(NASDAQ: OCUL)

OCULAR THERAPEUTIX

BUILDING A NEW STRATEGIC IN OPHTHALMOLOGY

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Eyecelerator at AAO 2022 | Retina Showcase
September 29, 2022

FORWARD LOOKING STATEMENTS

Any statements in this presentation about future expectations, plans, and prospects for the Company, including the commercialization of DEXTENZA®, ReSure® Sealant, or any of the Company's product candidates; the commercial launch of, and the effectiveness of and amounts of reimbursement codes for, DEXTENZA; the conduct of post-approval studies of and compliance with related labeling requirements for DEXTENZA and ReSure Sealant; the Company's sales and marketing strategy; the development and regulatory status of the Company's product candidates, such as the Company's development of and prospects for approvability of OTX-CSI for the chronic treatment of dry eye disease, OTX-DED for the short-term treatment of the signs and symptoms of dry eye disease, OTX-TIC for the treatment of primary open-angle glaucoma or ocular hypertension, and OTX-TKI for the treatment of retinal diseases including wet AMD; the Company's plan to advance the development of its product candidates; the ongoing development of the Company's extended-delivery hydrogel depot technology; the potential utility of any of the Company's product candidates; the potential benefits and future operations of Company collaborations, including any potential future costs or payments thereunder; projected net product revenue, in-market sales and other financial and operational metrics of DEXTENZA and ReSure Sealant; potential market sizes for indications targeted by the Company's product candidates, if approved; the expected impact of the COVID-19 pandemic on the Company and its operations; the sufficiency of the Company's cash resources and other statements containing the words "anticipate," "believe," "estimate," "expect," "intend", "goal," "may", "might," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," and similar expressions, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. Actual results may differ materially from those indicated by such forward-looking statements as a result of various important factors. Such forward-looking statements involve substantial risks and uncertainties that could cause the Company's preclinical and clinical development programs, future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the timing and costs involved in commercializing DEXTENZA, ReSure Sealant or any product candidate that receives regulatory approval, including the conduct of post-approval studies, the ability to successfully develop and commercialize products for the ophthalmology office setting, the ability to retain regulatory approval of DEXTENZA, ReSure Sealant or any product candidate that receives regulatory approval, the ability to maintain and the sufficiency of product, procedure and any other reimbursement codes for DEXTENZA, the initiation, timing, conduct and outcomes of clinical trials, whether clinical trial data such as the data reported in this presentation will be indicative of the results of subsequent clinical trials, availability of data from clinical trials and expectations for regulatory submissions and approvals, the Company's ability to enter into and perform its obligations under collaborations and the performance of its collaborators under such collaborations, the Company's scientific approach and general development progress, the availability or commercial potential of the Company's product candidates, the Company's ability to meet supply demands, the Company's ability to generate its projected net product revenue and in-market sales on the timeline expected, if at all, the sufficiency of cash resources, the Company's existing indebtedness, the ability of the Company's creditors to accelerate the maturity of such indebtedness upon the occurrence of certain events of default, the severity and duration of the COVID-19 pandemic including its effect on the Company's revenues and relevant regulatory authorities' operations, any additional financing needs, the Company's ability to recruit and retain key personnel, and other factors discussed in the "Risk Factors" section contained in the Company's quarterly and annual reports on file with the Securities and Exchange Commission. In addition, the forward-looking statements included in this presentation represent the Company's views as of the date of this presentation. The Company anticipates that subsequent events and developments will cause the Company's views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, the Company specifically disclaims any obligation to do so, whether as a result of new information, future events or otherwise, except as required by law. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this presentation.

This presentation discusses investigational agents in development. Their efficacy and safety profiles have not been established, and they have not been approved for marketing by the FDA.

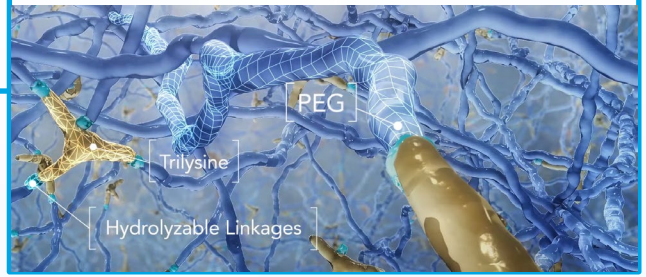
Ocular Therapeutix™

OTX-TKI: HYDROGEL DELIVERY OF AXITINIB

HYDROGEL DELIVERY PLATFORM

BIORESORBABLE, TARGETED, SUSTAINED DRUG DELIVERY

OTX's proprietary bioresorbable polymer matrix, a polyethylene glycol (PEG) hydrogel is a versatile platform for localized sustained drug delivery



