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# KODIAK

THE OPHTHALMOLOGY MEDICINES COMPANY

**Corporate Presentation**

June 2026

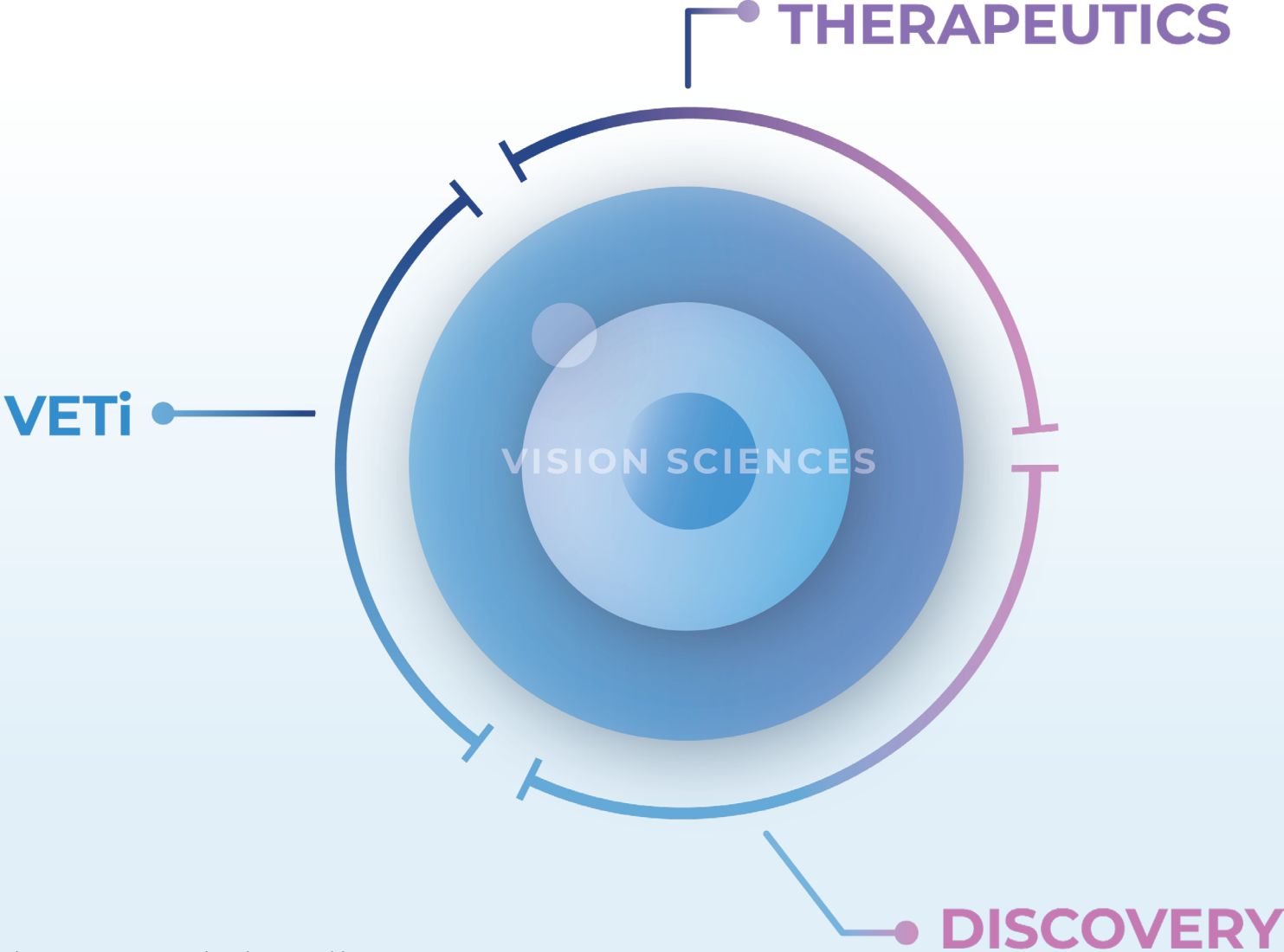
# Forward-Looking Statements

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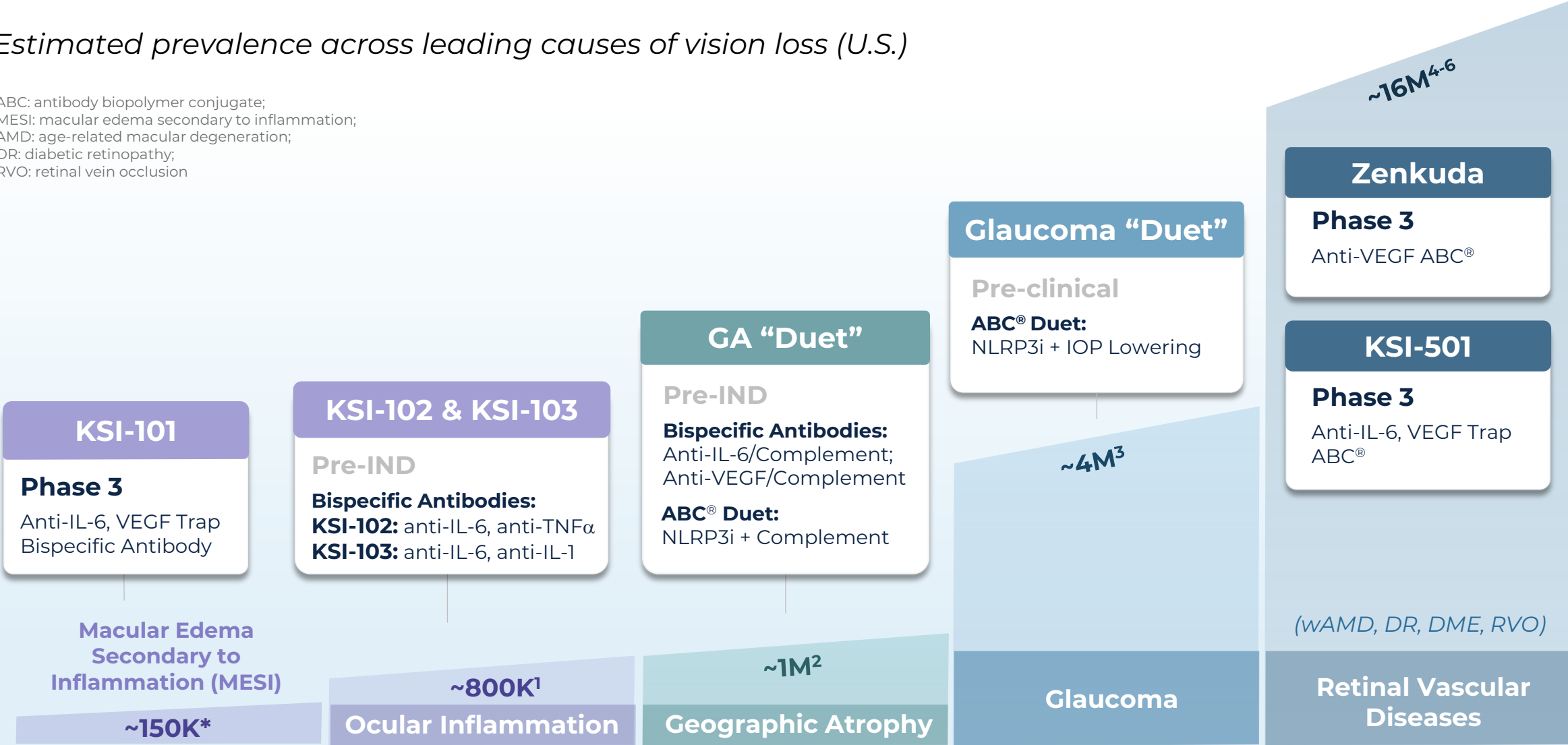
# Kodiak is emerging into a fully integrated Vision Sciences company



# We have both a late-stage clinical portfolio and an emerging pipeline that span multiple retina mechanisms of action, indications and drug types

Estimated prevalence across leading causes of vision loss (U.S.)

ABC: antibody biopolymer conjugate;  
 MESI: macular edema secondary to inflammation;  
 AMD: age-related macular degeneration;  
 DR: diabetic retinopathy;  
 RVO: retinal vein occlusion



\*KSI-101 initial addressable population in MESI. Kodiak Data on File and shared Investor R&D Day July 2025.  
 1. Nila Kirupaharan et al. *Invest. Ophthalmol. Vis. Sci.* 2024;65(7):6510. 2. Wong WL, et al. *Lancet Glob Health* 2014;2:e106-116. 3. Ehrlich JR et al. *JAMA Ophthalmol.* 2024;142(11):1046-1053. 4. Market Scope. 2024 Retinal Pharmaceuticals Market Report. 5. Roche epidemiology data 2025. 6. Kalva, P et al. *Baylor University Medical Center Proceedings*, 36(3), 335-340

# Our three late-stage clinical assets target leading causes of vision loss

**KSI-101**

**Phase 3**

Anti-IL-6, VEGF Trap  
Intravitreal Protein

*MESI*

**Zenkuda™**

**Phase 3**

Anti-VEGF  
Intravitreal ABC®

*wAMD, DR, RVO*

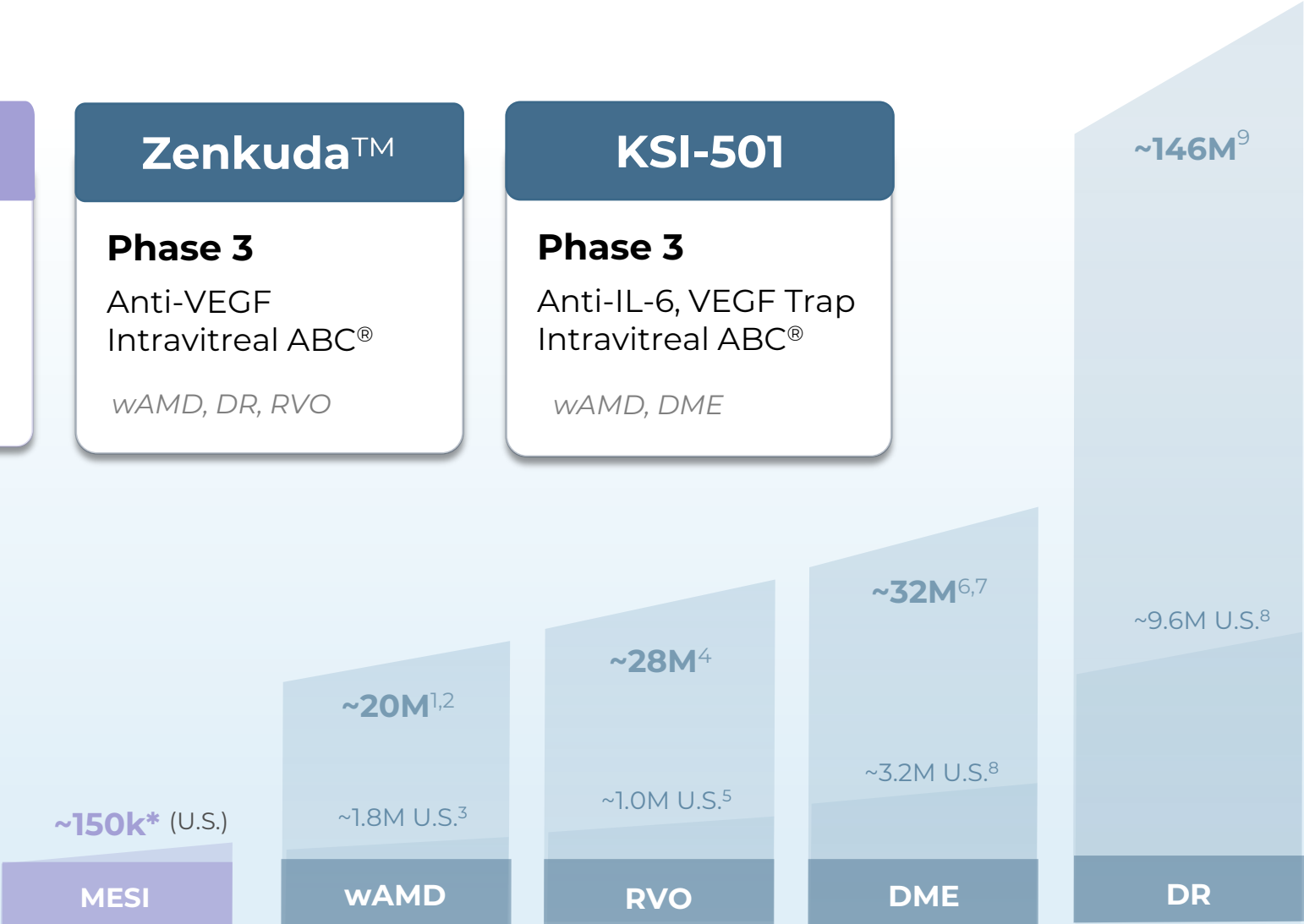
**KSI-501**

**Phase 3**

Anti-IL-6, VEGF Trap  
Intravitreal ABC®

*wAMD, DME*

## Estimated global prevalence



ABC: antibody biopolymer conjugate;  
MESI: macular edema secondary to inflammation;  
AMD: age-related macular degeneration;  
RVO: retinal vein occlusion  
DME: diabetic macular edema  
DR: diabetic retinopathy

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1. Fleckenstein M, et al. *JAMA*. 2024;331(2):147-157. 2. Boopathiraj N, et al. *Mayo Clinic Proceedings: Innovations, Quality & Outcomes*, 2024; 8, 364-374. 3. Market Scope. 2024 Retinal Pharmaceuticals Market Report. 4. Song, P., et al. (2019). *Journal of Global Health*. <https://doi.org/10.7189/jogh.09.010427>. 5. Kalva, P et al. *Baylor University Medical Center Proceedings*, 36(3), 335-340. 6. The Diabetes Atlas, Accessed May 2026. 7. James H.B. et al. *Survey of Ophthalmology*, 2022;67(4): 1244-1251. 8. Roche epidemiology data 2025. 9. WHO, 2019, World Report on Vision Executive Summary.

# We are gathering speed: all three clinical programs are in Phase 3 with topline data expected in 2026 and Zenkuda is BLA ready

## KSI-101

Anti-IL-6, VEGF trap  
**bispecific protein**

**Safe and potent control of MESI**

- **Positive** Phase 1b results in MESI
- Phase 3 PEAK and PINNACLE studies **actively enrolling**
- PEAK topline data 4Q2026

## Zenkuda

Anti-VEGF **ABC<sup>®</sup> biologic**

**Strong immediacy and industry-leading durability**

- **4 successful pivotal studies**
- **BLA-ready in DR, RVO, wAMD\***
- Phase 3 DAYBREAK study in wAMD with topline data 3Q2026
- BLA filing expected in 2026

## KSI-501

Anti-IL-6, VEGF trap  
**bispecific ABC<sup>®</sup> biologic**

**Differentiated efficacy, strong immediacy and industry-leading durability**

- Differentiated efficacy being explored in the Phase 3 DAYBREAK study in wAMD with topline data 3Q2026
- Phase 3 study in DME planned 3Q2026

# Four Phase 3 readouts in 2026, if successful, position Kodiak to file 3 licensing applications (BLA) in 2026 and 2027

- 4 successful pivotal studies completed
- 3 additional topline data readouts expected in 2026
- 3 Licensing applications (BLA) expected in 2026 and 2027

| ZENKUDA         |  | 3Q '26 | 4Q '26                      | 1Q '27 | 2Q '27 | 3Q '27 | 4Q '27 | 1Q '28 | 2Q '28 | 3Q '28 |
|-----------------|--|--------|-----------------------------|--------|--------|--------|--------|--------|--------|--------|
| RVO (BEACON)    |  |        |                             |        |        |        |        |        |        |        |
| DR (GLOW1)      |  |        |                             |        |        |        |        |        |        |        |
| DR (GLOW2)      |  |        | BLA*                        |        |        |        |        |        |        |        |
| wAMD (DAYLIGHT) |  |        |                             |        |        |        |        |        |        |        |
| wAMD (DAYBREAK) |  |        |                             |        |        |        |        |        |        |        |
| <b>KSI-101</b>  |  |        |                             |        |        |        |        |        |        |        |
| MESI (PEAK)     |  |        |                             |        | BLA*   |        |        |        |        |        |
| MESI (PINNACLE) |  |        |                             |        |        |        |        |        |        |        |
| <b>KSI-501</b>  |  |        |                             |        |        |        |        |        |        |        |
| wAMD (DAYBREAK) |  |        |                             |        |        |        | BLA*   |        |        |        |
| DME (ALTO)      |  |        | First Patient In (Expected) |        |        |        |        |        |        | sBLA*  |

### Upcoming catalysts (expected)

- **DAYBREAK** topline data expected 3Q 2026; licensing application in 4Q 2026
- Pivotal analysis 1 (**PEAK**) expected December 2026; potential licensing application in 1H 2027
- Pivotal analysis 2 (**PEAK+PINNACLE**) expected 2Q 2027
- **DAYBREAK** topline data expected 3Q 2026
- Phase 3 **ALTO** study in DME First Patient In expected 3Q 2026

\*Timing reflects current expectations; BLA timing pending discussions with regulatory bodies, subject to change  
 RVO: retinal vein occlusion; DR: diabetic retinopathy; AMD: age-related macular edema; DME: diabetic macular edema; MESI: macular edema secondary to inflammation;  
 BLA: biologics license application; sBLA: supplemental biologics license application; DAYBREAK: NCT06556368; PEAK: NCT06990399; PINNACLE: NCT06996080

# Significant investment in commercial manufacturing has positioned Kodiak well for potential launch of multiple ABC<sup>®</sup> products into large and growing markets

News Release

**Lonza**  
**KODIAK**

Grand Opening of Kodiak Sciences' Purpose-Built Bioconjugation Facility to Support Potential Commercial Manufacture of KSI-301, an Antibody Biopolymer Conjugate for Retinal Diseases

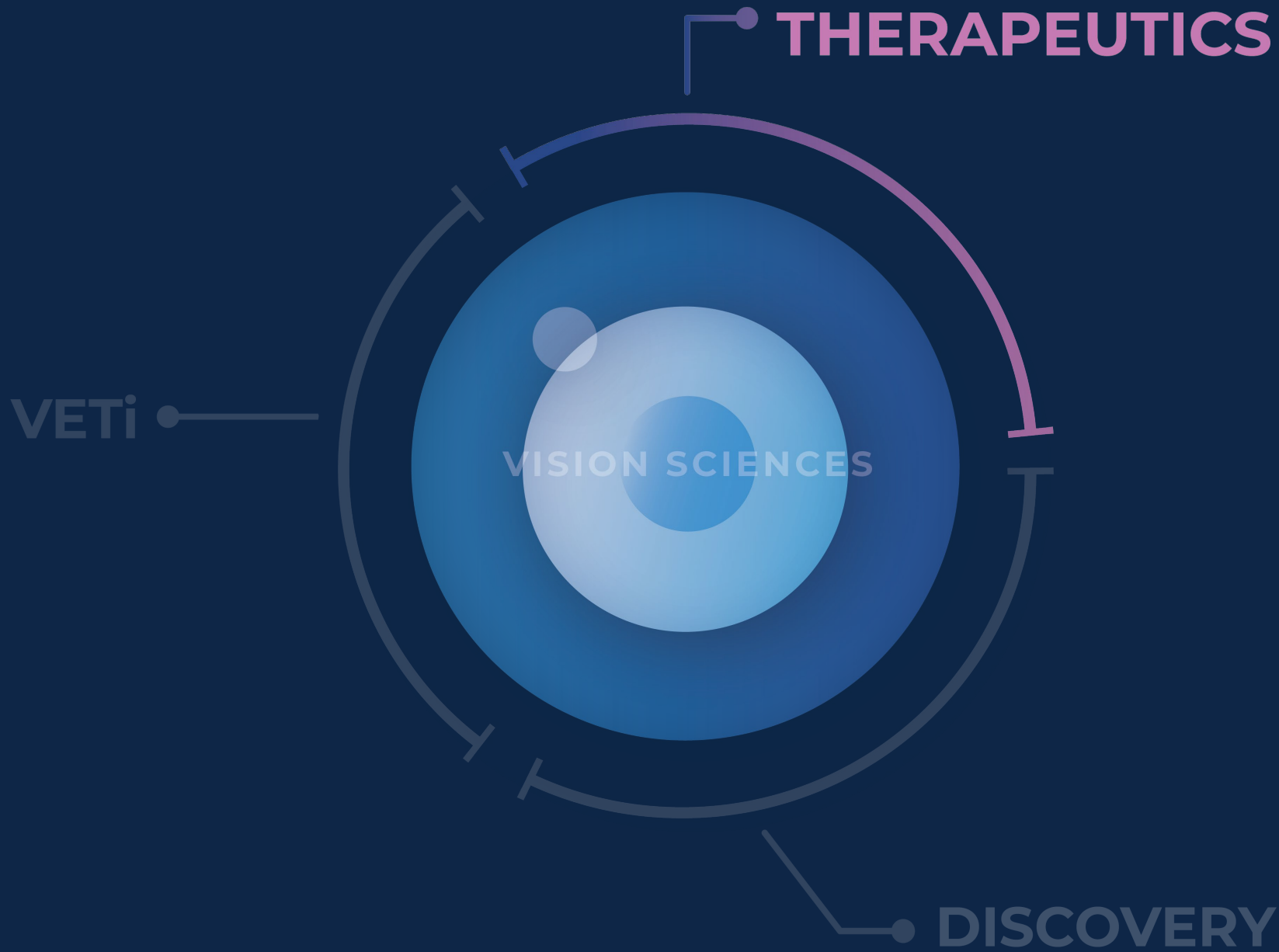
- Purpose-built bioconjugation facility in Lonza's Ibex<sup>®</sup> De to support the potential commercial launch of Kodiak's high-prevalence retinal diseases
- The opening ceremony took place on May 17, 2022 following facility in March 2022

**Basel, Switzerland and Palo Alto (CA), USA, 18 May 2022** – Kodiak Sciences, a biopharmaceutical company committed to researching, developing and commercializing transformative therapeutics to treat high prevalence retinal diseases, today announced the opening of a new, custom-built, bioconjugation facility at its manufacturing complex in Visp (CH).



## Ursus, a premium commercial manufacturing facility dedicated to the manufacture of Kodiak's ABC<sup>®</sup> medicines

- Custom designed for large scale **premium manufacturing of complex antibody conjugate biotherapies**
- Mechanical completion in 1H2022; commissioned as a cGMP facility for commercial supply in Jan 2023
- Successful cGMP manufacture and release commercial scale tarcocimab commercial formulation in Nov 2023
- **BLA-facing commercial-scale validation batches were manufactured and released in 2025 for antibody, biopolymer and bioconjugate**



ZENKUDA + KSI-501

# Kodiak's ABC<sup>®</sup> Platform Science for Retina

# The ABC Platform supports Kodiak's science of **immediacy and durability**



## **Designed-in Extended Tissue Residence Time**

A proprietary phosphorylcholine-based polymer is conjugated to an antibody to increase molecular size which extends ocular half-life

## **High In-Vitro Potency**

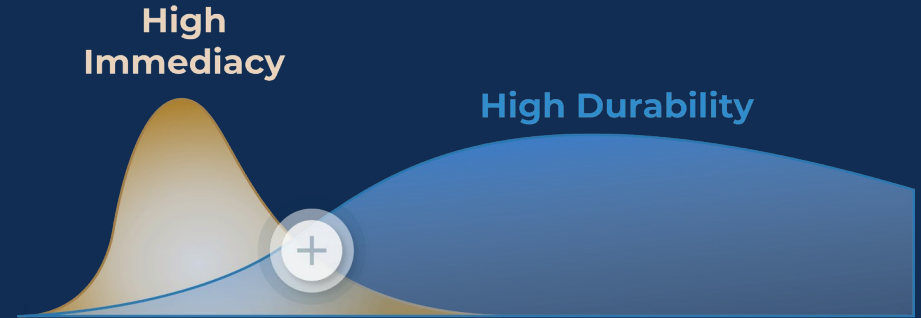
Both unconjugated protein and conjugated protein demonstrate high binding affinity and potency *in vitro*

## **Extended Ocular Half- Life in Animals**

3x the ocular  $t_{1/2}$  of approved intravitreal biologics when measured in rabbits following an intravitreal injection

## **Extended Ocular Half- Life in Humans**

3x the ocular  $t_{1/2}$  of faricimab when measured from aqueous humor in patients following an intravitreal injection



## **Powerful Immediacy via Unconjugated Antibody**

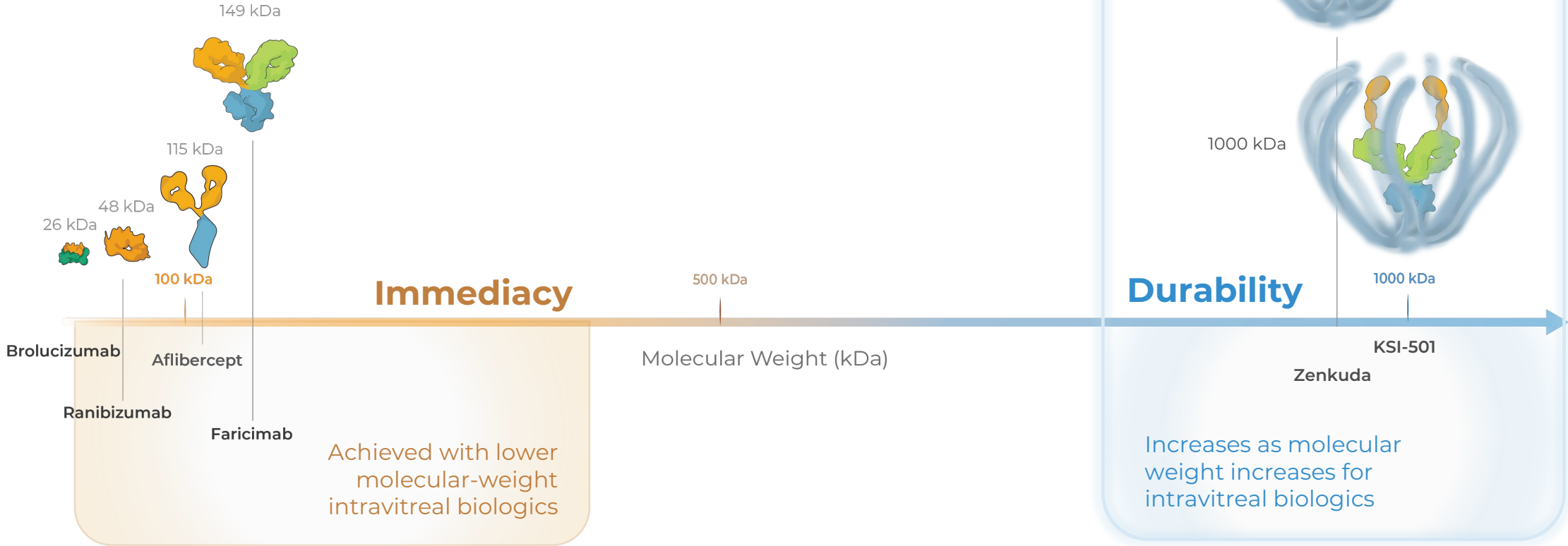
The unconjugated protein delivers a strong “pulse” of anti-VEGF inhibition during the loading phase, or to recapture control of the disease in patients whose disease has reactivated

## **Extended Clinical Durability via Conjugated Antibody**

The conjugated protein maintains the signature durability as seen in Kodiak's pivotal studies to date

# Durability: ABC<sup>®</sup> Platform-based medicines are designed for longer ocular durability

ABC<sup>®</sup> Platform-based medicines **have a high molecular weight which increases their ocular half-life** compared to today's intravitreal biologics



\*Kodiak's ABC platform-based medicines Zenkuda and KSI-501 combine unconjugated and conjugated protein in a single biologic

**Conjugated Portion of ABC<sup>®</sup> Platform-based medicines\***

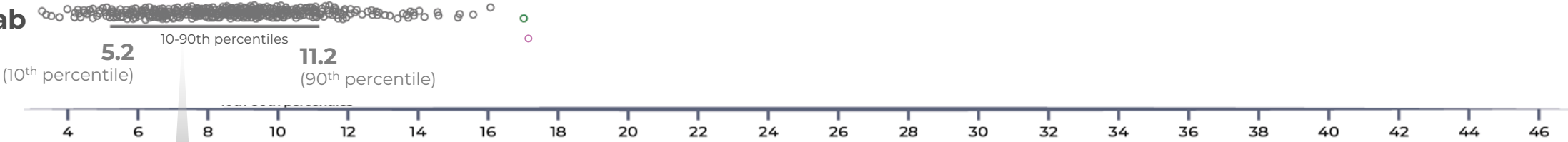
# Durability: Zenkuda has a mean ocular half-life in humans of 20 days, which is 3-fold longer than faricimab

**19.8 days**  
(Mean)  
~3x longer than faricimab

Zenkuda

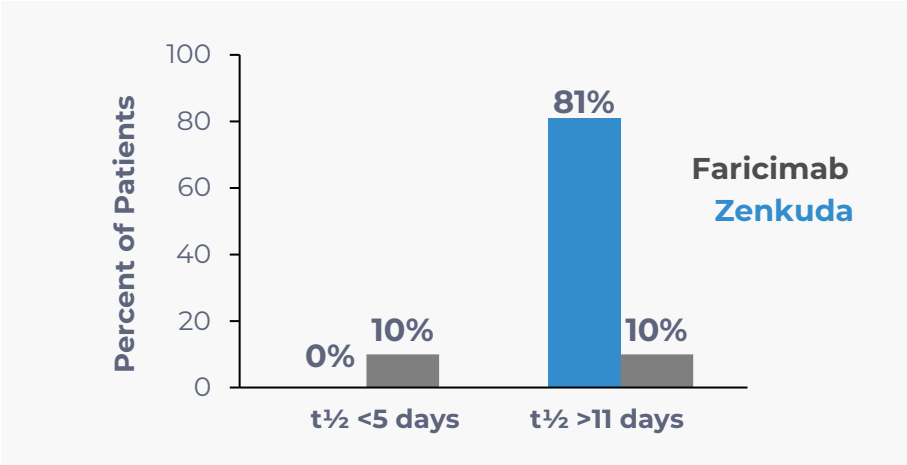


Faricimab



Human Ocular Half-Life (Days)

**7.5 days**  
(Mean)



# Zenkuda and KSI-501 combine **unconjugated** and **conjugated** protein, enabling **high immediacy** and **high durability** in a single biologic

## Zenkuda – 5 mg

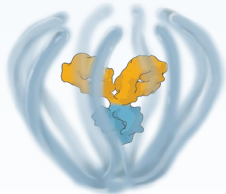


**IMMEDIACY**

**1.0 mg**

Unconjugated

+



**DURABILITY**

**4.0 mg**

ABC (conjugated)

## KSI-501 – 5 mg

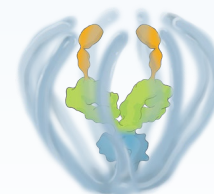


**IMMEDIACY**

**1.5 mg**

Unconjugated

+



**DURABILITY**

**3.5 mg**

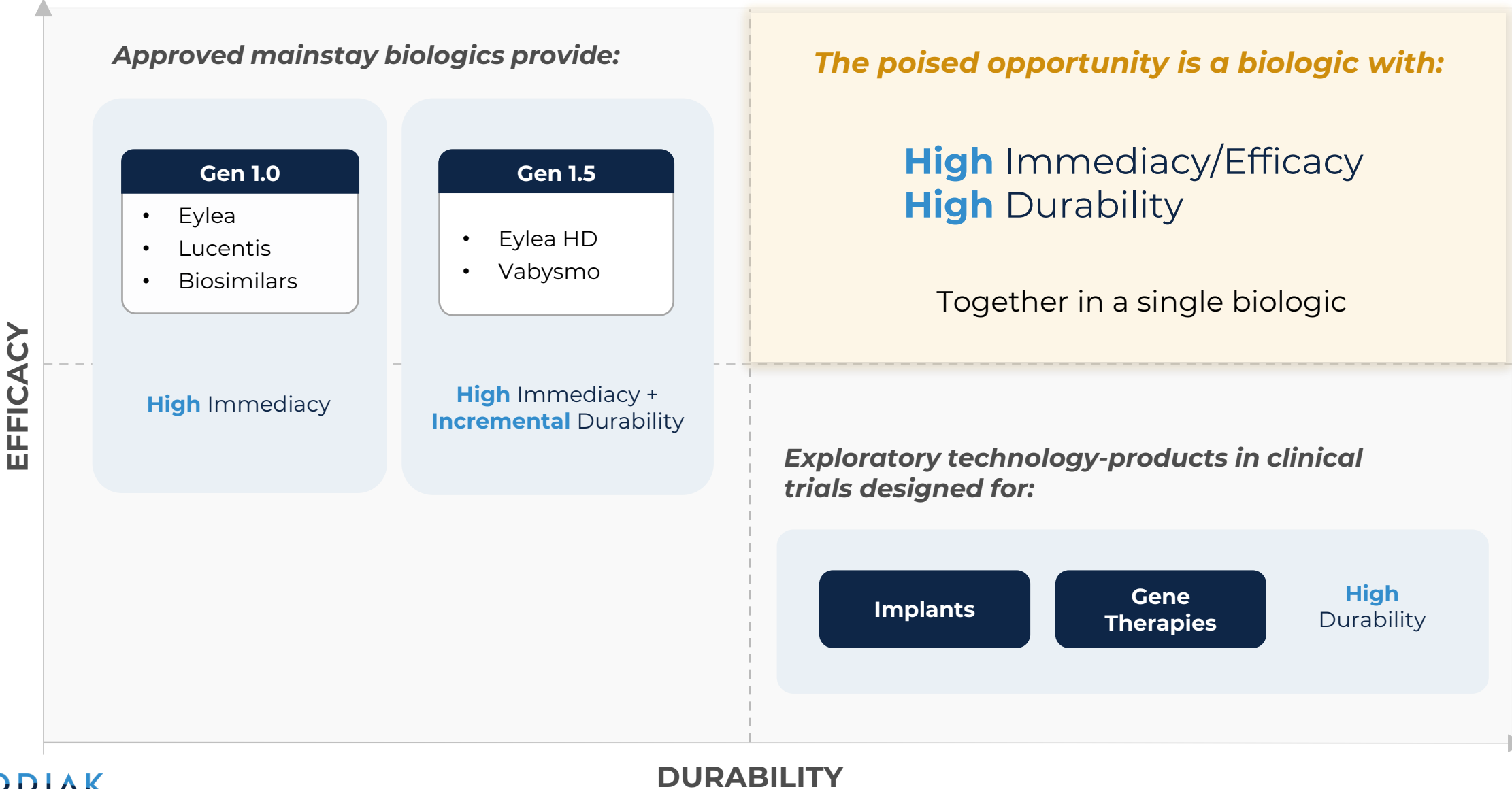
ABC (conjugated)

