A prospective, multi-center, open-label study to evaluate the safety, tolerability and efficacy of OTX-TIC (travoprost) intracameral implant in subjects with primary open-angle glaucoma (OAG) or ocular hypertension (OHT)

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Study Title	A prospective, multi-center, open-label study to evaluate the safety, tolerability and efficacy of OTX-TIC (travoprost) intracameral implant in subjects with primary open-angle glaucoma (OAG) or ocular hypertension (OHT).
Test Articles	**Treatment: OTX-TIC (**travoprost) intracameral implant (5 µg, 15 µg [2 different formulations], and 26 µg)
Phase of Clinical Study	1
Number of Sites	Approximately 5 sites in the United States
Study Objective	To assess the safety, tolerability and efficacy of a single sustained release dose of the OTX-TIC drug product in subjects with primary OAG or OHT.
Product Description	OTX-TIC is [redacted] The implant is designed to be injected in the irideocorneal angle. Hydration of OTX-TIC will initiate upon contact with biological fluids such as aqueous humor. OTX-TIC is retained in the irideocorneal angle for the entire duration of drug delivery (up to approximately 9 months, depending on the formulation). There are three doses (4 cohorts) of OTX-TIC used in this study to provide an extended release of travoprost over approximately 3 to 9 months, depending on the formulation: 1. Cohort 1: 15 µg (formulation 1) 2. Cohort 2: 26 µg (formulation 1) 3. Cohort 3: 15 µg (formulation 2) 4. Cohort 4: 5 µg (formulation 3) Only one implant may be placed in the study eye at a specified time depending on assignment to one of four cohorts.
Number of Subjects Planned	Approximately 20 subjects will be enrolled (~5 per a cohort).
Study Population	• Subjects with stable primary OAG or OHT *The contralateral eye, if needed, should only be treated with Travatan Z (if not contraindicated) once daily in the evening and the dose and frequency should remain unchanged for the duration of the study.*

Study Design and Overview	**Study Design:** This is a multicenter, open label, Phase 1 clinical study and will treat approximately 20 subjects in one of four cohorts (see table below). Each cohort may consist of 5 subjects each to receive a single implant to one eye.

Cohort	N	Age (yr)	Route of delivery	Total dose per eye (µg), formulation	Non-study eye treatment (if required)
1	~5	≥18	Intracameral Injection	15, formulation 1	Travatan *Z*
2	~5	≥18	Intracameral Injection	26, formulation 1	Travatan *Z*
3	~5	≥18	Intracameral Injection	15, formulation 2	Travatan *Z*
4	~5	≥18	Intracameral Injection	5, formulation 3	Travatan *Z*

The subjects will be followed for approximately 7 months (one month washout and 6 months follow-up after injected of the OTX-TIC implant). [redacted]

The Data Safety Monitoring Committee (DSMC) will review safety data from Cohort 1 prior to enrollment of any subject into Cohort 2.
All enrolled subjects on any glaucoma medication at time of screening will undergo a four to six week washout of all glaucoma medications prior to randomization.
Cohort 1 will be fully enrolled, and all safety and tolerability data of OTX-TIC for each subject in Cohort 1 (minimum follow up data for two weeks) will be assessed prior to any subject entering Cohort 2.
Dose escalation to Cohort 2 will be based on the recommendation of the DSMC and determined by the medical monitor (MM) or the Sponsor.
Cohort 3 and Cohort 4 may be initiated in parallel as Cohort 4 is a lower dose and the implant lasts for shorter duration than the doses studied in Cohorts 1, 2, and 3.
In the event that one dose limiting toxicity (DLT) is identified in the Cohort 2 dose group, enrollment will continue; however, if another DLT is identified, the previous (lower-Cohort 1) dose will be declared as the MTD.