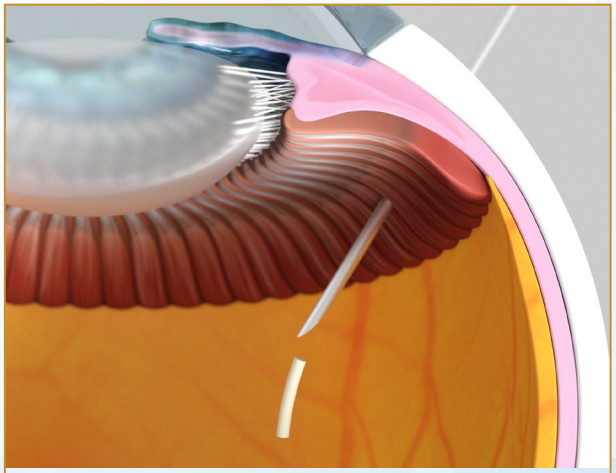
AXITINIB

MULTI-TARGET TYROSINE KINASE INHIBITOR FOR RETINAL VASCULAR DISEASES

Axitinib is a highly selective inhibitor of all VEGF and PDGF receptors with high affinity and low solubility compared to other ocular TKIs[1]

Drug	Inhibitory Concentrations for VEGFR2/KDR (IC_{50} in nM) (lower values indicate higher affinity)
Axitinib[2]	**0.2**
Sunitinib[3]	43
Vorolanib[3]	52

OTX-TKI: AXITINIB IN A HYDROGEL INTRAVITREAL IMPLANT



- **Single implant**
- **Completely bioresorbable over 6-9 months**
- **Administered by a 25G or smaller needle**
- **Covered by a US Patent that expires 2041[4]**

References: 1. Zhao Y, et al. *Oncologist*. 2015;20(6):660-673. 2. Gross-Goupil M, et al. *Clin Med Insights Oncol*. 2013;7:269-277. 3. Eyepoint Pharmaceuticals, Inc. Form 8-K. Published online September 15, 2020. Accessed August 24, 2022. https://sec.report/Document/0001564590-20-043596/ 4. Blizzard CD, Driscoll A, El-Hayek R, et al. Ocular implant containing a tyrosine kinase inhibitor. Published online September 13, 2022. Accessed September 26, 2022. Patent
Abbreviations: KDR, kinase insert domain receptor

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OTX-TKI PHASE 1 AUSTRALIA TRIAL

Key Inclusion Criteria

- Sub foveal neovascularization secondary to AMD
- **Treatment Naïve or Previously treated** with anti-VEGF injections and **with baseline retinal fluid**

Objectives

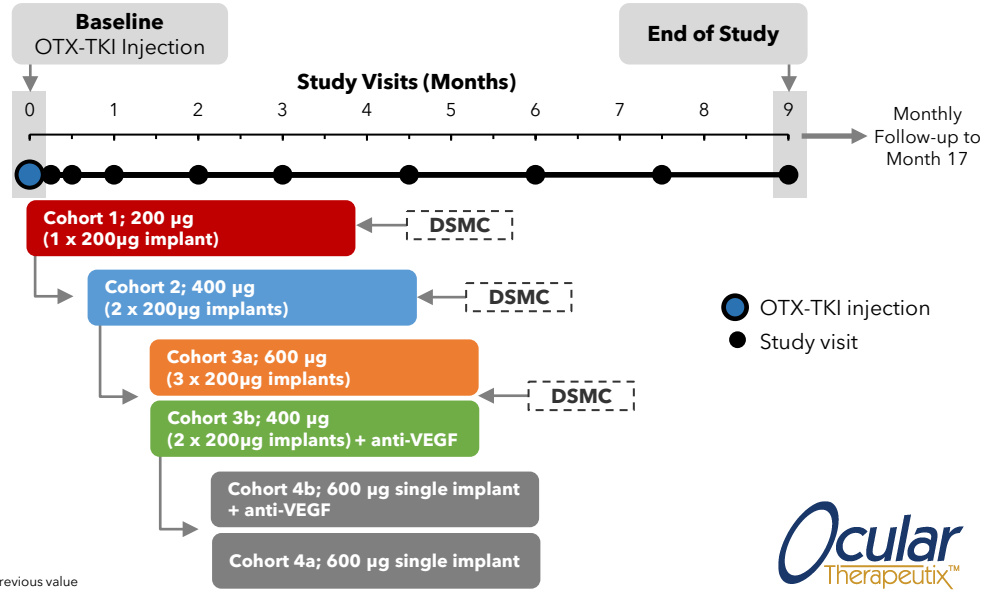
- Safety and tolerability
- Biological activity: mean change in central subfield thickness measured by SD-OCT, BCVA, and clinically-significant leakage on FA and/or OCT-A