**Single biologics engineered for high immediacy and high durability**

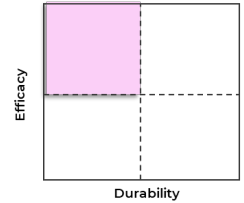
ZENKUDA + KSI-501

# Retinal Vascular Diseases and the Anti-VEGF Market

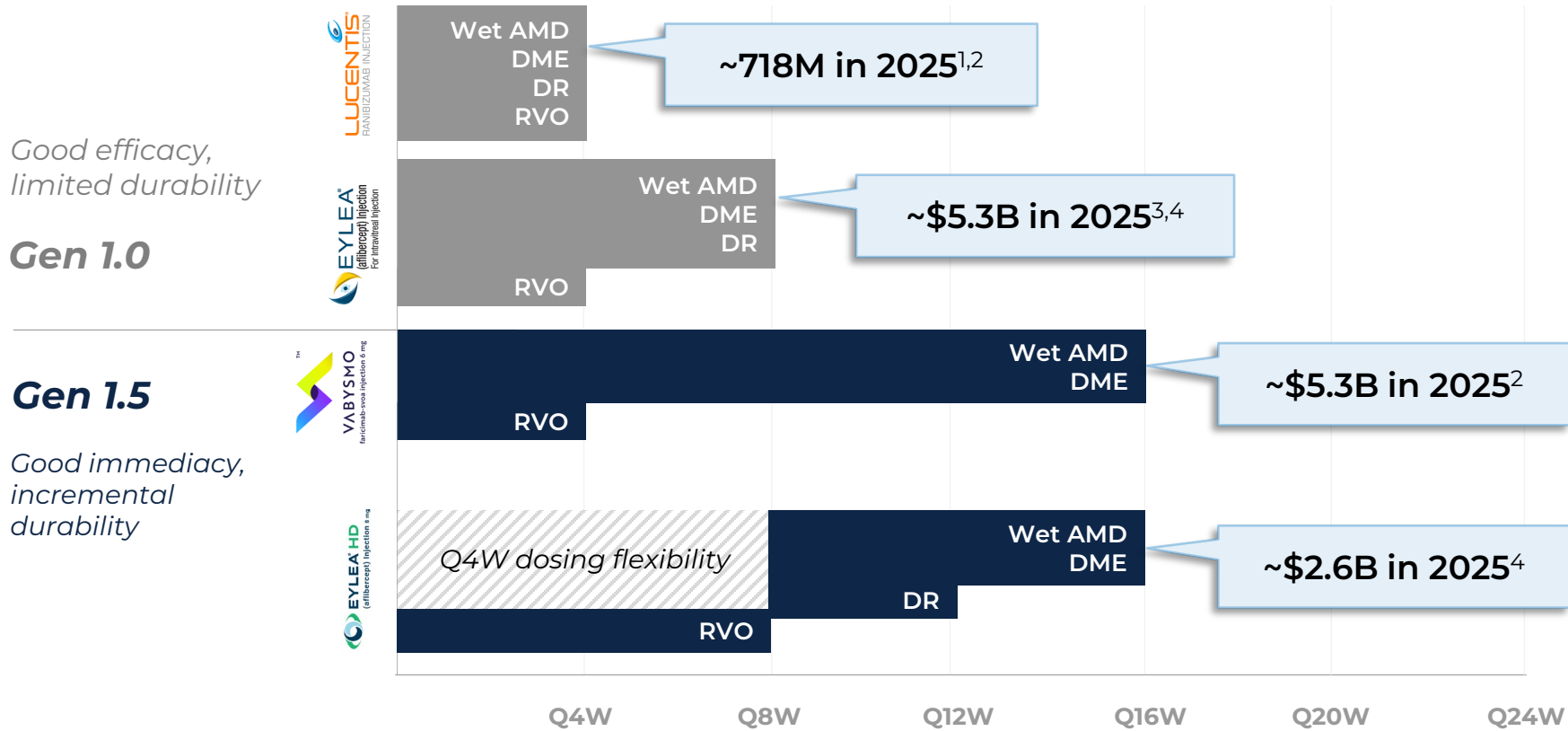
**There remains valuable open space in the ~\$15B retinal vascular diseases market, despite the availability of approved biologics and clinical trials of new exploratory technologies**



# The Gen 1.0 biologics that provide **immediacy** and the Gen 1.5 biologics that provide **immediacy** and **incremental durability** are meaningful for patients and physicians



Dosing regimen per label for approved intravitreal biologics and estimated worldwide sales in 2025

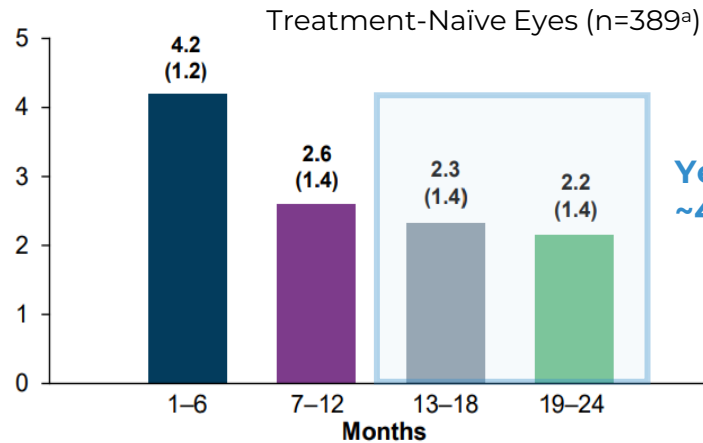
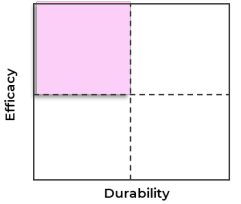


**The commercial success of new branded therapies is a testament to:**

- The **power of the intravitreal biologic** as the mainstay of therapy
- The **unmet need** that remains for patients

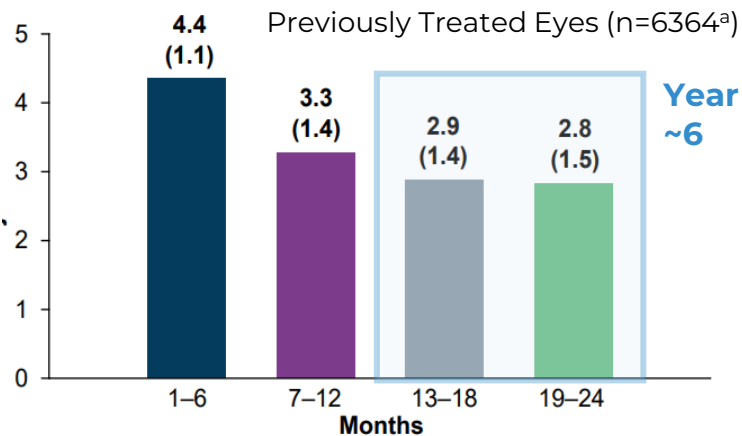
# Despite their commercial success, real-world data in wAMD show that most patients are falling short of the durability promise of the Gen 1.5 labels

Faricimab injections observed after the first 6 months of treatment through Year 2 in the FARENTINA study<sup>1</sup>



Year 2:  
~4.5

In Year 2, patients received 4.5 injections which is an average dosing interval of every 11.5 weeks



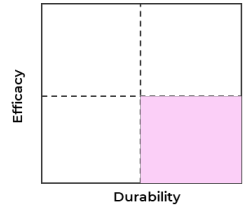
Year 2:  
~6

In Year 2, patients received 6.0 injections which is an average dosing interval of every 8 weeks

Most patients are on a Q8W-Q12W schedule in the real world in Year 2

<sup>a</sup> Only eyes with ≥ 1 injection after index and prior to censoring were included.

# Technologies being explored in clinical trials, including implants and gene therapies, are engineering for high durability but are lacking immediacy



## Implants

- Engineering for durability
- Long-term safety unknown

## Gene Therapies

- Engineering for durability
- Onerous monitoring and inflammation control
- Long-term safety unknown

Maintenance agents to be used in subset of patients but always **relying on mainstay biologics to (re)establish disease control**

Implants and gene therapies are being tested **on top of mainstay biologics**, which are given during the **loading phase** and then as needed during the **maintenance phase**.

# Zenkuda and KSI-501: Differentiated ABC platform mainstay biologics

Target product profiles

## ZENKUDA

Anti-VEGF ABC<sup>®</sup> biologic

## KSI-501

Anti-IL-6, VEGF trap **bispecific** ABC<sup>®</sup> biologic

Non-inferior efficacy

Better efficacy

Strong immediacy

Industry-leading durability

# Zenkuda and KSI-501's complementary and differentiated product profiles support a broad retinal franchise

| Phase 3 Study      | Primary Endpoint | 6-Month Durability |
|--------------------|------------------|--------------------|
| <b>ZENKUDA</b>     |                  |                    |
| RVO<br>(BEACON)    |                  |                    |
| DR<br>(GLOW1)      |                  |                    |
| DR<br>(GLOW2)      |                  |                    |
| wAMD<br>(DAYLIGHT) |                  | Not Applicable     |
| wAMD<br>(DAYBREAK) | Non-Inferiority  |                    |
| <b>KSI-501</b>     |                  |                    |
| wAMD<br>(DAYBREAK) | Non-Inferiority  | Not Applicable     |
| DME<br>(ALTO)      | Superiority      |                    |

Successfully completed

Planned

**Across 4 pivotal studies, Zenkuda demonstrated:**

- Non-inferior efficacy with 6-month predominant durability
- Favorable and well-tolerated safety profile
- In GLOW1 and GLOW2, Zenkuda reduced the risk of developing a Site Threatening Complication by  $\geq 85\%$  with 100% of patients on 6-month dosing at Year 1

**Ongoing DAYBREAK study in wAMD explores potential for immediacy and 6-month durability**

- Enrollment complete; topline data expected 3Q 2026

**Ongoing DAYBREAK study in wAMD explores potential for immediacy and differentiated efficacy**

- Enrollment complete; topline data expected 3Q 2026

**ALTO study in DME expected to start 3Q2026**

# Zenkuda in Retinal Vein Occlusion: Well-positioned to capture meaningful share in a large and growing >\$3B RVO market

- **RVO is a meaningful and growing market**

- **~3B** estimated RVO market<sup>1</sup>
  - ~20% of Eylea net sales derived from RVO in 2025<sup>2</sup>
- **~1M** people in the U.S. with RVO<sup>3</sup>
  - Prevalence of RVO is growing globally, driven by growth in aging population
- **~750,000** treatable with anti-VEGF

- **RVO is a chronic disease that requires long-term management**

- Despite acute onset, RVO often requires frequent **long-term** treatment
- Approved intravitreal biologics **require frequent injections** that can be burdensome for patients and physicians

**Zenkuda is designed to address key unmet needs in RVO<sup>4</sup>**

### **Strong efficacy**

Zenkuda **doubled** the treatment interval relative to aflibercept at month 6 (Q8W vs. Q4W)

### **6-month durability**

**75%** of patients achieved 6-month durability at Year 1 in the Phase 3 BEACON study

### **Fewer injections**

Potential to reduce treatment burden

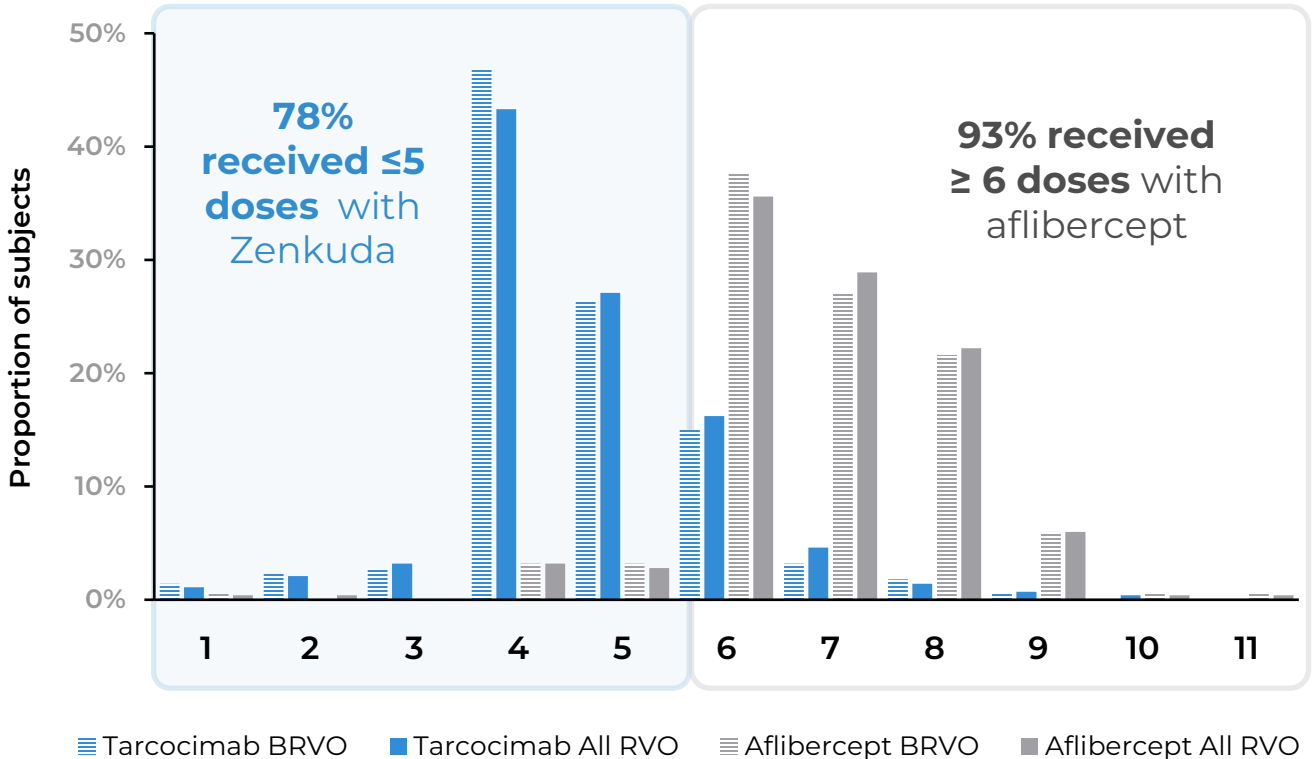
# Zenkuda in Retinal Vein Occlusion: Demonstrated high efficacy and industry-leading durability in the Phase 3 BEACON study

**Phase 3 BEACON**

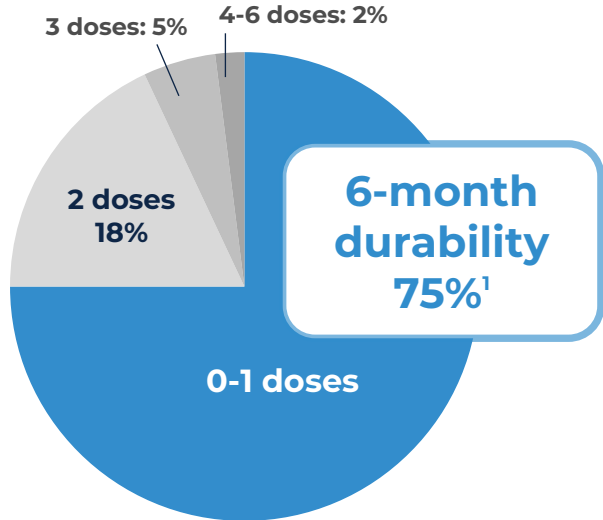
Primary Endpoint ✓

6-month Durability ✓

**Number of injections through Year 1**



**Zenkuda: Number of doses in the second 6 months of Year 1**



RVO: retinal vein occlusion; BRVO: branched retinal vein occlusion;  
 1. Durability interval calculated based on patients that received no injections (46%) or 1 injection (29%) over the second 6 months of Year 1.

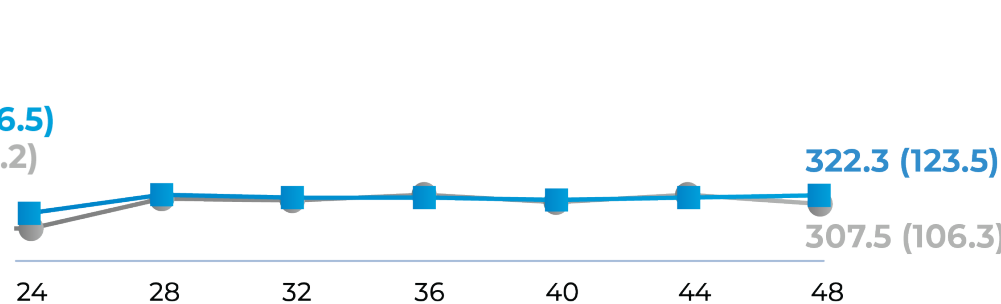
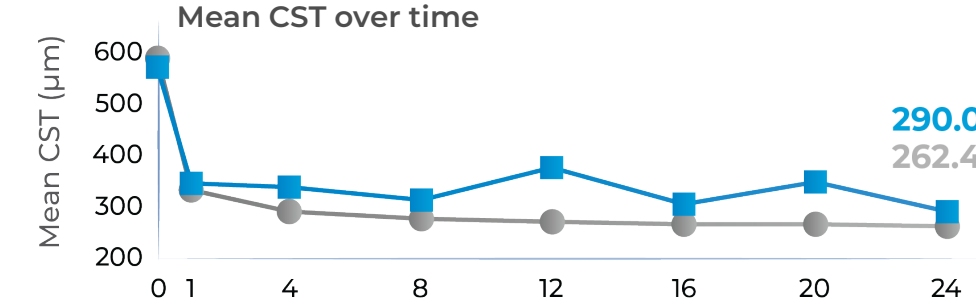
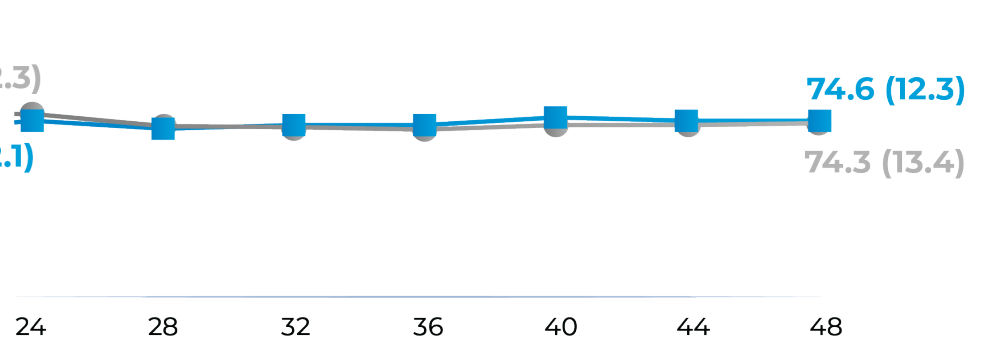
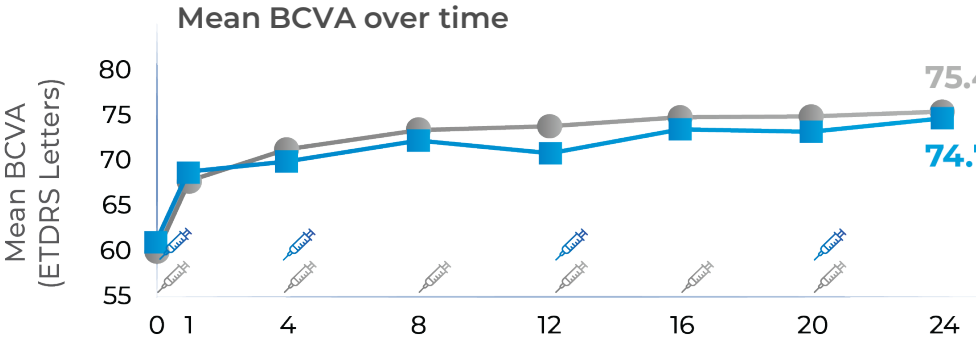
# Zenkuda achieved comparable visual and anatomical outcomes in all RVO patients, irrespective of the treatment paradigm used

**Fixed Dosing (0-24)**  
Doubling of treatment interval

**Head-to-head Individualized Dosing (24-48)**  
Zenkuda vs aflibercept

**With two fewer doses (4 vs 6), similar visual and anatomical gains**

**75% achieved 6-month durability, similar visual and anatomical gains**



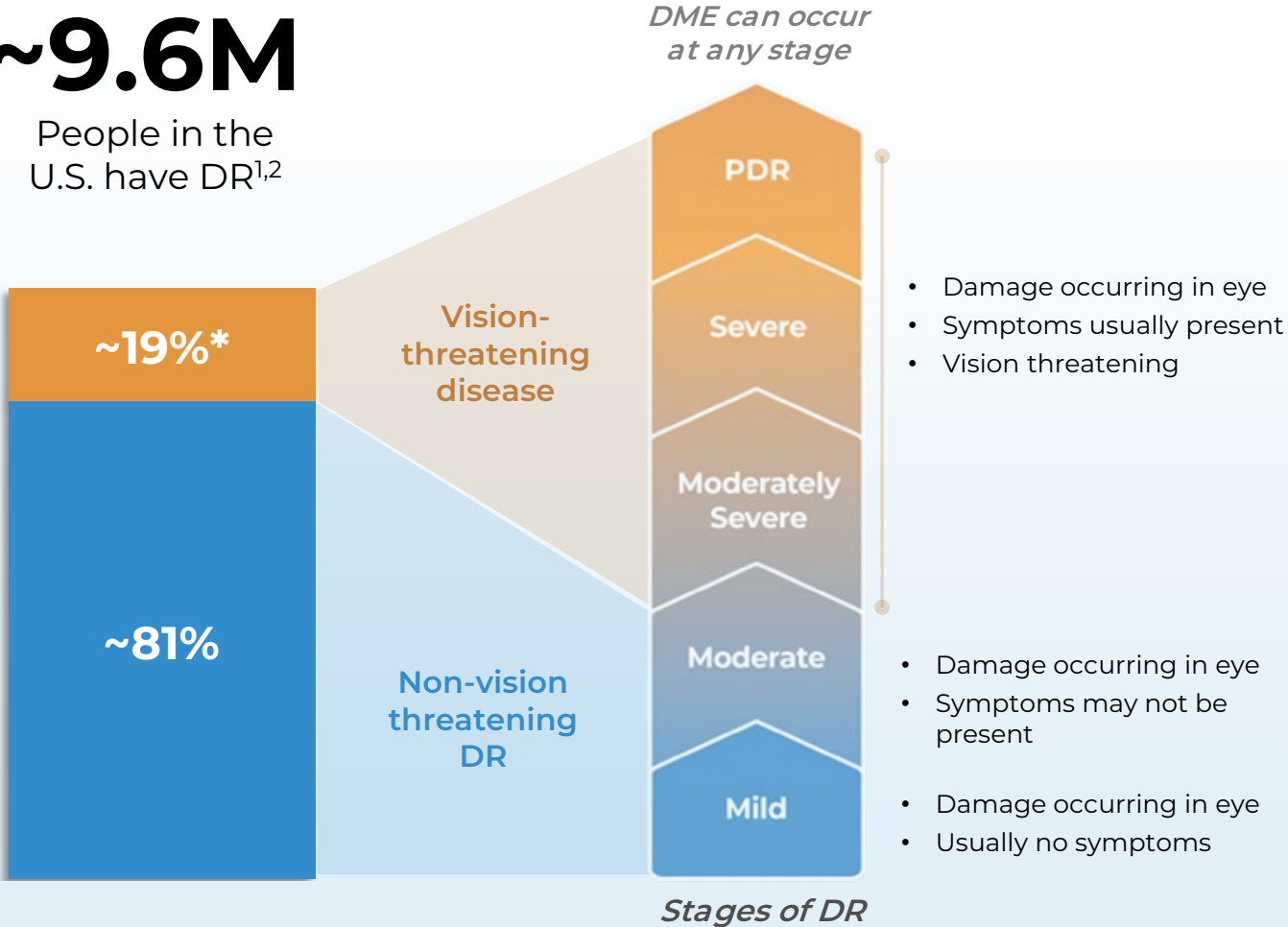
|   | Zenkuda     | Aflibercept |
|---|-------------|-------------|
| LSM change from BL BCVA at Week 48 (MMRM) | 11.7        | 12.8        |
| 95% CI for LSM difference                 | -3.11, 0.94 |             |
| P-value for non-inferiority <sup>a</sup>  | p = 0.001   |             |

Mean observed data; Week 24 and 48 datapoints are Mean (Standard Deviation). Results for BCVA are based on a mixed model repeated measures (MMRM) analysis, with the change from baseline value as the dependent variable; treatment, visit (Week 1 through Week 48), and treatment by visit interaction as fixed effects; randomization stratification variables [baseline BCVA, disease duration, RVO type) and geographical location], as well as continuous covariates of baseline BCVA value and baseline OCT CMM value, as fixed effects; and subject as a random effect. a. Nominal p-value. Non-inferiority margin = 4.5 ETDRS letters.

# Zenkuda in Diabetic Retinopathy: A large, undertreated disease with meaningful risk progression

**~9.6M**

People in the U.S. have DR<sup>1,2</sup>



## DR can progress quickly into vision-threatening PDR or DME<sup>3</sup>

- DME can occur at any stage, but the risk increases as DR worsens
- **50%** of moderate NPDR and **60%** of severe NPDR eyes developed vision-threatening DME by Year 4

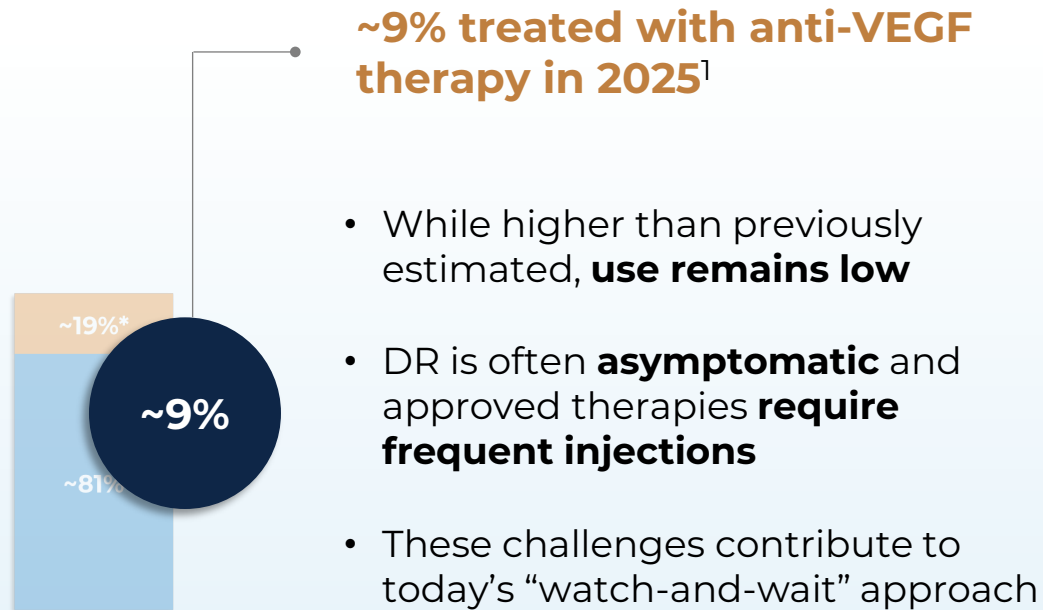
## Anti-VEGF therapy reduces the risk of PDR or DME development by ~50%<sup>3,4</sup>

- Compared to laser or no treatment
- Repeated anti-VEGF injections are required to maintain the benefits of therapy

\*The CDC defines VTDR as severe NPDR, PDR, and/or DME

1. Roche epidemiology data from 2025. 2. CDC accessed May 13: <https://www.cdc.gov/vision-health-data/prevalence-estimates/dr-prevalence.html>. 3. Moshfeghi AA, et al. BMC Ophthalmol. 2024 May 31;24(1):229. 4. Maturi RK et al; DRCR Retina Network. JAMA Ophthalmol. 2021 Jul 1;139(7):701-712.

