

# UNITY BIOTECHNOLOGY

## Corporate Overview

April 2024

NASDAQ: UBX



# Special Note Regarding Forward-Looking Statements

This presentation and the accompanying oral commentary contain forward-looking statements including statements related to Unity Biotechnology Inc.'s ("UNITY's") understanding of cellular senescence and the role it plays in diseases of aging, the potential for UNITY to develop therapeutics to slow, halt, or reverse diseases of aging, including for ophthalmologic and neurologic diseases, UNITY's expectations regarding potential benefits, activity, effectiveness, and safety of UBX1325, the potential for UNITY to successfully commence and complete clinical studies of UBX1325 for DME, AMD, and other ophthalmologic diseases, the expected timing of enrollment and results of the clinical trials in UBX1325, and UNITY's expectations regarding the sufficiency of its cash runway. These statements involve substantial known and unknown risks, uncertainties, and other factors that may cause our actual results, levels of activity, performance, or achievements to be materially different from the information expressed or implied by these forward-looking statements, including the risk that the COVID-19 worldwide pandemic may continue to negatively impact the development of preclinical and clinical drug candidates, including delaying or disrupting the enrollment of patients in clinical trials, risks relating to the uncertainties inherent in the drug development process, including the risk that interim results of our clinical studies may not be indicative of future results, and risks relating to UNITY's understanding of senescence biology. We may not actually achieve the plans, intentions, or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we make. The forward-looking statements in this presentation represent our views as of the date of this release. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should, therefore, not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this release. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to the business of UNITY in general, see UNITY's most recent Annual Report on Form 10-K for the year ended December 31, 2023, filed with the Securities and Exchange Commission on April 15, 2024, as well as other documents that may be filed by UNITY from time to time with the Securities and Exchange Commission. This presentation concerns drug candidates that are under clinical investigation which have not yet been approved for marketing by the U.S. Food and Drug Administration. They are currently limited by Federal law to investigational use, and no representation is made as to their safety or effectiveness for the purposes for which they are being investigated. This presentation does not constitute an offer or invitation for the sale or purchase of securities and has been prepared solely for informational purposes.



# Executive Leadership Team



ANIRVAN GHOSH, PhD  
Chief Executive Officer



LYNNE SULLIVAN, MS  
Chief Financial Officer



SHARON KLIER, MD, MPH  
Chief Development Officer



ALEX NGUYEN, JD  
Chief Legal Officer  
and Head of  
Operations



MIKE SAPIENZA, PhD  
Chief Scientist



ROBERT B. BHISITKUL MD, PhD  
Senior Clinical Advisor



## Steering Team

Arshad Khanani, MD, MA  
Raj Maturi, MD  
Dante Pierameci, MD  
Victor Gonzales, MD  
Quan Nguyen, MD

## Advisory Team

Jeff Heier, MD  
David Boyer, MD  
Bob Bhisitkul, MD, PhD  
Quan Nguyen, MD, MSc  
Diana Do, MD

# Developing Transformative Medicines to Slow, Halt, or Reverse Diseases of Aging

Targeting cellular senescence and aging-related biology



## Focus Area: Ophthalmology

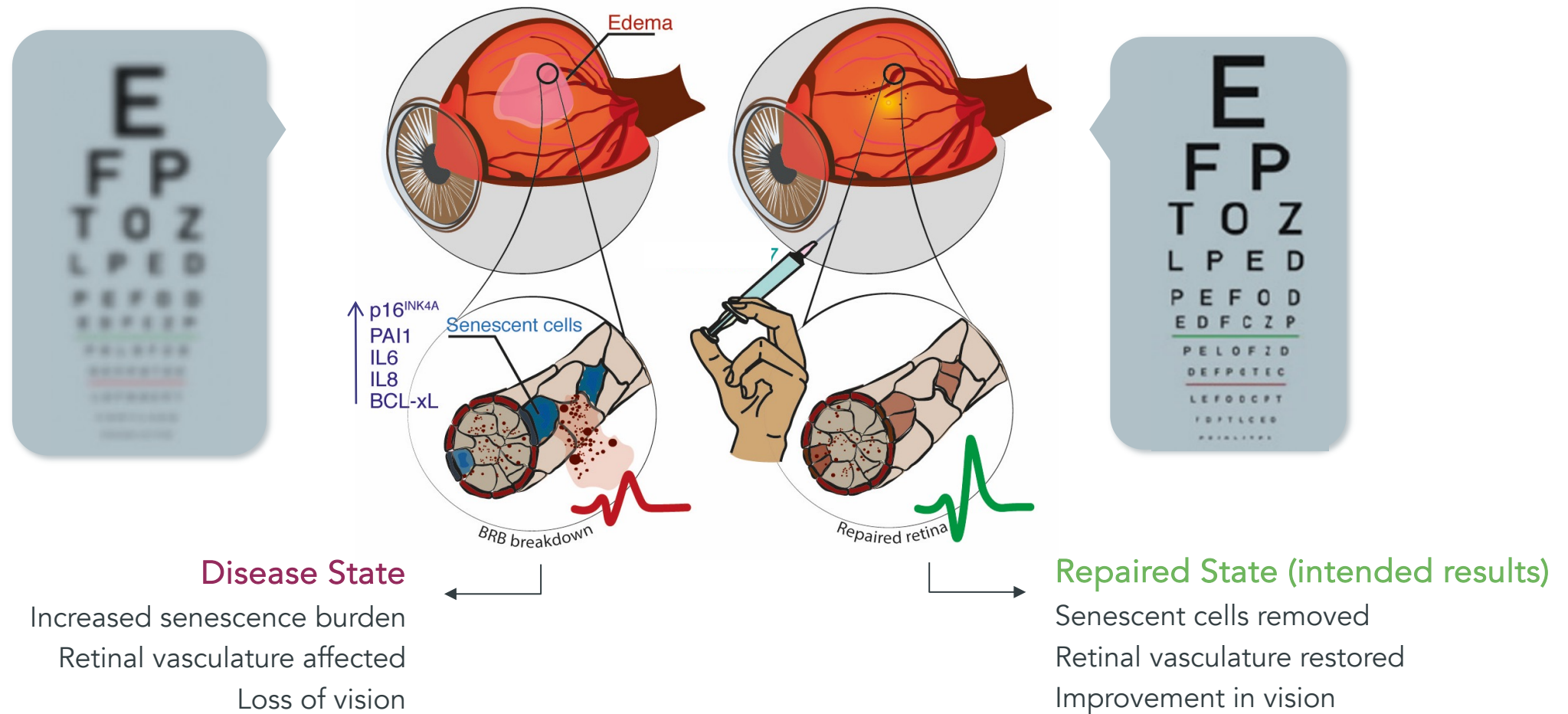
DME (Diabetic Macular Edema),  
AMD (Age-Related Macular Degeneration),  
Diabetic Retinopathy



## Growth Area: Neurology

Alzheimer's, PSP (and other Tauopathies),  
Cognitive Disorders

# UNITY is Developing Senolytic Medicines to Eliminate Senescent Cells to Restore Vascular Health and Improve Vision



UNITY illustration of proposed mechanism of action

# Investment Highlights: Recent Achievements and Ongoing Studies

## Senolytic platform to develop transformative therapeutics

Developing a novel therapeutic approach to remodel the retina

Potential to be valuable as monotherapy or in combination with anti-VEGF agents to shift the treatment paradigm for progressive vision loss

## Lead asset UBX1325 (foselutoclax) has best in class potential for DME

Novel MOA to overcome limitations of current standard of care with favorable safety, efficacy, durability and disease modification potential

A single dose of foselutoclax led to **strong visual acuity gains through 48 weeks** in Phase 2 BEHOLD study in patients with DME

## Recent achievements and ongoing studies

Completed foselutoclax 48-week data from Part B of Ph2 ENVISION study in AMD in 3Q23; Treatment effects of foselutoclax were durable and well tolerated

Foselutoclax Phase 2b ASPIRE study, head-to-head against aflibercept in DME, first patients dosed in **24-week data expected in 1Q25** and **36-week data expected in 2Q25**



# Foselutoclax Clinical Program in Diabetic Macular Edema – BEHOLD and ASPIRE



# UNITY Pipeline

Targeting Cellular Senescence and Aging-Related Biology in Indications with Established Endpoints and Well-Defined Regulatory Pathways to Approval

	Mechanism	Indication	Research	Lead Optimization	IND-enabling	Phase 1	Phase 2	Phase 3
Ophthalmology	Bcl-xL Inhibition	Diabetic Macular Edema (ASPIRE)	Foselutoclax (Phase 2b)					
		Diabetic Macular Edema (BEHOLD)	Foselutoclax (Phase 2)					
	Tie2/aVEGF bi-specific	Retinal Vascular Diseases	UBB2048					
	Tie2 Agonist	Retinal Vascular Diseases	UBB2048					
Neurology	α-Klotho	Cognitive Disorders	UBX2089					
			Partnered with Jocasta Neuroscience					

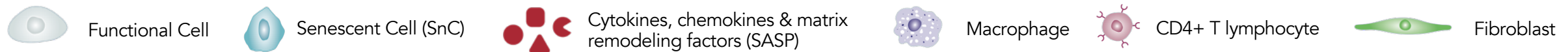
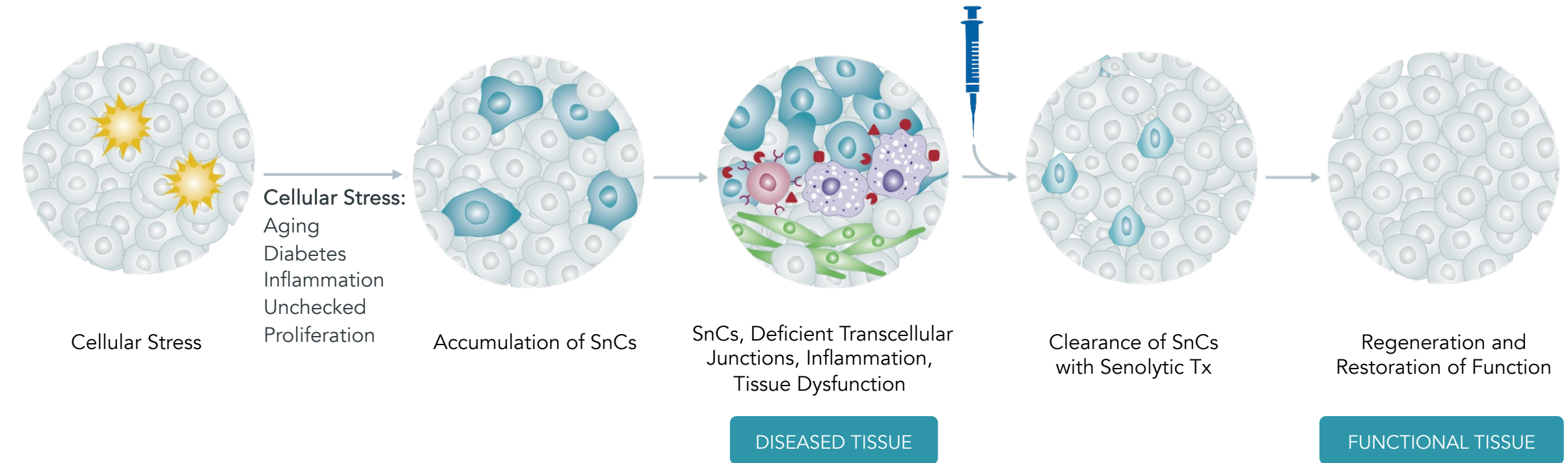
# **Senolytic Therapeutic Hypothesis**