Key Differences in Study Design:

	US Phase 1 Study	Australia Phase 1 Study
Inclusion Criteria	Controlled fluid	**Presence of retinal fluid**
OTX-TKI Implant	One 0.6 mg (600 µg) single implant	**Cohorts 1-3 used one to three 0.2 mg implants to achieve different doses (0.2, 0.4 and 0.6 mg)**
Anti-VEGF Induction	Yes, all subjects	**Only in Cohort 3b and 4b**
Rescue Criteria	i. Investigator discretion ii. Loss of ≥10 letters[a] iii. Evidence of >75µm CSFT & ≥5 letters loss[b] iv. New macular hemorrhage	**i. Investigator discretion** **ii. Loss of ≥15 letters[a]** **iii. Loss of ≥10 letters on 2 consecutive visits[a]** **iv. Evidence of >75µm CSFT[b]**

[a]From best previous BCVA due to AMD, with current BCVA not better than baseline
[b]Evidence of worsening disease activity manifest by greater than 75 µm CSFT from previous best value; letter loss compared to best previous value

Open-label, Dose Escalation Study



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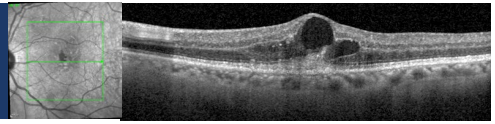
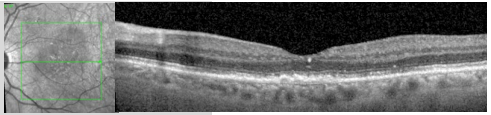
AUS PHASE I OTX-TKI TRIAL
BIOLOGIC ACTIVITY IN TREATMENT NAÏVE PATIENTS (N=11)

Cohort 3a (600 µg): **Treatment Naïve**

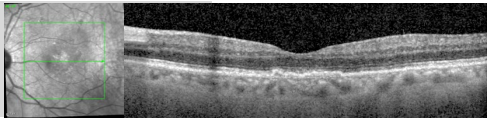
Baseline
CSFT: 484µm
BCVA: 56 letters (20/80)



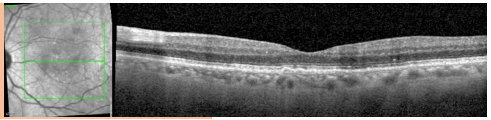
Month 2
CSFT: 236µm
BCVA: 74 letters (20/30)



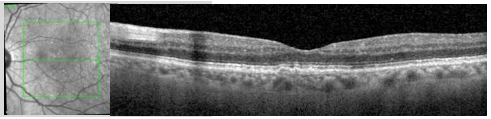
Month 3
CSFT: 232µm
BCVA: 73 letters (20/40)



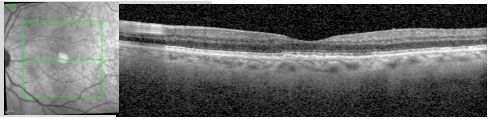
Month 6
CSFT: 239µm
BCVA: 80 letters (20/25)
+24 letters/-245µm