# Zenkuda in Diabetic Retinopathy: A durable anti-VEGF therapy could expand treatment in DR



**A reduced treatment burden could catalyze the DR market**

~19%

~81%

**Zenkuda's 6-month dosing has the potential to expand anti-VEGF adoption**

**Fewer injections with all patients on 6-month dosing at Year 1\*<sup>2</sup>**

- Potential to increase patient compliance
- May catalyze more at-risk patients to seek earlier treatment, given risk of disease progression

**Strong efficacy<sup>2</sup>**

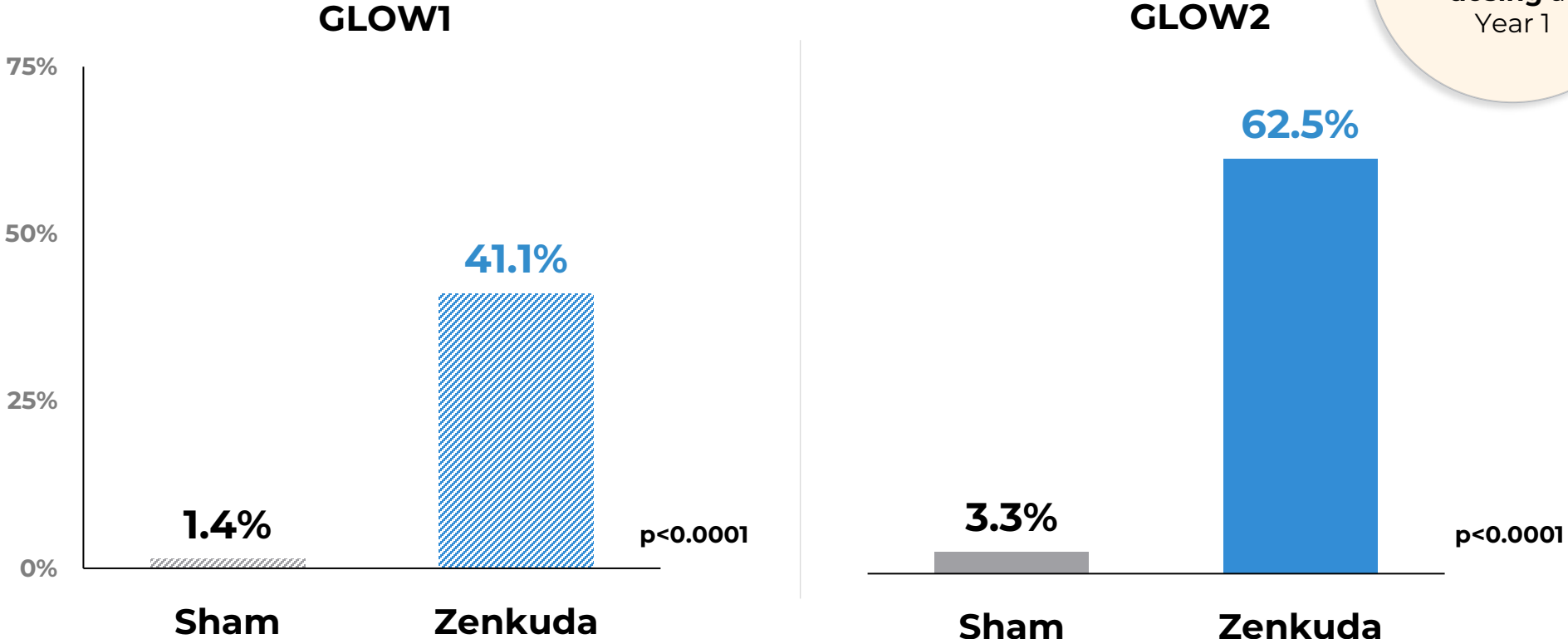
- Superior  $\geq 2$ -step improvement in DRSS
- Reduced risk of developing sight-threatening complications by  $\geq 85\%$

# Zenkuda in Diabetic Retinopathy: Established superiority in $\geq 2$ -step improvement in DRSS in GLOW1 *and* GLOW2

**Phase 3**  
GLOW1  
GLOW2

Superiority ✓  
6-month Durability ✓

Proportion of patients with  $\geq 2$ -Step improvement in Diabetic Retinopathy Severity Score (DRSS) from Baseline to Week 48



100% of patients on 6-month dosing at Year 1

**GLOW1:** Sham (n=125); Zenkuda (n=128). **GLOW2:** Sham (n=125); Zenkuda (n=130); Week 48 (LOCF) represents the last available observation while on randomized treatment, within the Week 48 visit window. Note: Weighted percentages are based on weighted average of observed estimates across strata using CMH weights. p-values are based on the difference in response rates

# Zenkuda in Diabetic Retinopathy: Reduced the risk of developing sight-threatening complications by $\geq 85\%$ in GLOW1 *and* GLOW2

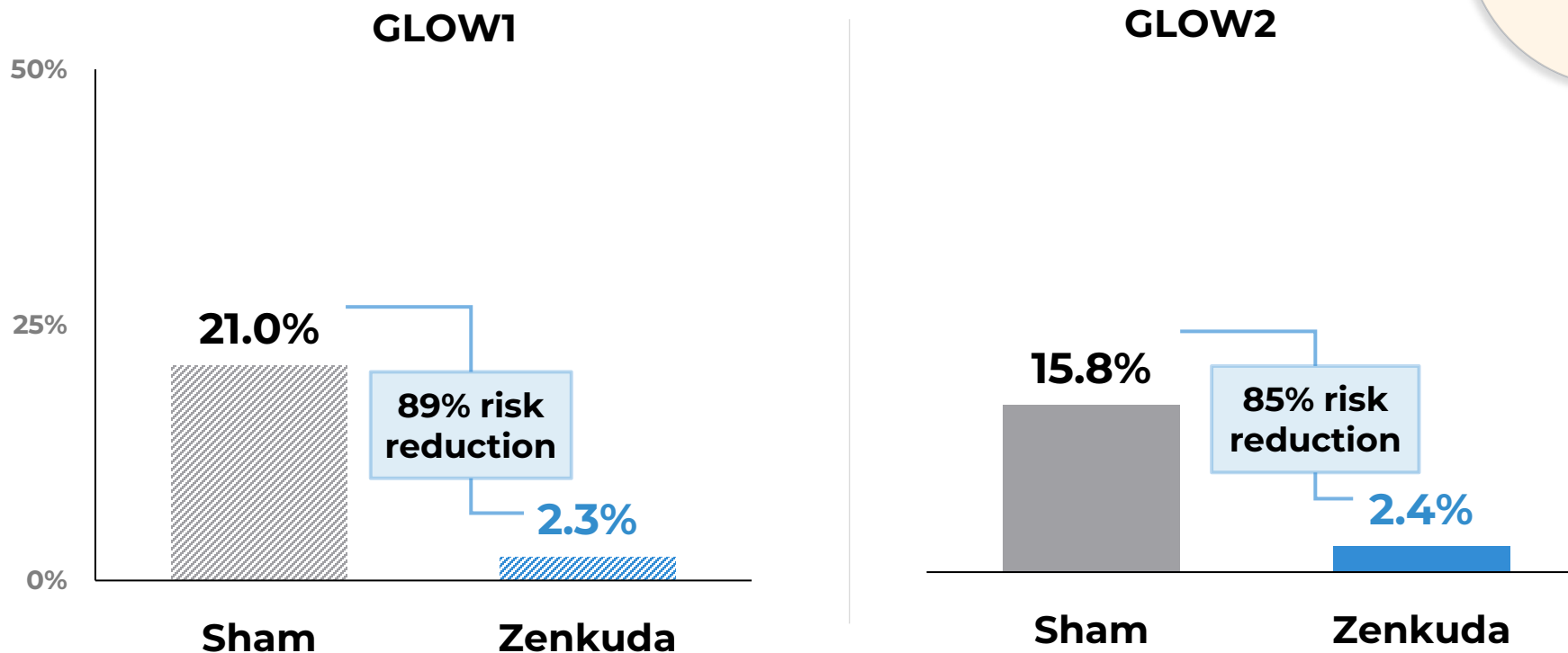
Phase 3  
GLOW1  
GLOW2

Superiority ✓

6-month  
Durability ✓

Proportion of patients developing sight-threatening complications from Baseline through Week 48

100% of patients on 6-month dosing at Year 1



**GLOW1:** Sham (n=125); Zenkuda (n=128). **GLOW2:** Sham (n=125); Zenkuda (n=130). Weighted percentages are based on weighted average of observed estimates across strata using CMH weights. p-values are based on the difference in response rates. Sight threatening complications include: diabetic macular edema, new or worsening proliferative diabetic retinopathy; anterior segment neovascularization; neovascularization of the disc and elsewhere, vitreous hemorrhage and neovascular glaucoma.

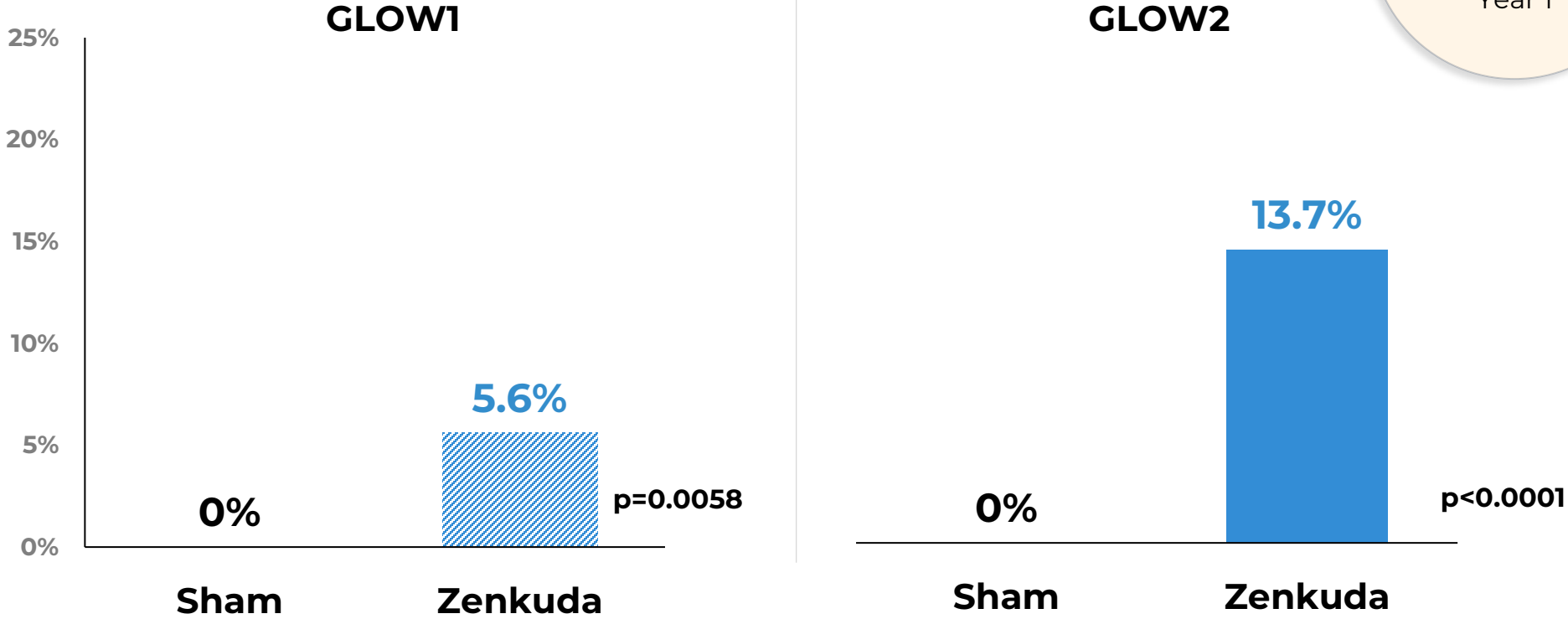
# Zenkuda in Diabetic Retinopathy: Zenkuda established superiority in $\geq 3$ -step improvement in DR Severity Score (DRSS) in GLOW1 *and* GLOW2

**Phase 3**  
GLOW1  
GLOW2

Superiority ✓

6-month Durability ✓

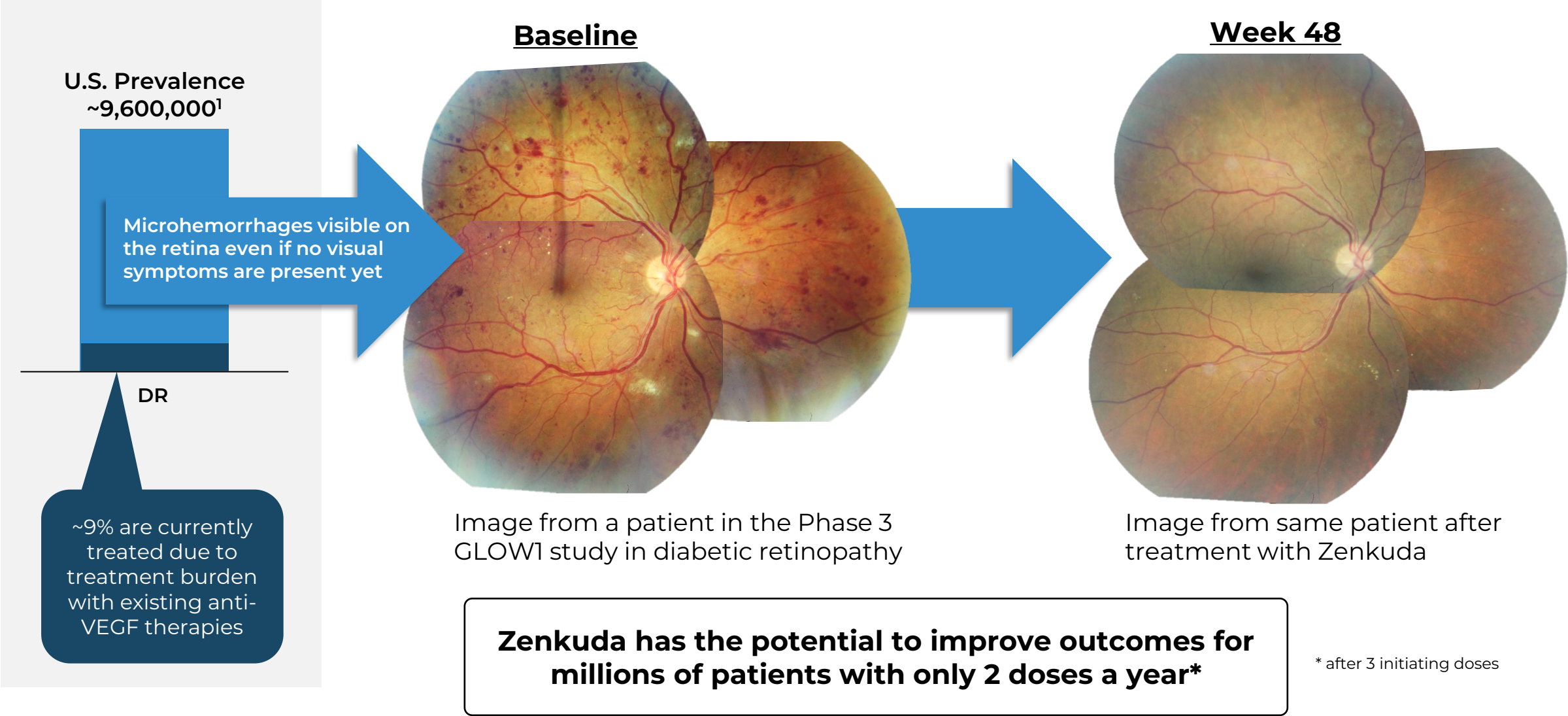
Proportion of patients with  $\geq 3$ -Step improvement in DRSS from Baseline to Week 48



100% of patients on 6-month dosing at Year 1

**GLOW1:** Sham (n=125); Zenkuda (n=128). **GLOW2:** Sham (n=125); Zenkuda (n=130); Week 48 (LOCF) represents the last available observation while on randomized treatment, within the Week 48 visit window. Weighted percentages are based on weighted average of observed estimates across strata using CMH weights. p-values are based on the difference in response rates

# The GLOW studies show that Zenkuda opens the door to earlier treatment with only 2 doses a year – a transformative potential for millions of patients



# Zenkuda and KSI-501 in wAMD: The ongoing Phase 3 DAYBREAK study is designed to evaluate immediacy, real-world durability and efficacy

**Phase 3  
DAYBREAK**

**Noninferiority**

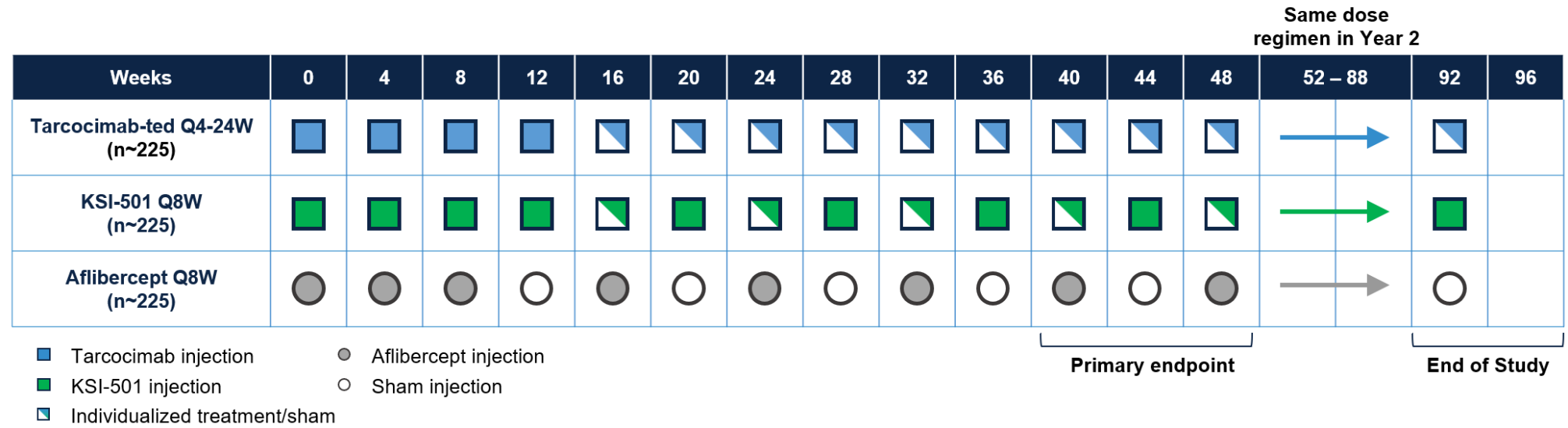
**Zenkuda  
6-month  
durability**

**KSI-501  
efficacy  
exploration**

**Topline data  
3Q 2026**

**Zenkuda objective:** Assess **6-month durability** potential in wAMD

**KSI-501 objective:** Explore **efficacy potential** of bispecific IL-6 and VEGF inhibition in wAMD



## AI-based tool precisely measures fluid in the eye to optimize treatment per patient

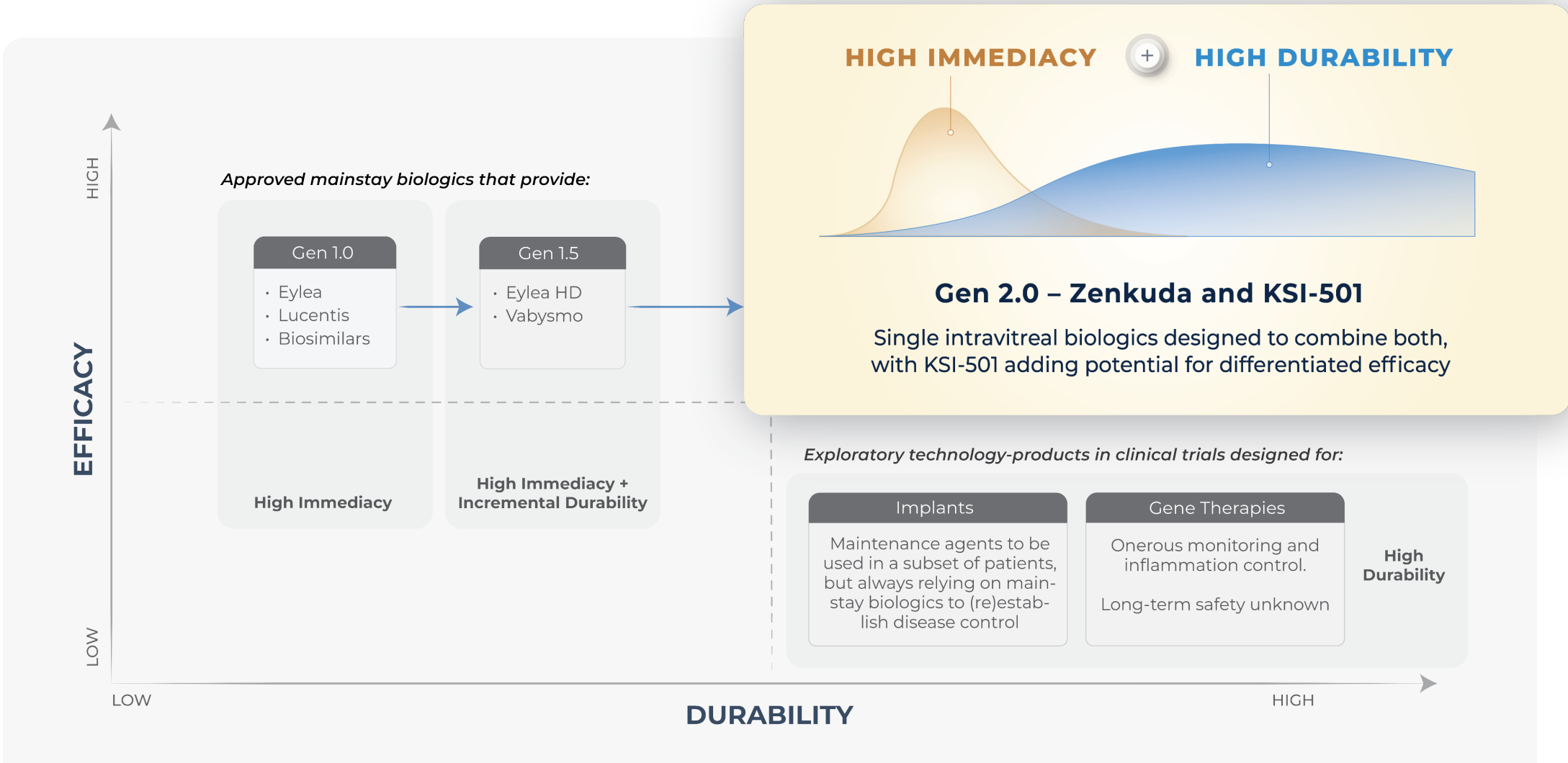
- High-need patients: treats until dry, enables monthly dosing and detects disease reactivation earlier
- Long-durability patients: allows patients without active disease to safely go to every 6-month dosing

# What are the potential implications and upsides for Zenkuda and KSI-501 in DAYBREAK, if successful?

|   | ZENKUDA | KSI-501                  |
|---|---------|--------------------------|
| <b>Strong and immediate</b> disease control (closing the 'immediacy' gap)                   | ✓       | ✓                        |
| <b>Better vision</b> gains vs anti-VEGF monotherapy (aflibercept Q8W) with good OCT control |         | ✓                        |
| <b>Non-inferior vision</b> gains to aflibercept Q8W   | ✓       |                          |
| <b>Long-interval</b> dosing with flexible 1-month through 6-month label                     | ✓       | Not assessed in DAYBREAK |

# Revisiting the core unmet need: Kodiak's Gen 2.0 biologics are designed to occupy the high-immediacy, high-durability golden quadrant

Gen 2.0 biologics designed to combine:

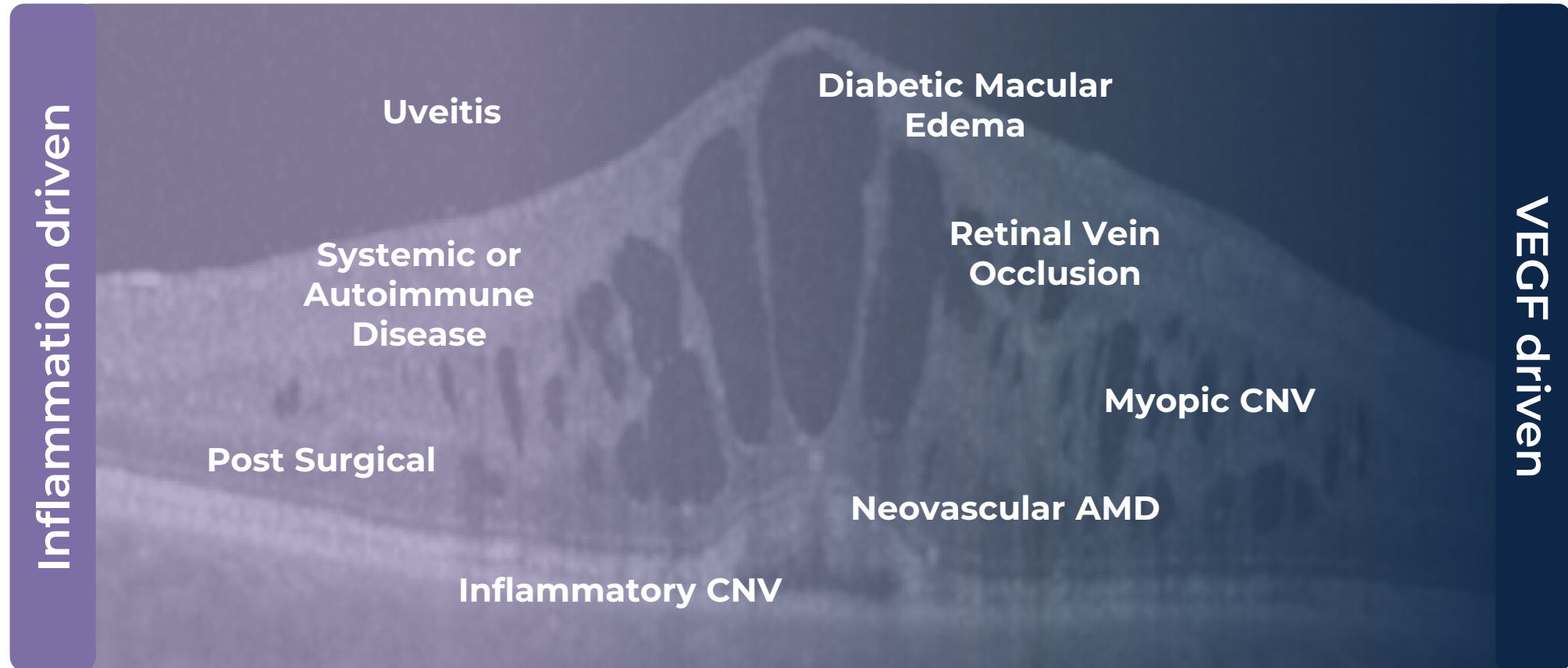


KSI-101

# Macular Edema Secondary to Inflammation

# Macular edema, the common clinical presentation of a wide spectrum of diseases, can be caused by inflammation and/or by VEGF over-expression

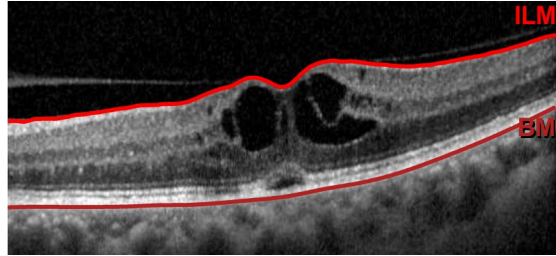
*Macular Edema Spectrum of Diseases*



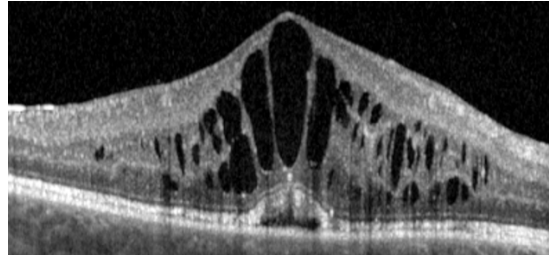
**Macular edema secondary to inflammation**

**Retinal vascular and degenerative diseases**

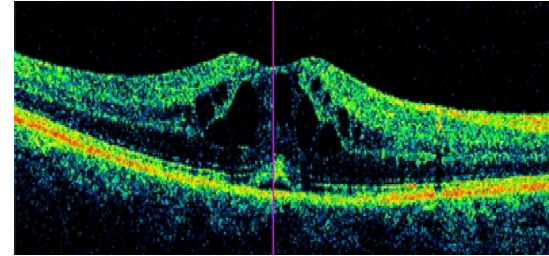
# Macular edema and visual impairment are shared clinical features irrespective of etiology or location of inflammation



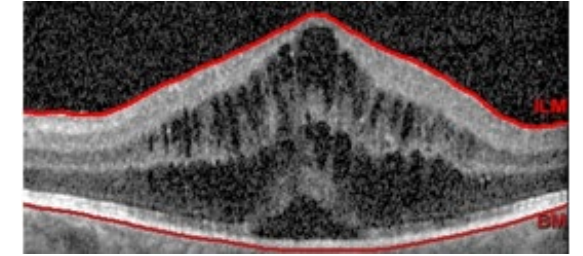
Anterior



Intermediate



Posterior



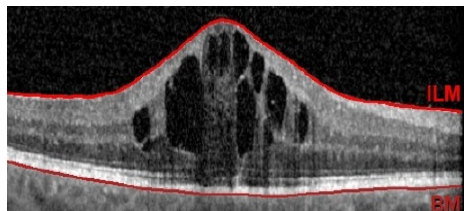
Panuveitis

Location of Inflammation

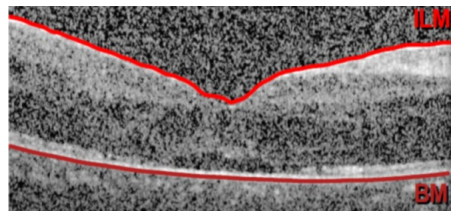
Macular edema is a shared clinical feature irrespective of the anatomical location of inflammation or specific etiology

Specific Etiology

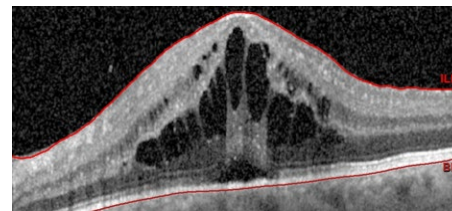
Idiopathic



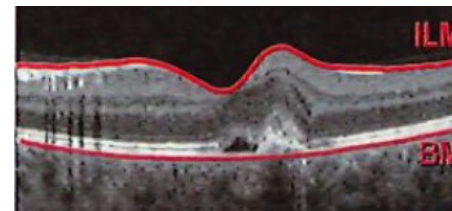
Juvenile Idiopathic Arthritis



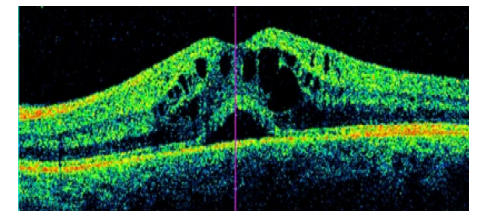
Focal Chorioretinal inflammation



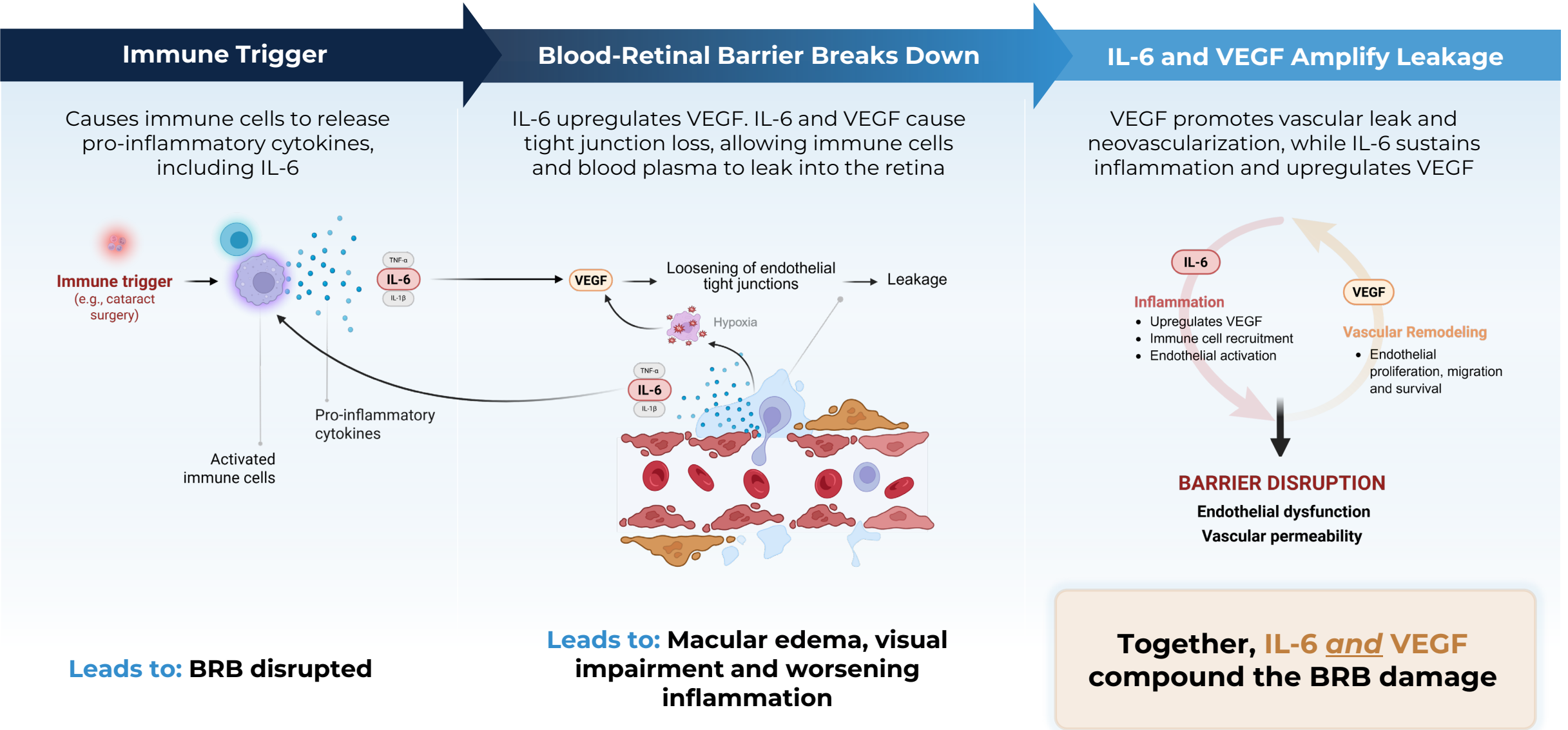
Punctate Inner Choroidopathy



Post-Operative Macular Edema (refractory)

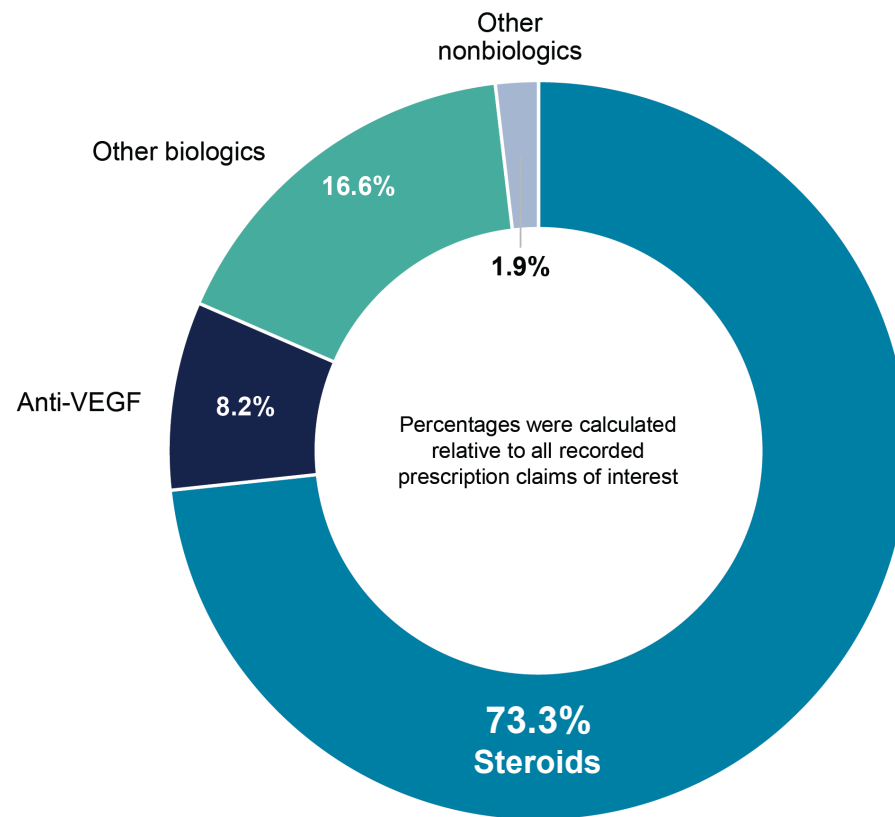


# MESI is caused by immune dysregulation, leading to blood-retinal barrier breakdown and release of inflammatory mediators



# Corticosteroids are used most often for MESI, but carry significant safety risks and efficacy can be limited

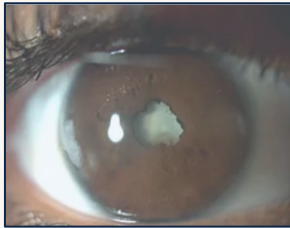
**Most frequently prescribed medications in patients with macular edema due to noninfectious uveitis, across any line of therapy<sup>1</sup>**



- Steroids were the most common medication class and remain the standard of care<sup>1</sup>
- XIPERE® (suprachoroidal triamcinolone acetonide) is the only approved local ocular treatment in the U.S.
- **Approximately 30-40% of patients do not fully respond to intraocular steroids<sup>2,3</sup>**
- Intraocular steroids are avoided in the pediatric population and **used with caution in adults due to high risk of permanent glaucoma damage and cataract formation**

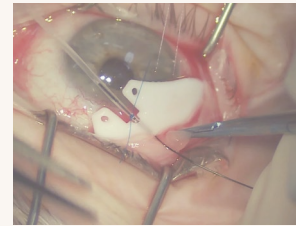
# Adverse effects from current MESI treatments can lead to complex, repeated surgeries and irreversible vision loss

## Cataract repair is complex in MESI and can be contraindicated, leading to permanent vision loss



- Even with good inflammation control, surgeries can trigger intractable inflammation, often leaving the eyes with no intraocular lens implant and/or suboptimal results (synechiae/scarring)

## Visual damage from glaucoma can be irreversible and can lead to legal blindness



- Concerns about permanent IOP elevation limit steroid use and dose
- Supplemental topical drops to control elevated IOP are often insufficient, requiring invasive glaucoma surgeries
- Once the optic nerve is damaged due to glaucoma (high eye pressure), the visual loss can be irreversible

**RETISERT® Label**  
(fluocinolone acetonide  
intraocular implant)

- **60% of patients will require chronic IOP lowering medications to control IOP**
- **37% will require filtering procedures to control IOP**
- Within an average post-implantation period of approximately 2 years, **nearly all phakic eyes are expected to develop cataracts and require cataract surgery**

*Surgeries in MESI patients are complicated and require complete control of inflammation before, during and after each procedure*

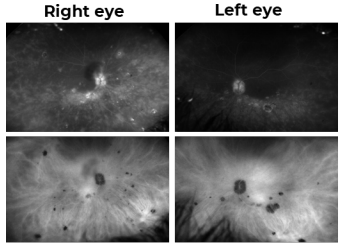
# Patient journey case: steroids induced glaucoma with recurrent MESI over the course of approximately 2 years

1 

Patient presented in Aug. 2023 with a 12-year history of **panuveitis of both eyes** and **multiple failed treatments**



Minimum macular edema initially



- Failed treatments**
- Weekly adalimumab
  - Methotrexate
  - Cellcept
  - Azathioprine
  - Oral steroids
  - Difluprednate eyedrops

2

Developed worsening of chorioretinal lesions and **macular edema**

**Intraocular pressure (IOP) spikes to 40s with any steroids (topical eyedrops and intravitreal)**

 REFERRED

**Surgery #1:**

A combined cataract surgery and glaucoma surgery (OMNI canaloplasty) of the right eye in Jan 2024

**IOP continue to rise despite surgery**

3

Worsening **macular edema** with taper of **difluprednate eyedrops**

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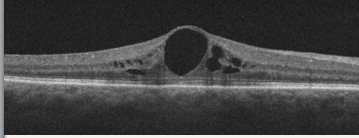
For alternate **immunomodulatory therapy (IMT)**

Attempted authorization for tocilizumab but insurance denied twice.

