 (2/4)	20 (1/5)
Cohort 2 (26 µg) N=4	**100**(4/4)	**100**(4/4)	**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)	**80**(4/5)	**80**(4/5)	NA	NA	NA	NA
Total	100 (19/19)	89 (17/19)	74 (14/19)	74 (14/19)	68 (13/19)	50 (7/14)	43 (6/14)	39 (5/13)	20 (1/5)

Unmonitored data (8AM measurements)

Visualization of the Travoprost Implants

- No implant movement was observed at the slit lamp
- **Cohorts 1 & 2**: Implant biodegraded by 5-7 Months
- **Cohorts 3 & 4**: Fast-degrading hydrogel-based implants biodegraded by 3-5 Months in majority of subjects

Cohort 1: Subject 01-001



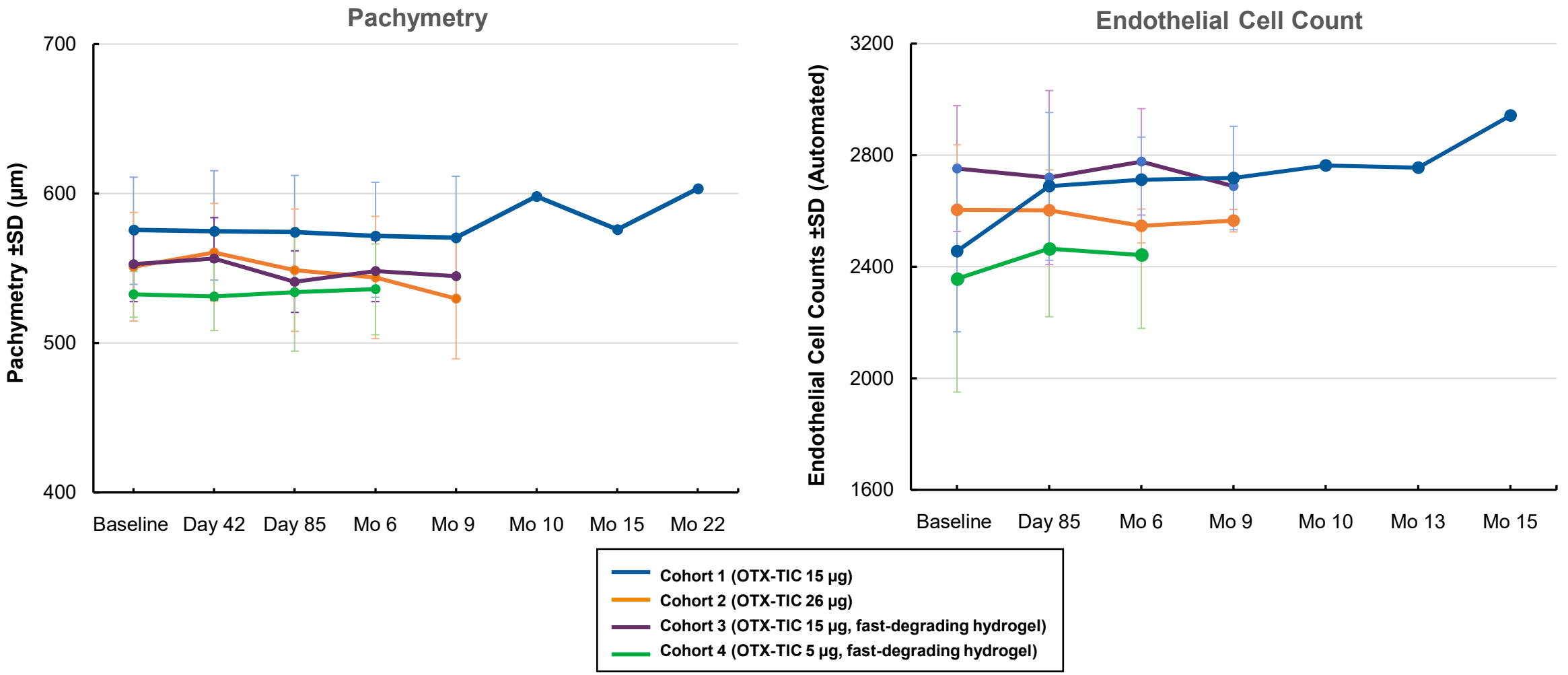
OTX-TIC Safety Summary

No serious AEs were reported

Ocular AEs in the Study Eye, n	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	2	2	1	1	6
Peripheral anterior synechiae	3	0	0	0	3
Corneal edema	0	1	2	0	3
Elevated IOP	0	0	3	0	3
Transient BCVA decrease	0	1	1	0	2
Subconjunctival hemorrhage	0	0	1	0	1
Posterior vitreous detachment	1	0	0	0	1
Inferior corneal keratic precipitates	0	1	0	0	1
Total AEs	**6**	**5**	**8**	**1**	**20**

Pachymetry and Endothelial Cell Counts

- No clinically meaningful change from baseline in corneal health were observed for any cohort



Conclusions

OTX-TIC demonstrates potential as a durable, sustained-release glaucoma therapy

- A single OTX-TIC implant produced IOP lowering effects comparable to topical travoprost therapy as early as two days following administration and lasted 6+ months in Cohorts 1 & 2 and 3-6 months in Cohorts 3 & 4
- Visualization of the implant indicated no movement within the anterior chamber and biodegradation in 5-7 and 3-5 months for Cohorts 1& 2 and Cohorts 3 & 4, respectively
- OTX-TIC was generally safe and well tolerated with no clinically meaningful changes in endothelial cell counts and pachymetry assessments
- Phase 2 study is expected to initiate in Q4 2021