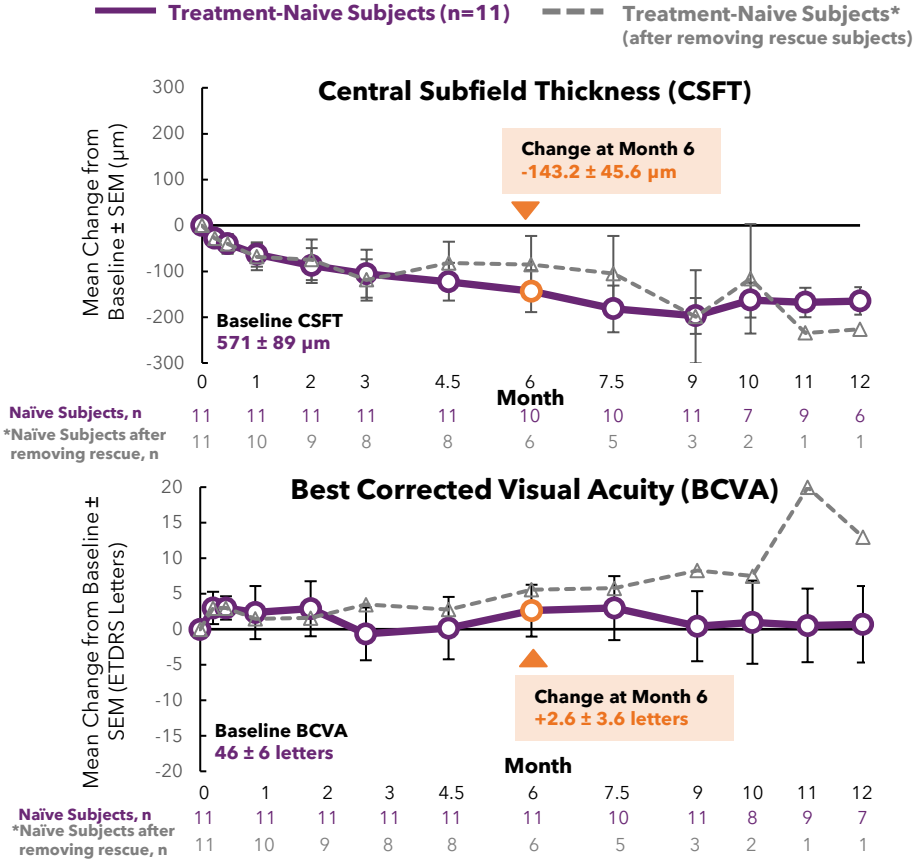
Month 9
CSFT: 244µm
BCVA: 81 letters (20/25



Month 11
CSFT: 249µm
BCVA: 76 letters (20/30)



Patient only received OTX-TKI, no anti-VEGF injections



Interim review, unmonitored data: data cut off August 5, 2022
Number of treatment-naïve subjects in each cohort. Cohort 1 (n=2), Cohort 2 (n=2), Cohort 3a (n=5), and Cohort 3b (n=2)

OTX-TKI PHASE 1 US TRIAL

Key Inclusion Criteria

- Subfoveal neovascularization secondary to AMD
- **Previously treated** with anti-VEGF injections and **controlled fluid** per investigator

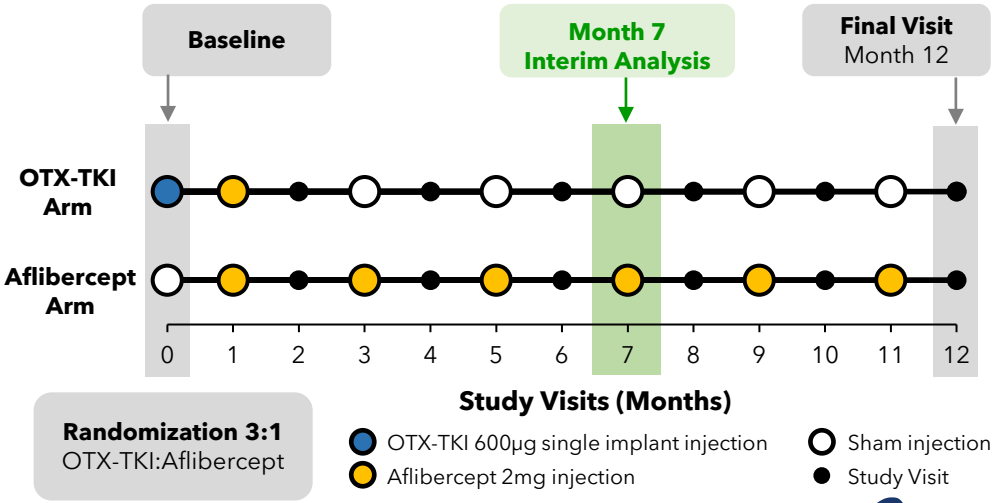
Objectives

- Safety, tolerability, durability and biological activity
- BCVA, mean change in CSFT measured by SD-OCT and safety evaluations

Key Differences in Study Design:

	US Phase 1 Study	Australia Phase 1 Study
Inclusion Criteria	**Controlled fluid**	Presence of retinal fluid
OTX-TKI Implant	**One 0.6 mg (600 µg) single implant**	Cohorts 1-3 used one to three 0.2 mg implants to achieve different dose levels (0.2, 0.4 and 0.6 mg)
Anti-VEGF Induction	**Yes, all subjects**	Only in Cohort 3b and 4b
Rescue Criteria	**i. Investigator discretion** **ii. Loss of ≥10 letters[a]** **iii. Evidence of >75µm CSFT & ≥5 letters loss[b]** **iv. New macular hemorrhage**	**i. Investigator discretion** **ii. Loss of ≥15 letters[a]** **iii. Loss of ≥10 letters on 2 consecutive visits[a]** **iv. Evidence of >75µm CSFT[b]**