Unable to get authorization for infliximab either

4

Trial of bromfenac drops with initial improvement then worsening of **macular edema**



**Placed back on difluprednate drops QID with spike of IOP to 38**

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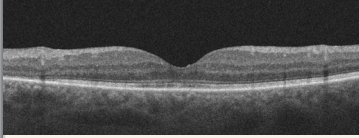
**Surgery #2:**

Glaucoma tube shunt surgery of the right eye in May 2025




**IOP now stable**

5

**IOP stable** and macular edema now resolved after **fluocinolone intravitreal injections**



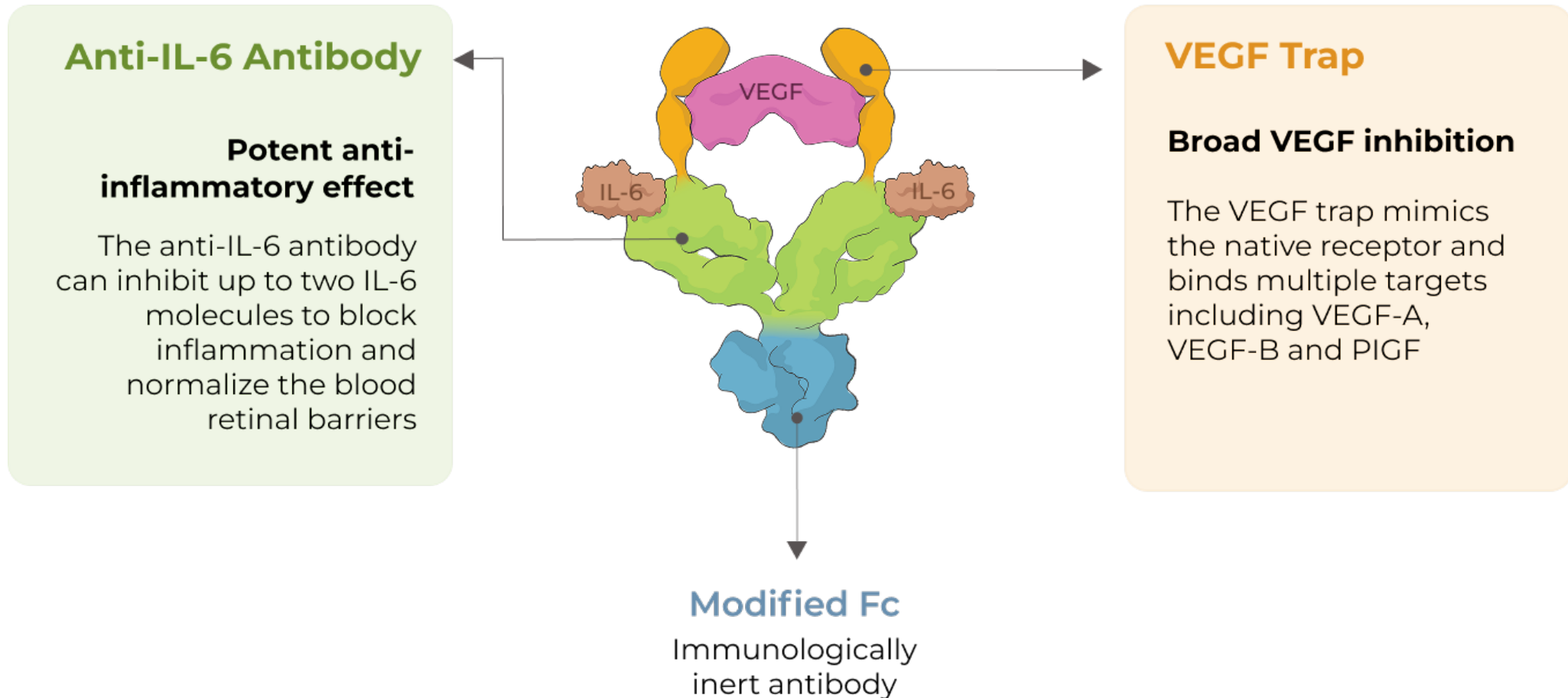
Will evaluate further need for IMT next visit

-  Patient presented to uveitis specialist
-  Glaucoma specialist
-  Rheumatologist

This representative case is based on Dr. Quan Nguyen's clinical experience, literature, and reviewed by uveitis consultants.

# KSI-101 is a first-in-class, high-strength intravitreal biologic designed to target IL-6 mediated inflammation and VEGF-mediated vascular permeability simultaneously

KSI-101: high formulation strength (100 mg/mL)



# IL-6 and VEGF each disrupt the blood-retinal barrier independently. When combined, they cause an even greater loss of barrier integrity

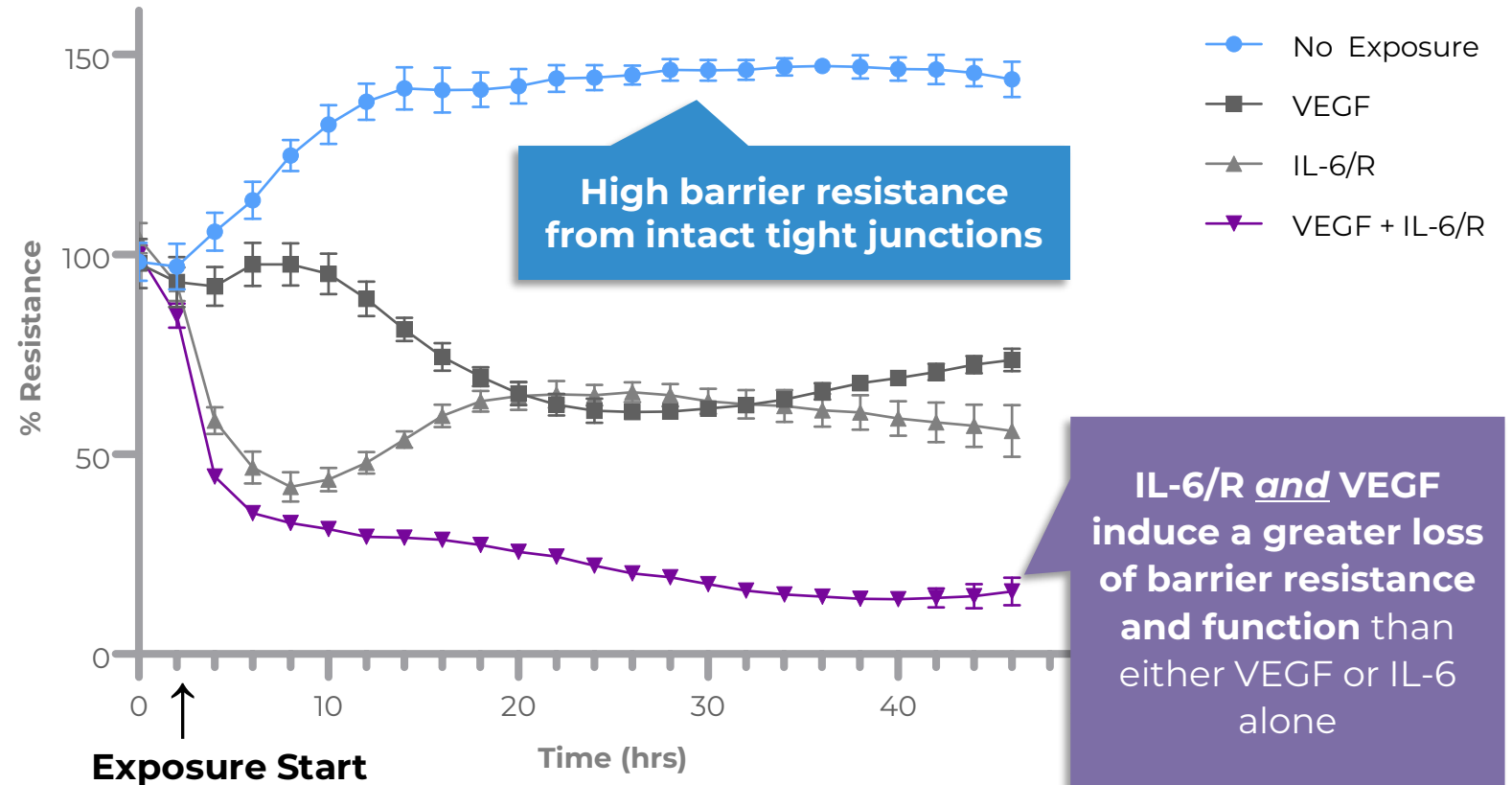
## Ocular inflammation damages tight junctions between endothelial cells

- This compromises the integrity of the blood retina barrier, which increases vascular permeability
- The integrity of the blood-retinal barrier can be measured by barrier resistance

## Exposure to both IL-6/R and VEGF additively induces greater loss in barrier function than either IL-6 or VEGF alone

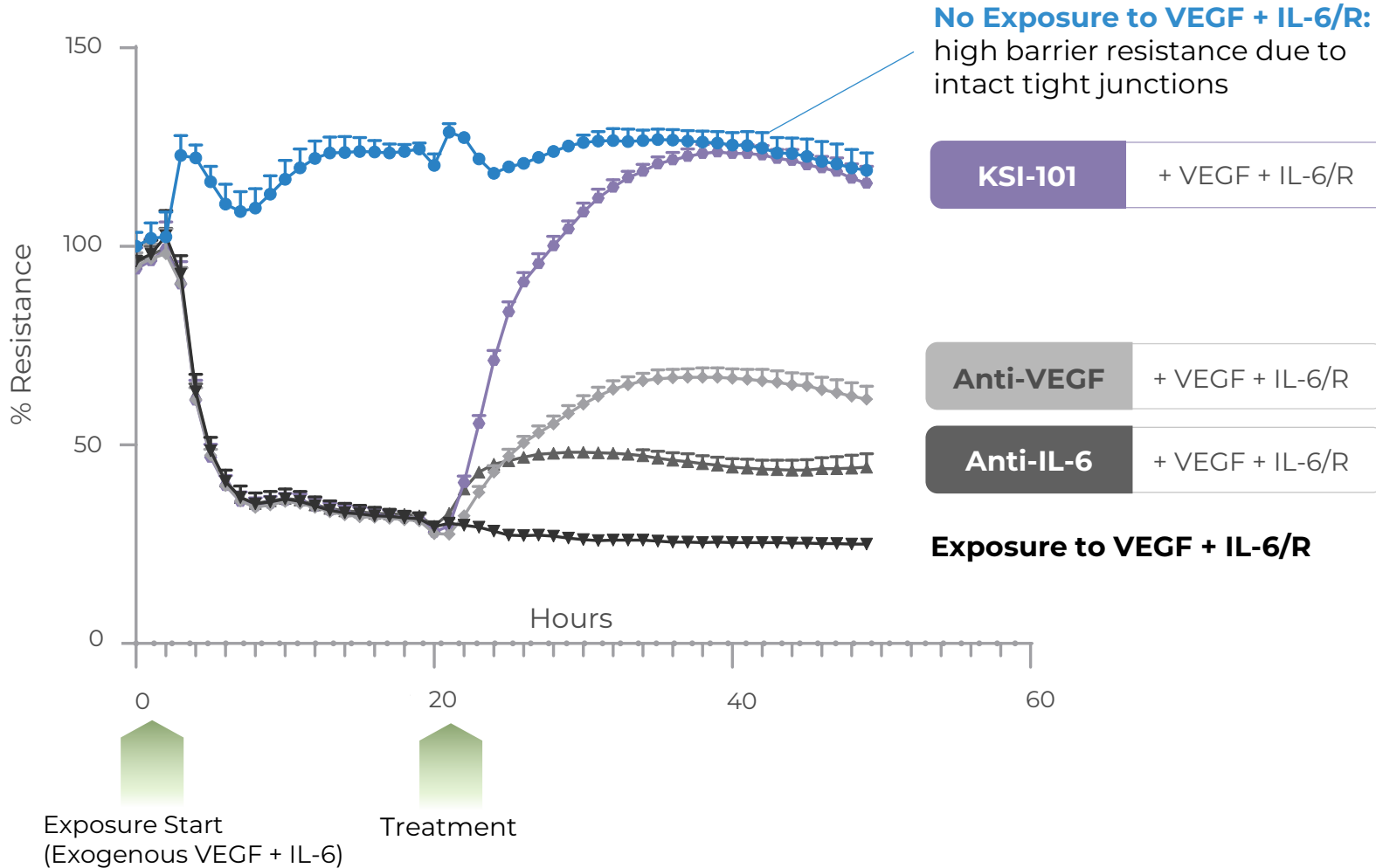
- As measured by decreased barrier resistance in human umbilical vein endothelial cells (HUVEC)

## Assessing vascular endothelial barrier integrity using electrical resistance measurements



# Bispecific KSI-101 restores barrier resistance from pre-existing insult greater than anti-IL-6 or anti-VEGF monotherapies alone

Preclinical model of endothelial cells simulating the blood-retinal barrier

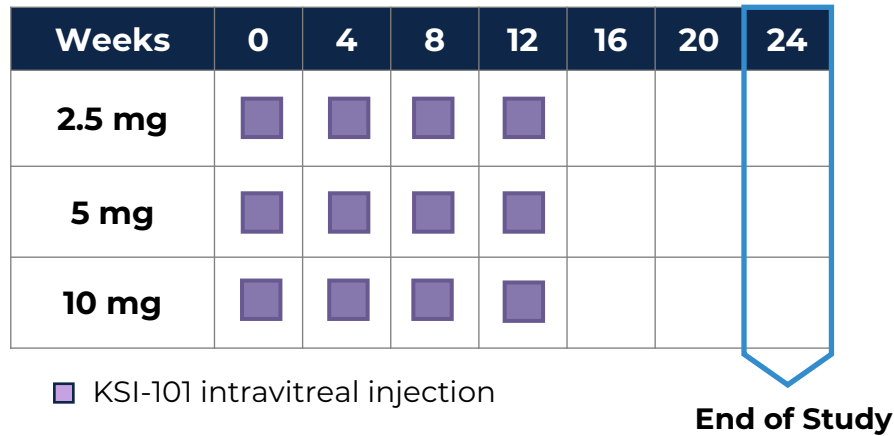


**KSI-101 restores barrier integrity to no exposure levels**

**Anti-VEGF and anti-IL-6 monotherapy only partially restore barrier function**

# KSI-101 in MESI: Multiple-dose results from APEX Phase 1b study in the U.S. and a clinical cohort of Asian patients from tertiary uveitis centers

## Study Design: Open-label Phase 1b in MESI



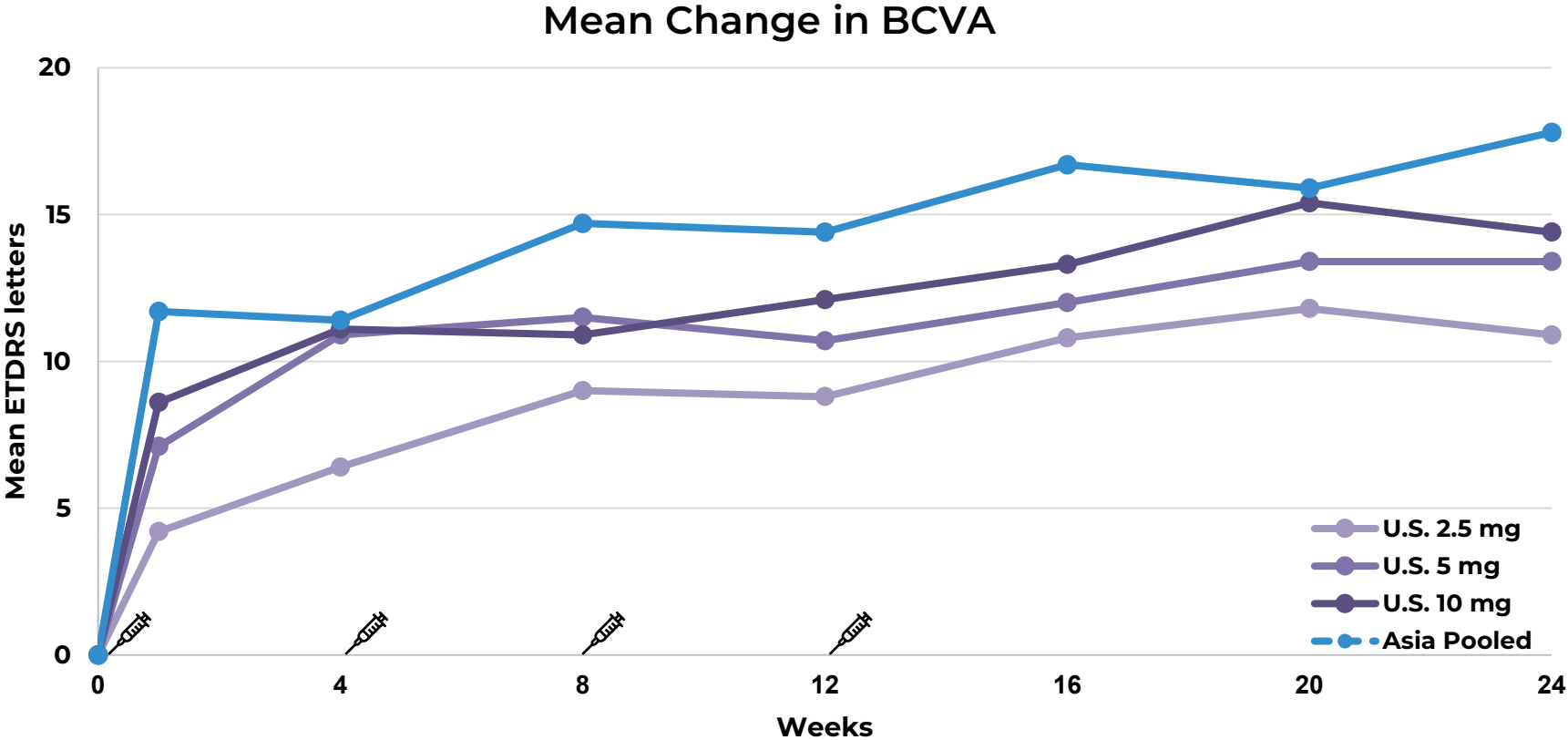
### Key inclusion criteria

- Macular edema secondary to inflammation (MESI)
- Diagnosis of active or inactive non-infectious intraocular inflammation, acute or chronic
- Active leakage as evidenced by fluorescein angiogram
- OCT CST of  $\geq 320$  microns
- BCVA score  $\leq 75$  and  $\geq 25$  (20/32 to 20/320 Snellen equivalent)

## Baseline Characteristics

|   | APEX U.S. (N=41)      |                     |                      | Asia*                 |
|---|-----------------------|---------------------|----------------------|-----------------------|
|   | KSI-101 2.5 mg (n=13) | KSI-101 5 mg (n=14) | KSI-101 10 mg (n=14) | KSI-101 pooled (N=13) |
| <b>Age, years, mean (SD)</b>  | 74.2 (11.6)           | 67.4 (8.1)          | 67.5 (18.8)          | 49.9 (22.6)           |
| <b>Female, n (%)</b>  | 8 (61.5)              | 7 (50.0)            | 8 (57.1)             | 11 (84.6)             |
| <b>Race, Asian, n (%)</b>   | 0                     | 1 (7.1%)            | 0                    | 13 (100)              |
| <b>Race, White, n (%)</b>   | 11 (84.6)             | 11 (78.6)           | 14 (100)             | 0                     |
| <b>MESI disease duration, months, mean (SD)</b>                     | 12.2 (21.0)           | 1.7 (1.2)           | 15.8 (37.2)          | 2.3 (1.9)             |
| <b>Inflammation anatomical location, n (%)</b>                      |                       |                     |                      |                       |
| Anterior  | 0                     | 2 (14.3)            | 0                    | 1 (7.7)               |
| Intermediate  | 1 (7.7)               | 0                   | 2 (14.3)             | 2 (15.4)              |
| Posterior   | 10 (76.9)             | 6 (42.9)            | 10 (71.4)            | 6 (46.2)              |
| Panuveitis  | 2 (15.4)              | 6 (42.9)            | 2 (14.3)             | 5 (38.5)              |
| <b>Patients with active inflammation, n (%)</b>                     | 3 (23.1)              | 11 (78.6)           | 5 (35.7)             | 12 (92.3)             |
| <b>Unilateral MESI, n (%)</b>                                       | 9 (69.2)              | 6 (42.9)            | 5 (35.7)             | 4 (30.8)              |
| <b>BCVA, ETDRS Letters, mean (SD)</b>                               | 62.7 (7.4)            | 65.6 (7.9)          | 62.1 (8.4)           | 58.5 (14.1)           |
| Snellen equivalent  | ~20/50                | ~20/50              | ~20/63               | ~20/63                |
| <b>OCT CST, <math>\mu\text{m}</math>, mean (SD) (Site reported)</b> | 461.7 (137.7)         | 487.0 (124.1)       | 528.6 (157.3)        | 429.8 (76.3)          |
| <b>Lens Status, pseudophakic, n (%)</b>                             | 9 (69.2)              | 13 (92.9)           | 11 (78.6)            | 7 (53.8)              |

# Meaningful vision gains of >10 letters were observed after a single injection with continued improvement through 24 weeks



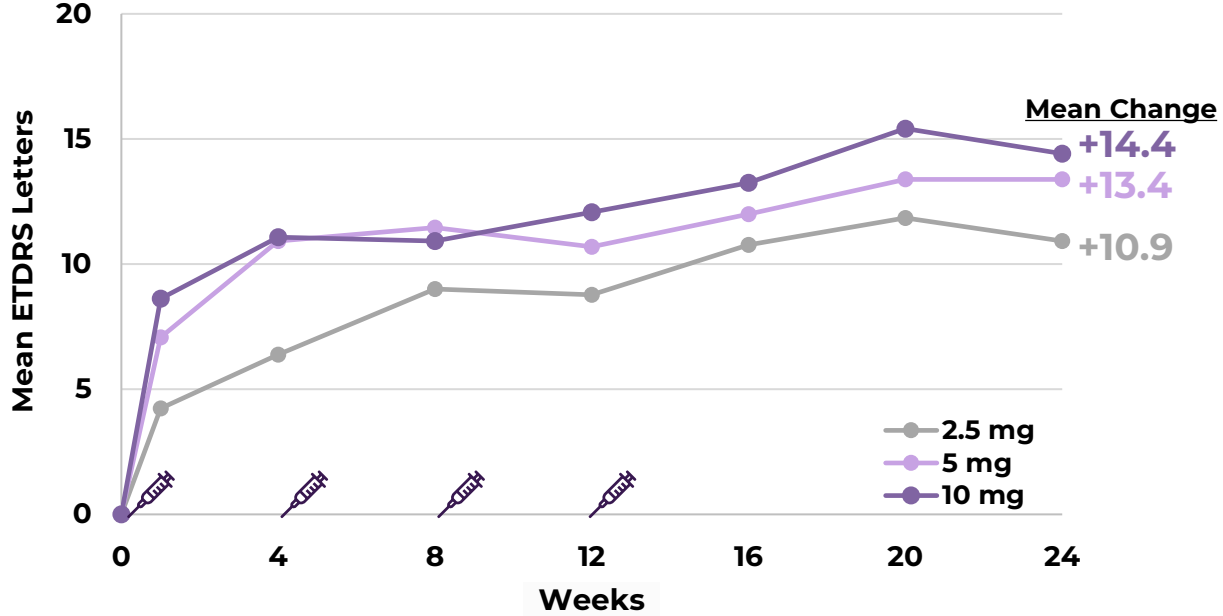
|      |        | 0  | 4  | 8  | 12 | 16 | 20 | 24 |
|------|--------|----|----|----|----|----|----|----|
| U.S. | 2.5 mg | 13 | 13 | 13 | 13 | 13 | 13 | 12 |
|      | 5 mg   | 13 | 13 | 13 | 13 | 13 | 13 | 13 |
|      | 10 mg  | 13 | 13 | 13 | 13 | 12 | 12 | 12 |
| Asia | Pooled | 12 | 12 | 12 | 12 | 11 | 11 | 11 |

Sample Size

Final results of the APEX study in MESI. Includes patients in the per protocol set that completed the Week 4 visit and met all the eligibility criteria. US: Excludes one patient in the 5 mg dose that discontinued treatment before Week 4, and one patient in the 10 mg dose with a significant epiretinal membrane at baseline (exclusion criterion). One patient in the 10 mg dose level discontinued after Week 12 due to recurrent uveitis flare-up. Asian cohort: excludes one patient with a significant epiretinal membrane at baseline (exclusion criterion). One patient discontinued after Week 12 due to a spinal fracture.

