

KSI-101: Bispecific Intravitreal Biologic Targeting IL-6 and VEGF for the Treatment of Macular Edema Secondary to Inflammation (MESI)

Results from the Phase 1b APEX Study

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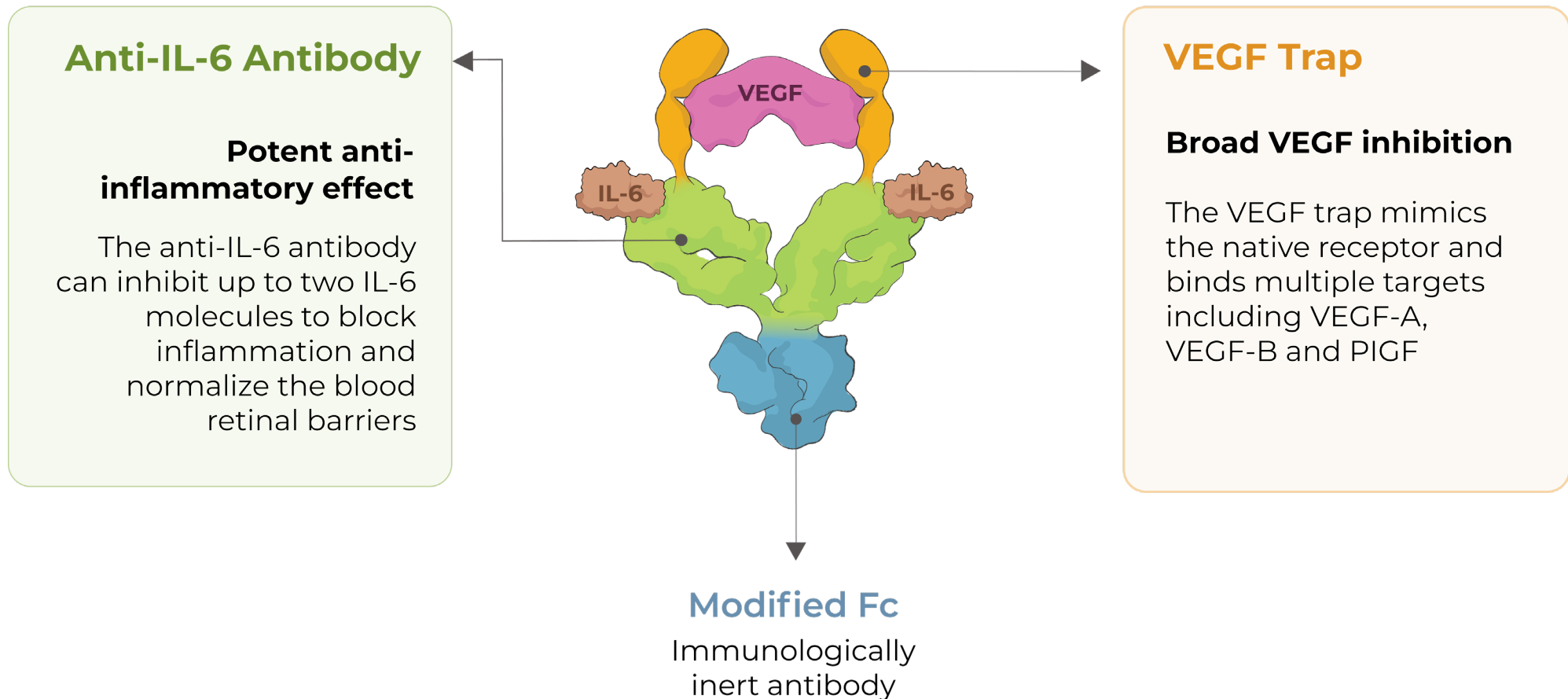
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- Consultant: Kowa, Oculis, ANI Pharmaceuticals, AstraZeneca, AbbVie, Alfasigma, Kodiak Sciences, Genentech, VivaVision.

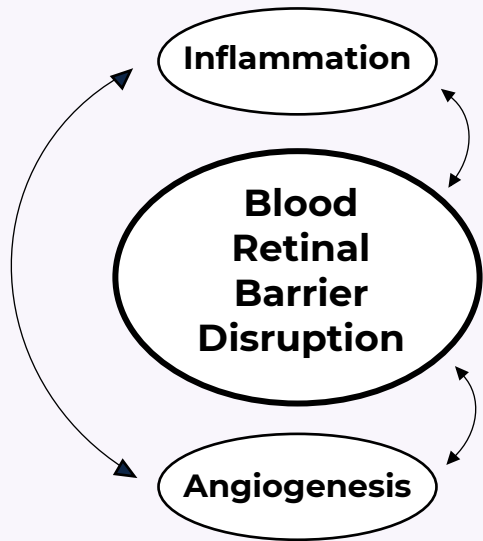
KSI-101 is a first-in-class, high-strength intravitreal biologic designed to target IL-6 mediated inflammation and VEGF-mediated vascular permeability simultaneously