Multicenter, Randomized, Double-masked Trial



[a]From best previous BCVA due to AMD, with current BCVA not better than baseline
[b]Evidence of worsening disease activity manifest by greater than 75 µm CSFT from previous best value; letter loss compared to best previous value

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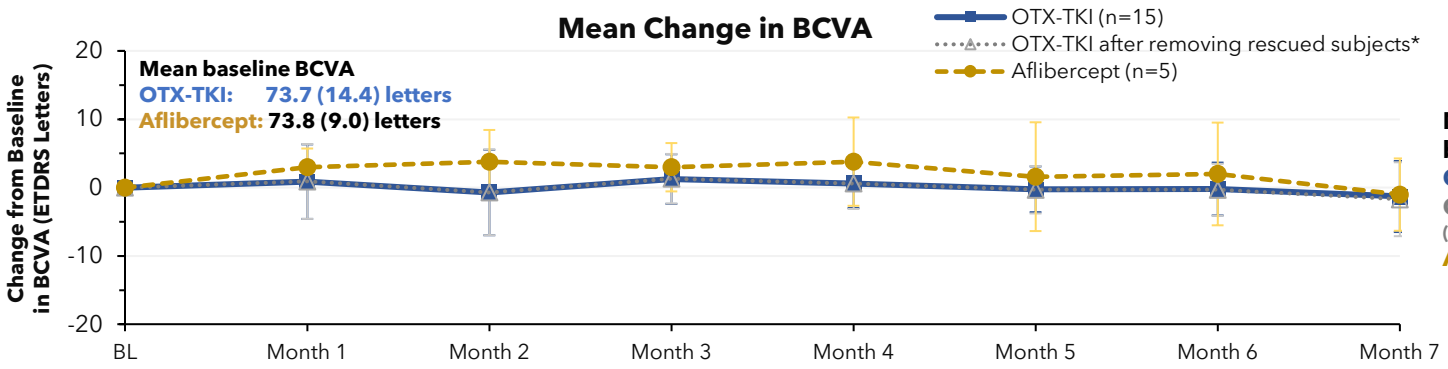
EFFECT OF OTX-TKI ON BCVA AND CSFT FOR 7 MONTHS

Sustained and stable effect with a single OTX-TKI implant comparable to aflibercept Q8W



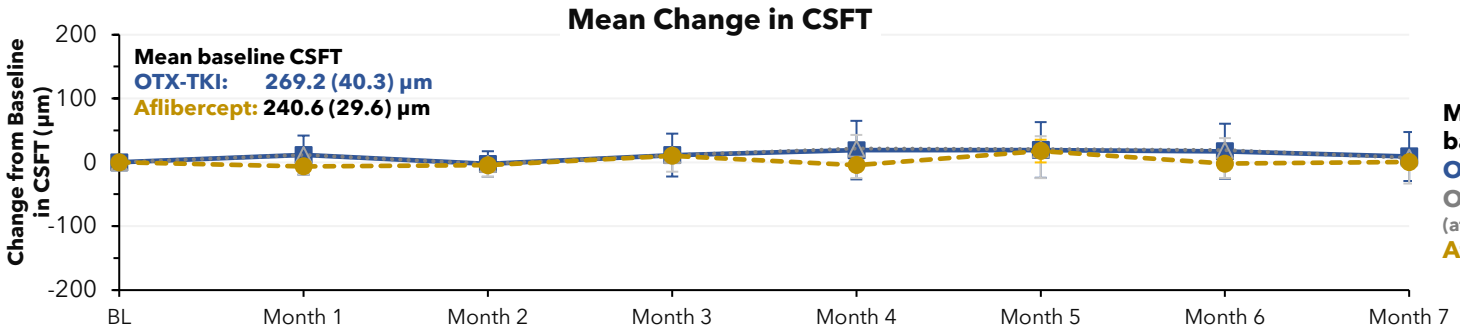
Mean change in BCVA from baseline to Month 7:

OTX-TKI: -1.3 (5.2) letters

OTX-TKI: -1.7 (5.4) letters

(after removing rescue subjects)

Aflibercept: -1.0 (5.3) letters



Mean change in CSFT from baseline to Month 7:

OTX-TKI: +9.2 (38.6) µm

OTX-TKI: +7.3 (40.8) µm

(after removing rescue subjects)

Aflibercept: +0.4 (9.1) µm

Interim review: data cut off August 24, 2022

Error bars represent standard deviation; n=14 in OTX-TKI arm at Months 2 and 7 due to missed visits.