Mechanism of Action



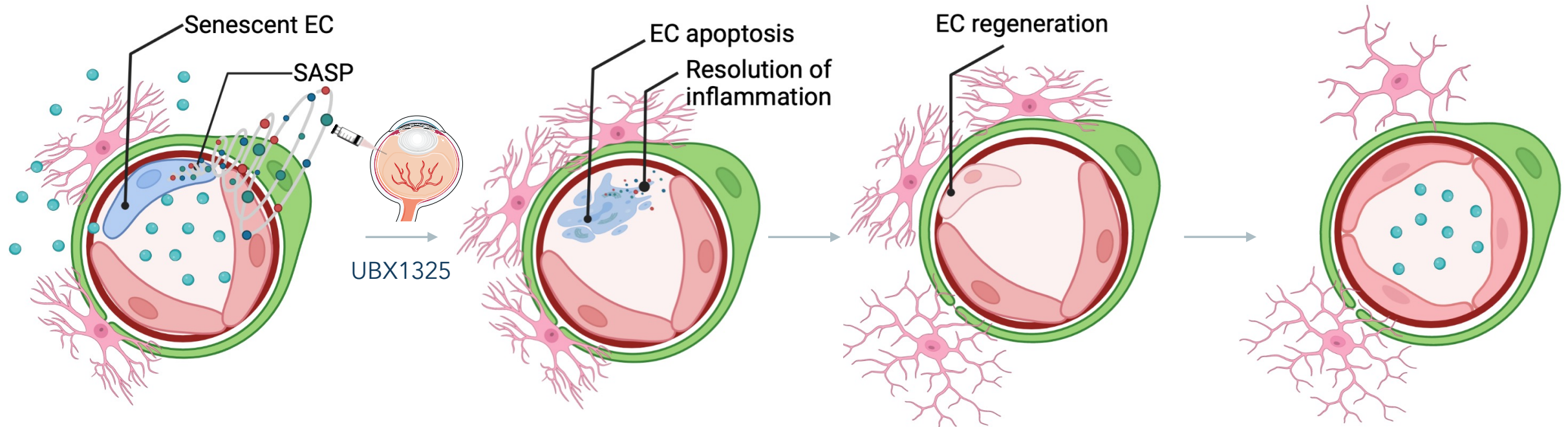
# Targeting Senescent Cells to Restore Tissue Health

Target senescent cells to neutralize SASP factors and eliminate dysfunctional cells that are the root cause of disease progression





# Proposed Mechanism of Action for UBX1325 in Retinal Disease



## Diabetic blood vessel

Senescent (Sn) ECs accumulate in diabetic retinas in areas of disease activity

## Vessel remodeling

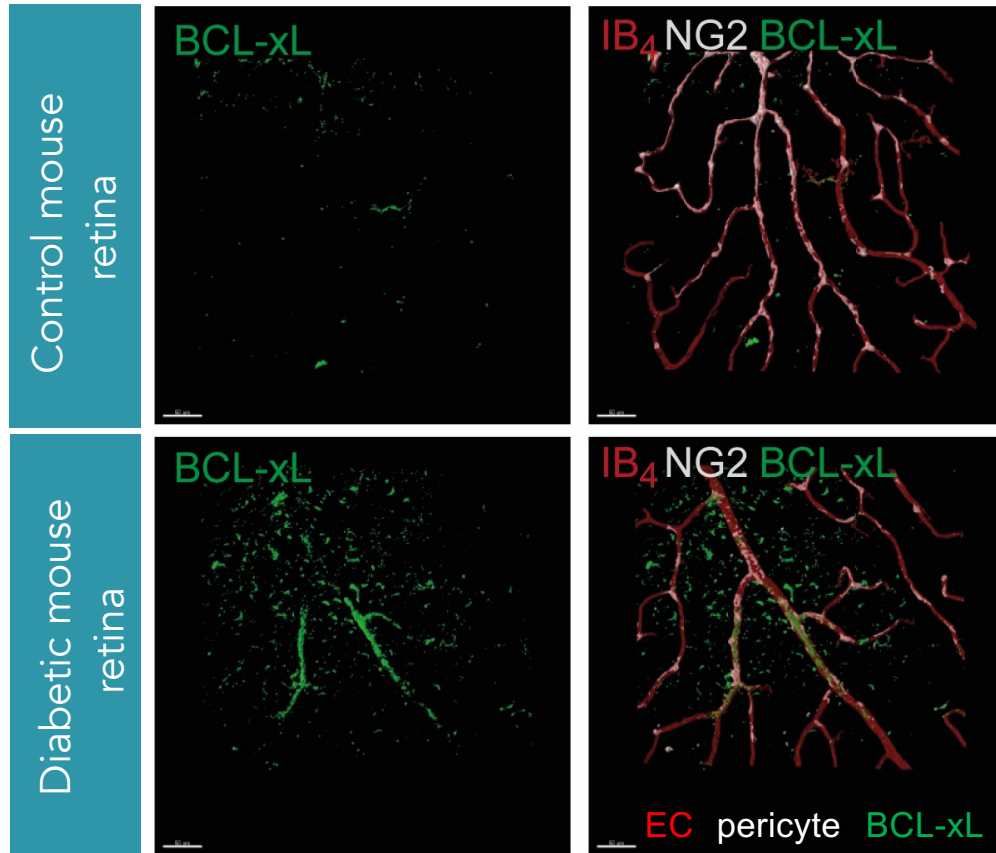
UBX1325 selectively triggers cell death of Sn ECs. UBX1325 reduces retinal inflammation and leakage

## Repaired blood vessel

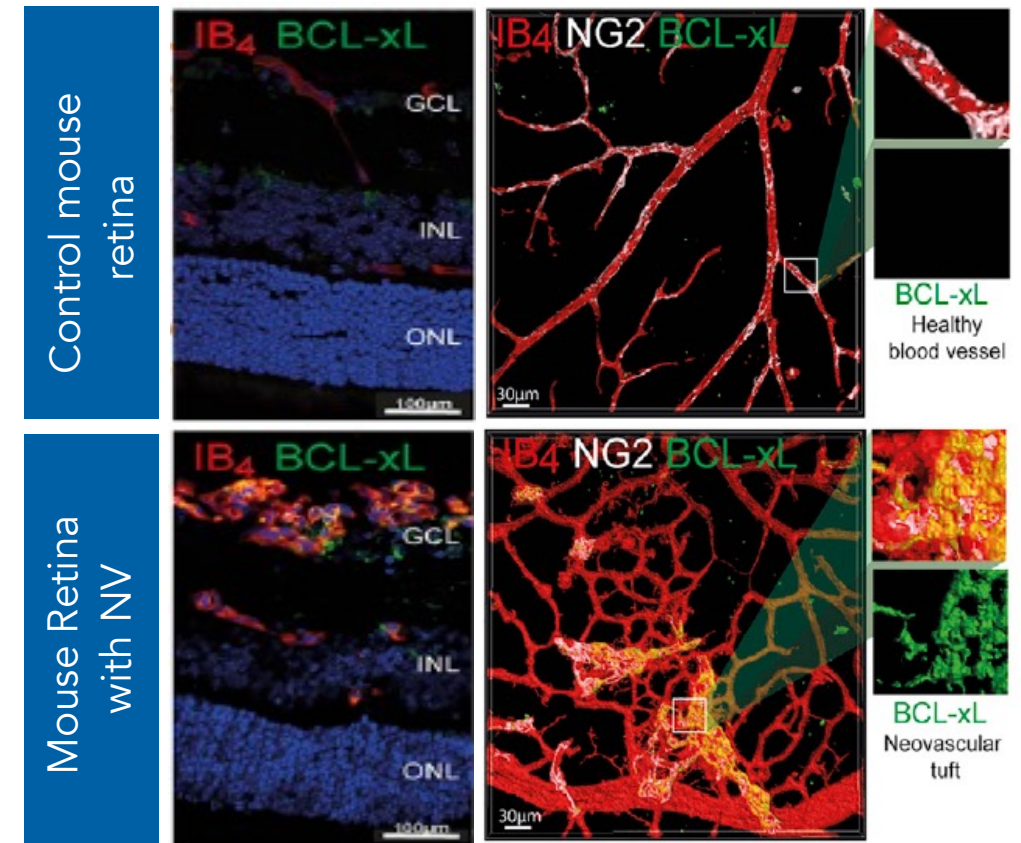
Preclinical data predicts progressive disease modification through vascular remodeling

# Senescent Vascular Units Express Bcl-xL and are Associated with Models of Retinal Vasculopathies

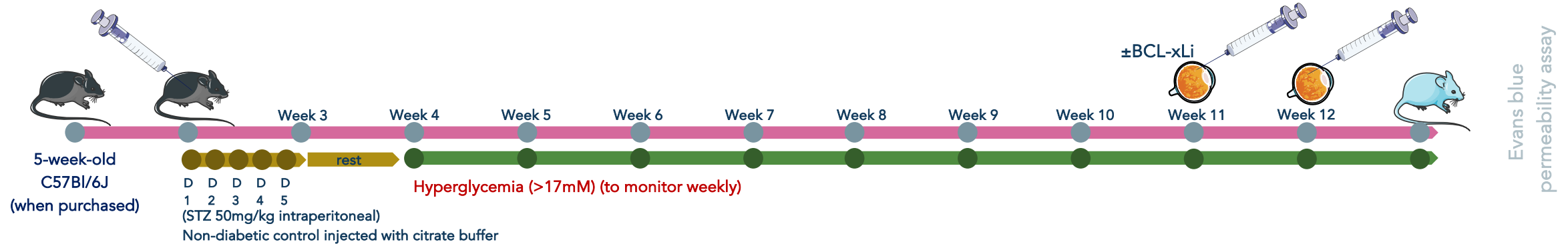
Diabetes induces cellular senescence in the vascular unit



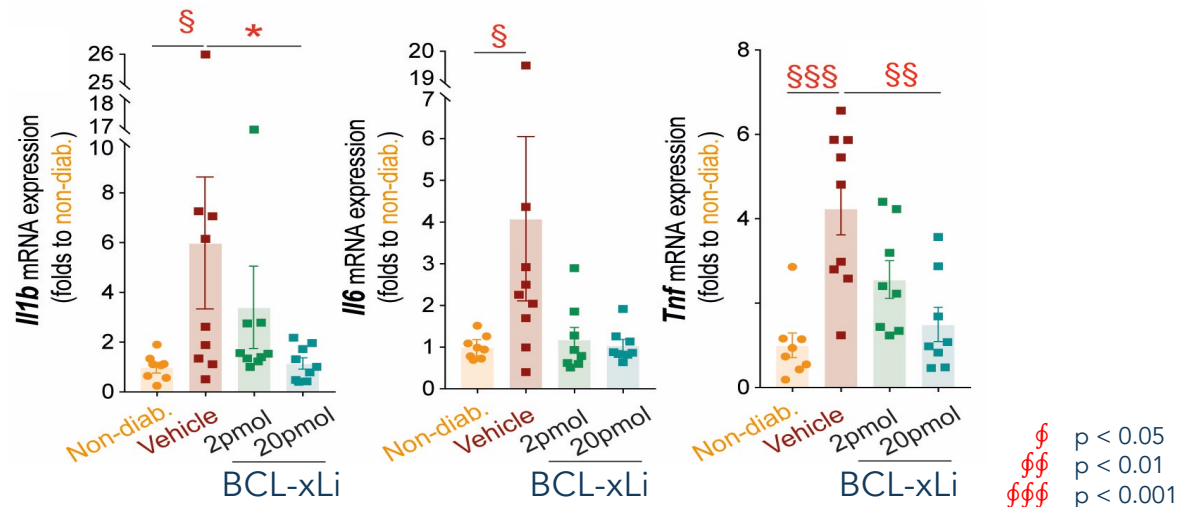
Markers of cellular senescence are found in preretinal neovascularization