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



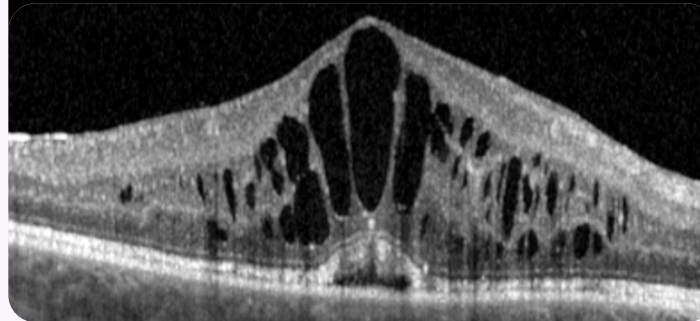
What is macular edema secondary to inflammation (MESI)?

Common Pathophysiology

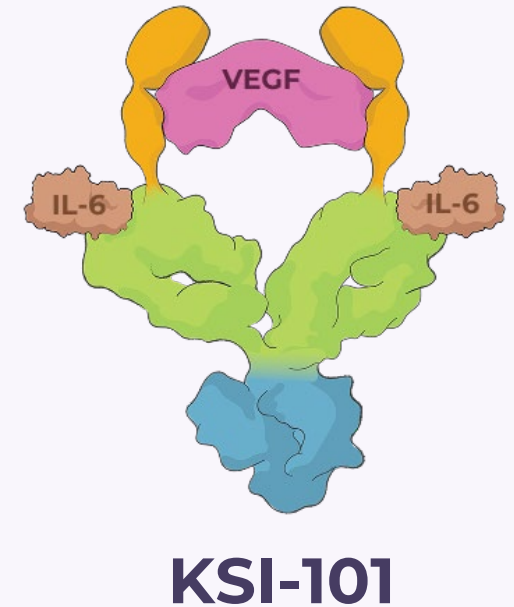


Common Clinical Presentation

Macular edema with
visual impairment

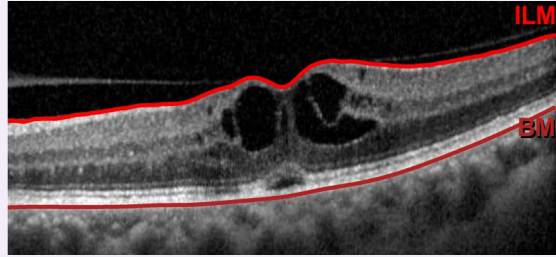


Unifying Therapy?

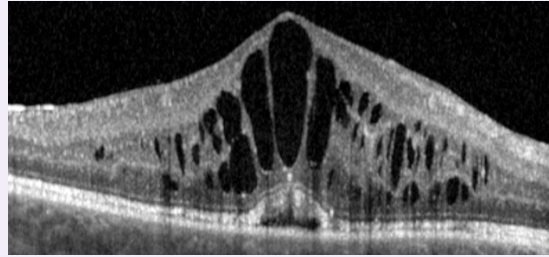


MESI is a heterogenous group of diseases that clinically present with macular edema and visual impairment, which are caused by a common pathophysiology: inflammation and blood retinal barrier disruption

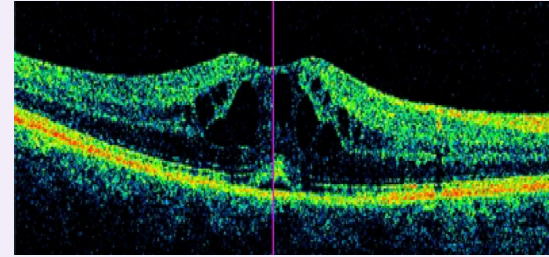
MESI comprises a heterogenous group of diseases with a common, readily identifiable clinical presentation: macular edema with visual impairment



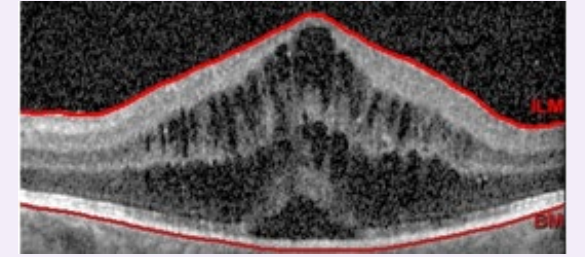
Anterior



Intermediate



Posterior



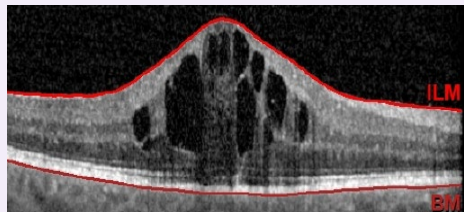
Panuveitis

Location of Inflammation

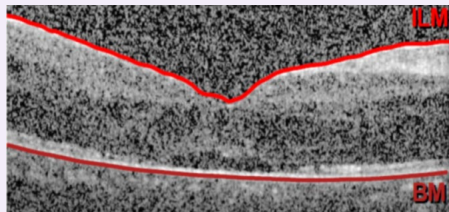
Irrespective of the anatomical location of the inflammation or the specific etiology, the clinical presentation is the same: macular edema