*Sample size for OTX-TKI after removing rescued subjects: n=15 at Baseline and Months 1 and 3; n=14 at Month 2 (missed visit) and Months 4 and 5; n=12 at Month 6 and n=11 at Month 7

Abbreviations: BCVA, best corrected visual acuity; BL, baseline; CSFT, central subfield thickness; ETDRS, Early Treatment Diabetic Retinopathy Study

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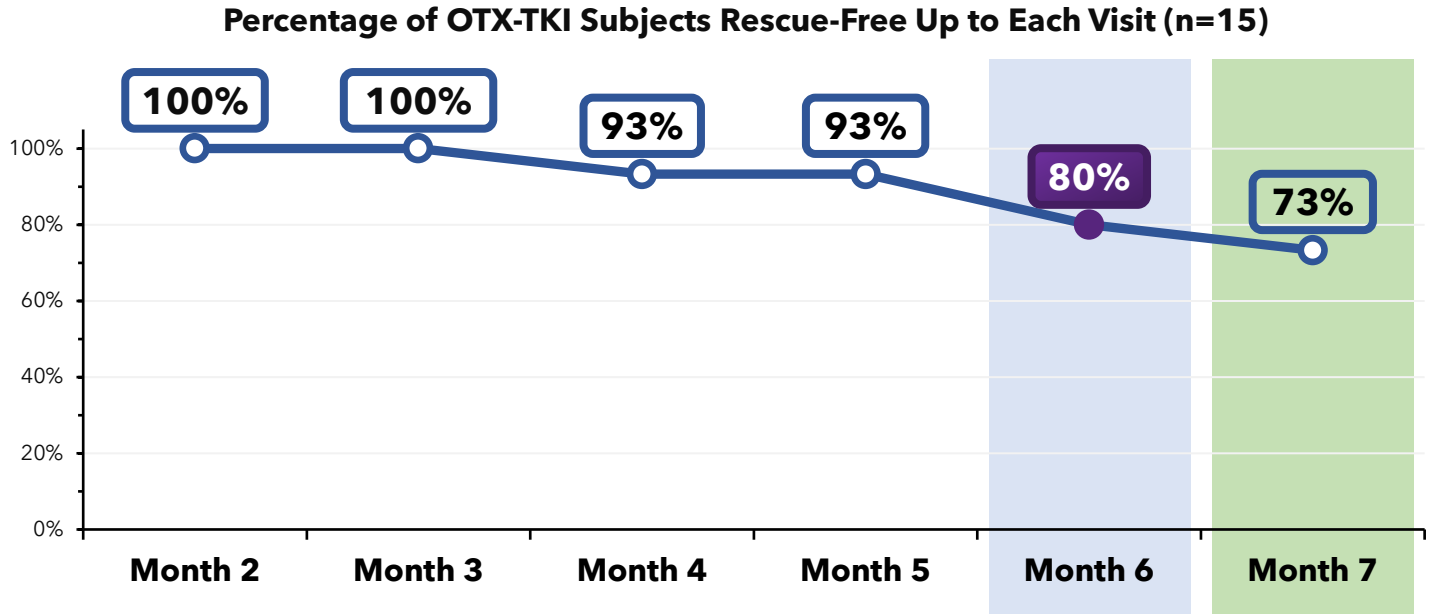
OTX-TKI DEMONSTRATED EXTENDED DURATION OF ACTION

80% of subjects were rescue-free up to 6 months and 73% of subjects were rescue-free up to 7 months



Interim review: data cut off August 24, 2022

Rescue-free rate calculations: If subjects received rescue anti-VEGF therapy at a study visit, they were counted as rescued at the following study visit in the graph above.