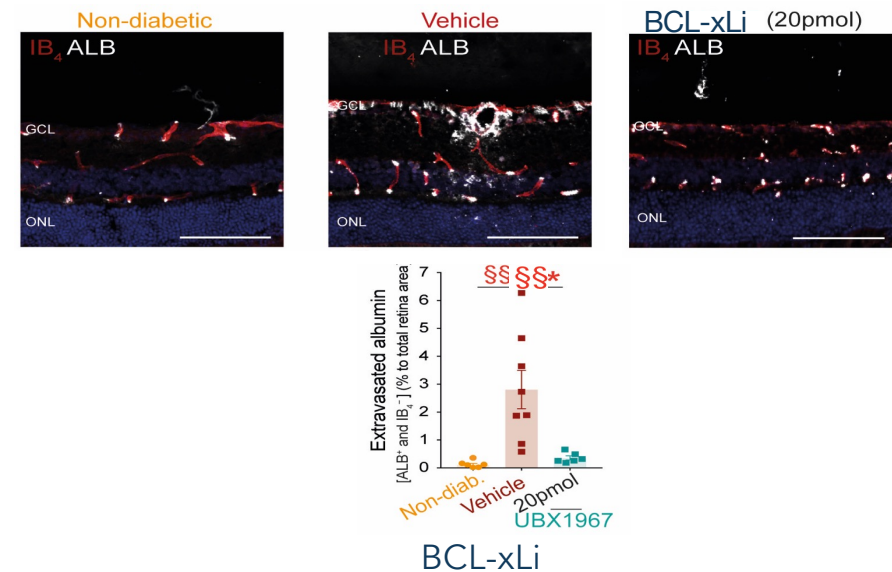
# Bcl-xL Inhibition Reduces Inflammation and Vascular Leakage in a Mouse Model of Diabetes



## Inflammation

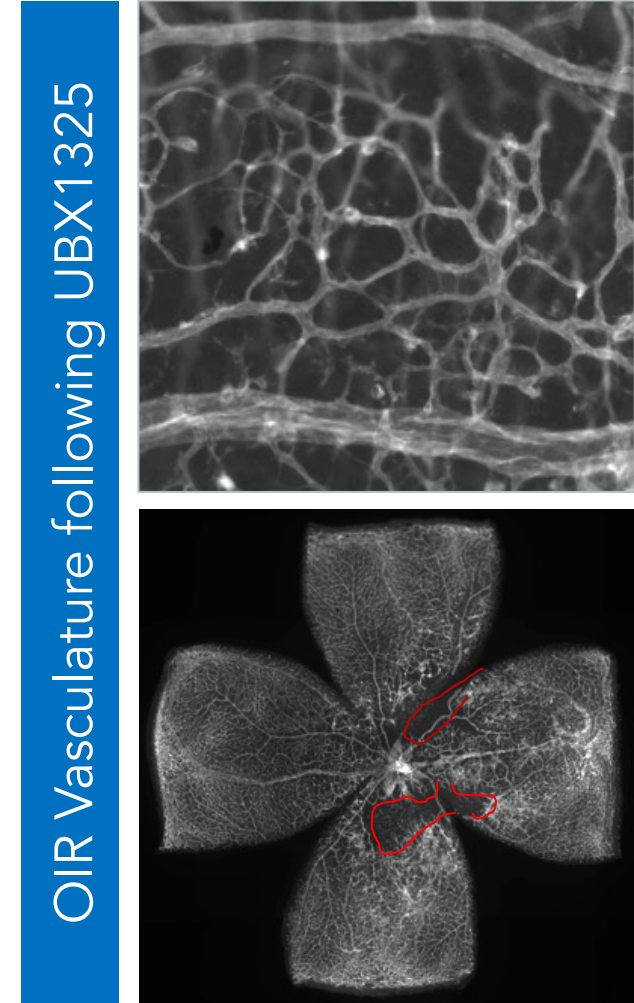
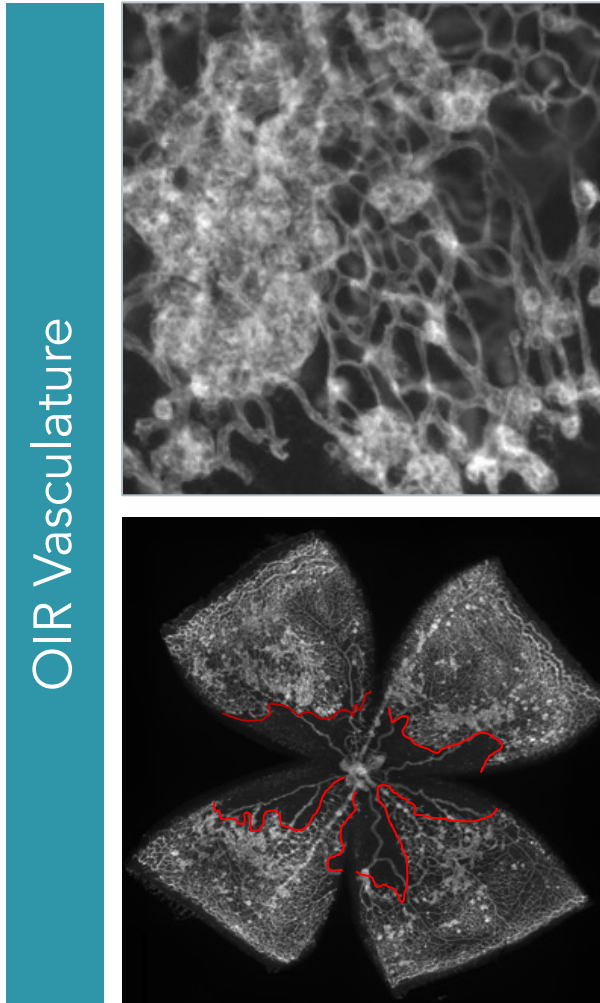
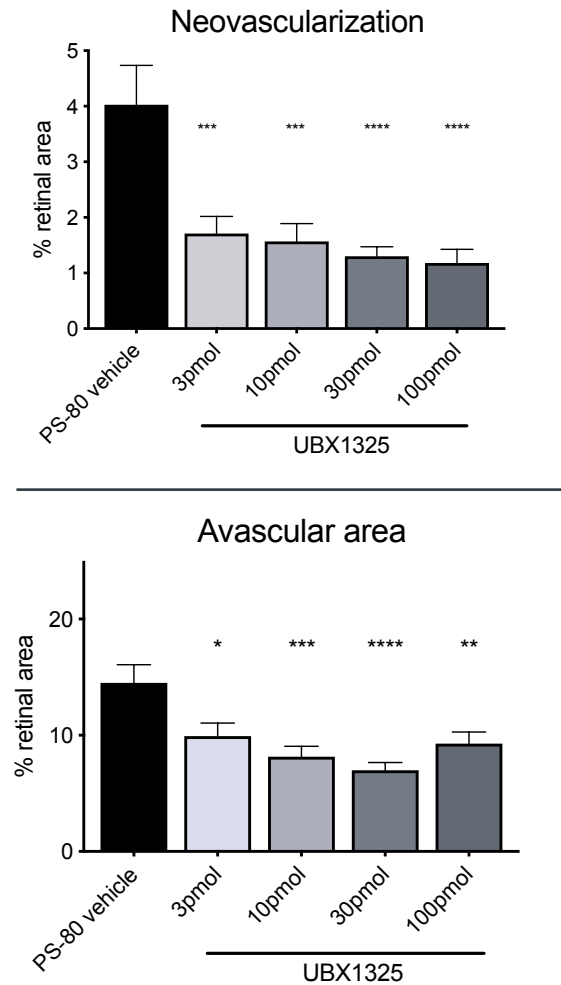


## Vascular Permeability





# UBX1325 Improves Retinal Vasculature in Mouse Model of Neovascularization







# **Unmet Need in Ophthalmology and the Opportunity for Senolytic Therapies**

UBX1325 – Bcl-xL inhibitor

# UBX1325 Has a Differentiated Profile With Best-In-Disease Potential in DME

Safety and Efficacy Profile	Current standard of care (Aflibercept)	aVEGF/Ang2 bispecific (Faricimab)	UBX1325
Favorable safety and PK profile	✓	✓	✓
Strong efficacy signal in broad patient population including sub-optimal anti-VEGF responders	✗	✗	✓
>50% patients achieve 6-month treatment free interval after single injection	✗	✗	✓
Reduction of ischemic regions of the retina and potential for disease modification	✗	✗	✓