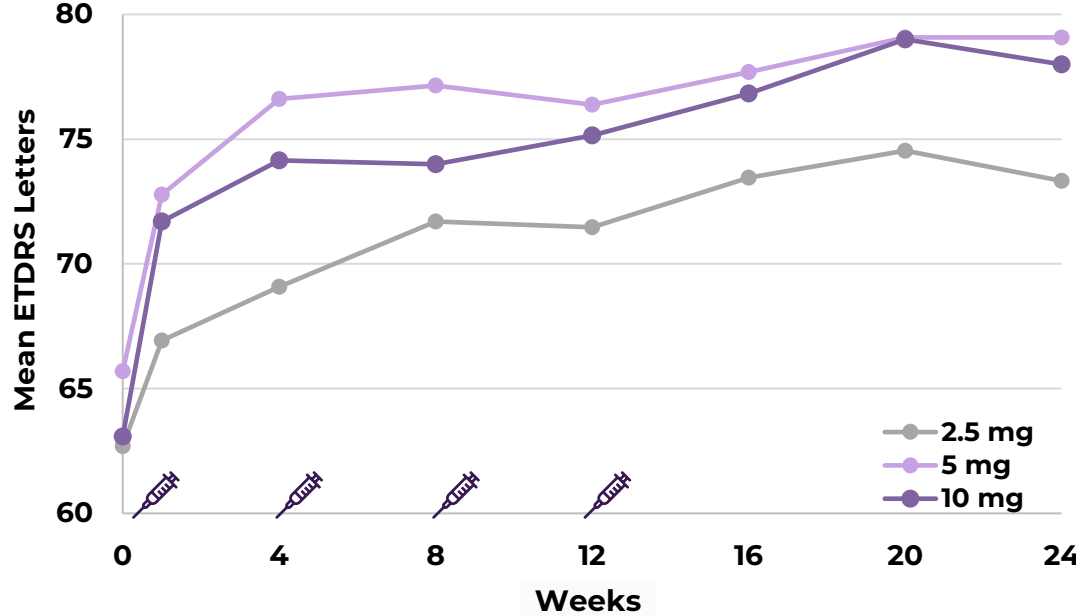
# In APEX U.S., the top two dose levels achieve meaningful vision gains of >10 letters by Week 4 and continue to improve over time, achieving a 20/25 Snellen visual acuity by Week 20

Mean Change in BCVA over time



| Dose Level | 0  | 4  | 8  | 12 | 16 | 20 | 24 |
|------------|----|----|----|----|----|----|----|
| 2.5 mg     | 13 | 13 | 13 | 13 | 13 | 13 | 12 |
| 5 mg       | 13 | 13 | 13 | 13 | 13 | 13 | 13 |
| 10 mg      | 13 | 13 | 13 | 13 | 12 | 12 | 12 |

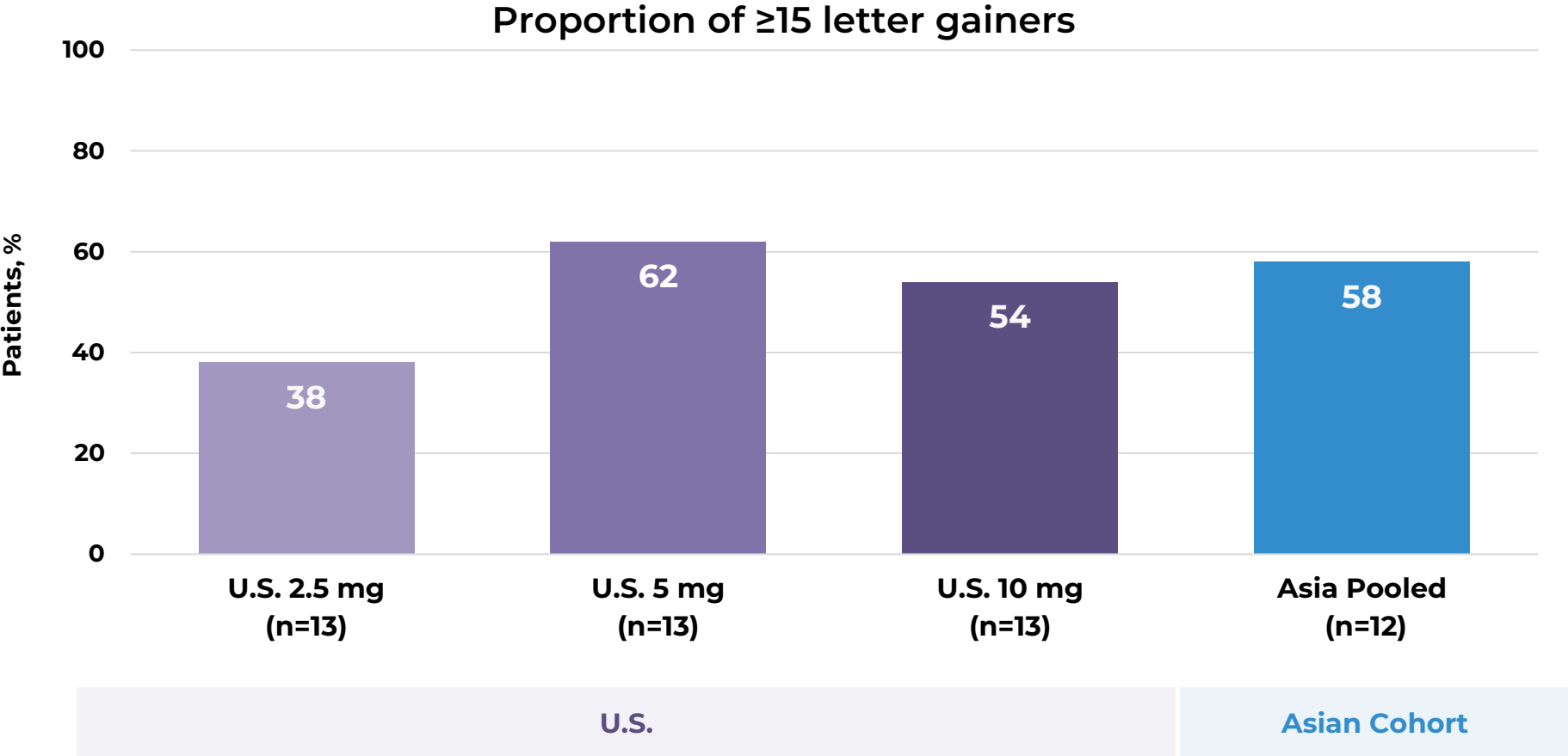
Observed BCVA over time



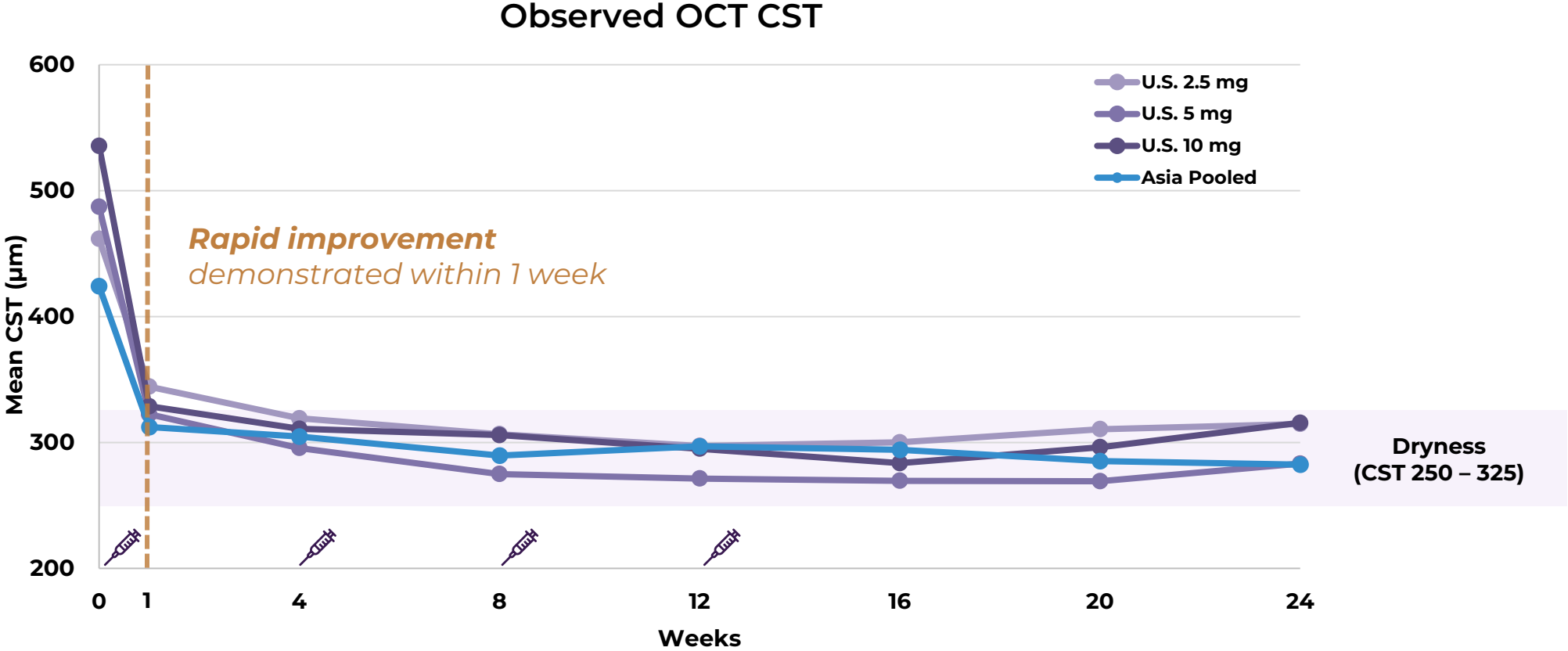
| Dose Level | 0  | 4  | 8  | 12 | 16 | 20 | 24 |
|------------|----|----|----|----|----|----|----|
| 2.5 mg     | 13 | 13 | 13 | 13 | 13 | 13 | 12 |
| 5 mg       | 13 | 13 | 13 | 13 | 13 | 13 | 13 |
| 10 mg      | 13 | 13 | 13 | 13 | 12 | 12 | 12 |

Final results of the APEX study in MES1. Includes patients in the per protocol set that completed the Week 4 visit and met all the eligibility criteria. Excludes one patient in the 5 mg dose that discontinued treatment before Week 4, and one patient in the 10 mg dose with a significant epiretinal membrane at baseline (exclusion criterion). One patient in the 10 mg dose level discontinued after Week 12 due to recurrent uveitis flare-up

# More than half of patients achieved a $\geq 15$ letter gain, with additional benefit observed in the top dose levels in the U.S.



# KSI-101 consistently achieved dryness (CST 250-325 μm) after a single injection, with sustained dryness observed during follow-up

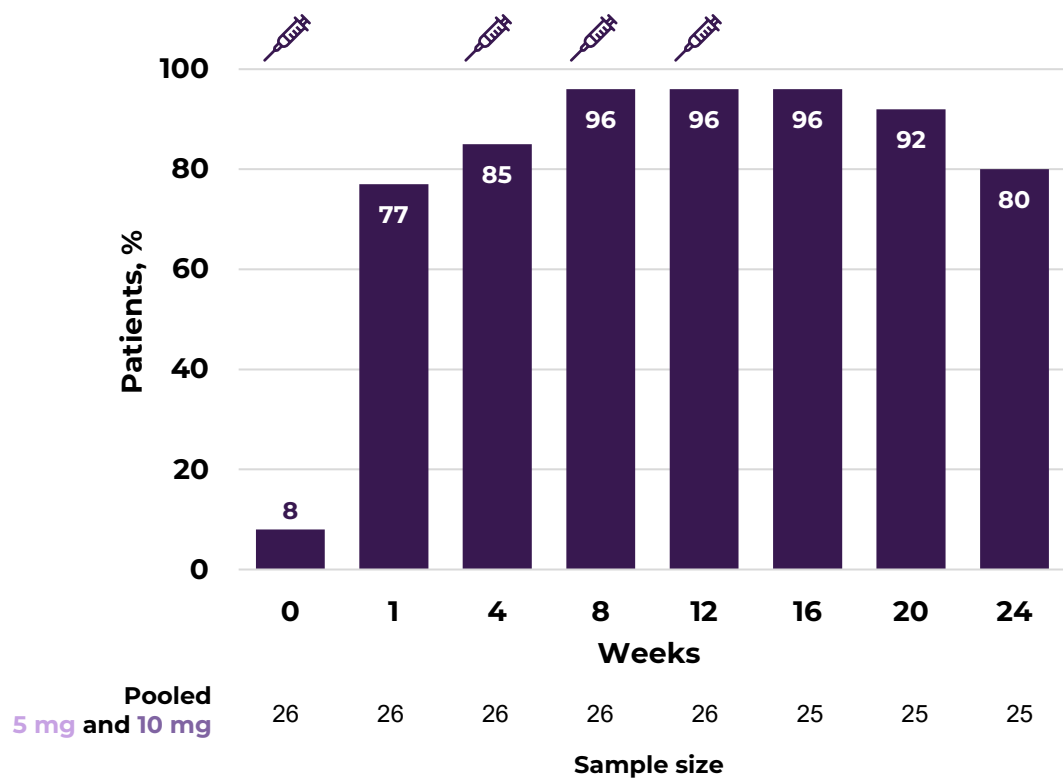


|      |        | 0  | 1  | 4  | 8  | 12 | 16 | 20 | 24 |
|------|--------|----|----|----|----|----|----|----|----|
| U.S. | 2.5 mg | 13 | 12 | 13 | 13 | 13 | 13 | 13 | 12 |
|      | 5 mg   | 13 | 13 | 13 | 13 | 13 | 13 | 13 | 13 |
|      | 10 mg  | 13 | 13 | 13 | 13 | 13 | 12 | 12 | 12 |
| Asia | Pooled | 12 | 12 | 12 | 12 | 12 | 11 | 11 | 11 |

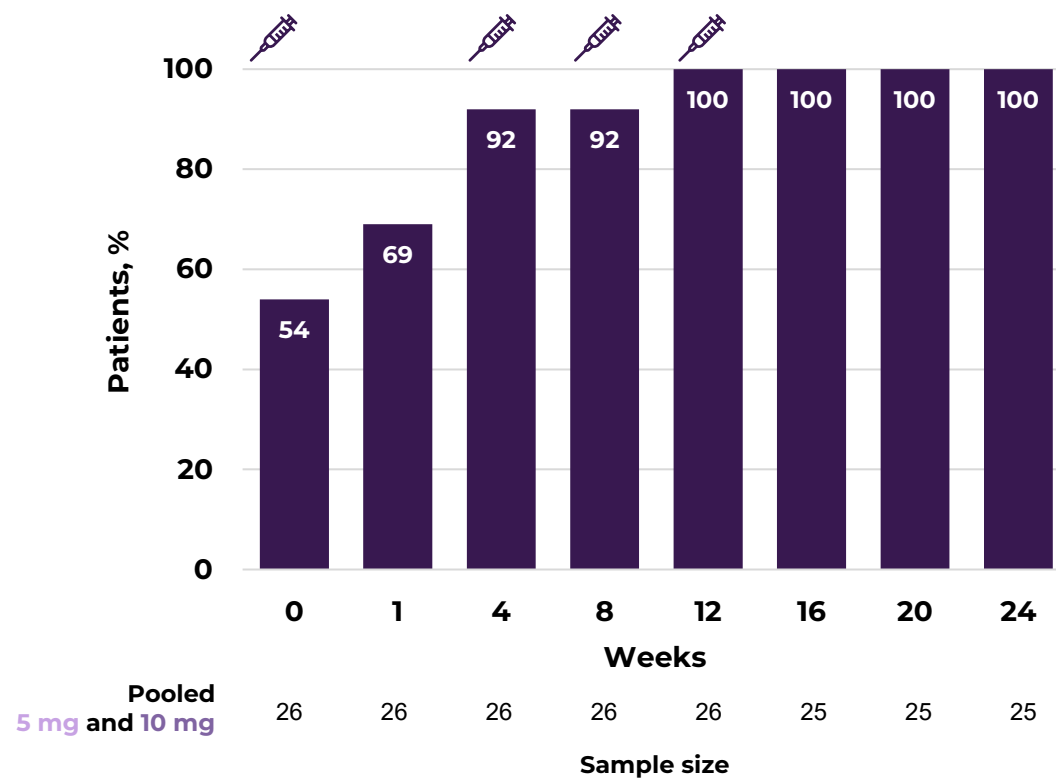
**Sample Size**

# In APEX U.S., $\geq 90\%$ of patients in the top two dose levels achieved absence of both IRF and SRF. A recurrence in IRF was observed in some patients 8 to 12 weeks after the last study treatment

Proportion of patients in the 5 and 10 mg (pooled) dose level achieving absence of **IRF**



Proportion of patients in the 5 and 10 mg (pooled) dose level achieving absence of **SRF**



IRF: intraretinal fluid; SRF: subretinal fluid

Final results of the APEX study in MESI. Includes patients in the per protocol set that completed the Week 4 visit and met all the eligibility criteria. Excludes one patient in the 5 mg dose that discontinued treatment before Week 4, and one patient in the 10 mg dose with a significant epiretinal membrane at baseline (exclusion criterion). One patient in the 10 mg dose level discontinued after Week 12 due to recurrent uveitis flare-up.

# KSI-101 has been well-tolerated

|   | KSI-101 2.5 mg<br>(n=13) | KSI-101 5 mg<br>(n=14) | KSI-101 10 mg<br>(n=14) | All KSI-101<br>(N=41) | Asia KSI-101<br>pooled<br>(N=13) |
|---|--------------------------|------------------------|-------------------------|-----------------------|----------------------------------|
| <b>Summary of AEs in the Study eye, n (%)</b>         |                          |                        |                         |                       |                                  |
| Subjects with ≥1 AEs                                  | 2 (15.4)                 | 3 (21.4)               | 2 (14.3)                | 7 (17.1)              | 3 (23.1)                         |
| Treatment-related AEs                                 | 1 (7.7) <sup>a</sup>     | 1 (7.1) <sup>b</sup>   | 0                       | 2 (4.9)               | 0                                |
| Serious AEs   | 0                        | 0                      | 0                       | 0                     | 0                                |
| Treatment-related serious AEs                         | 0                        | 0                      | 0                       | 0                     | 0                                |
| Severe AEs  | 0                        | 0                      | 0                       | 0                     | 0                                |
| AEs leading to study discontinuation                  | 0                        | 1 (7.1) <sup>b</sup>   | 0                       | 1 (2.4)               | 0                                |
| <b>Selected AEs in the Study Eye, n (%)</b>           |                          |                        |                         |                       |                                  |
| Intraocular inflammation (recurrent uveitis flare-up) | 1 (7.7) <sup>a</sup>     | 1 (7.1) <sup>b</sup>   | 0                       | 2 (4.9)               | 0                                |
| Occlusive retinal vasculitis                          | 0                        | 0                      | 0                       | 0                     | 0                                |
| Cataract  | 0                        | 0                      | 0                       | 0                     | 0                                |
| Elevated IOP  | 0                        | 0                      | 0                       | 0                     | 0                                |
| Eye pain  | 1 (7.7) <sup>a</sup>     | 0                      | 0                       | 1 (2.4)               | 0                                |
| Vitreous hemorrhage                                   | 1 (7.7) <sup>a</sup>     | 0                      | 0                       | 1 (2.4)               | 0                                |

Final results from the APEX Study in MESI.

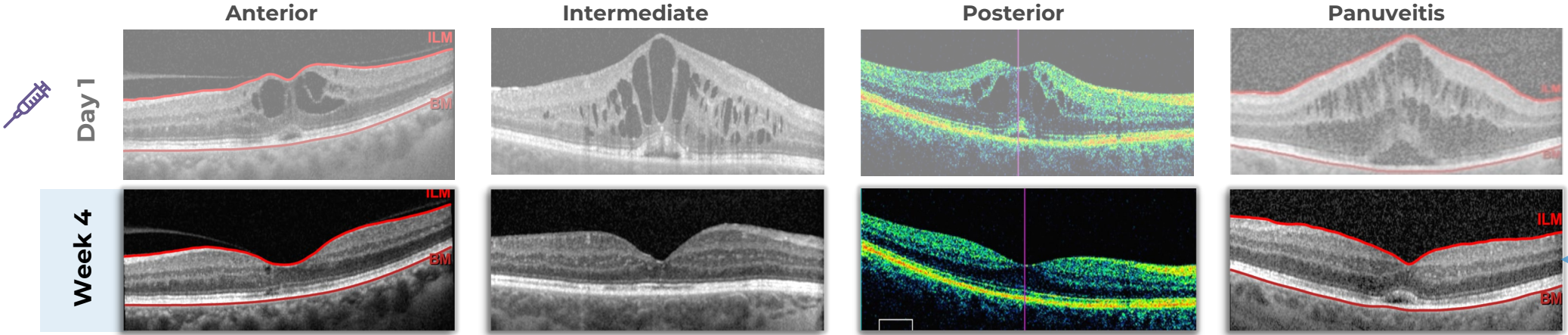
AE, Adverse event; IOP, intraocular pressure. Events are investigator reported. Adverse events are treatment-emergent events with start date ≥first study drug date and ≤last study drug date + 28 days.

<sup>a</sup> Same patient. Vitreous hemorrhage secondary to aqueous humor sampling at the Day 1 visit (pre-dose). The patient had 3+ AC cells and flare and 2+ vitreous haze **prior** to the Day 1 KSI-101 dose. The patient safely received all 4 doses of KSI-101 and is +26 letters in BCVA at their last visit and no intraocular inflammation.

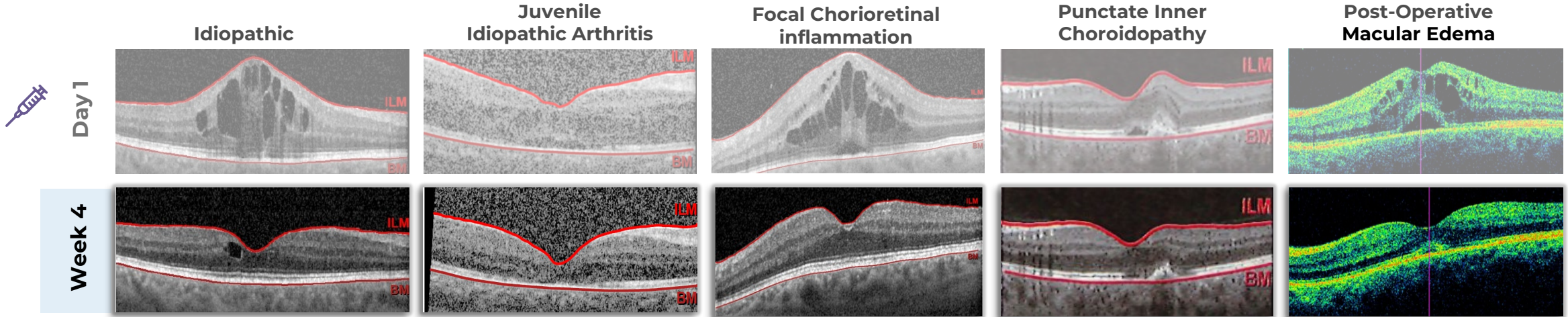
<sup>b</sup> Same patient. Uveitis flare-up consistent with underlying disease.

# Single-dose KSI-101 demonstrates rapid, meaningful responses in MESI, independent of inflammation location or macular edema etiology

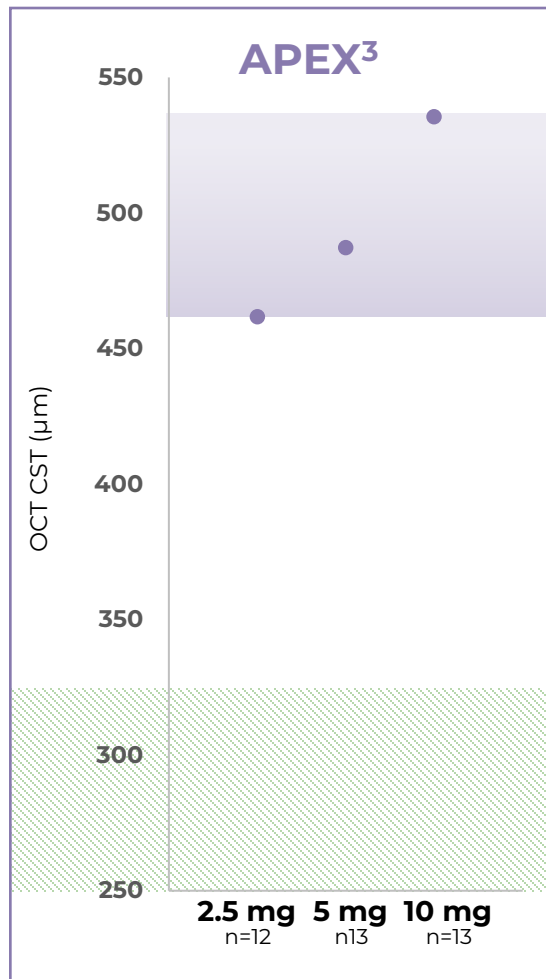
## Location of Inflammation



## Specific Macular Edema Etiology

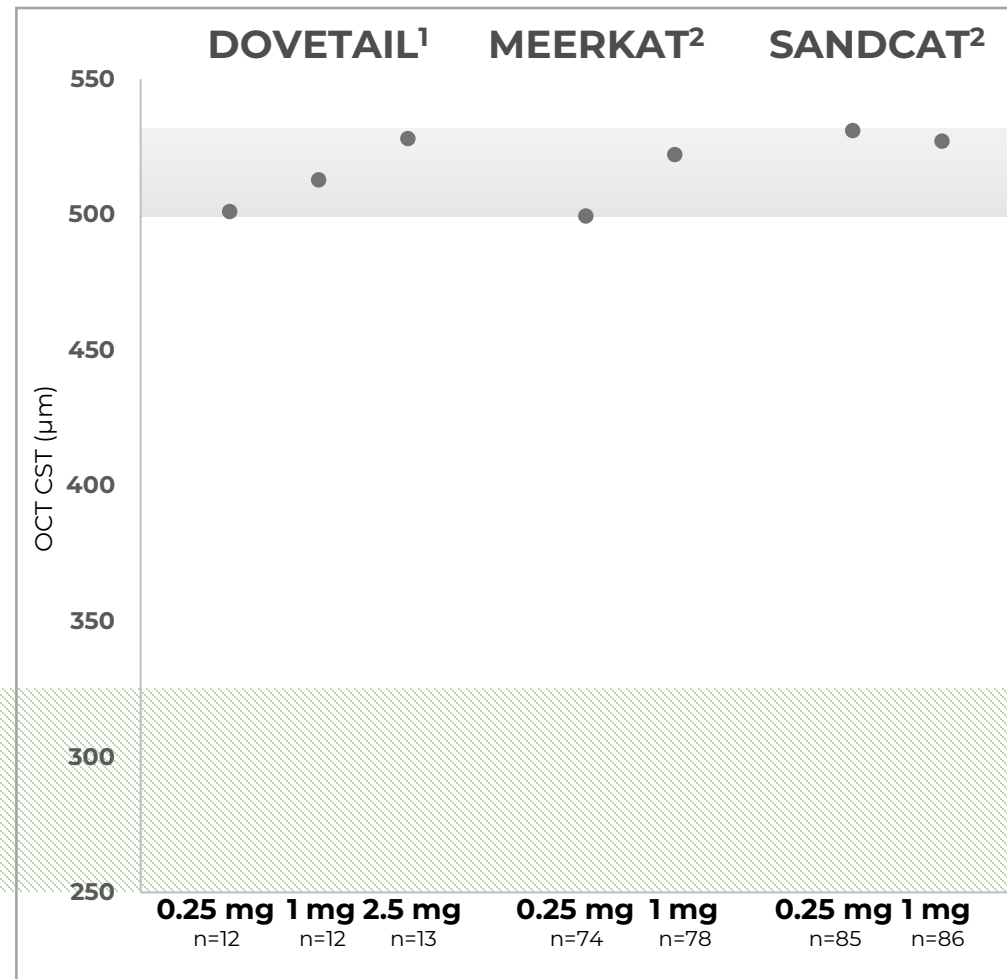


## Mean Change in OCT CST and Absolute CST



Day 1 

 Day 1



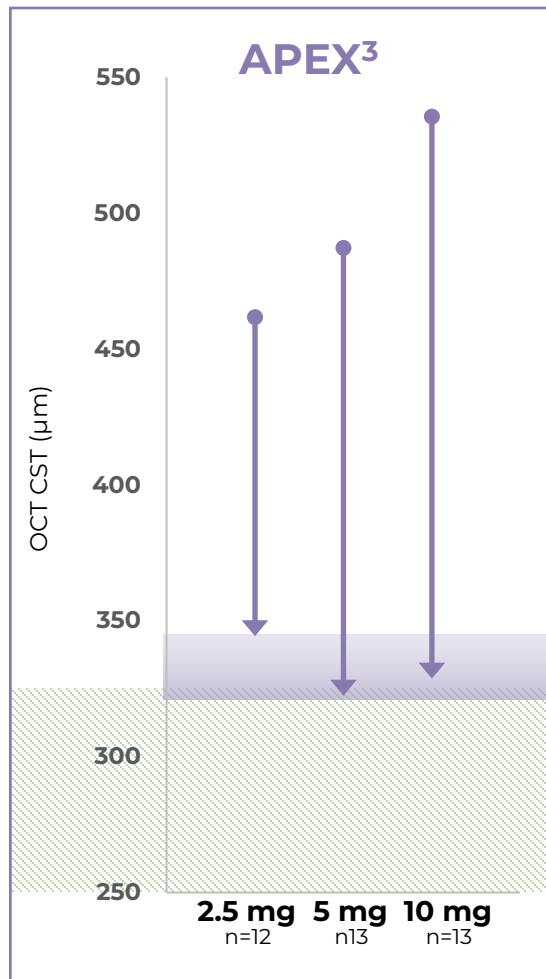
**Dryness  
(CST 250 – 325)**

**Anti-IL-6, VEGF trap  
KSI-101**

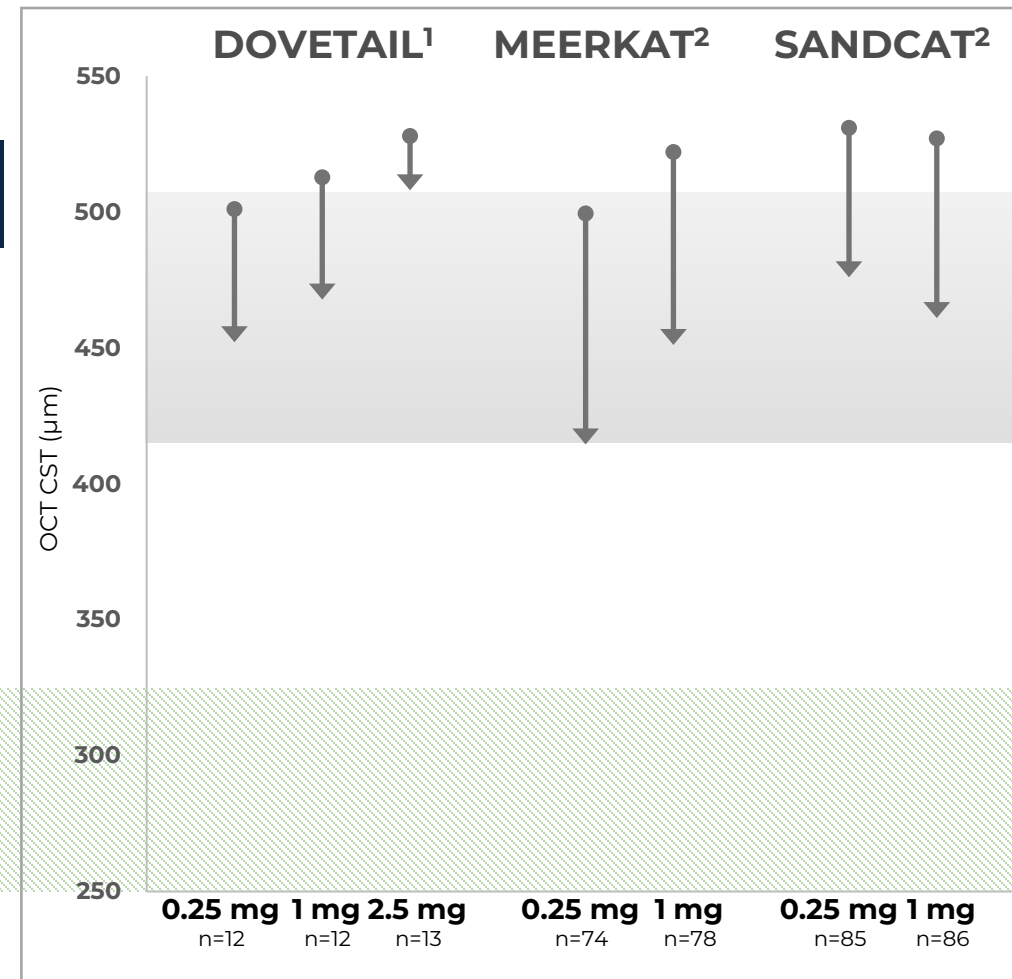
**Anti-IL-6  
Vamikibart**

**For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.**

## Mean Change in OCT CST and Absolute CST



Anti-IL-6, VEGF trap  
KSI-101

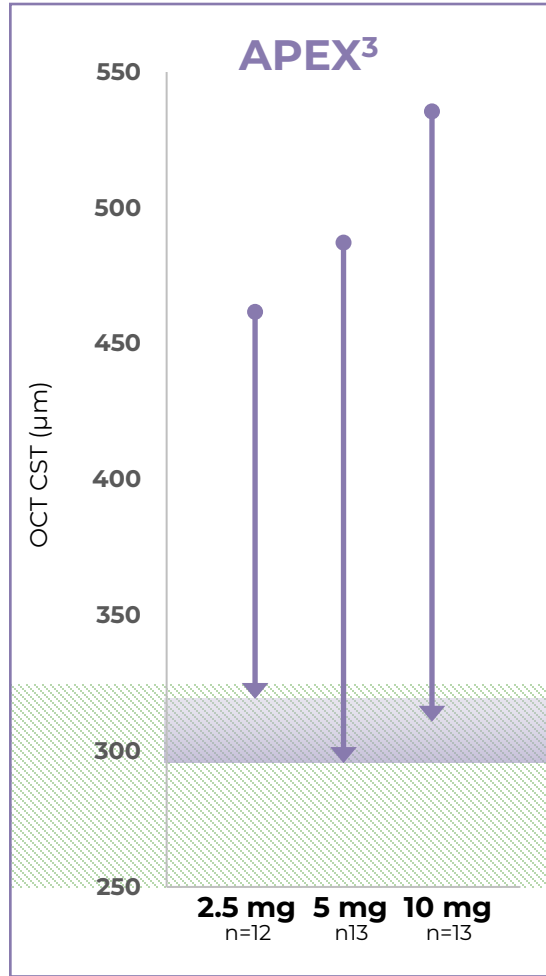


Anti-IL-6  
Vamikibart

**Rapid onset of action observed with KSI-101**

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## Mean Change in OCT CST and Absolute CST

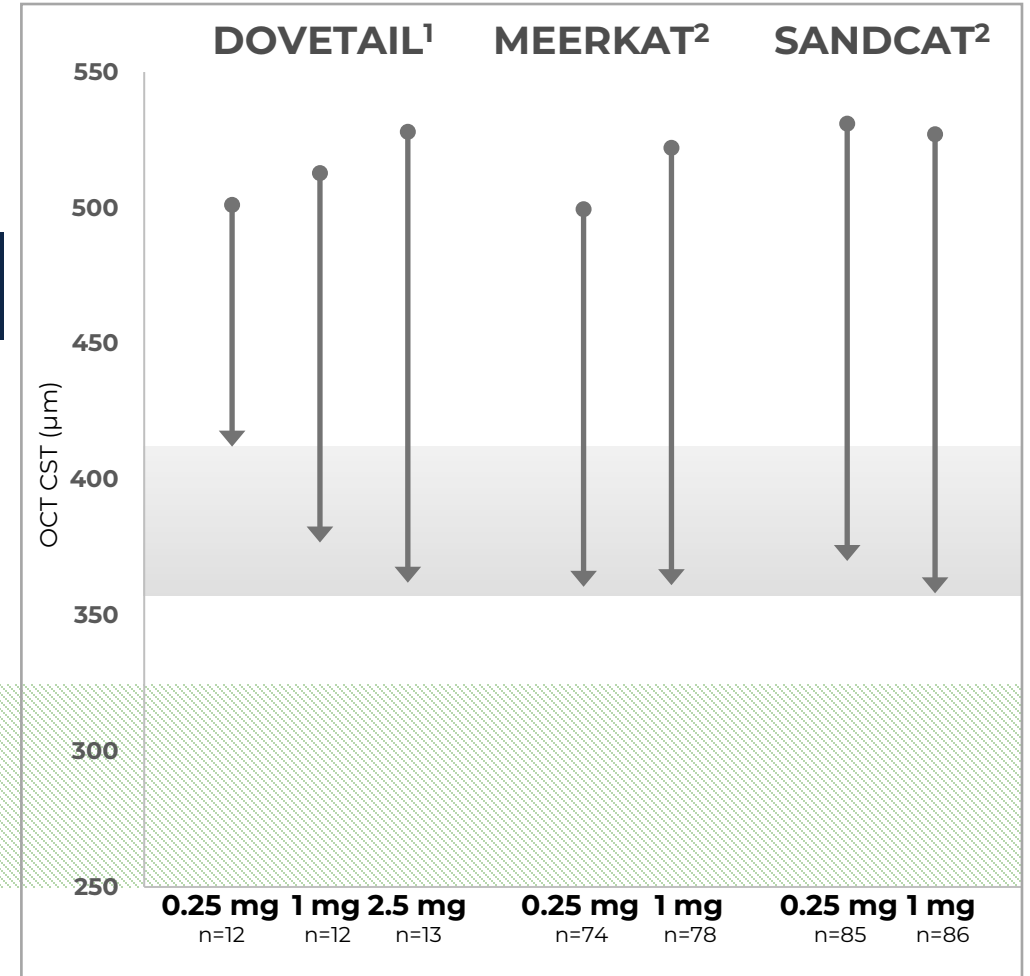


Anti-IL-6, VEGF trap  
KSI-101



Dryness  
(CST 250 – 325)