	All enrolled subjects on any glaucoma medication at time of screening will undergo a four to six-week washout of all glaucoma medications prior to randomization. Subject can have only 1 eye treated with OTX-TIC as part of this study; that eye will be designated as the **SE**. If both eyes qualify for study entry the **SE** will be selected on the basis of the eye with the highest IOP after the protocol described washout period. If both eyes have the same IOP after the washout period, the right eye will be chosen as the **SE.** The contralateral eye, designated as the **non-study eye (NSE)**, if needed, will be treated with *Travatan Z if not contraindicated)*. The treatment of the **NSE** should remain consistent for the duration of the study.
Study Duration and Study Visits	The study is intended to last for approximately 7 months (including washout period prior to the injection and six months follow-up); there will be a two-part screening visit to allow for washout of any IOP lowering medications followed by the Day 1 visit with up to 12 visits (See Study Schedule). Visit 1 is a screening visit and should take place approximately 4 to 6 weeks prior to baseline visit. Subjects will begin washout of glaucoma medications, if needed. They will return in approximately 4 to 6 weeks for Visit 2 to confirm they meet eligibility criteria including IOP. Subjects will then be asked to return for Visit 3 where the OTX-TIC implant will be placed. Subjects will return for follow-up visit 2-3 days and 7 days later for post-operative evaluation and IOP check at Visits 4 and Visit 4.1. Subjects will then return in approximately two weeks (Visit 5) for a safety evaluation and diurnal IOP check. Subjects will return for follow-up Visit 6 (28 days), Visit 7 (6 weeks, diurnal IOP check), Visit 8 (12 weeks, diurnal IOP check), Visit 9 (Month 4, diurnal IOP check), and Visit 10 (Month 5) for safety evaluations and IOP check. Subjects will be asked to return approximately four weeks later for Visit 11 (Month 6) where they will have final safety evaluations, diurnal IOP measurements and be discharged from the study. [redacted]
Inclusion Criteria	Individuals of either gender will be eligible for study participation if they: 1. Are 18 years of age or older at the time of screening 2. Have a documented diagnosis of OHT, or primary OAG in the **study eye**

	3. Have IOP that is currently controlled (as assessed by the Investigator) [redacted] 6. Are able to comply with all study requirements 7. Have provided a written signed informed consent
Exclusion Criteria	Individuals are not eligible for study participation if they: [redacted] 3. Are unwilling to discontinue use of contact lenses prior to pachymetry (3 days) and throughout the entire study 4. Have a known or suspected allergy and/or hypersensitivity to a prostaglandin (i.e., travoprost), fluorescein or to any component of the study products [redacted]

	[redacted] 12. Have a history of significant ocular trauma within the past six months in the **study eye** 13. Have a history of peripheral iridotomy/iridectomy in the inferior 180° of the iris in the **study eye** 14. Have any history of bleeding disorder of use of medications which in the Investigator's opinion places at the subject at high risk during insertion of the implant 15. Had any ophthalmic surgical procedures (e.g., glaucoma laser, minimally invasive glaucoma surgery, refractive surgery) in the **study eye** within the last 6 months or will require ophthalmic surgery during the study period. Subjects currently or planning to be treated during the study with a CyPass implant will be excluded. 16. Have a history of penetrating keratoplasty in the **study eye** 17. Have proliferative diabetic retinopathy, or have a history of macular edema in **either eye** 18. Have an uncontrolled systemic disease or a debilitating disease (e.g., cardiovascular, hypertension, uncontrolled diabetes, or cystic fibrosis). 19. Have participated in any study involving an investigational drug either in the U.S. or outside the U.S. within the past 30 days 20. Are an employee of the site that is directly involved in the management, administration, or support of the study, or are an immediate family member of the same 21. Are currently pregnant or breast-feeding or of childbearing potential without the use of adequate contraceptive methods during the length of the study
Safety Evaluations	The Investigator will grade the ease of the procedure. Subjects will be monitored for approximately 1 hour immediately following injection. Safety evaluations include: • Adverse event reporting (Adverse Events will be assessed to determine if they are procedure related) [redacted] • BCVA • Slit lamp biomicroscopy • Gonioscopy • Fundus exam • Endothelial cell count with specular microscopy • Pachymetry

	• Anterior segment (AS)-OCT • Automatic Visual Field [redacted]
Study Outcome Measure	• Diurnal IOP (8 a.m., 10 a.m., 4 p.m.) will be checked at baseline, Day 14 (Visit 5), Day 42 (Visit 7), Day 85 (Visit 8), Month 4 (Visit 9), and Month 6 (Visit 11). IOP will continue to be measured if biological activity is noted at Month 6. • Intraocular pressure (at 8 a.m. on the day of insertion; Days 3, 7, and 28; and Month 5 [Visit 10])
Procedural Exclusion Criteria	Unsuccessful intracameral injection (record reason for injection failure on the electronic Case Report Form, i.e., eCRF); in the case of injection failure do not attempt another injection. The study will be supplemented with additional subjects to account for these subjects in order to ensure that the necessary number of subjects receive the implant to inform on safety, tolerability and efficacy.