supported by clinical data



supported by preclinical data

Not based on head-to-head trials

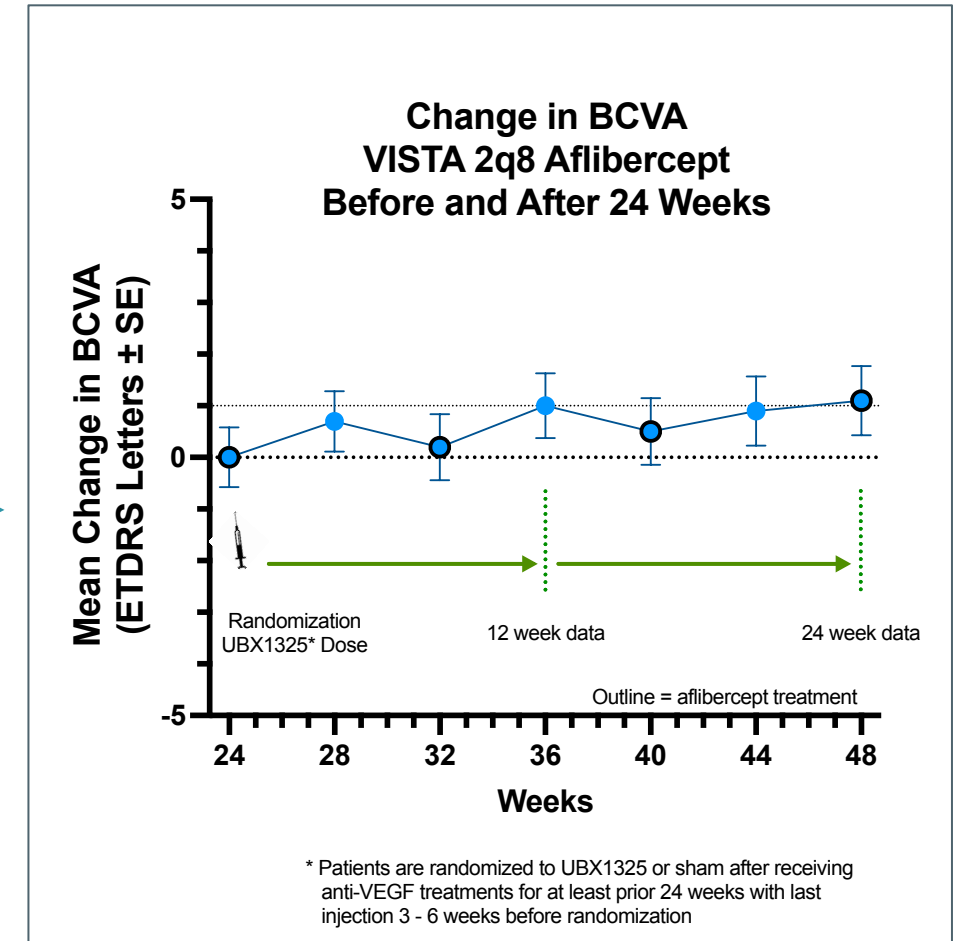
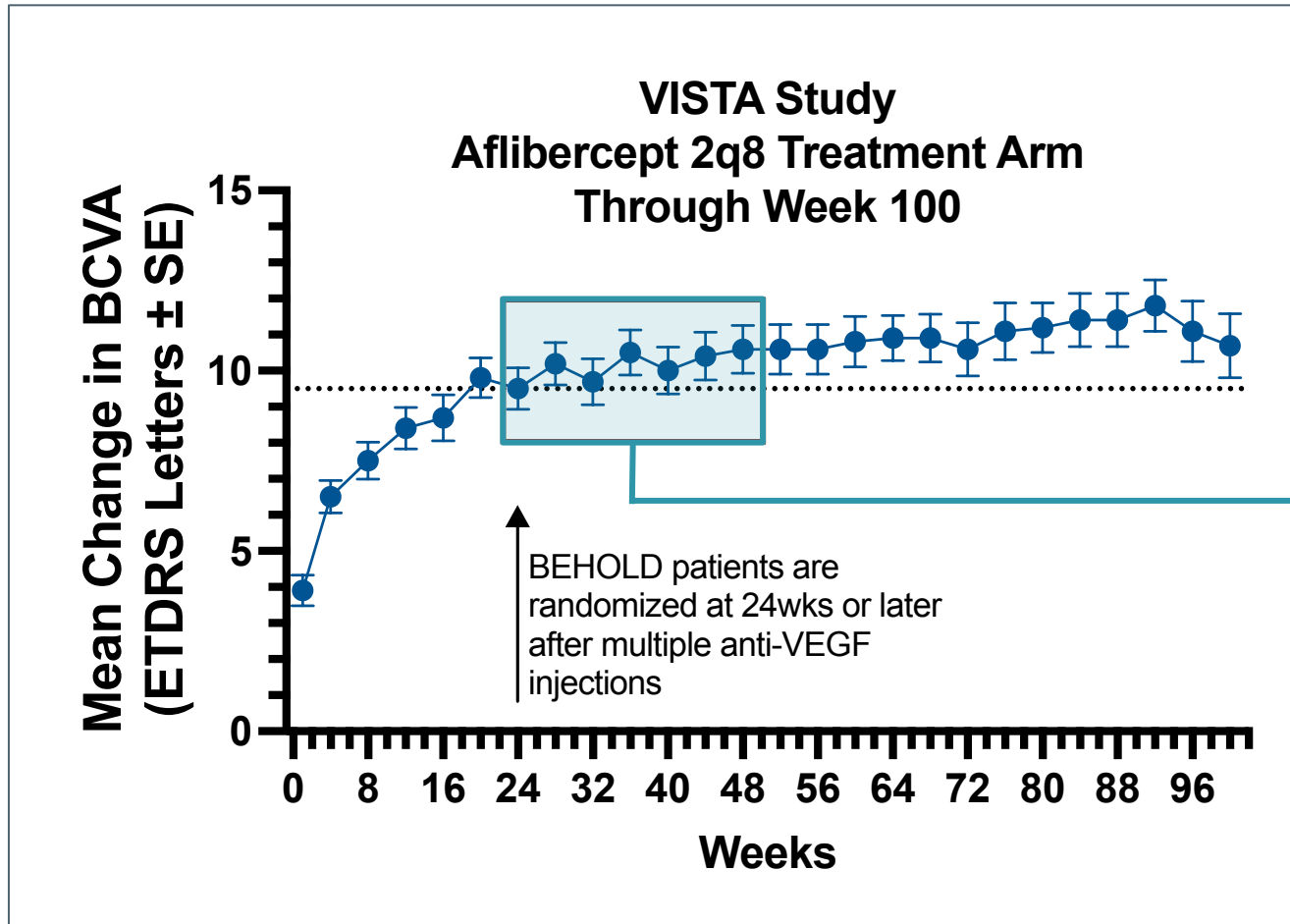




**UBX1325 Phase 2  
BEHOLD Study in  
Patients with DME**



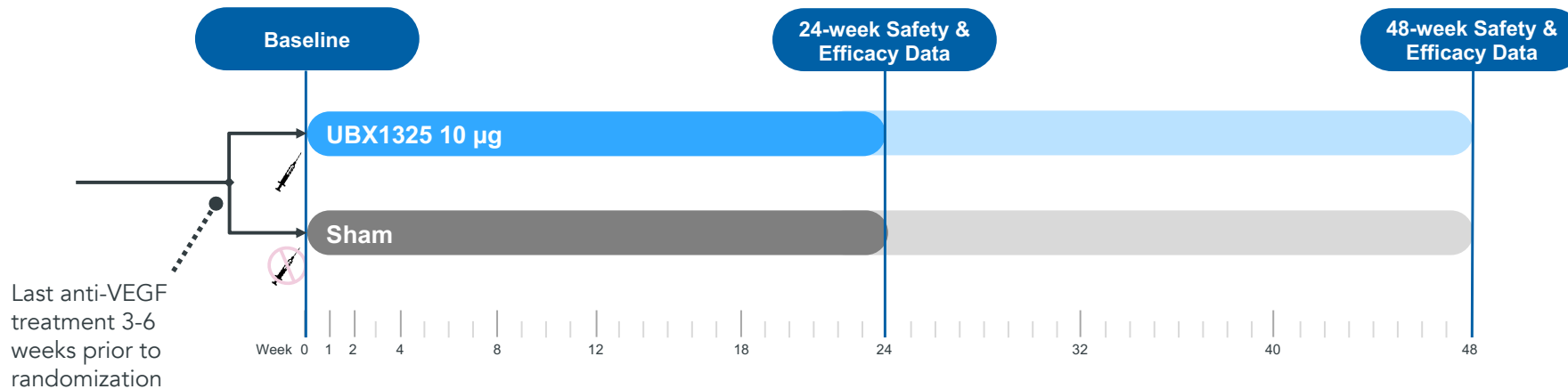
# Context for 48wk DME Data: After Anti-VEGF Effect Has Plateaued, Patients Gain Approximately 1 Letter in Subsequent 6 Months on Aflibercept Treatment



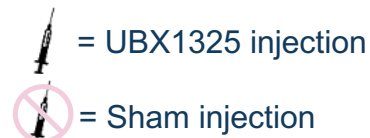
# BEHOLD Study Design, Patient Population, and Endpoints

## Patient Population

- Individuals with **Diabetic Macular Edema**
- **Repeated anti-VEGF** treatments ( $\geq 2$  injections/6 months) – Actual: 4.1 injections in prior 6 months
- **Residual retinal fluid** ( $\geq 300$   $\mu\text{m}$ ) – Actual: 439.6  $\mu\text{m}$
- **Visual acuity deficit** (73 ETDRS letters or worse) – Actual: 61.4 ETDRS letters



	Sham	UBX	Total
Full Analysis Set	33	32	65
Completed to 24 Weeks only	4	5	9
Lost to follow-up	1	3	4
Site Closure	1	0	1
Patient withdrawal	1	0	1
Available through 48 Weeks	26	24	50



## Endpoints

Safety and tolerability

BCVA change from baseline

Durability of response

Sub- and intra-retinal fluid, CST changes

Proportion of UBX1325 patients requiring 2 or more rescue treatments





## **UBX1325 Phase 2 BEHOLD Study**

48-Week Topline Data  
in Patients With DME



# UBX1325 Led to a Statistically Significant and Clinically Meaningful Improvement in Visual Acuity in Patients with Diabetic Macular Edema Through 48 Weeks

## Phase 2 BEHOLD Study Data Highlights

A single dose of  
UBX1325 demonstrated:

- UBX1325-treated patients had a **significant improvement in BCVA** of +6.2 ETDRS letters from baseline and +5.6 ETDRS letters compared to sham at 48 weeks
- Approximately **50% of UBX1325-treated patients did not require any additional injection through 48 weeks**
- There was more than a **30-week difference in median time-to-first-rescue** favoring UBX1325 over sham
- **Retinal structure was maintained** in UBX1325-treated patients with a central subfield thickness that was lower than baseline and was -37.9  $\mu\text{m}$  compared to sham at 48 weeks
- UBX1325 had a **favorable safety and tolerability profile** with no evidence of intraocular inflammation

UBX1325 may be an important future therapeutic option for patients with diabetic macular edema

# Patient Characteristics at Baseline Were Well Balanced Between Groups

	Sham (n=33)	UBX1325 (n=32)
Age (Mean / Median)	61.4 (9.09)	63.6 (9.33)
HBA1c, %	7.4 (1.36)	8.0 (1.68)
Diabetes Dx, Years	17.5 (10.53)	17.2 (11.41)
DME Dx, Years	3.0 (2.32)	3.5 (3.60)
BCVA, ETDRS letters	61.8 (9.61)	60.9 (9.97)
CST, $\mu\text{m}$	456.2 (98.07)	422.5 (84.16)
Anti VEGF prior 190 days		
Aflibercept	13	13
Aflibercept, bevacizumab	4	1
Bevacizumab	15	16
Ranibizumab	1	2

Balanced on other parameters at baseline: ethnicity & race, BMI, DRSS score



# UBX1325-treated Patients had Marked Reduction in Need for Anti-VEGF Rescue Compared to Sham-treated Patients Through 48 weeks

- Median Time-To-First-Rescue in UBX arm was >48 weeks (at least 30 weeks greater than Sham arm)
- ~50% of UBX-treated patients went without rescue through 48 weeks
- ~80% of sham-treated patients required rescue before 48 weeks

