Evaluating Safety, Tolerability and Efficacy of a Hydrogel-based Intracameral Travoprost Implant in Glaucoma Patients

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FINANCIAL DISCLOSURES

Thomas R. Walters, MD; Damien Goldberg, MD; and Jason Bacharach, MD were investigators in this clinical trial

Elizabeth Braun, PhD; Fabiana Q. Silva, MD; Matthew Cheung, PharmD; Srilatha Vantipalli, PhD; Jamie L. Metzinger, MPH; and Michael H. Goldstein, MD are employees 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

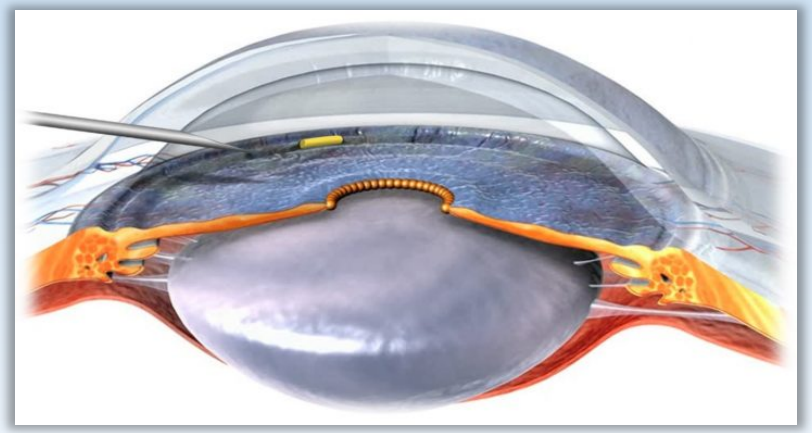
- Poor adherence to regimen[1,4,5]
- Limited bioavailability[6]
- Dissatisfaction with local side effects[7]
  - Hyperemia with topical travoprost eye drops
- Limitations with topical drops application[8]
  - Difficulty with handling the bottle
  - Limited instillation accuracy
  - Potential washout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

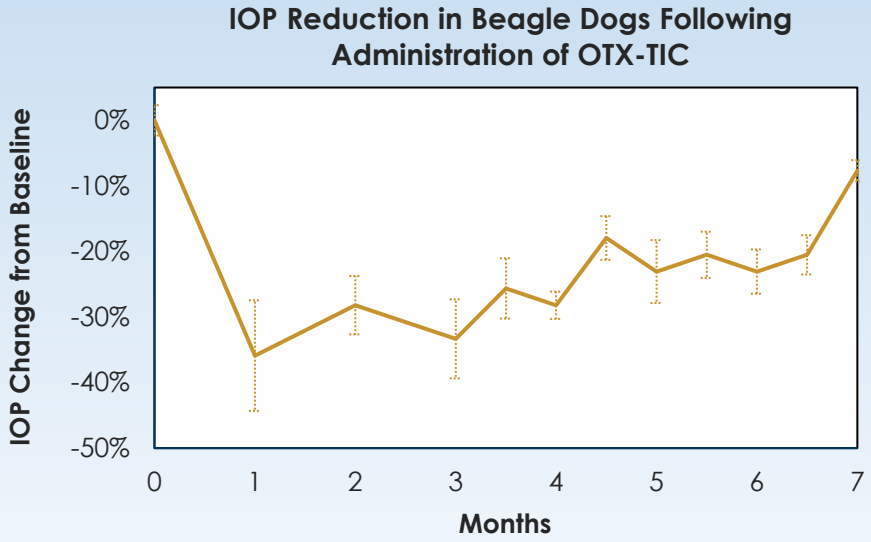
Travoprost Intracameral Implant

- 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.

