TITLE:

A PROSPECTIVE, MULTICENTER, OPEN LABEL EXTENSION STUDY TO EVALUATE THE LONG TERM SAFETY OF OTX-TP (SUSTAINED RELEASE TRAVOPROST INTRACANALICULAR INSERT)

NCT#: NCT04061044

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Study Title	A Prospective, Multicenter, Open Label Extension Study to Evaluate the Long Term Safety of OTX-TP (sustained release travoprost) Intracanalicular Insert
Test Article	OTX-TP (sustained release travoprost) Intracanalicular Insert
Phase of Clinical Study	3
Study Objective	To evaluate the long term safety of repeat dose OTX-TP, a sustained release travoprost drug product, placed in the canaliculus of the eyelid in the treatment of subjects with open-angle glaucoma or ocular hypertension.
Product Description	The OTX-TP drug product is a dried polyethylene glycol (PEG) based, rod-shaped hydrogel intracanalicular insert designed to be placed in the superior or inferior canaliculus. The hydrogel swells on contact with moisture to occlude the lumen, thus holding the intracanalicular insert in place. Once OTX-TP swells to fill the canaliculus, it is contained in the canaliculus until the hydrogel is resorbed. [redacted] The intracanalicular insert also has an inert PEG tip to aid in insertion. Travoprost is a synthetic prostaglandin F2α analogue used for reducing elevated intraocular pressure in subjects with open-angle glaucoma or ocular hypertension. Travoprost is the active pharmaceutical ingredient in Travatan®, Travatan Z® and Izba™ (Alcon Laboratories Inc., Fort Worth, TX) which have been approved by the US FDA for this indication. OTX-TP is an extended release drug delivery insert designed to release travoprost over a period of up to 12 weeks. As both the hydrogel [redacted] degrade by hydrolysis, OTX-TP softens, liquefies and is cleared through the nasolacrimal duct.
Study Design and Overview	Study Design: This is a prospective, multicenter, open label trial, to evaluate the long term safety of OTX-TP, a sustained release drug product placed in the canaliculus of the eye in subjects with open-angle glaucoma or ocular hypertension. A total of up to 100 subjects (200 eyes) who have completed the OTX-16-002 trial, A Prospective, Multicenter, Randomized, Parallel-Arm, Double Masked, Vehicle Controlled Phase 3a Study Evaluating the Safety and Efficacy of OTX-TP in the Treatment of Subjects with Open-Angle Glaucoma or Ocular

	Hypertension, will receive OTX-TP in this trial to evaluate the long term safety of the OTX-TP drug product and will be followed for approximately 12 months. The study will be conducted at up to 15 qualified investigative sites in the United States. Study arms and treatments: OTX-TP: In the OTX-16-002 trial, subjects were randomized to receive either OTX-TP or a placebo vehicle. In this long term safety study, all subjects will receive OTX-TP in both eyes. Masking from the OTX-16-002 will remain in place until all data review has been completed.
Study Duration and Study Visits	Each subject's participation in the study is intended to last for approximately 12 months. Once a subject has successfully completed OTX-16-002, and has provided written informed consent, the subject will be screened for entry into this open label extension trial. Visit 1 is a screening and insertion visit that should take place within 7 days from when the subject exits the OTX-16-002 trial. This visit may be conducted on two separate days. At the end of Visit 1, subjects will have the OTX-TP intracanalicular insert placed in both eyes. Subjects in this study will not be randomized. All subjects will receive OTX-TP in both eyes. Subjects will be followed every 6 weeks during this study for approximately 12 months. All subjects will undergo follow-up visits at 1.5 months (Visit 2), 3 months (Visit 3), 4.5 months (Visit 4), 6 months (Visit 5), 7.5 months (Visit 6), 9 months (Visit 7), 10.5 months (Visit 8), and 12 months (Visit 9). If at any visit, the investigator deems it necessary to initiate IOP-lowering drops as rescue therapy due to an increase in IOP, the subject will begin the IOP-lowering drops at the Investigator's discretion and continue to be followed until the intracanalicular insert is no longer present and patency is confirmed. Tear fluid samples will be collected at specified study visits, if possible. At visits where no insertion is required, tear fluid samples should be collected following the visualization assessment. At visits requiring an insertion, tear fluid samples should be collected approximately an hour prior to insertion, and again up to two hours post insertion. Insertions will be attempted at 3 months (Visit 3), 6 months (Visit 5), and 9 months (Visit 7). Insert placement is to be performed after patency confirmation only if prior insert is not present, whether or not IOP is controlled. If IOP is controlled and insert is present, insertion may be deferred until the next study visit. If IOP is not controlled and insert is present, the insert will be removed and another insert will be placed.