## Rescue Criteria (Either)

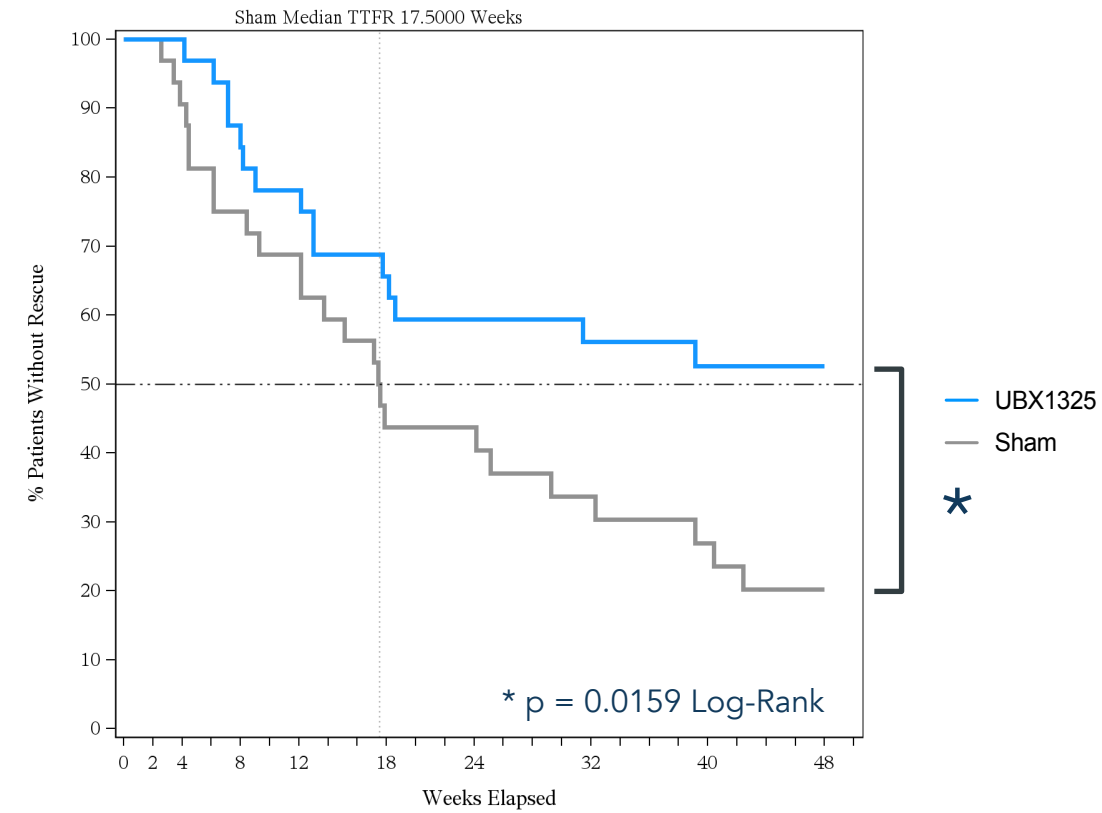
Decrease of 10 ETDRS or more letters from any peak value

Increase in CST of 75  $\mu\text{m}$  or more from baseline

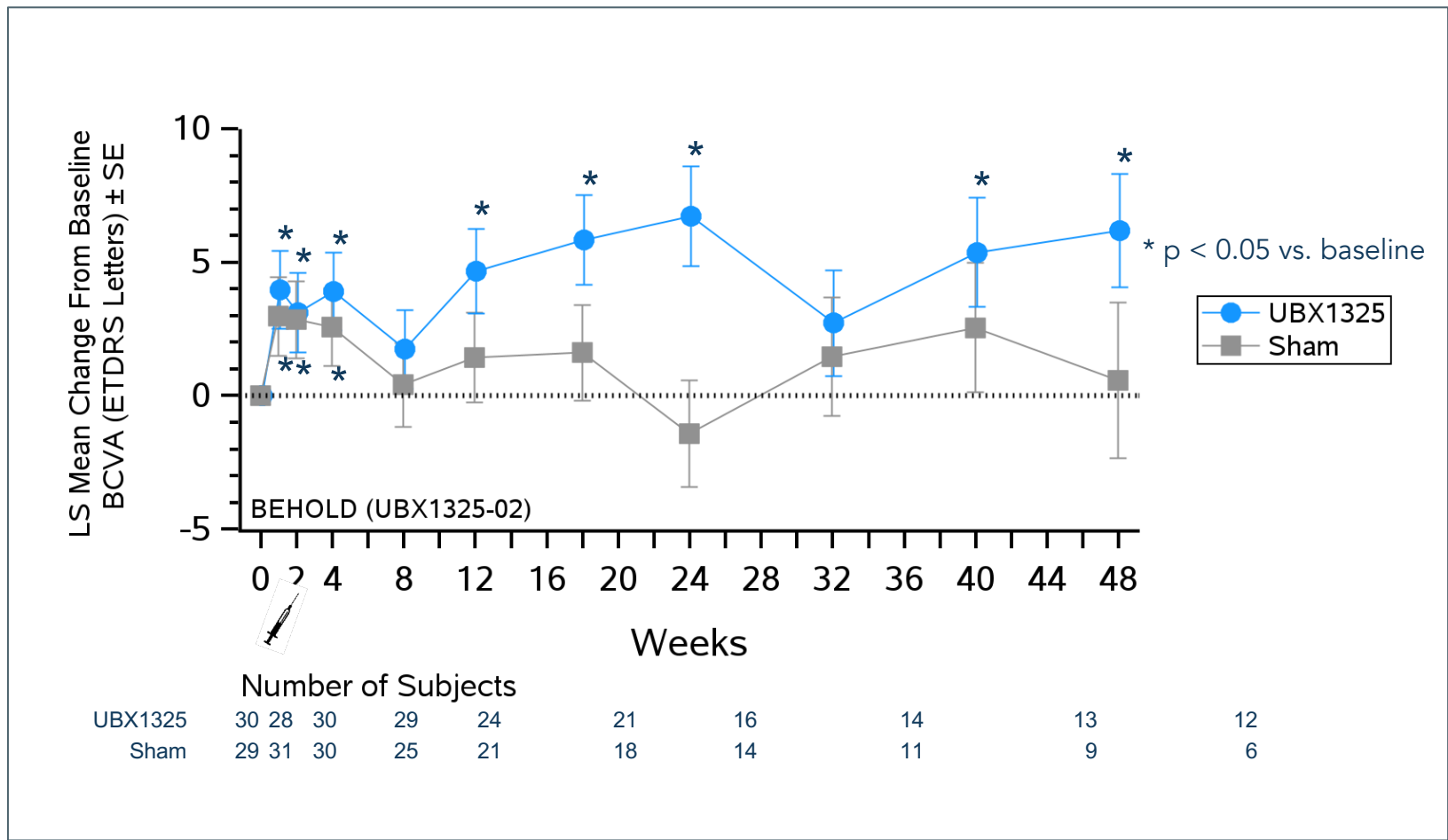
Physician discretion

Efficacy analyses *excluding* and *including* data post anti-VEGF rescue show a treatment benefit of UBX1325

## Median Time to First Rescue Sham: 17.5 Weeks



# UBX1325-treated Patients had a Significant Improvement in BCVA from Baseline† of 6.2 Letters at 48 Weeks (Excluding Data Post-rescue)

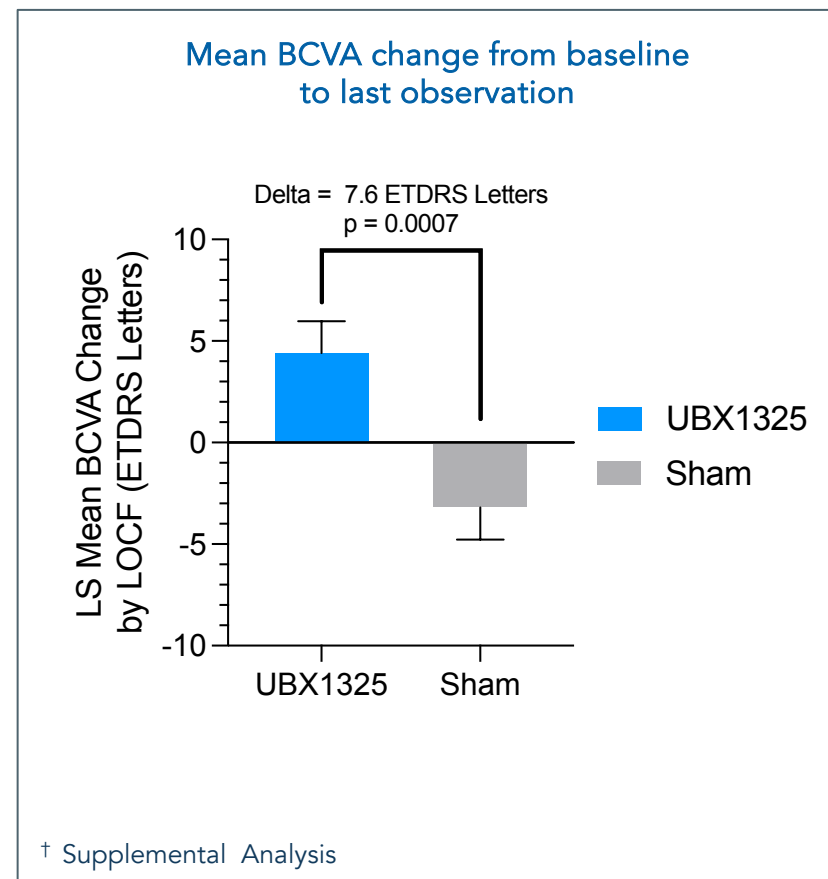
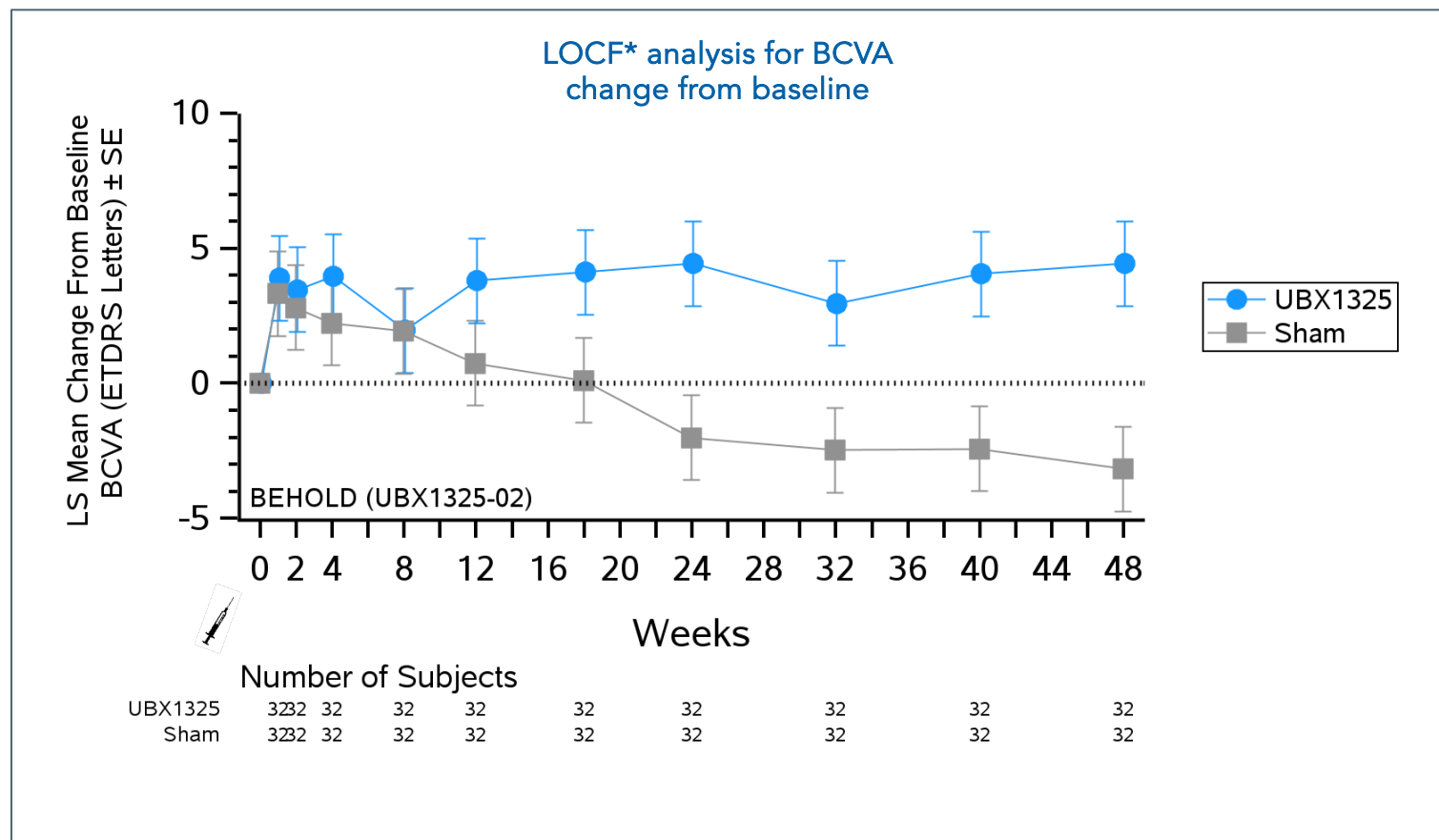