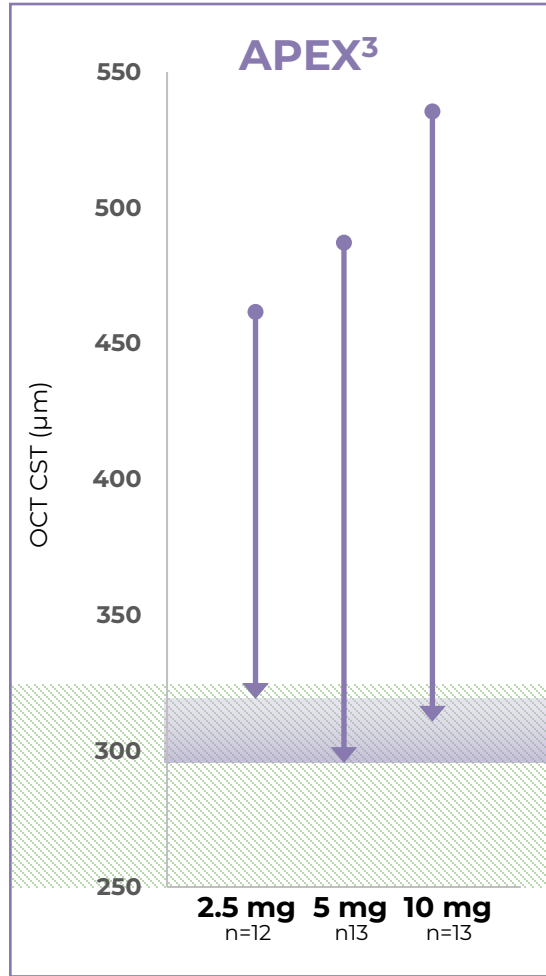
Dryness levels observed with  
a single dose of KSI-101



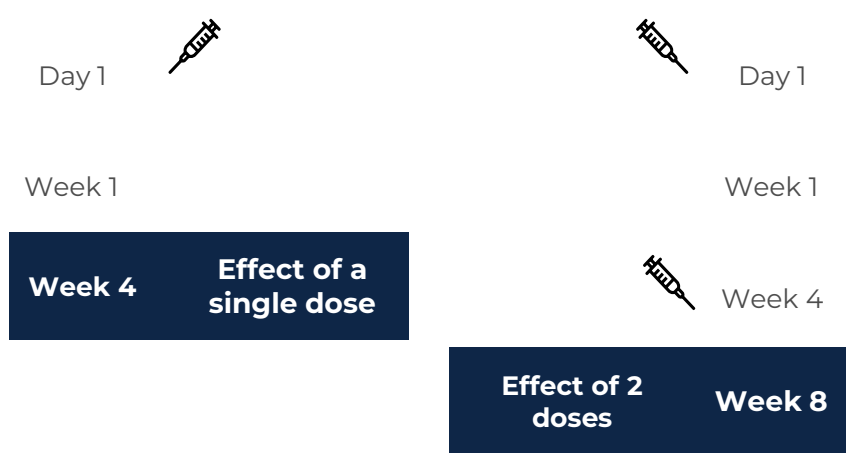
Anti-IL-6  
Vamikibart

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## Mean Change in OCT CST and Absolute CST

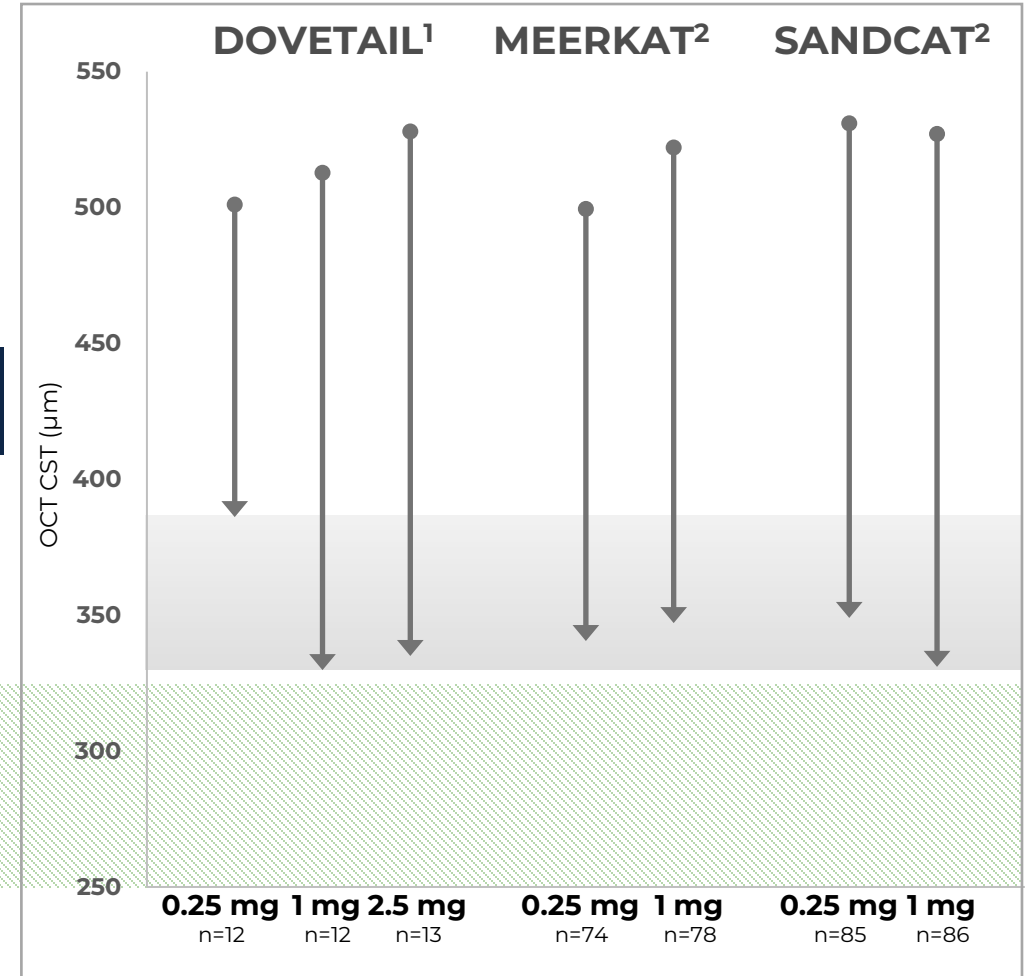


Anti-IL-6, VEGF trap  
KSI-101



Dryness  
(CST 250 – 325)

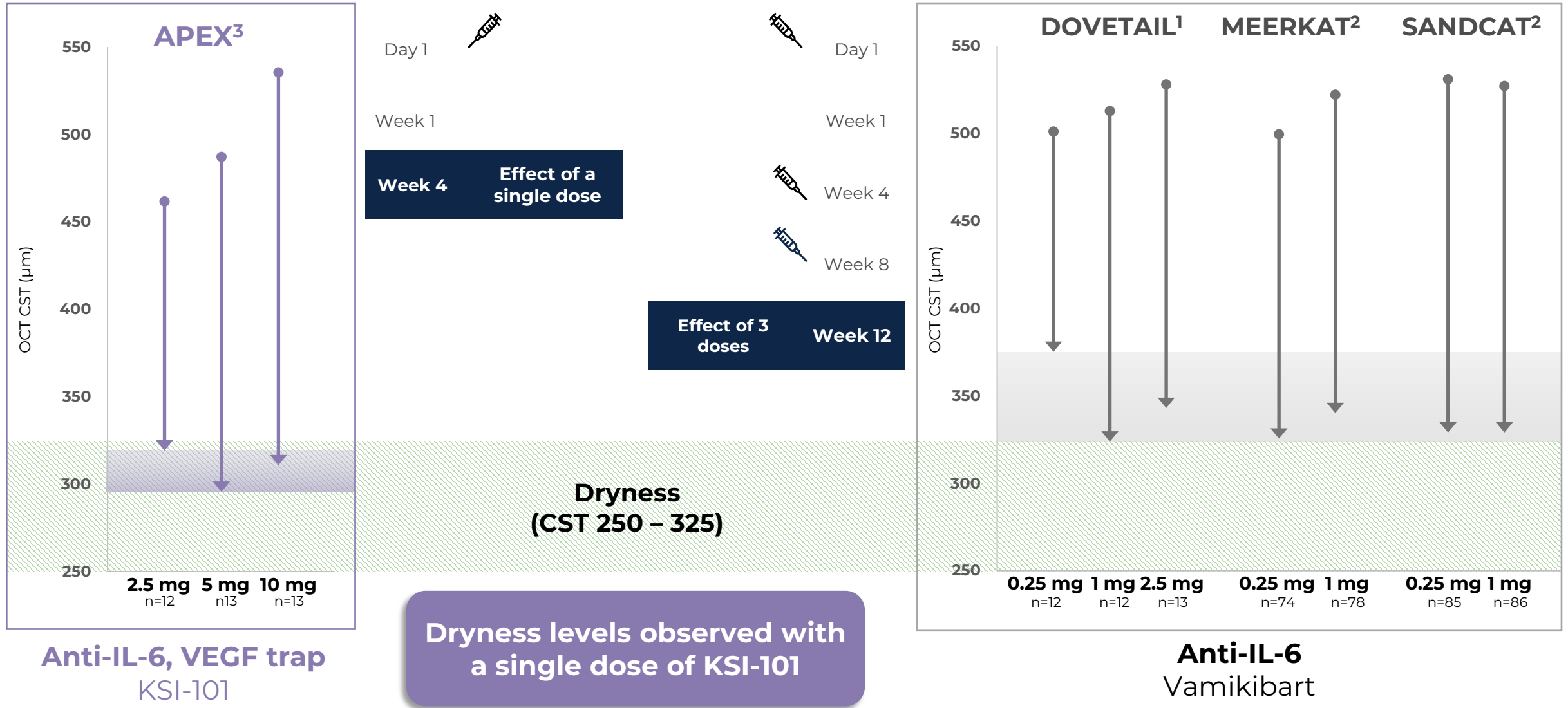
Dryness levels observed with  
a single dose of KSI-101



Anti-IL-6  
Vamikibart

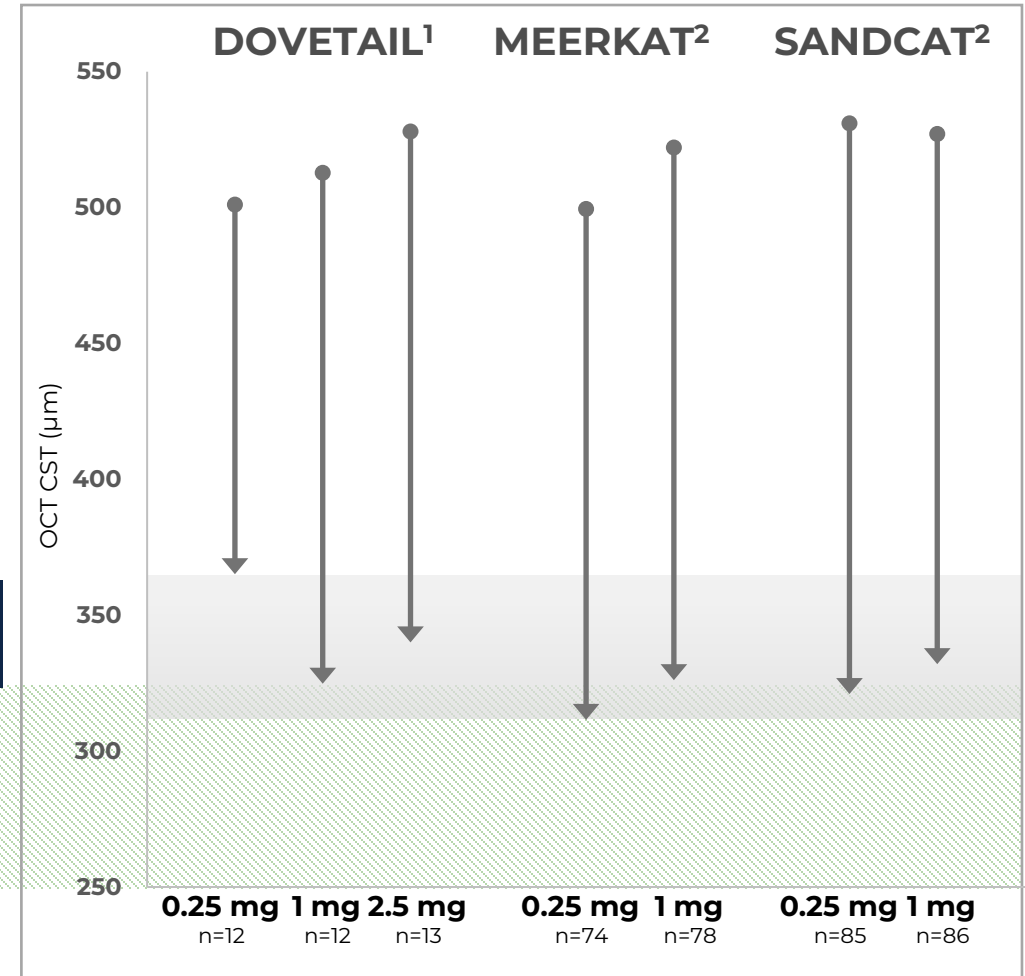
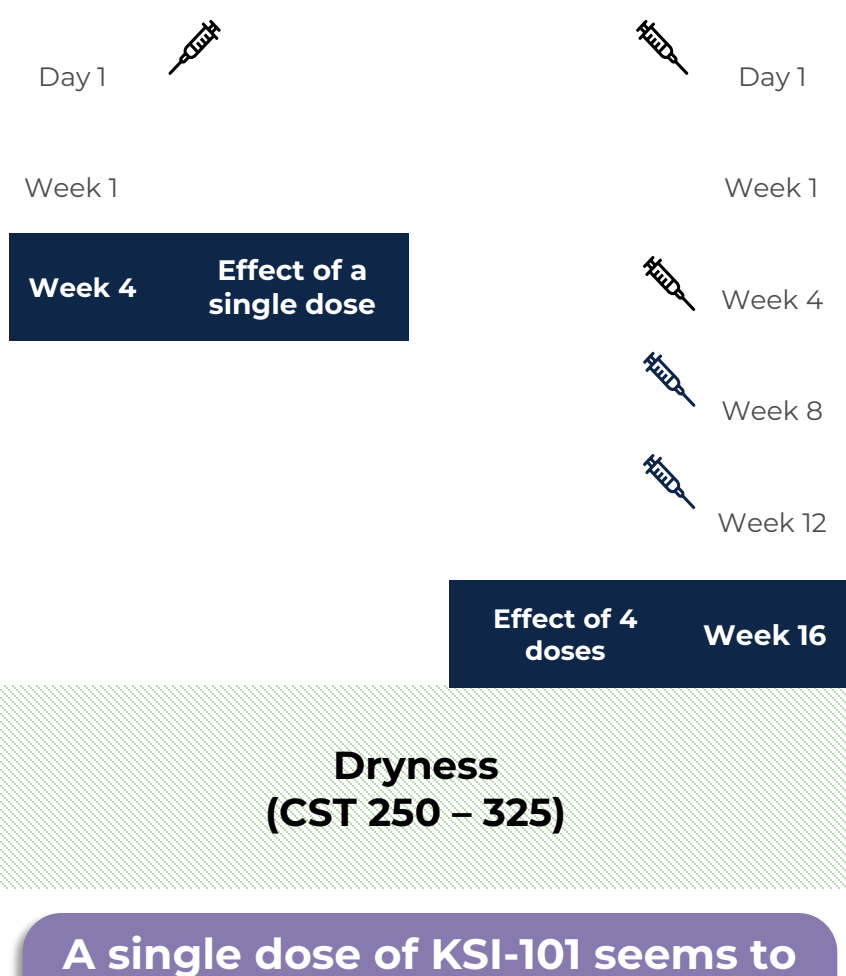
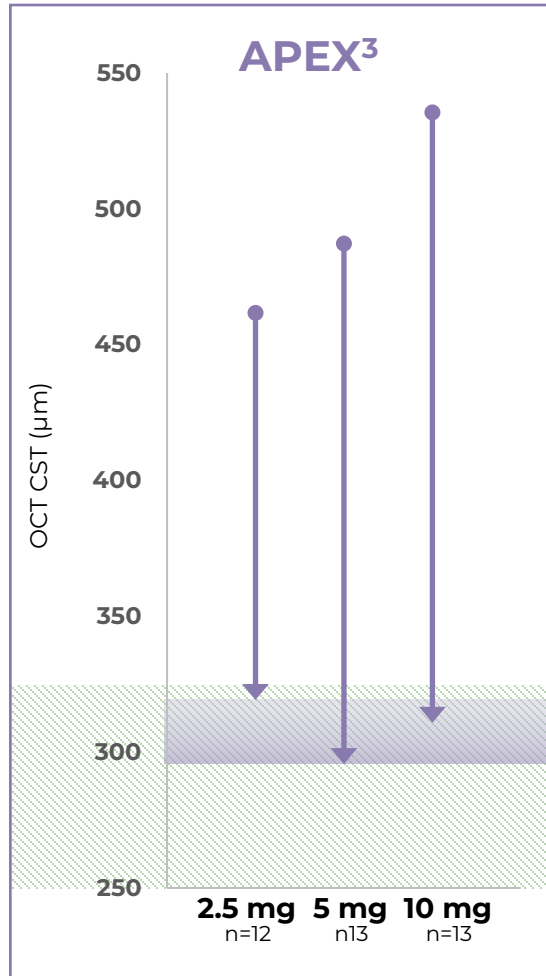
For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.

## Mean Change in OCT CST and Absolute CST



**For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.**

## Mean Change in OCT CST and Absolute CST



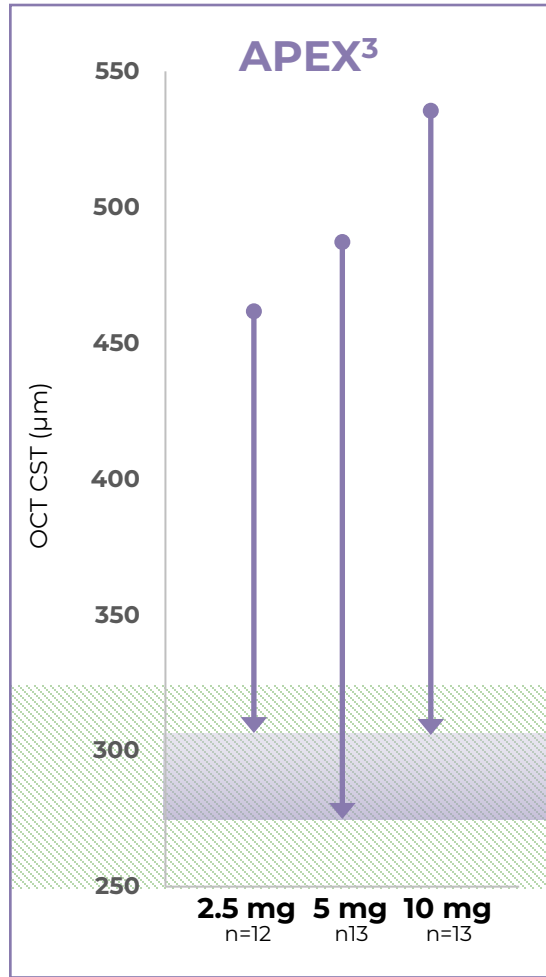
Anti-IL-6, VEGF trap  
KSI-101

A single dose of KSI-101 seems to provide a deeper drying effect than 4 doses of anti-IL-6 monotherapy

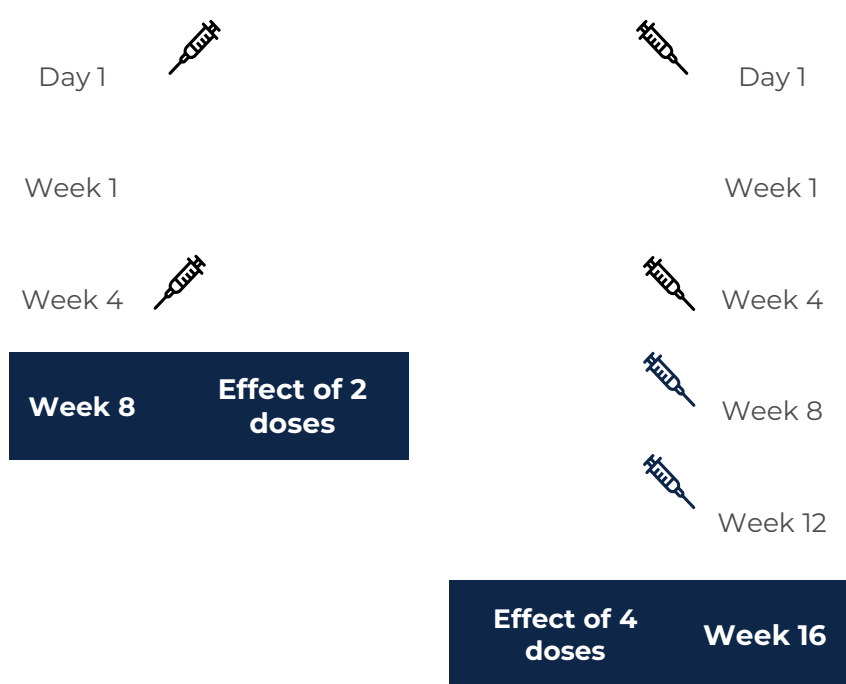
Anti-IL-6  
Vamikibart

For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.

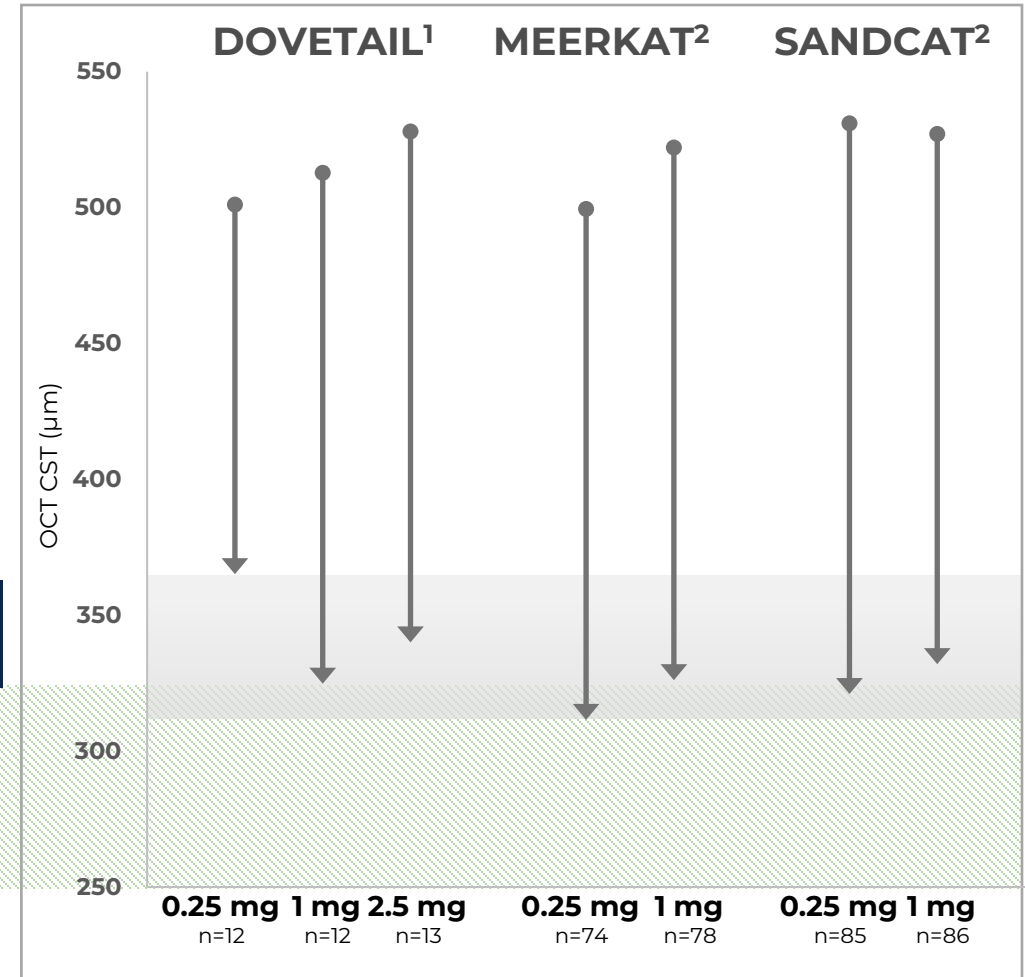
## Mean Change in OCT CST and Absolute CST



Anti-IL-6, VEGF trap  
KSI-101



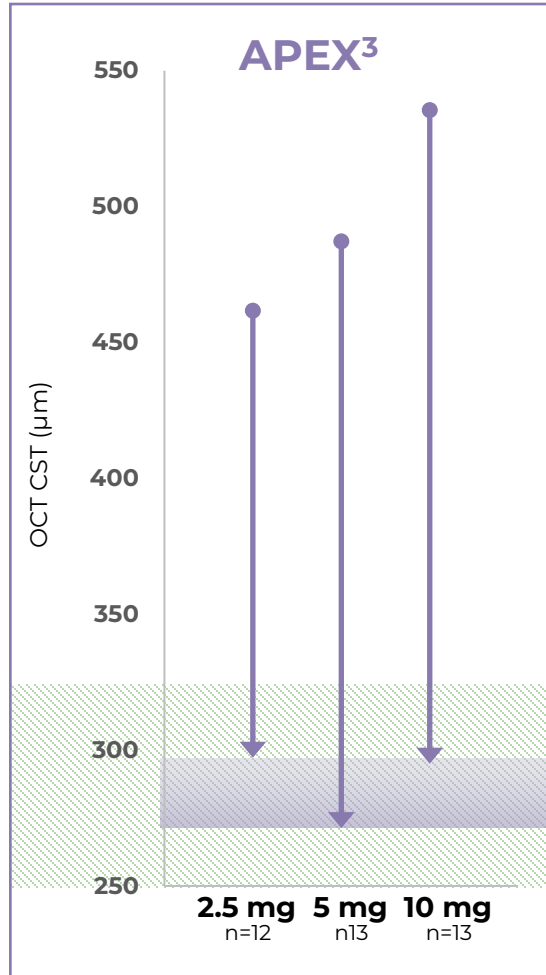
**Continued dosing with KSI-101 provides further deepening into the dryness corridor**



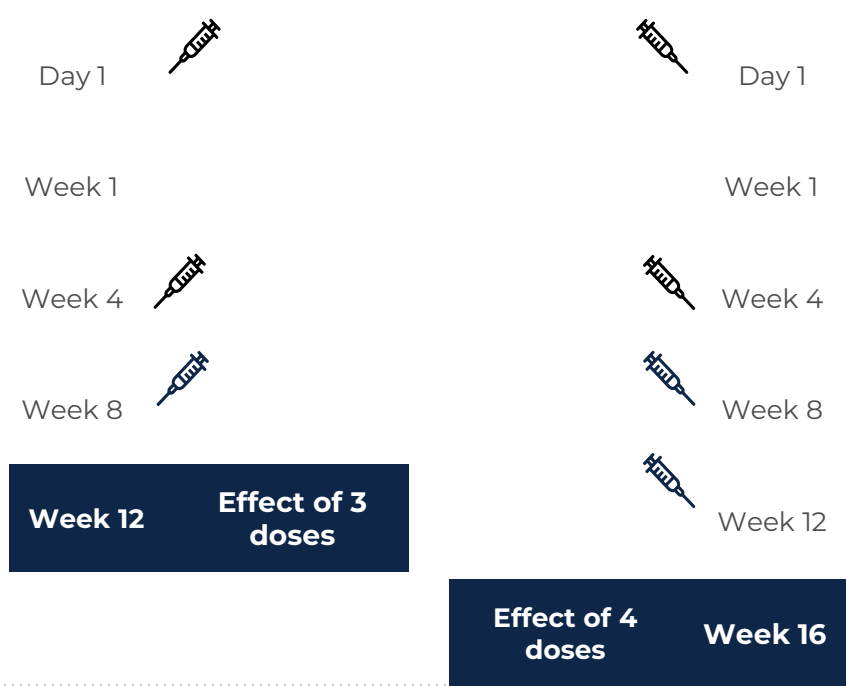
Anti-IL-6  
Vamikibart

**For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.**

## Mean Change in OCT CST and Absolute CST

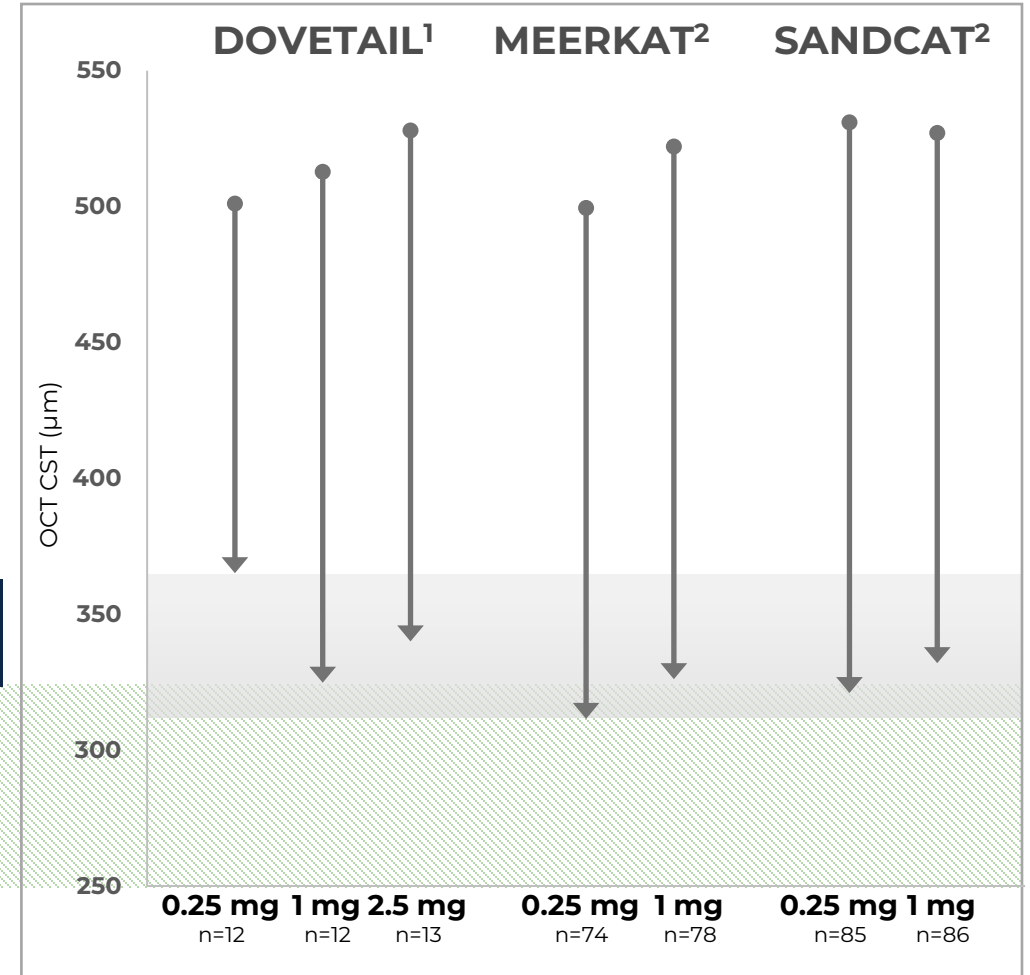


Anti-IL-6, VEGF trap  
KSI-101



Dryness  
(CST 250 – 325)

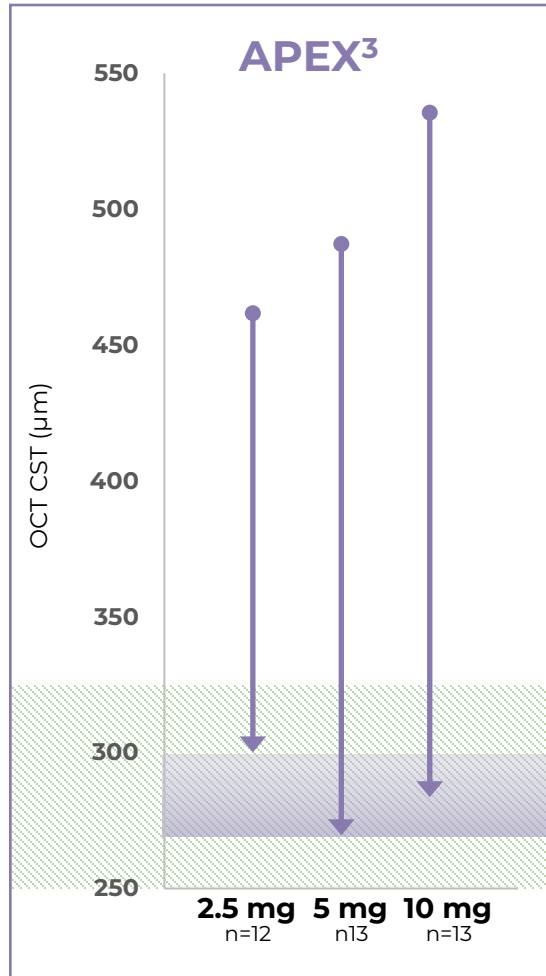
Continued dosing with KSI-101  
provides further deepening into  
the dryness corridor



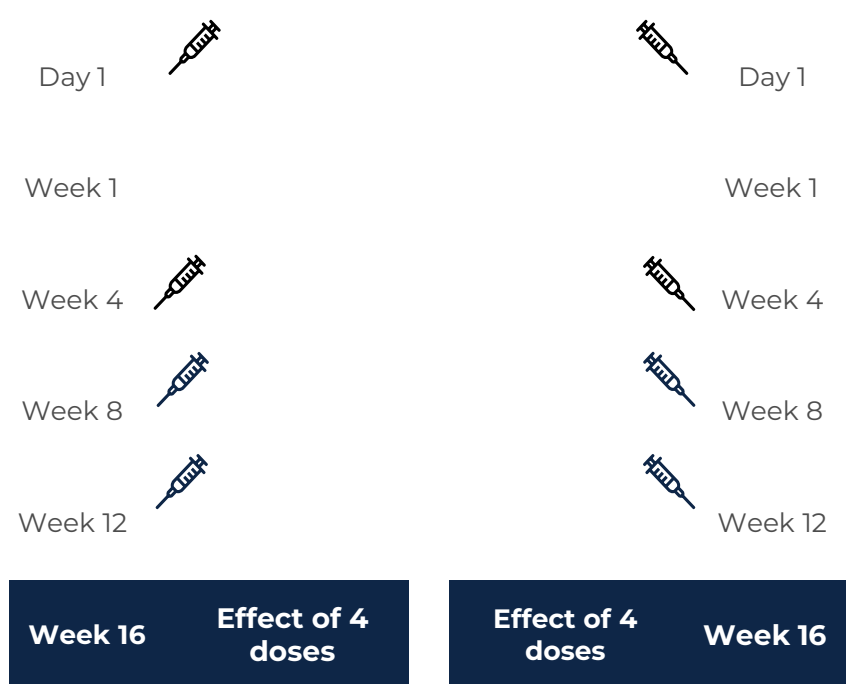
Anti-IL-6  
Vamikibart

For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.