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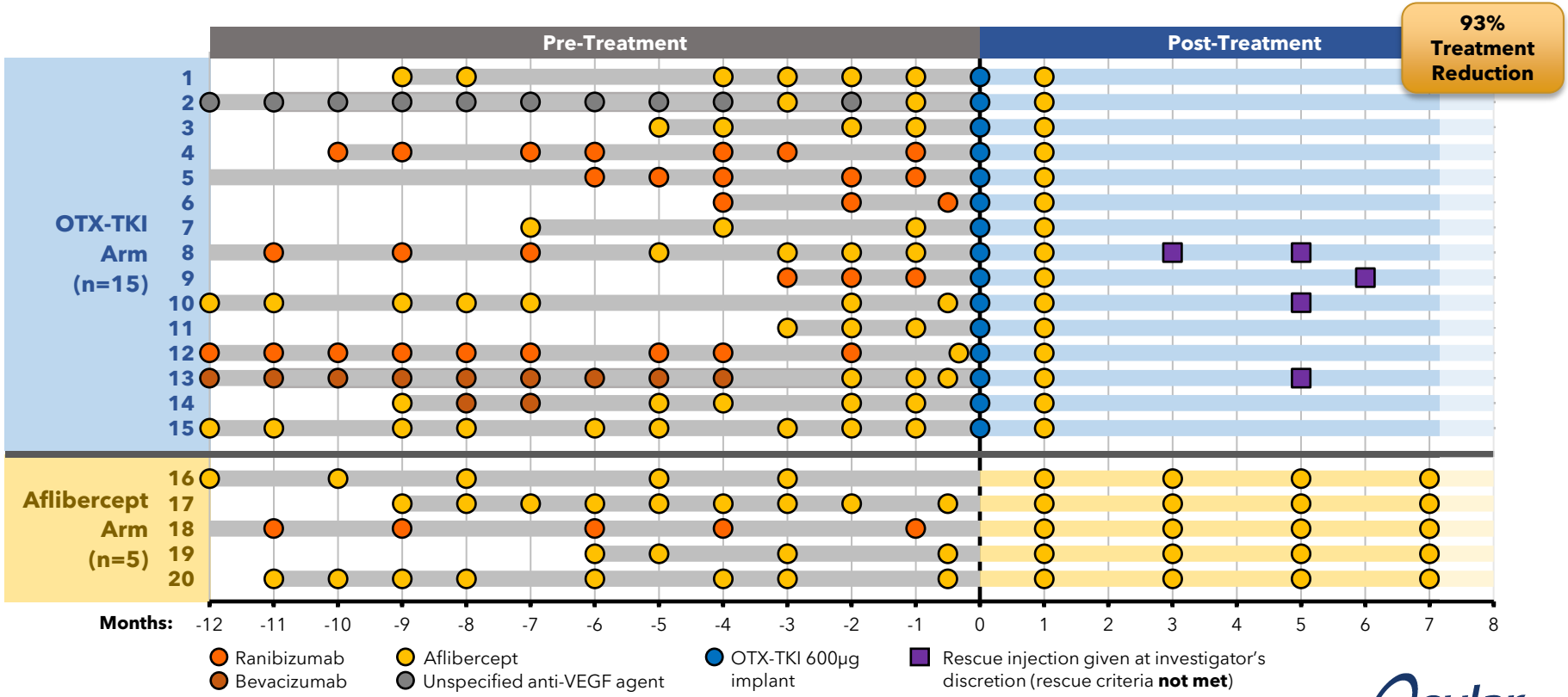
OTX-TKI DEMONSTRATED REDUCTION IN TREATMENT BURDEN

Clinically meaningful reduction in treatment burden and all rescues were given at investigator's discretion



Sham injection was given at Month 0 in the Aflibercept Arm and at Month 3, 5 & 7 in the OTX-TKI Arm (not shown). Interim review: data cut off August 24, 2022; per protocol analysis

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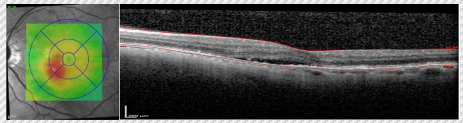
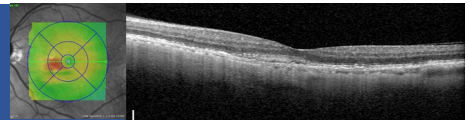
ACUTE ENDOPHTHALMITIS CASE: OTX-TKI PATIENT 8

Acute endophthalmitis reported 6 days after aflibercept injection at Month 1 visit

Historical OCT
(~5 months prior to baseline)
CSFT: 315 µm

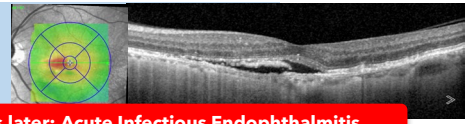


Baseline
CSFT: 290 µm
BCVA: 81 letters



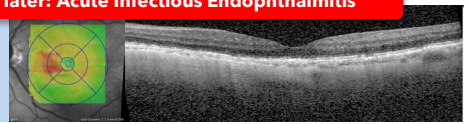
Mandated aflibercept

Month 1
CSFT change: +58 µm
BCVA change: +4 letters



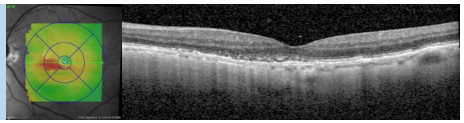
6 days later: Acute Infectious Endophthalmitis