BCVA CFBL (ETDRS Letters)	UBX1325	Sham	Delta	Between Group p-value
Week 24	6.7	-1.4	8.1	0.0031
CFBL p-value	0.0004	NS		
Week 48	6.2	0.6	5.6	0.1198
CFBL p-value	0.0037	NS		

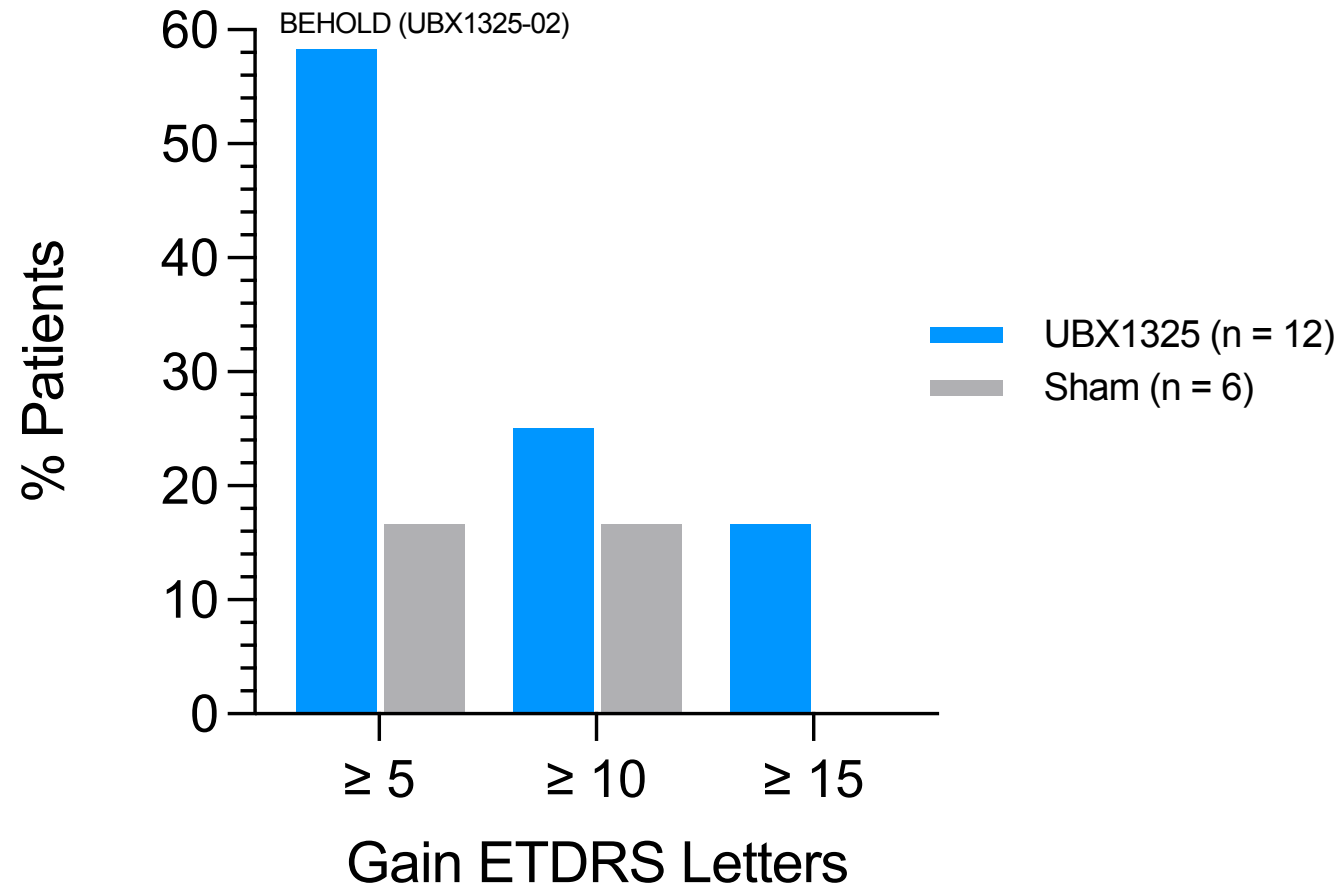
NS: not significant  
† MMRM Analysis



# UBX1325-treated Patients had Significant Visual Acuity Gains Compared to Sham Based on Analysis of Last Observation Prior to Rescue or End of Study†

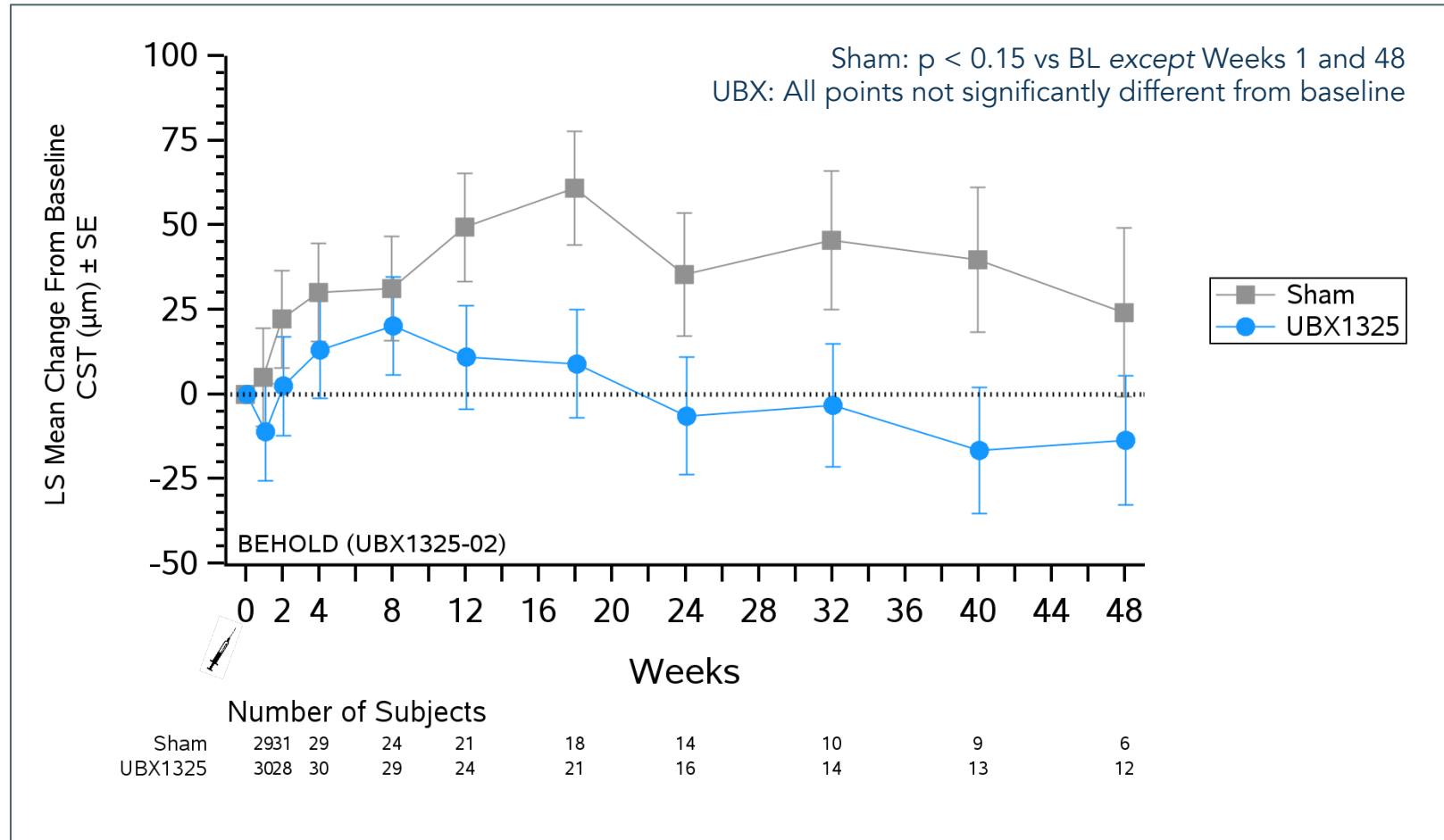


Last observation carried forward (to rescue or end of study participation)



58% of UBX1325-treated Patients Gained At Least 5 Letters of Vision Through 48 Weeks, with 25% Gaining At Least 10 Letters (*Excluding Post-rescue Data*)