Open-label, Active Comparator-Controlled, Phase 1 Trial of OTX-TIC in Glaucoma

Status

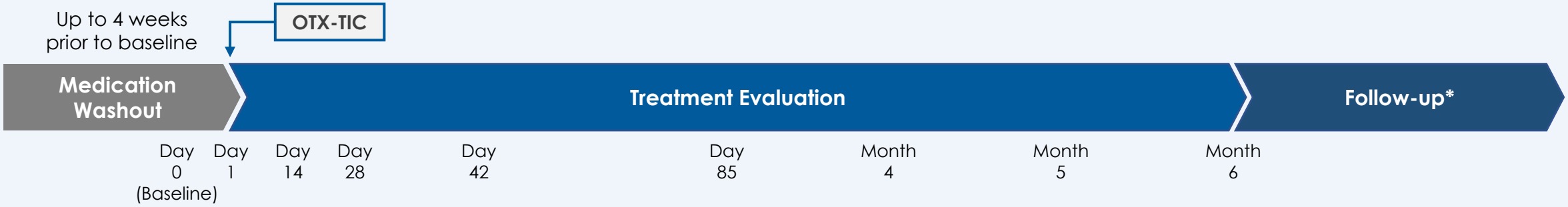
- 4 cohorts complete

Objective

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

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

Treatment

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

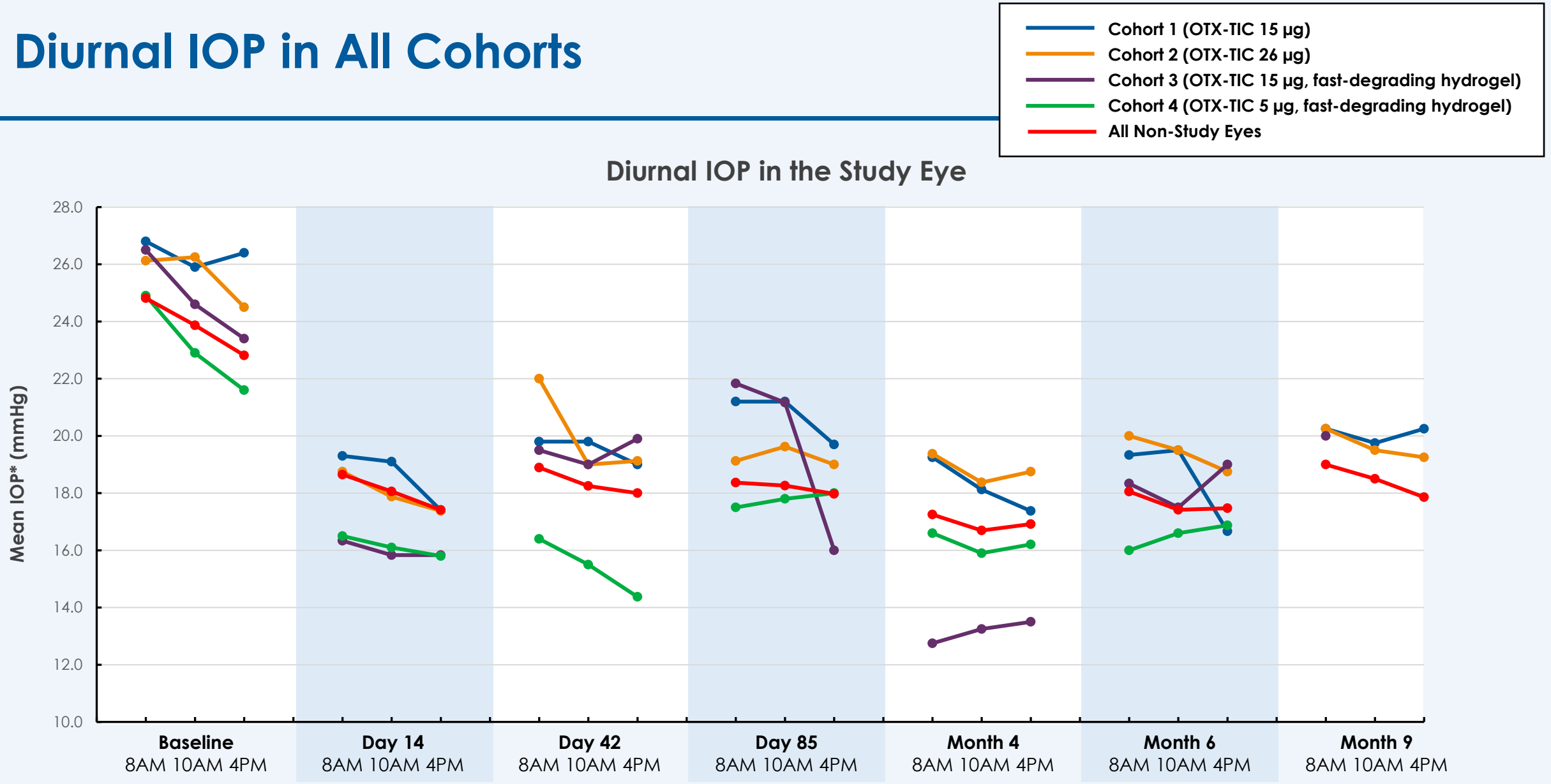
	OTX-TIC Dose
Cohort 1 (n=5)	15 µg
Cohort 2 (n=4)	26 µg
Cohort 3 (n=5)	15 µg (fast-degrading hydrogel)
Cohort 4 (n=5)	5 µg (fast-degrading hydrogel)