Month 2
CSFT change: -9 µm
BCVA change: -20 letters



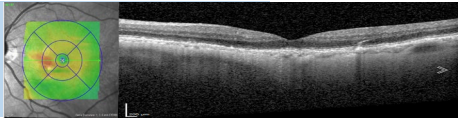
Rescue injection (criteria not met)

Month 3
CSFT change: +44 µm
BCVA change: -3 letters

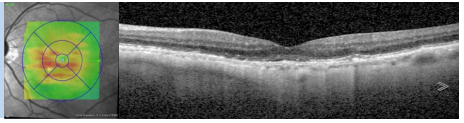


Rescue injection (criteria not met)

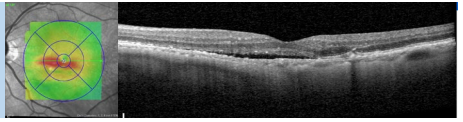
Month 4
CSFT change: -15 µm
BCVA change: 0 letters



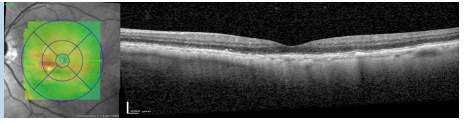
Month 5
CSFT change: +3 µm
BCVA change: 0 letters

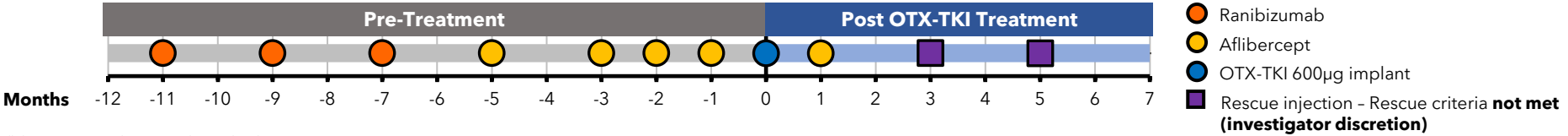


Month 6
CSFT change: +66 µm
BCVA change: 0 letters



Month 7
CSFT change: -6 µm
BCVA change: +5 letters





All changes in CSFT and BCVA are relative to baseline visit

SAFETY EVENTS

7-month interim analysis to be presented at Retina Subspecialty Day: Late Breaking Developments (Friday, September 30th @ 3:24PM in Arie Crown)

OTK-TKI was well tolerated with a favorable safety profile

Adverse Events in the Study Eye	OTX-TKI n=16	Aflibercept n=5
Elevated IOP	0	1**
Retinal detachment	0	0
Retinal vasculitis	0	0
Implant migration into the anterior chamber	0	NA
Acute Endophthalmitis	1*	0
Ocular Adverse Events Reported by Severity		
Ocular AEs	10	3
Mild	9	2
Moderate	1*	1**
Severe	0	0
Serious AEs	1*	0

*Moderate and Serious ocular AE in OTX-TKI arm was Acute Endophthalmitis 6 days after Eylea injection
**Moderate AE in Aflibercept arm was Elevated Intraocular pressure

Interim review: data cut off August 24, 2022
Abbreviations: IOP, intraocular pressure; SAE, serious adverse event

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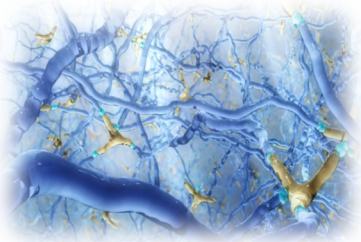
OCULAR'S RETINA PORTFOLIO BEYOND OTX-TKI

Our Commitment to Retinal Diseases

Versatile Hydrogel Platform

Continuing development of OTX's hydrogel for sustained delivery of small molecules, peptides and large proteins



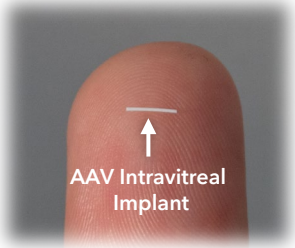
Complement Inhibition for Geographic Atrophy

Investigating antibody drug candidates with extended duration in collaboration with Mosaic Biosciences

mosaic

Ocular Gene Therapy Program

Exploring extended release of viral vectors for reduced inflammation and improved transduction



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