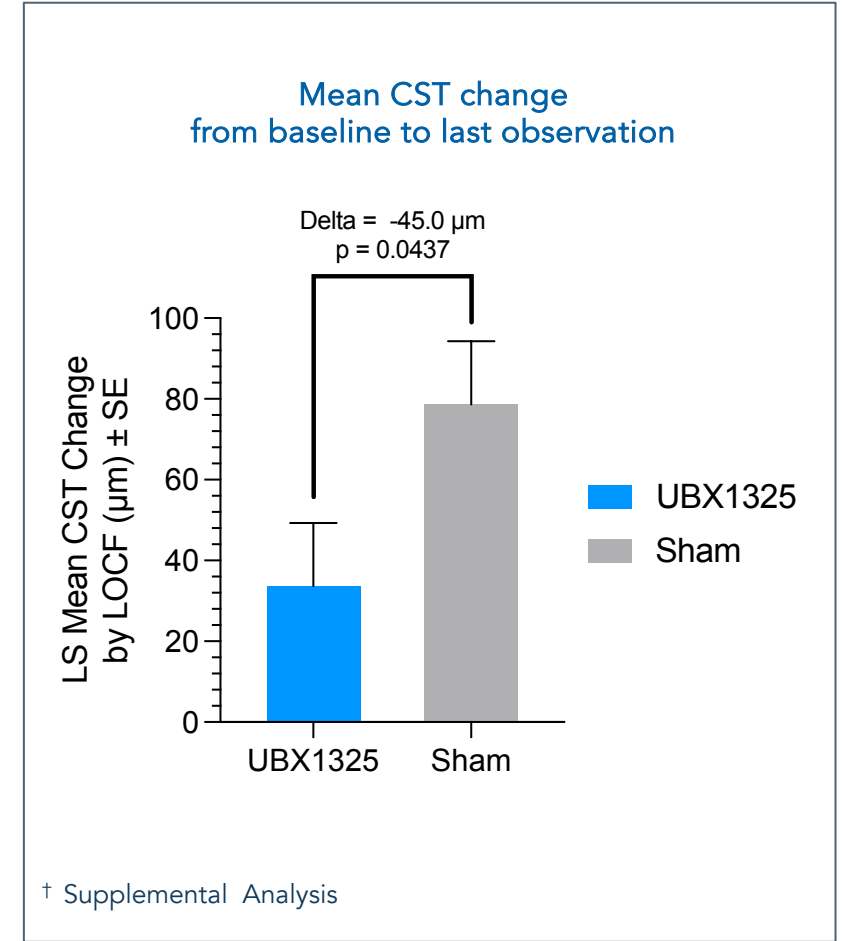
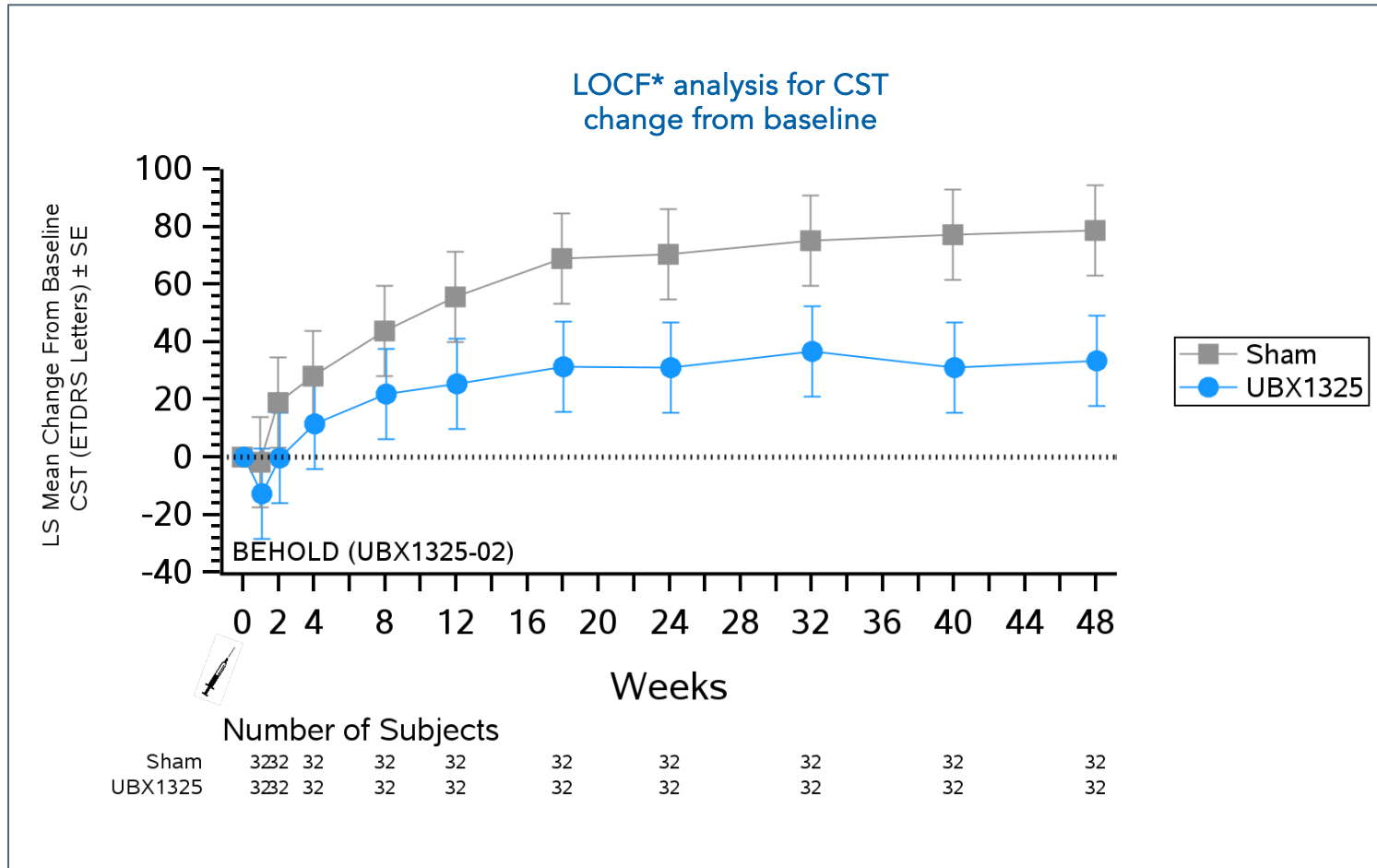
# CST Remained Stable in UBX1325-treated Patients Compared to Worsening in Sham Patients (*Excluding Post-rescue Data*)



BCVA CFBL (ETDRS Letters)	UBX1325	Sham	Delta	Between Group p-value
Week 24	-6.4	35.4	-41.8	0.0985
CFBL p-value	NS	0.0534		
Week 48	-13.7	24.2	-37.9	NS
CFBL p-value	NS	NS		

NS: not significant

# UBX1325-treated Patients had Significantly Lower CST Compared to Sham Based on Analysis of Last Observation Prior to Rescue or End of Study†

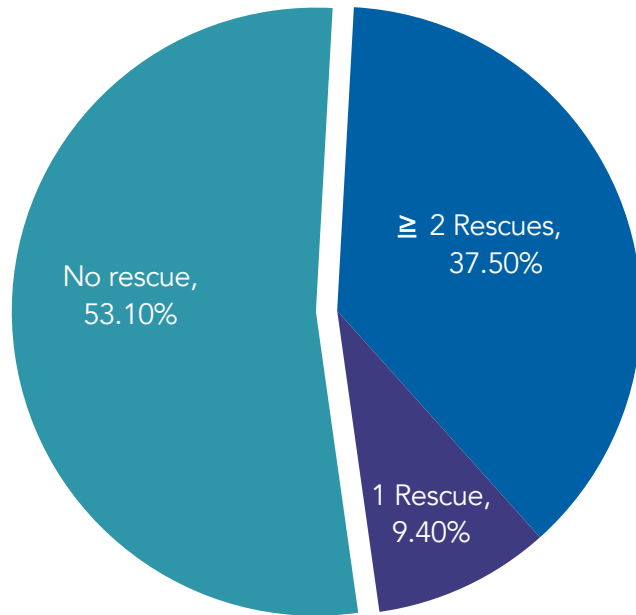


- Last observation carried forward (to rescue or end of study participation)

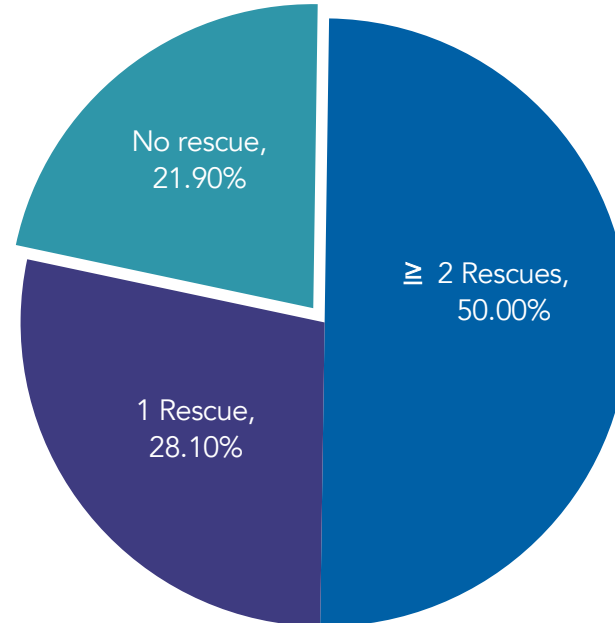


UBX vs. Sham

P = 0.0096



n = 32  
UBX1325



n = 32  
Sham

Rescue Criteria (EITHER)

Decrease of 10 ETDRS or more letters from any peak value

Increase in CST of 75 μm or more baseline

Physician discretion

53.1% of UBX1325-treated Patients in the Study Did Not Require Anti-VEGF Rescue Compared to 21.9% of Sham Patients

# UBX1325 Demonstrated a Favorable Overall Safety and Tolerability Profile with no Instances of Intraocular Inflammation

Parameter	Sham (n=33)	UBX1325 10 µg (n=32)
Subjects with at least one TEAE	31 (93.9)	26 (81.3)
Related TEAE	3 (9.1)	6 (18.8)
Grade $\geq 3$ TEAE	4 (12.1)	5 (15.6)
Serious TEAE	3 (9.1)	5 (15.6)
Ocular TEAE for Study Eye	28 (84.8)	23 (71.9)
Treatment-related Ocular TEAE for Study Eye	3 (9.1)*	6 (18.8)*
TEAE leading to death	0	0
Intraocular inflammation, endophthalmitis, retinal artery occlusion, or vasculitis	0	0

\* Most are likely procedural related, all were mild-mod, and self-limited: Sham: 1 conj. hemorrhage, 1 conj. hyperemia, 1 diabetic macular edema. UBX: 5 conj. hemorrhage, 1 ant. chamber pigmentation, 1 eye irritation

## In the BEHOLD Study, UBX1325:

- Improved visual acuity at 48 weeks by 6.2 letters from baseline after a single injection
- Led to ~50% of patients achieving a **rescue-free** interval of at least **48 weeks** and may represent the **potential** for disease modification
- **Maintained retinal structure** throughout the duration of the study without the need for anti-VEGF rescue
- Had a **generally favorable safety and tolerability** profile with no intraocular inflammation

UBX1325 may be an important future therapeutic option for patients with diabetic macular edema