*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)	All Cohorts (N=19)
Mean age (SD), years	72.8 (5.6)	74.3 (7.1)	65.8 (7.9)	66.0 (14.4)	69.5 (10.2)
Range	65-80	63-82	53-76	47-84	47-84
Female, n (%)	3 (60%)	4 (100%)	4 (80%)	4 (80%)	15 (78.9%)
Race, n (%)					
White	5 (100%)	2 (50%)	2 (40%)	5 (100%)	14 (73.4%)
Black	0	2 (50%)	3 (60%)	0	5 (26.3%)
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)	26.1 (2.8)
Non-study eye (Topical travoprost)	25.8 (2.5)	25.1 (0.9)	25.2 (4.0)	22.9 (1.9)	24.7 (2.7)
IOP Lowering Treatments Prior to Washout, n (%)					
Naïve	1 (20%)	0	0	3 (60%)	4 (21%)
1 Medication	2 (40%)	3 (75%)	5 (100%)	2 (40%)	12 (63%)
2 Medications	1 (20%)	1 (25%)	0	0	2 (11%)
≥3 Medications	1 (20%)	0	0	0	1 (5%)

Diurnal IOP in All Cohorts

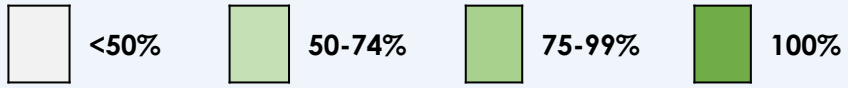


* Subjects who received rescue therapy (ie, IOP lowering medication other than OTX-TIC) were excluded from analysis

Cohorts 2 and 4 had the Highest Percentage of Subjects with Duration of Effect to Month 6

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)

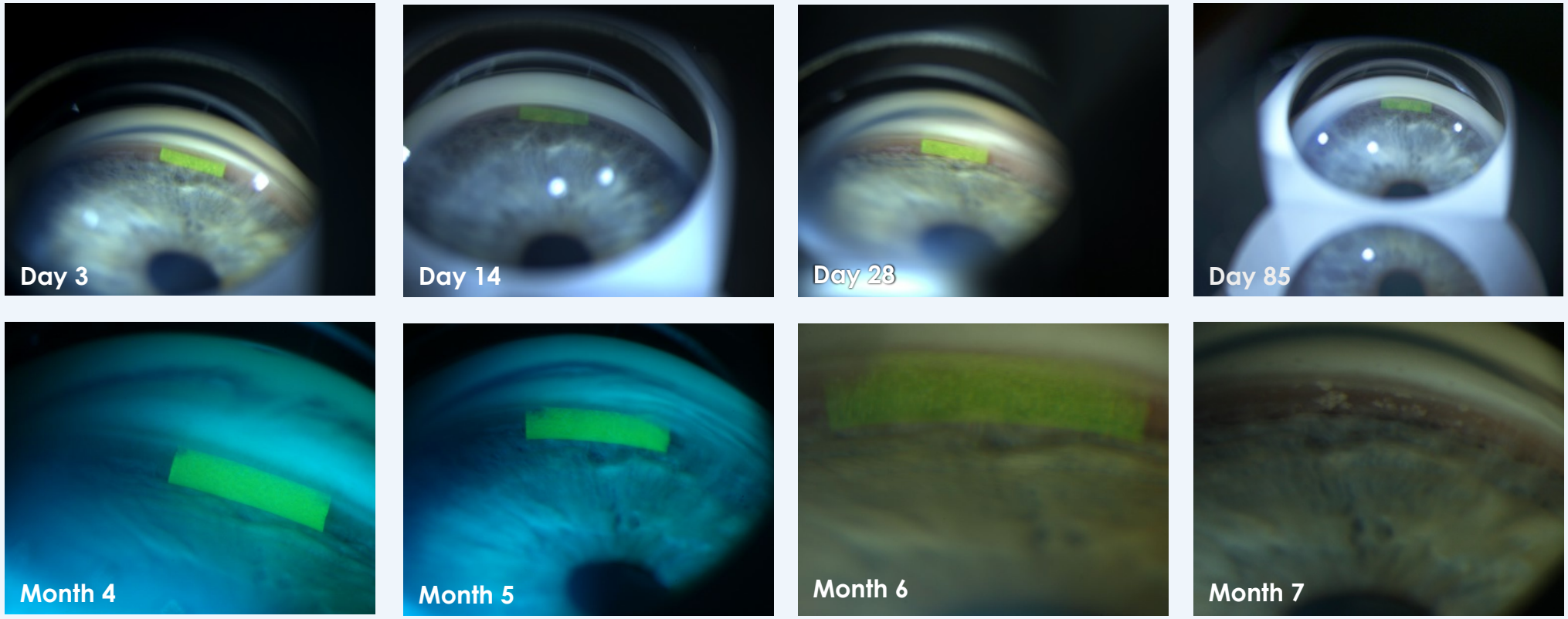


Unmonitored data (8AM measurements)

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 was Generally Well-tolerated with a Favorable Safety Profile

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 Indicate No Clinically Meaningful Changes from Baseline in Corneal Health in All Cohorts

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