## Mean Change in OCT CST and Absolute CST

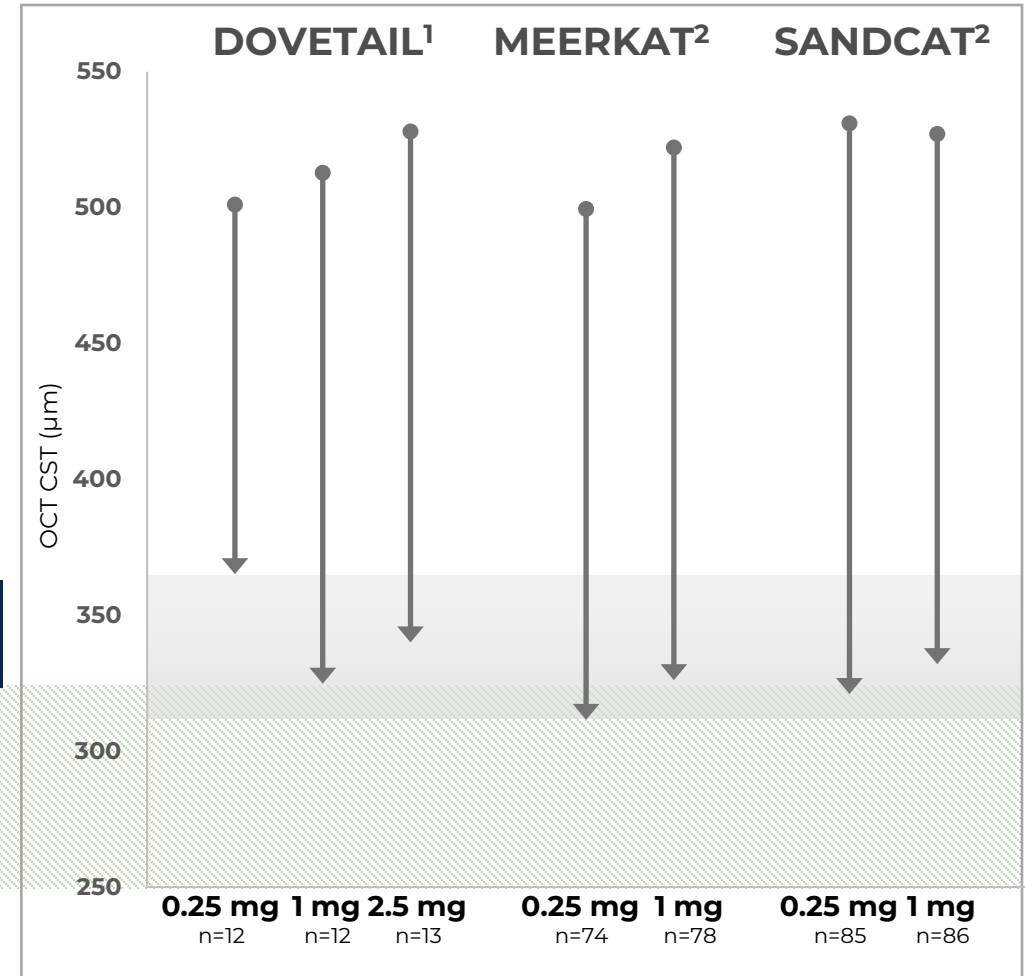


Anti-IL-6, VEGF trap  
KSI-101



Dryness  
(CST 250 – 325)

Dual inhibition of IL-6 and VEGF seems to provide a synergistic drying effect



Anti-IL-6  
Vamikibart

For illustrative purposes only. Not a head-to-head comparison. Differences exist between trial designs and subject characteristics, and caution should be exercised when comparing data across studies.

# The Phase 3 Program in MESI – PEAK and PINNACLE study design

| Weeks         | Fixed monthly dosing |   |   |    |    |    | Individualized dosing |    |    |    |    |    |    |
|---------------|----------------------|---|---|----|----|----|-----------------------|----|----|----|----|----|----|
|               | D1                   | 4 | 8 | 12 | 16 | 20 | 24                    | 28 | 32 | 36 | 40 | 44 | 48 |
| KSI-101 5 mg  | □                    | □ | □ | □  | □  | □  | ◻                     | ◻  | ◻  | ◻  | ◻  | ◻  |    |
| KSI-101 10 mg | ■                    | ■ | ■ | ■  | ■  | ■  | ◻                     | ◻  | ◻  | ◻  | ◻  | ◻  |    |
| Sham          | ●                    | ● | ● | ●  | ●  | ●  | ◐                     | ◐  | ◐  | ◐  | ◐  | ◐  |    |

- KSI-101 5 mg injection
- KSI-101 10 mg injection
- Sham injection
- ◻ Individualized treatment (PRN)
- ◐ Sham PRN

Primary endpoint

- Individualized treatment criteria (Week 24-44)**
- Increase in OCT CST  $\geq 50 \mu\text{m}$  compared to lowest previous measurement, or
  - OCT CST  $> 320 \mu\text{m}$

## Primary endpoint

BCVA change from baseline to the average of Week 20 and 24

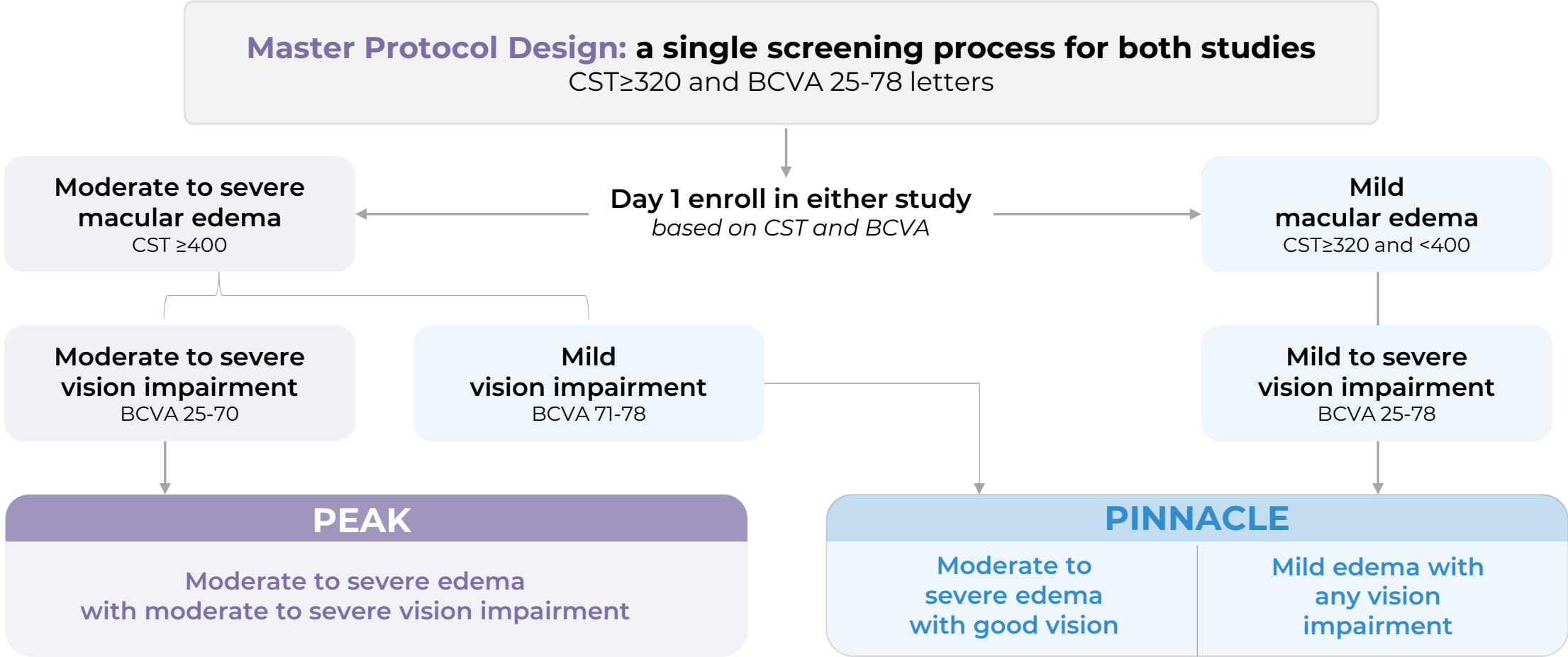
## Key secondary endpoint

Proportion of patients in whom BCVA had improved by  $\geq 15$  letters from baseline to 24 weeks

## Key inclusion criteria

- Macular edema secondary to inflammation (MESI)
- Diagnosis of active or inactive non-infectious intraocular inflammation, acute or chronic
- Active leakage as evidenced by fluorescein angiogram
- OCT CST of  $\geq 320$  microns
- BCVA score  $\leq 78$  and  $\geq 25$  (~20/25 to 20/320 Snellen)

# PEAK and PINNACLE master protocol design: a single screening process that enrolls distinct and complementary MESI patient populations



Two **distinct and complementary sub-populations** will be studied  
 Both studies to **run concurrently** in all study sites  
 Covers a **wide spectrum** of MESI patients

# We have increased the size of the KSI-101 MESI pivotal program

- Patient enrollment faster than expected
- No major changes to expected timelines are anticipated
- Pivotal program aligned with FDA in type C meeting

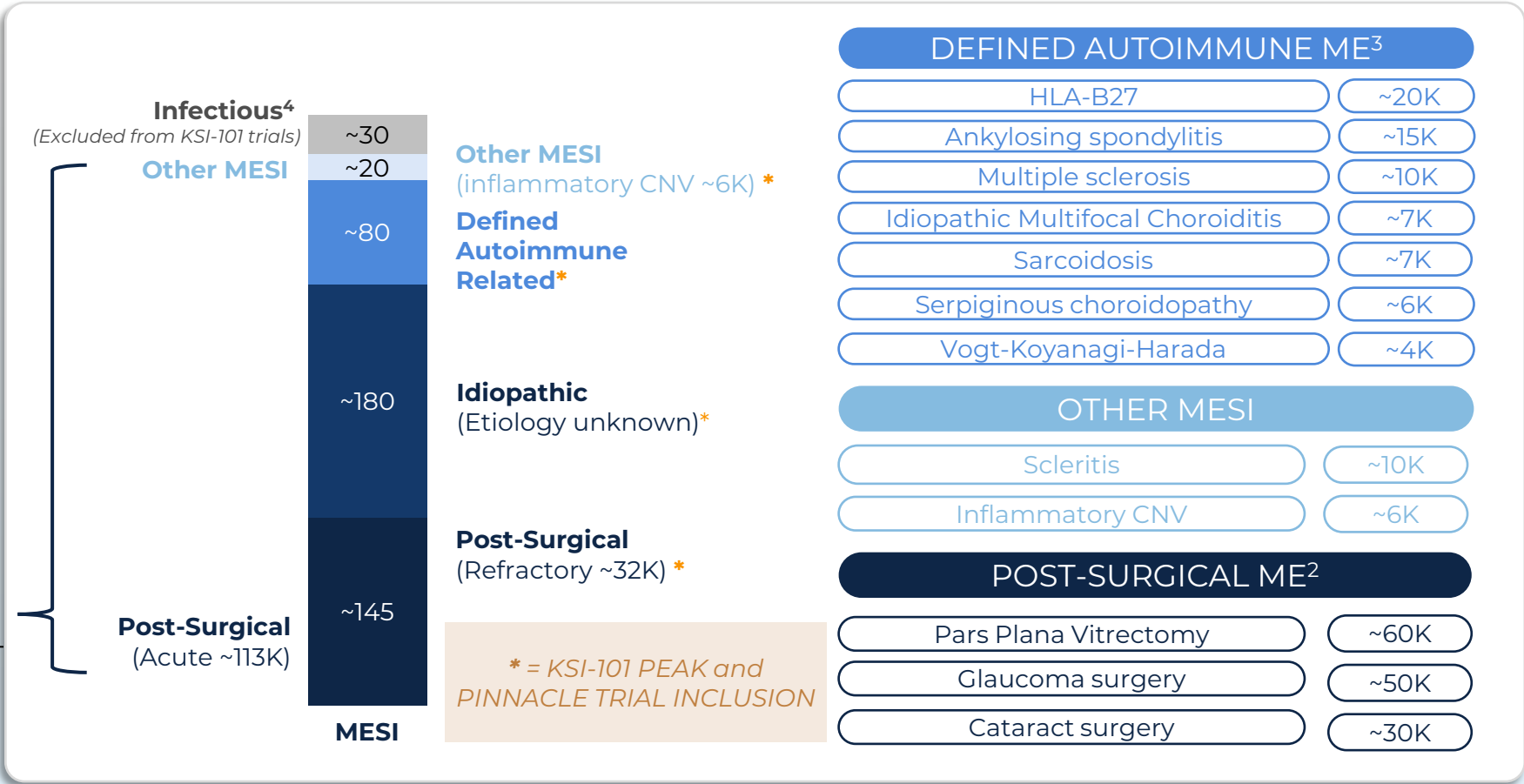
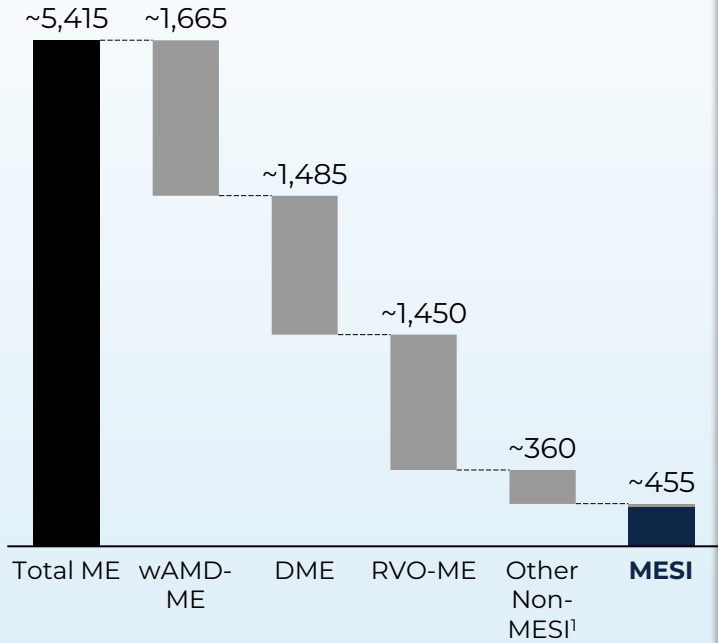


# MESI affects ~450,000 US patients (~300,000 trial eligible) often reported by etiology (defined autoimmune, idiopathic, surgical, infectious and other)

~455K out of 5.4M ME patients in the U.S. may be classified under MESI, ~298K meet KSI-101 trial inclusion

### U.S. MESI EPIDEMIOLOGY

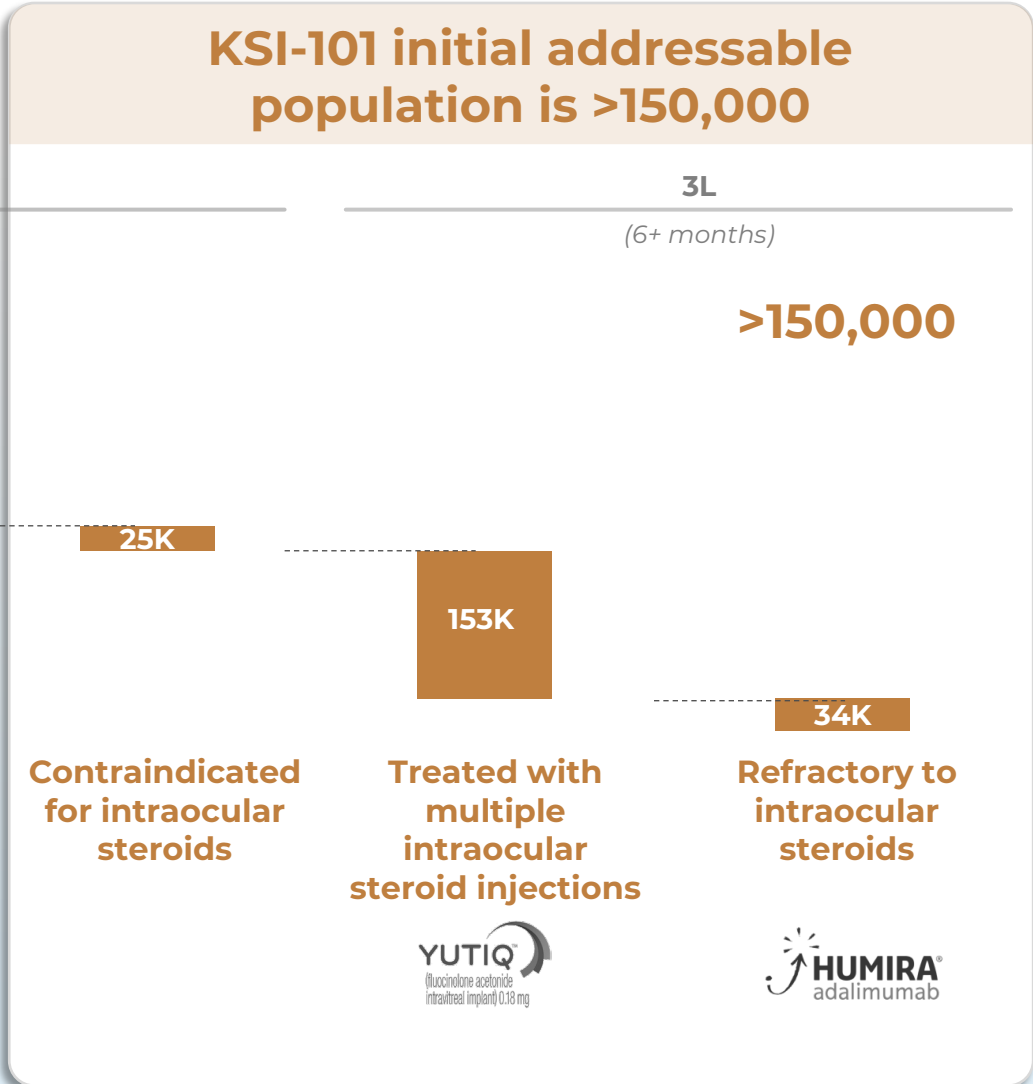
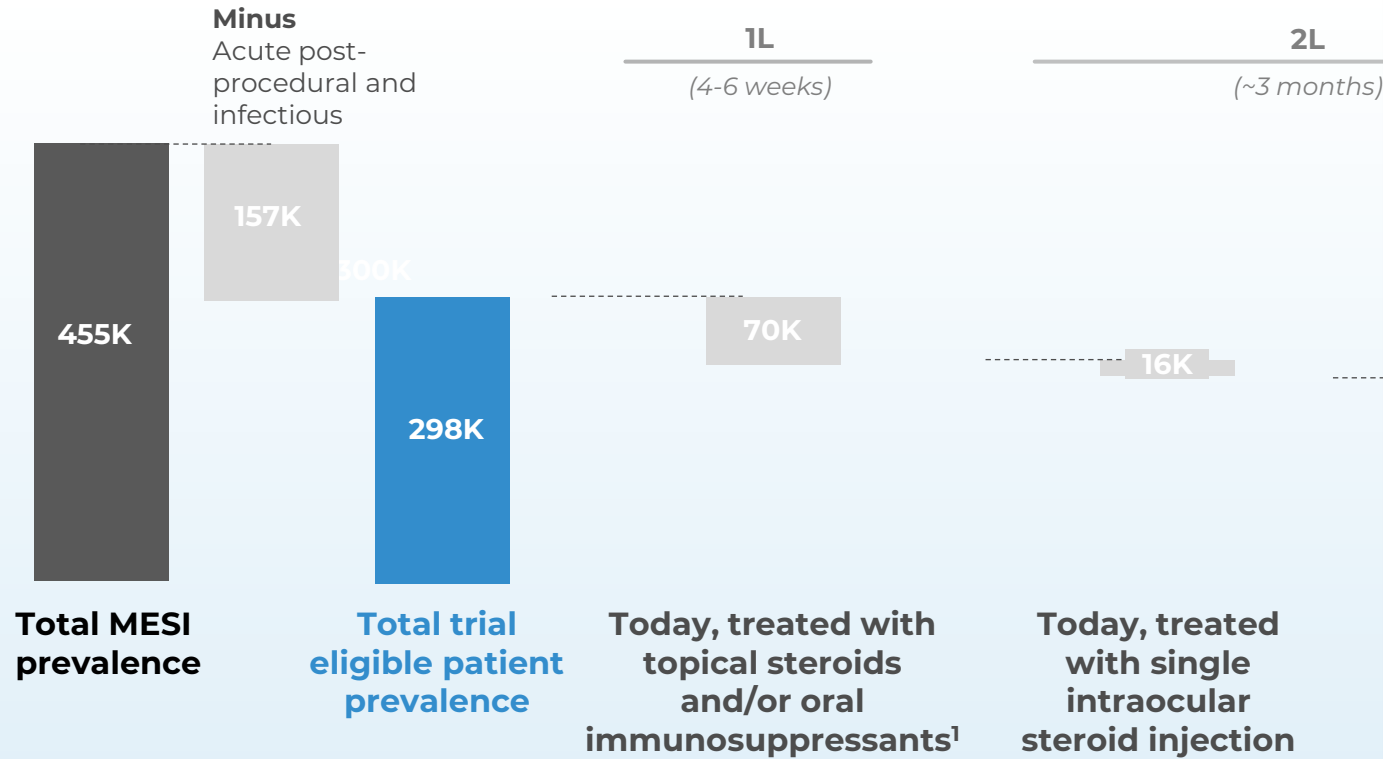
Estimated by two methodologies – method 1 (2025) Thousands of patients



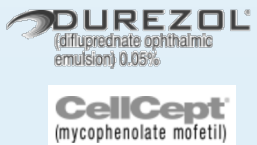
<sup>1</sup> Other Non-MESI includes epiretinal membrane ME and RP-associated ME; <sup>2</sup> Non-exhaustive list, other types include laser photocoagulation, DMEK, DSEAK-ME, IOL replacement, scleral buckling, pneumatic retinopathy; <sup>3</sup> Non-exhaustive list, others include birdshot choroidopathy, multiple evanescent white dot syndrome, punctate inner choroidopathy, and more; <sup>4</sup> Non-exhaustive list, others include bartonella sp. Tuberculosis, endophthalmitis; DME = Diabetic Macular Edema; ERM = Epiretinal Membrane; HLA = Human Leukocyte Antigen, ME = Macular Edema; MESI = Macular Edema Secondary to Inflammation; RP = Retinitis Pigmentosa; RVO = Retinal Vein Occlusion; UME = Uveitic Macular Edema; wAMD = Wet Age-Related Degeneration

# KSI-101 initial addressable population is greater than 150,000 MESI patients in the US

## KSI-101 ADDRESSABLE POPULATION # of Patients



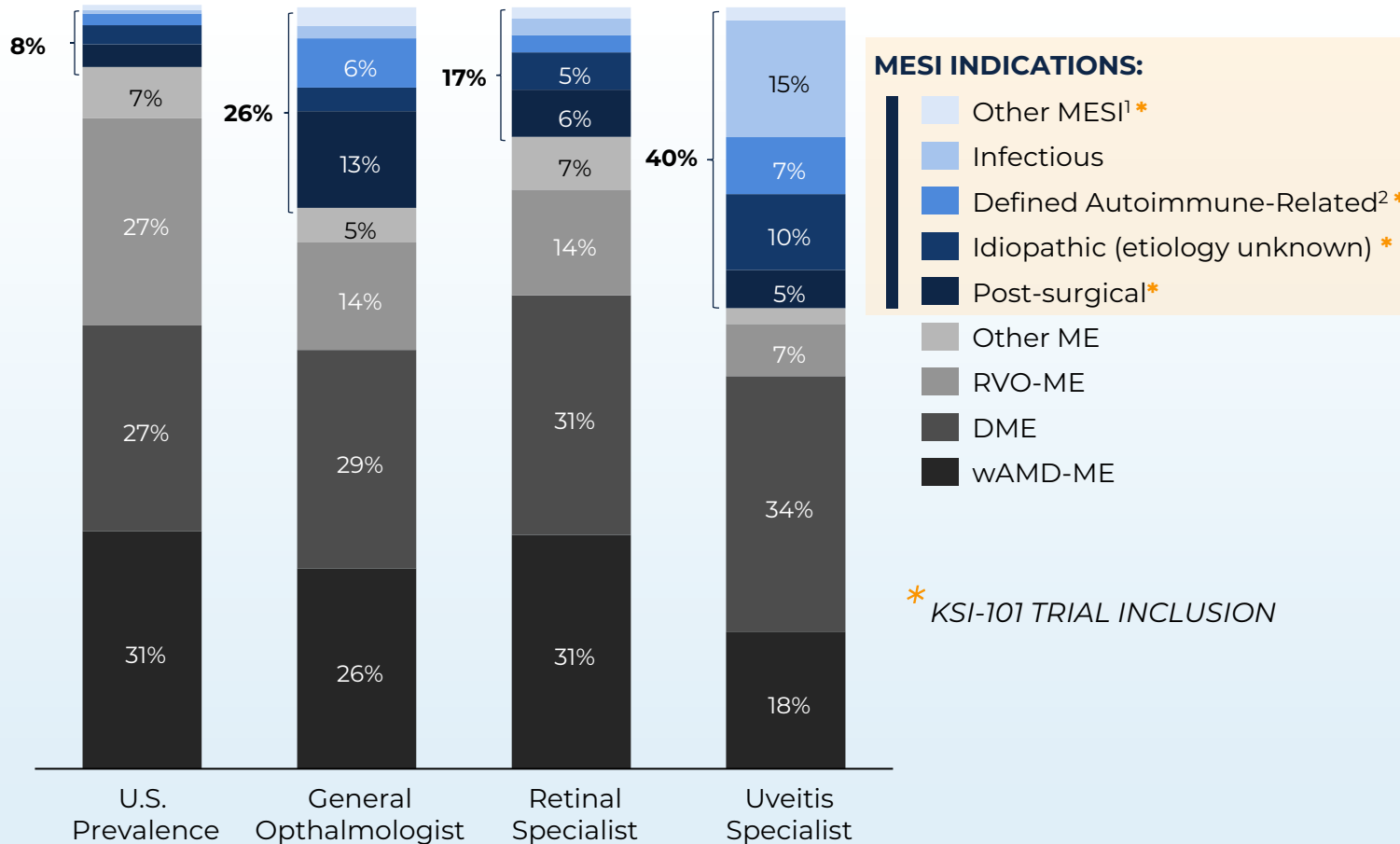
Example therapies:



Note: <sup>1</sup> First line includes eye drops or systemic immunosuppressants. Eyedrops prescribed by physicians includes steroidal and non-steroidal anti-inflammatory drops; IO = Intraocular; ME = Macular Edema; MESI = Macular Edema Secondary to Inflammation;  
 Source: Bellocq et al., *BMJ* (2014); Birnbaum et al., *JAMA Ophthalmol.* (2011); Erden et al., *Ocular Immunol. Inflamm.* (2019); Kao et al., *A.A. Ophthalmol.* (2022); Expert Interviews (JUN 2025); MUST Research Group, *Ophthalmol.* (2019); Schallhorn et al., *Am. J. Ophthalmol.* (2018)

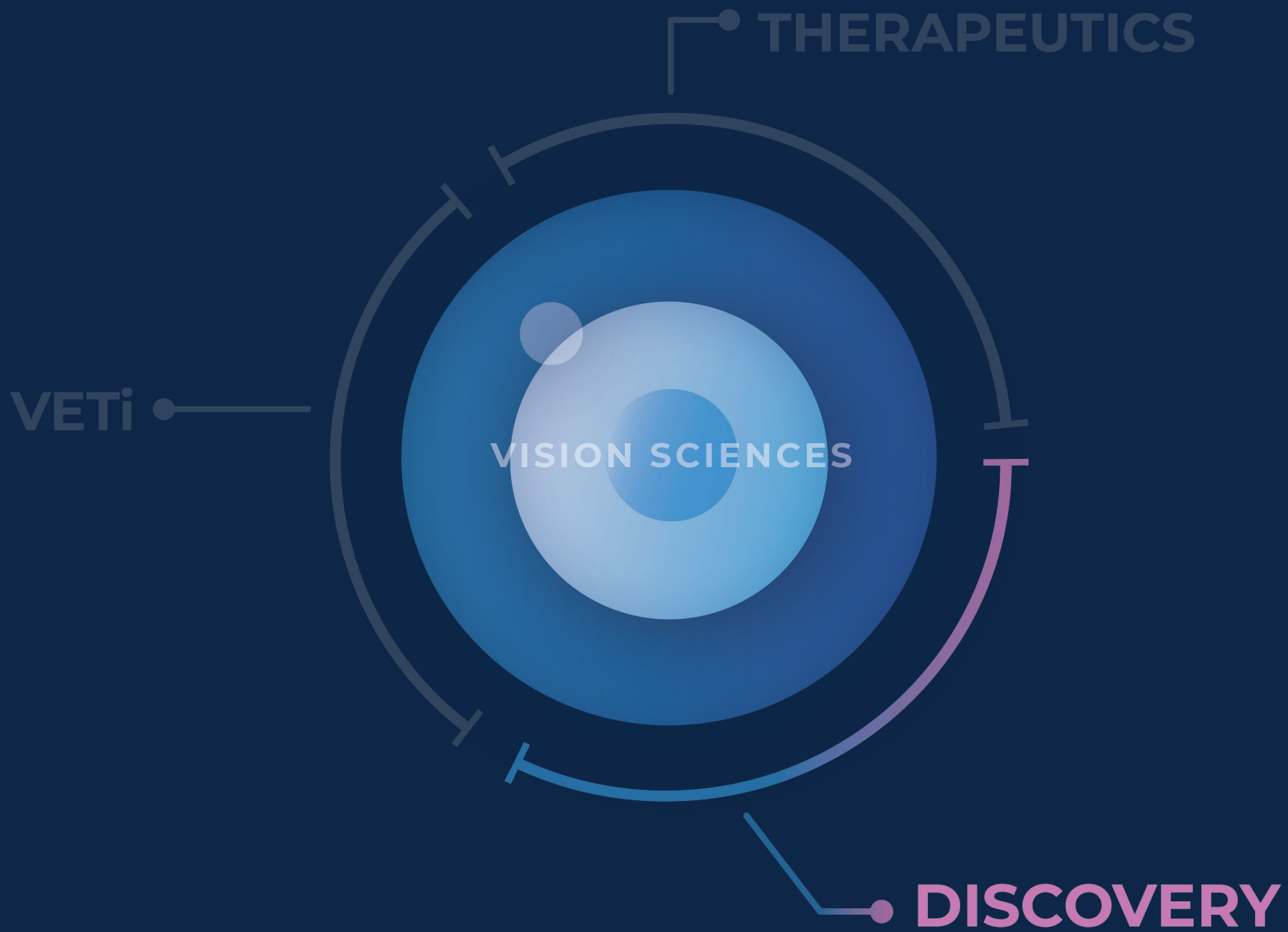
# Most MESI patients are in the care of General Ophthalmologists and Retinal Specialists; complex cases are referred out to Uveitis Specialists