UBX1325

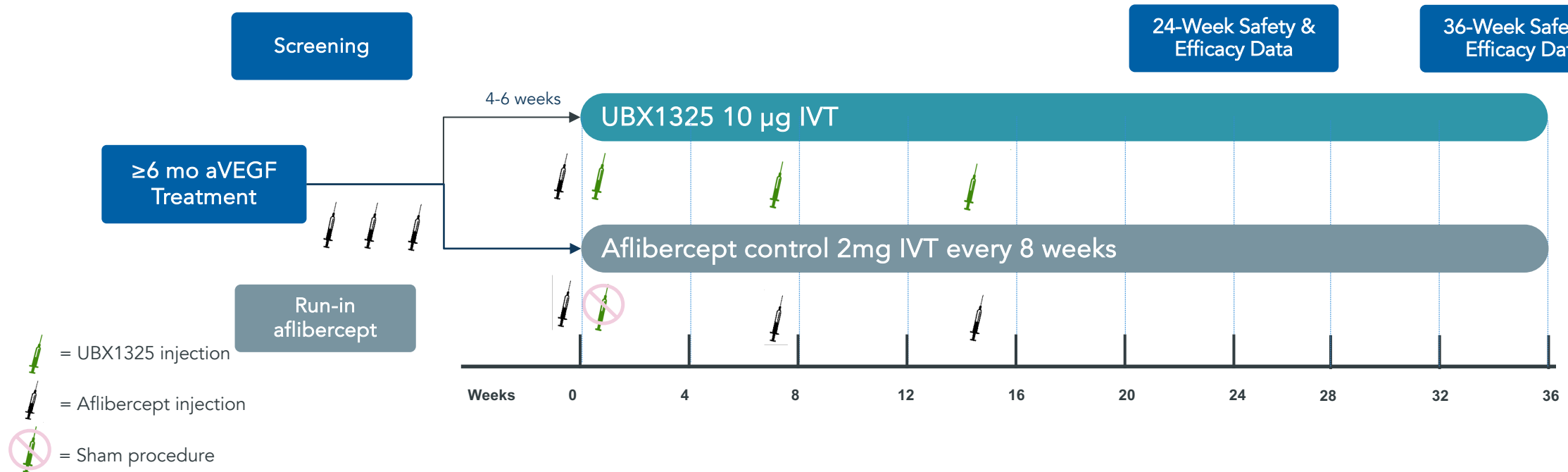
Summary of Findings  
and Concordance of  
Evidence Supporting  
a Treatment Effect of  
UBX1325 in Diabetic  
Macular Edema

**ASPIRE Ph2b Study**  
**UBX1325 head-to-head**  
**against aflibercept in patients**  
**with DME**





# ASPIRE: DME Phase 2b Study Design (Head-to-head against aflibercept)



**Patient Population:** Participants with NPDR who have active DME despite treatment with  $\geq 3$  anti-VEGF injections in preceding 6 months; BCVA 70 – 30 ETDRS letters; CST  $> 325\mu\text{m}$

- Duration: 36 Weeks; Randomization: 1:1**
- Size: n=50 (25 /arm)**

## Endpoints

**Primary endpoint:** BCVA change from baseline to week 24 (noninferiority)

**Secondary endpoints include:** BCVA change from BL over time • CST change from BL over time • proportion of patients gaining  $\geq 15$ ,  $\geq 10$ ,  $\geq 5$ , or  $\geq 0$  letters from BL • safety and tolerability • proportion of participants who do not require anti-VEGF rescue

**Exploratory endpoints:** DRSS change from BL at weeks 24 and 36



**Preclinical Pipeline**  
**Tie2/ $\alpha$ VEGF**  
**Bispecific Program**



# Tie-2 mAb Represents an Orthogonal Approach Restoring Vascular Integrity

Tie-2 mAb explores restoring vascular function in DME/DR independent of Bcl-xLi

1

## Senescence biology

### DR & DME

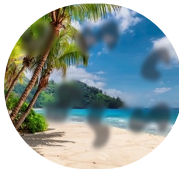
SnCs accumulate  
diabetic in the retina  
with age and disease



SASP → ocular  
inflammation abnormal  
blood vessel growth



Disease → vision loss



2

## Vascular biology

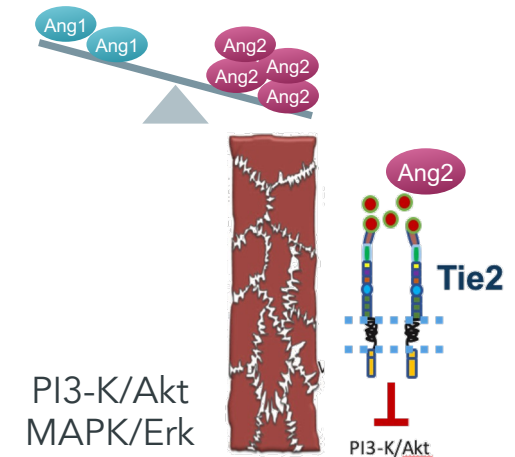
Vascular and endothelial  
growth factor (VEGF)



3

## Tie2 biology

Diseased Vasculature  
Tie2 inactivated by Ang2



PI3-K/Akt  
MAPK/Erk

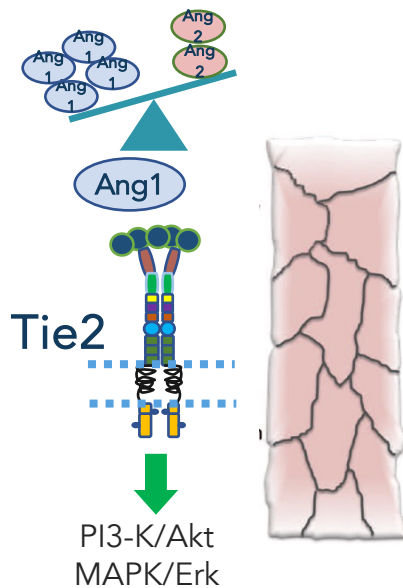
Junctional instability and pericyte  
death. Barrier integrity lost:  
Ocular edema/critical organ edema



# Tie2/VEGF Bispecific Mechanism of Action

## Healthy Vasculature

Tie2 is constitutively activated by Ang1

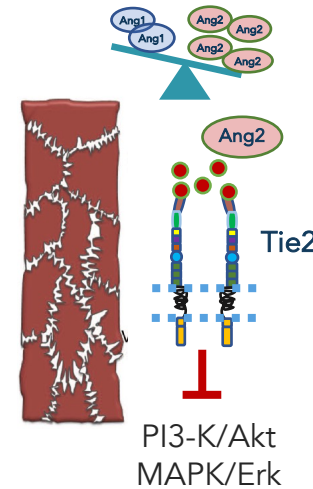
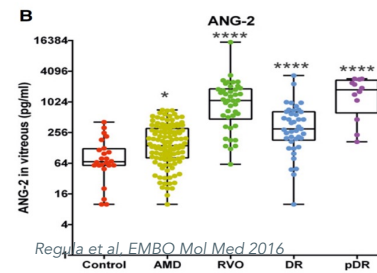


Junctional stability  
Barrier integrity maintained

## Diseased Vasculature

Tie2 is inactivated by Ang2

Inducers of Ang-2:  
Hyperglycemia,  
Hypoxia



## SCIENTIFIC REPORTS

**OPEN** Elevated angiopoietin 2 in aqueous of patients with neovascular age related macular degeneration correlates with disease severity at presentation

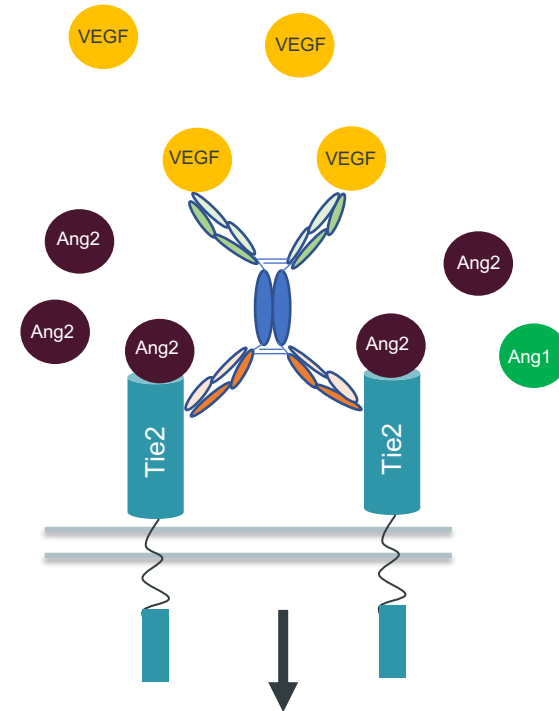
Received: 27 October 2016  
Accepted: 27 February 2017  
Published: 27 March 2017

Danny S. Ng, Yohenda W. Yip, Malini Balakrishna, L.J. Chen, Tie K. Ng, Timothy Y. Lai, Calvin P. Pang & Mårten E. Brelvi

Junctional instability

Barrier integrity lost: vascular leak in eye

## Vasculature Homeostasis Restored by Tie2/aVEGF Bispecific Molecule



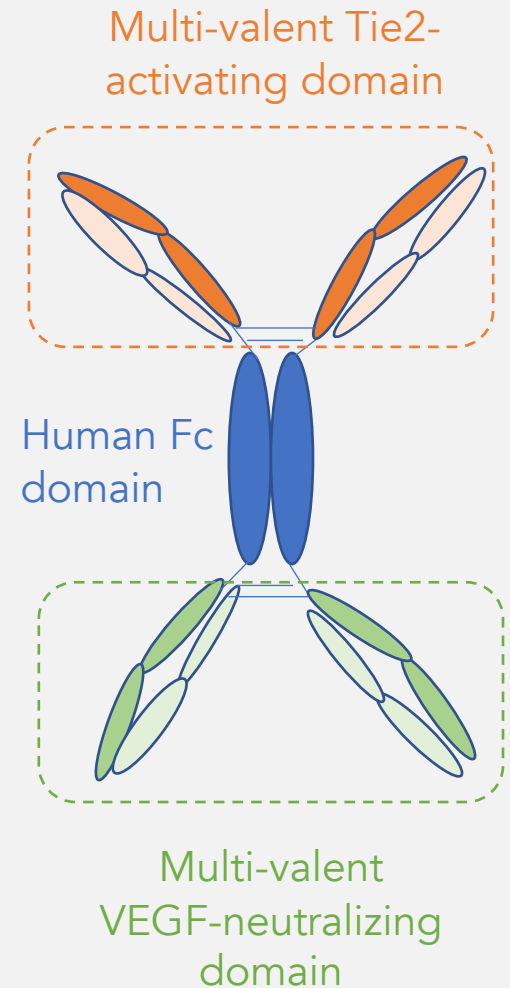
Junctional stability, Restoration of choriocapillaris,  
Inhibition of neovascularization

Barrier integrity restored



# UNITY's Tie2/VEGF Bispecific Molecules Are Differentiated from Competition

	Current standard of care (Aflibercept)	Anti-VEGF-Ang1 Bispecific (Faricimab)	Tie2/VEGF bispecific (Target Profile)
Neutralization of VEGF-A	✓	✓	✓
Neutralization of VEGF-B, PlGF and other angiogenic factors	✓	✗	✓
Ang1-independent activation of Tie2	✗	✗	✓
Potential to improve ischemic areas of eye (preclinical data)	✗	✗	✓



Symmetric molecules with dual functionality on two validated targets for retinal diseases

# Financial Metrics

A woman with long dark hair is wrapped in a light-colored, textured blanket. She is smiling and looking out over a body of water under a bright, hazy sky. The image has a soft, warm feel with a blue gradient overlay on the left side.

UNITY  
BIOTECHNOLOGY



## Financials: Market Snapshot

\$43.2 million cash, cash equivalents and marketable securities as of December 31, 2023

UNITY believes that focused capital allocation are sufficient to fund operations into the third quarter of 2025