	If insertion is not successful at any visit, re-insertions may be attempted at the Investigator's discretion within seven days of the failed attempt. If insertion is again unsuccessful, sites should discuss potential for re-insertion with Ocular Therapeutix on a case by case basis. For subjects with Early Loss of Intracanalicular Insert: At any visit, including unscheduled visits, prior to the scheduled replacement visits (3 months, 6 months, and 9 months), if the intracanalicular insert is not visualized in one or both eyes by the Investigator, the Investigator will insert a new intracanalicular insert in the respective eye(s) after confirming patency. For any insert replacements, IOP assessments should be completed prior to replacement. The subject will continue to return for follow-up visits per the study schedule. The number of replacements will be tracked and documented on the appropriate Case Report Form (CRF).
Inclusion Criteria	Subjects must meet all of the following criteria to be eligible: - Had prior bilateral treatment and completion, through a minimum of week 12, of the OTX-16-002 trial - Are informed of the nature of the study and subject is able to comply with study requirements and visit schedule for one year - Have provided written informed consent, approved by the appropriate Institutional Review Board
Exclusion Criteria	Subjects who meet any of the following criteria are not eligible: - Had more than 1 replacement, per eye, during participation in the OTX-16-002 trial - Had punctal or canaliculi related adverse events during the OTX-16-002 trial which required discontinuation (e.g., canaliculitis) - Used prohibited medications during the OTX-16-002 study, or the period between OTX-16-002 and this trial (with the exception of short term medication used to treat an adverse event or rescue therapy) - Missed more than 2 visits during participation in the OTX-16-002 trial - Had IOP $\geq$ 34 mmHg at the Screening/Insertion Visit, or any visit during the OTX-16-002 trial - Require contact lens use at any point during the study including the Screening/Insertion Visit(s) - Have planned intraocular surgery or laser over the one year study period - Have a cup to disc ratio > 0.80 (horizontal or vertical measurement) in either eye - Are currently pregnant or breast-feeding or who wishes to become pregnant during the length of study participation

	- Are determined by the Investigator to be ineligible for reasons not already specified (e.g., systemic or other ocular disease/abnormality, not a candidate for topical prostaglandin, therapy, specifically travoprost) if the health of the subject or the validity of the study outcomes may be compromised by the subject's enrollment - 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. - Are participating or plan to participate in any other investigational drug or device study during this study
Pharmacokinetics Parameters	The following pharmacokinetic parameters will be analyzed from tear fluid samples collected from subjects: The pharmacokinetic profile of travoprost and travoprost acid concentrations in tear fluid versus time. The maximum (C_{max}) and minimum (C_{min}) concentration of travoprost and travoprost acid in tear fluid. Calculations will be completed by the PK lab for tear fluid analysis.
Safety Evaluations	Safety evaluations include: - Adverse events - Subject ocular comfort assessment - Best corrected visual acuity (BCVA) - Slit lamp biomicroscopy including assessment and grade of ocular hyperemia (at slit lamp) and punctum exam - Intraocular pressure (IOP) - Fundus examination - Optical Coherence Tomography of optic nerve on nerve fiber layer - Automated perimetry - Number of subjects who need rescue therapy over the study period
Exploratory Evaluations	- Visualization of intracanalicular insert by the Investigator at each time point - Ease of placement of intracanalicular insert - Number of intracanalicular inserts required in each eye for the study period per subject
Procedural Exclusion Criteria	Unsuccessful punctal dilation of either eye (if needed) or punctum of either eye is too small to allow transient dilation to 0.7 mm prior for insertion of OTX-TP.