OPHTHALMOLOGY PRACTICE BREAKDOWN – Method 2  
% of ME patients by patient subtype across physician types



- **General ophthalmologists** act as the referral gatekeepers, being the most common physician subtype (~18K in the U.S.)
- **Retinal specialists** (~3K in the US) tend to treat a diverse set of macular edema patients (**~17% of their current case load is MESI today**)
- **Uveitis specialists** are rare (~200 in the U.S.) but are the most familiar with MESI subtypes as it makes up **~40%** of their **practice**

Notes: <sup>1</sup>Other causes can include RP, scleritis, neoplasms, drug-induced, and trauma-induced; <sup>2</sup>Non-exhaustive drivers include sarcoidosis, systemic lupus erythematosus, scleroderma, rheumatoid arthritis, Behcet's disease, Vogt-Koyanagi-Harada disease, and others; trauma-induced; DME = Diabetic Macular Edema, ERM = Epiretinal Membrane, ME = Macular Edema, MESI = Macular Edema Secondary to Inflammation, RP = Retinitis Pigmentosa, RVO = Retinal Vein Occlusion, wAMD = Wet Age-Related Degeneration  
Source: Expert Interviews (JUN 2025); Review of Optometry (2024); Ho and Avery, *Retina Today* (2025); Tsui et al., *J Acad Ophthalmol* (2022)



# Discovery: We are broadening our portfolio of investigational medicines to tackle additional high prevalence causes of severe vision loss

**Ocular Inflammation**

**Pre-IND**

**Bispecific Antibodies:**

**KSI-102:** anti-IL-6, anti-TNF $\alpha$

**KSI-103:** anti-IL-6, anti-IL-1

**Geographic Atrophy**

**Pre-clinical**

**Bispecific Antibodies:**  
anti-IL-6 , anti-complement;  
anti-VEGF, anti-complement

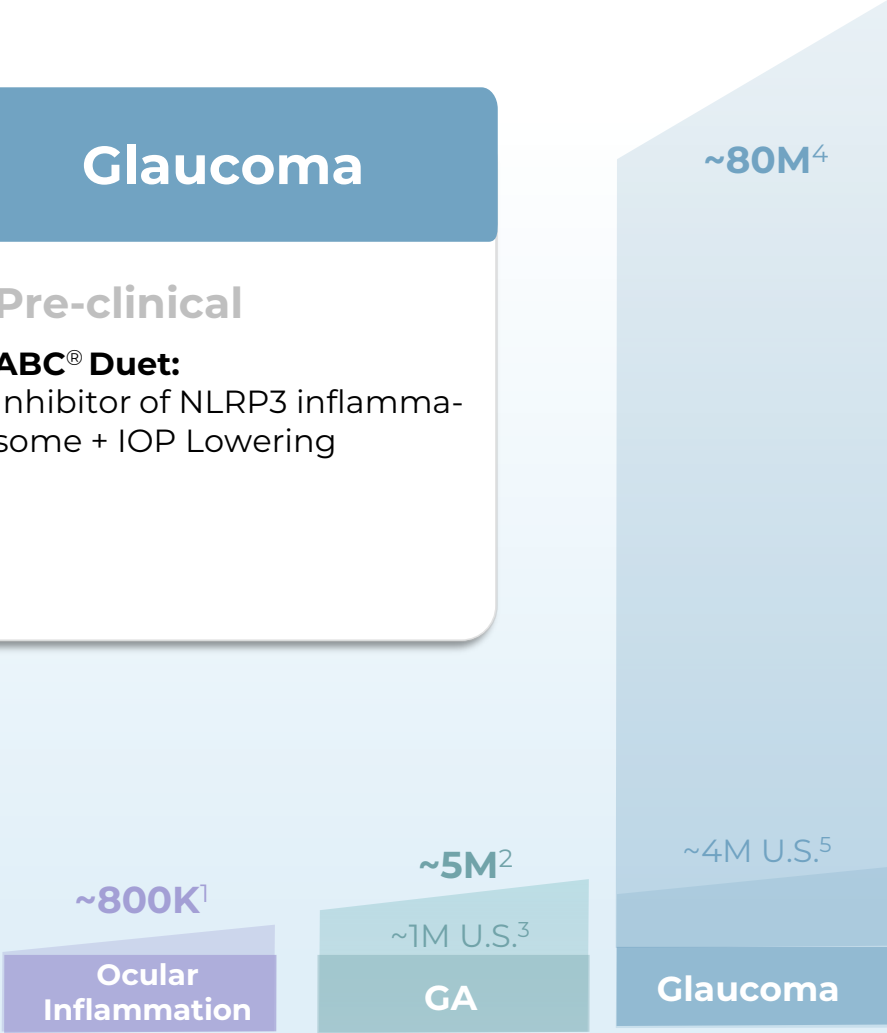
**ABC<sup>®</sup> Duet:**  
Inhibitor of NLRP3 inflamma-  
some + Complement

**Glaucoma**

**Pre-clinical**

**ABC<sup>®</sup> Duet:**  
Inhibitor of NLRP3 inflamma-  
some + IOP Lowering

*Estimated global prevalence*

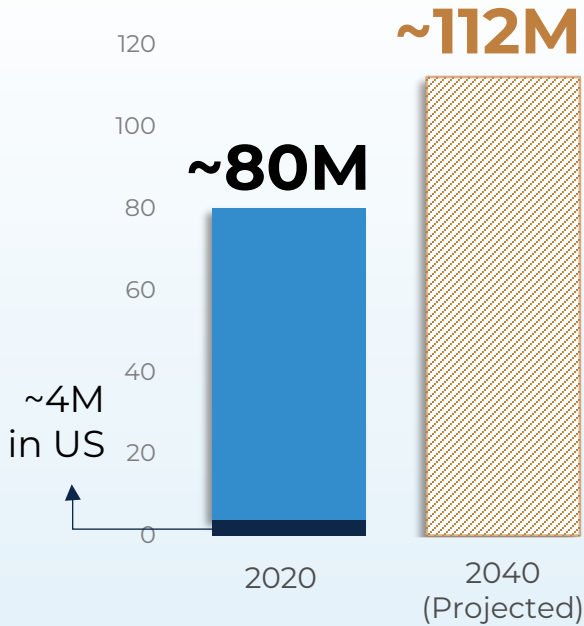


ABC: antibody biopolymer conjugate  
GA: geographic atrophy

1. Nila Kirupaharan et al. *Invest. Ophthalmol. Vis. Sci.* 2024;65(7):6510. 2. Rudnicka AR, et al. *Ophthalmology* 2012;119:571-580. 3. Wong WL, et al. *Lancet Glob Health* 2014;2:e106-116. 4. Allison K et al. *Cureus.* 2020 Nov 24;12(11):e11686. 5. Ehrlich JR, et al. *JAMA Ophthalmol.* 2024;142(11):1046-1053.

# Glaucoma is the leading cause of irreversible blindness worldwide with no approved neuroprotective treatments

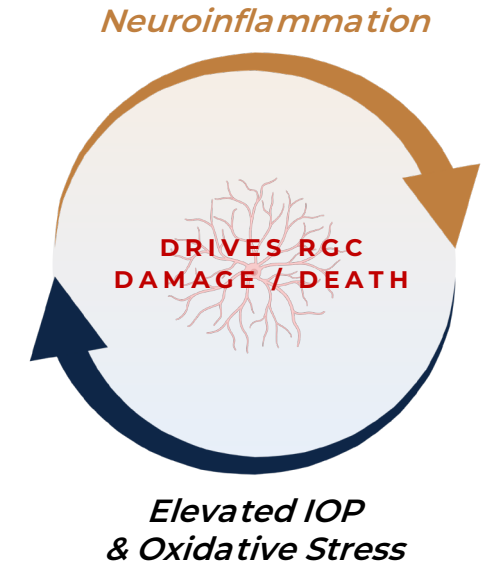
Worldwide prevalence of glaucoma<sup>1</sup>



- U.S. represents largest single market<sup>2</sup>
- Global market expected to grow due to aging population; valued at **~\$9B in 2025<sup>2</sup>**

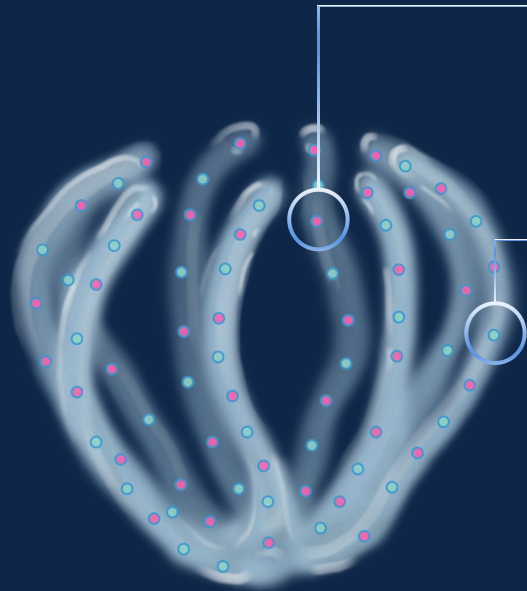
## Glaucoma is a progressive optic neuropathy driven by neuroinflammation

- **Current therapies focus on lowering intraocular pressure (IOP)** as it is the only modifiable risk factor
- **The NLRP3 inflammasome complex is a key driver of neuroinflammation** that results in optic neuropathy<sup>3</sup>
- Today's small molecule delivery technologies (eye drops, orally, intravitreally) **are limited in their ability** to reach retinal and optic nerve targets



**There is an unmet need to develop new therapies that target the underlying neuroinflammation that drives optic neuropathy**

# Glaucoma “duet”: a single molecule designed to target neuroinflammation (that causes optic neuropathy) *and* elevated IOP simultaneously



## Glaucoma “Duet”

Biopolymer with two small molecules (“BCD”)

### Disease Modifying NLRP3 Inhibitor

Targets the NLRP3 inflammasome complex that drives neuroinflammation causing optic neuropathy

### IOP Lowering Small Molecule

Addresses the IOP elevation stressor; NLRP3 inhibitor demonstrates potential to provide *additional* IOP reduction effects

### ABCD Platform for Extended Durability

High molecular weight to increase ocular half-life, providing potential for a quarterly dosed intravitreal therapy

### Favorable Safety Demonstrated

Zenkuda and the ABCD platform demonstrated a favorable safety profile across multiple pivotal studies (>13,000 intravitreal injections)

Neuroprotective

+

Reduces IOP

+

Durable

+

Safe

**4 key attributes needed in a next generation glaucoma therapy**

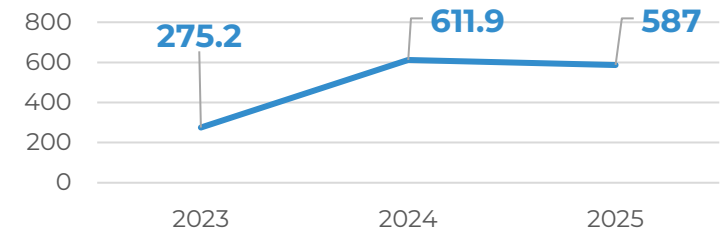
Administered via intravitreal injection

# Geographic atrophy is a valuable market with a high unmet need

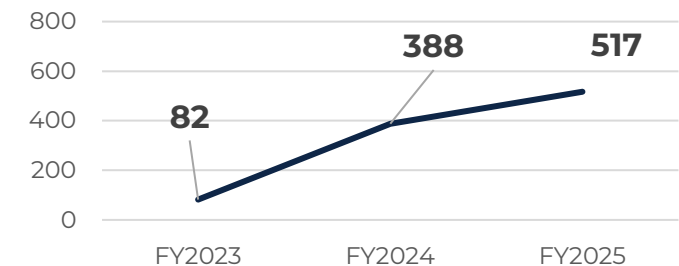
- Geographic atrophy (GA) is the advanced form of dry age-related macular degeneration, **affecting ~1M people in the U.S.**
- GA is characterized by progressive retinal atrophy that can extend to the macula and fovea, **leading to irreversible vision loss**
- **GA is driven by multiple inflammatory pathways, and current single target therapies have limitations**
  - The C3 complement inhibitor (Syfovre) and C5 complement inhibitor (Izervay) have been validated for GA. Despite their commercial success, monotherapies:
    - Provide modest clinical benefit
    - Require frequent intravitreal injections
    - Have been associated with an increased risk of conversion to choroidal neovascularization

**~\$1B in net sales for GA monotherapies in 2025**

**SYFOVRE Net Sales (in Millions)**



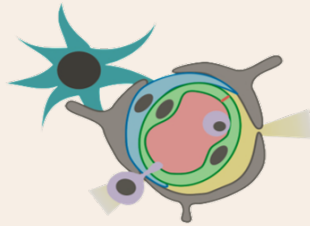
**IZERVAY Net Sales (in Millions)**



# GA is a complex interplay of complement, inflammation, and angiogenic pathways

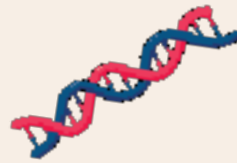
Smoking  
Age  
Diabetes

**NLRP3**  
inflammasome, IL-  
1 $\beta$ , IL-6



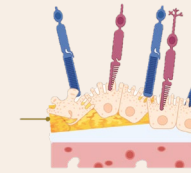
Inflammation

**Complement**



Human Genetics

**VEGF**

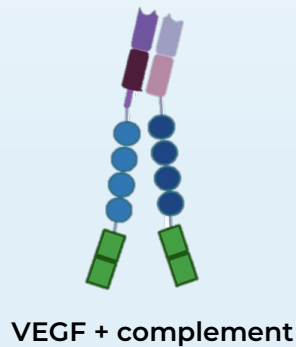
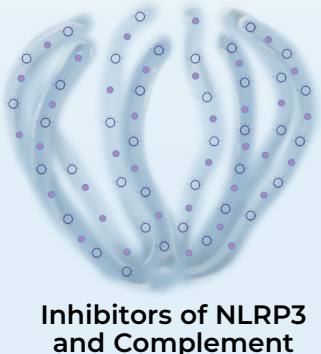
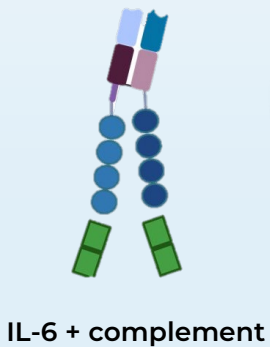
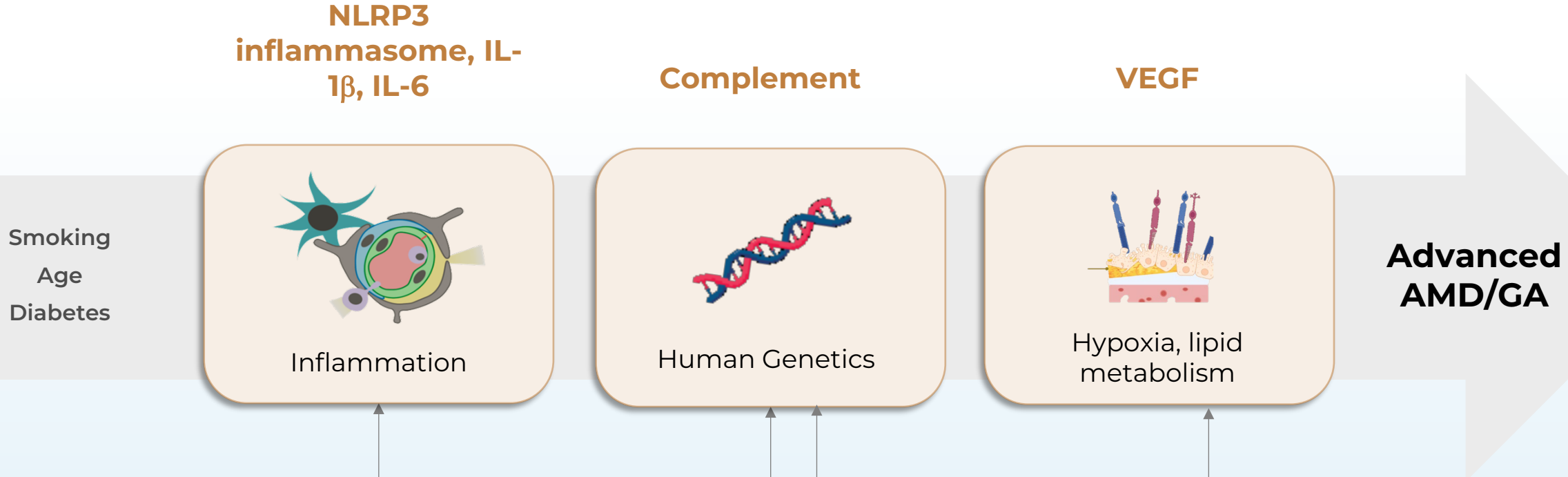


Hypoxia, lipid  
metabolism

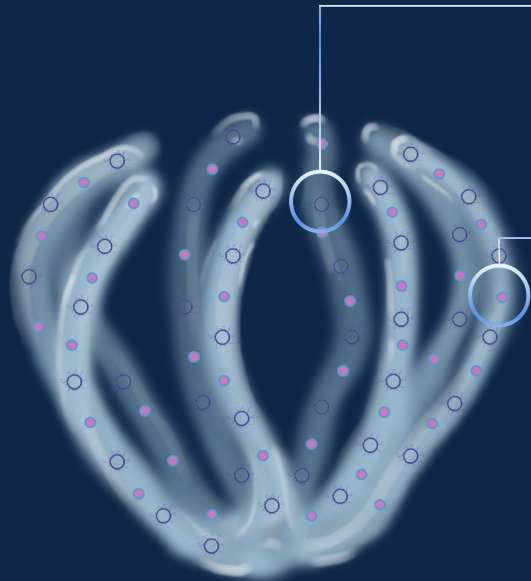
**Advanced  
AMD/GA**

This interplay drives both GA and neovascular AMD, which may co-exist within the same patient or eye—**emphasizing the need for therapeutic strategies that address multiple mechanisms**

# Kodiak's multi-asset pipeline in GA is designed to address the multifactorial nature of the disease



# GA “duet”: Dual inhibition of validated complement pathways along with the inflammasome pathway (NLRP3)



## GA “Duet”

Biopolymer with one macrocycle peptide and one small molecule

### Peptide Inhibitor of Complement

Anti-C3 and anti-C5 have been validated for GA, but current therapies do not sufficiently halt disease progression and are limited by frequent injections

### NLRP3 Inhibitor Small Molecule

Prevents inflammasome activation that contributes to AMD pathology

### ABCD Platform for Extended Durability

High molecular weight to increase ocular half-life, providing potential for a **quarterly dosed intravitreal therapy**

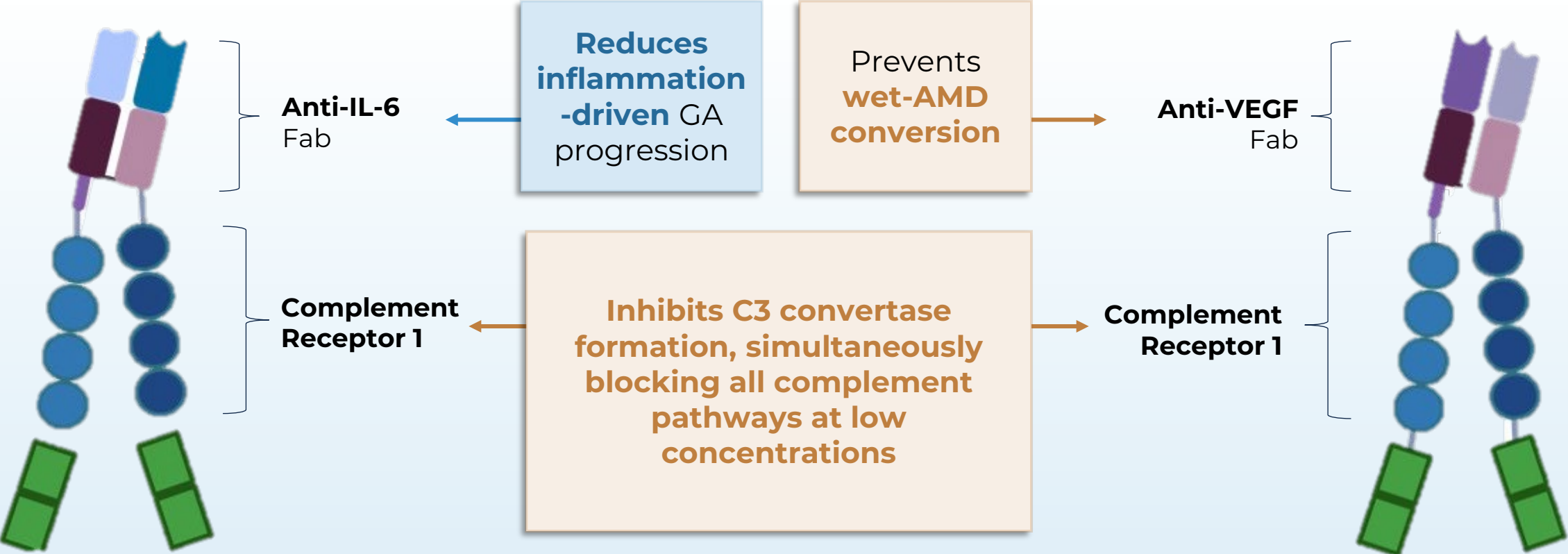
**Dual inhibition of inflammatory and complement pathways may better address the multifactorial biology driving GA progression**

*Administered via intravitreal injection*

# GA bispecific antibody: Combining validated complement regulation with VEGF or IL-6 inhibition as a therapeutic target for GA

## IL-6 + Complement

## VEGF + Complement



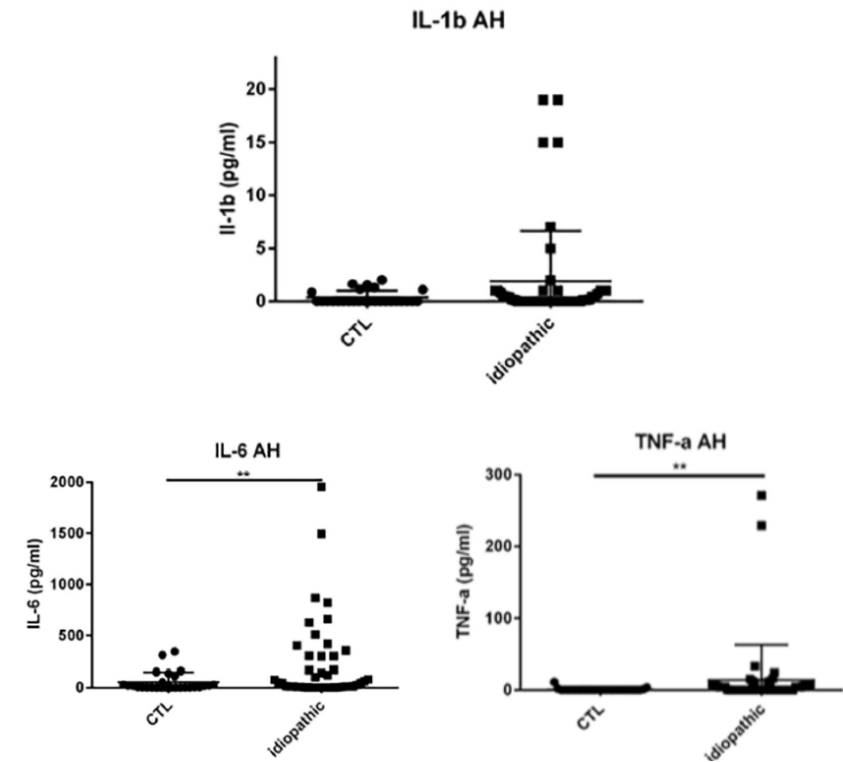
Administered via intravitreal injection

# Ocular inflammatory disease: the 4<sup>th</sup> leading cause of vision loss among working-age adults with no approved biologics

- ~1/3 of patients with ocular inflammation **develop macular edema**, the leading cause of vision loss in this population
- **Steroids** remain the mainstay treatment but can **cause significant and permanent ocular adverse effects**, especially with long-term use or high doses
- Elevated levels of pro-inflammatory cytokines including TNF- $\alpha$  and IL-6 play distinct yet complementary roles in driving inflammation and vascular permeability

**Therapies targeting these cytokines individually may not fully address both disease drivers**

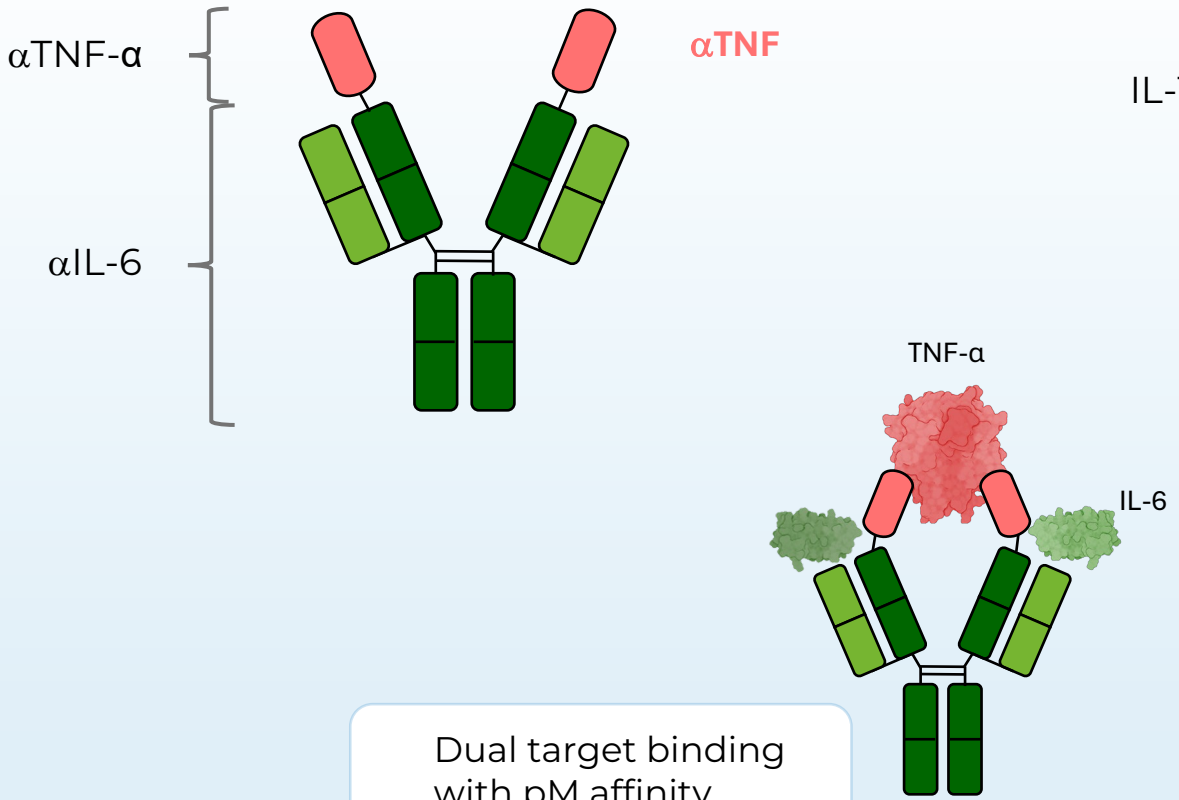
## TNF- $\alpha$ , IL-6 and IL-1 levels are upregulated in patients with ocular inflammation



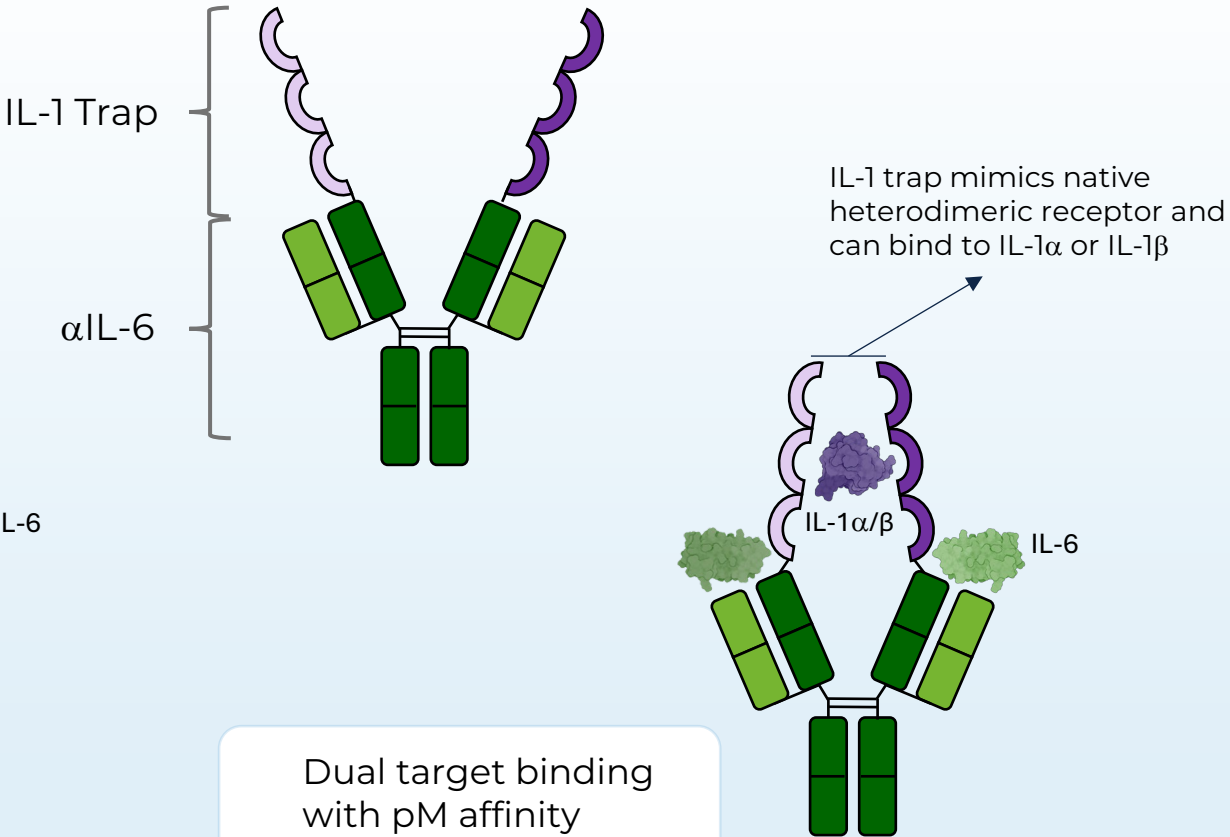
Dot plots comparing immune mediator levels in aqueous humor (AH) of patients with idiopathic uveitis and non-inflammatory controls patients (cataract age-related)

# KSI-102 and KSI-103: Engineered to inhibit TNF- $\alpha$ /IL-6 and IL-1/IL-6 through dual cytokine targeting

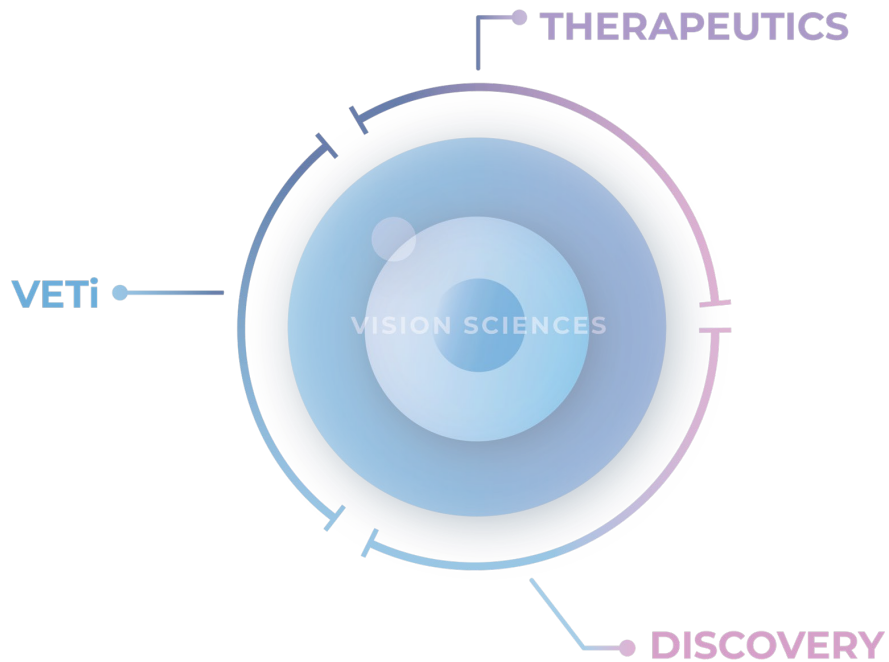
**KSI-102**  
( $\alpha$ TNF- $\alpha$  /  $\alpha$ IL-6 bispecific)



**KSI-103**  
(IL-1 trap /  $\alpha$ IL-6 bispecific)



# Kodiak is gathering speed. Our position at the intersection of retinal biology, therapeutics and optics/AI is a genuine source of differentiation



## 15+ years experience

Retinal biology, disease and therapeutics development