Specific Etiology

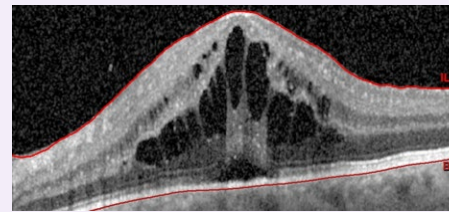
Idiopathic



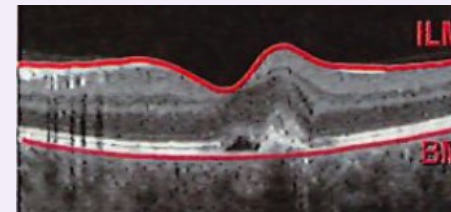
Juvenile
Idiopathic Arthritis



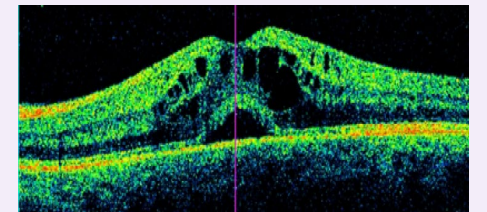
Focal Chorioretinal
inflammation



Punctate Inner
Choroidopathy

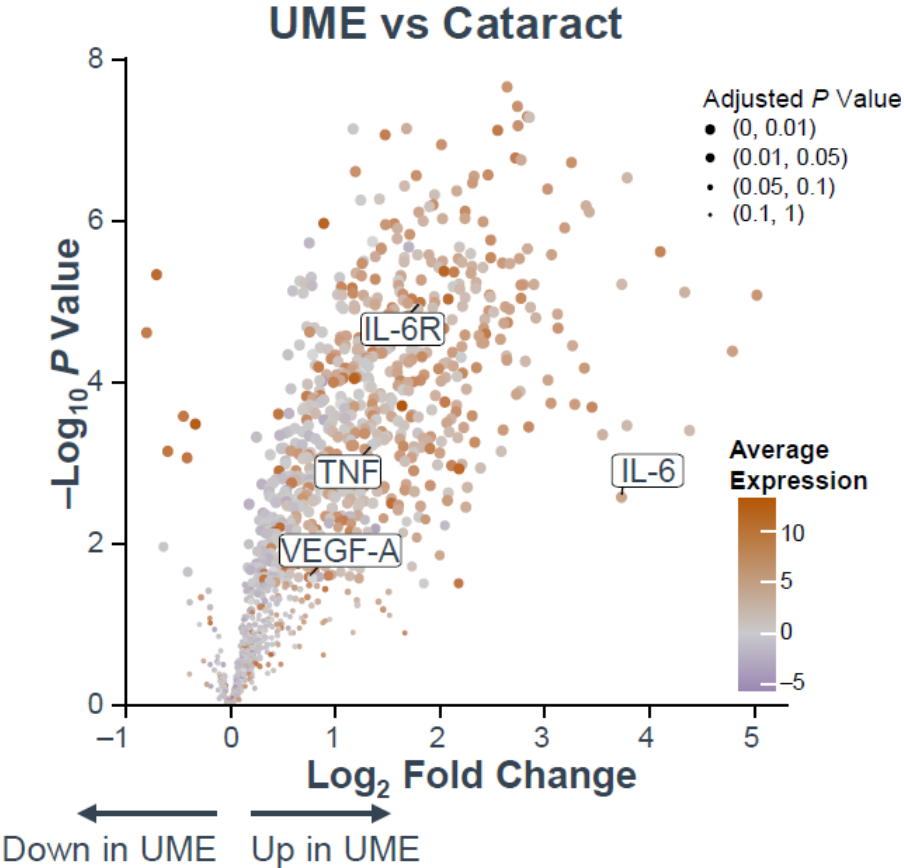


Refractive Post-Procedural
Macular Edema



In MESI, both VEGF and IL-6 are elevated and play an important role in disease pathology

- IL-6, soluble IL-6R and VEGF are significantly upregulated in UME eyes vs cataract control eyes¹
- This suggests that both IL-6 and VEGF play key roles in MESI



Protein Name	Fold Change ($\log_2$)	Fold Change	<i>P</i> Value	FDR
IL-6	3.7	14	0.0023	0.006
IL-6R	1.8	3.5	1.03E-05	9.88E-05
VEGF-A	0.75	1.7	0.026	0.043
TNF	1.4	2.6	0.0006	0.0017

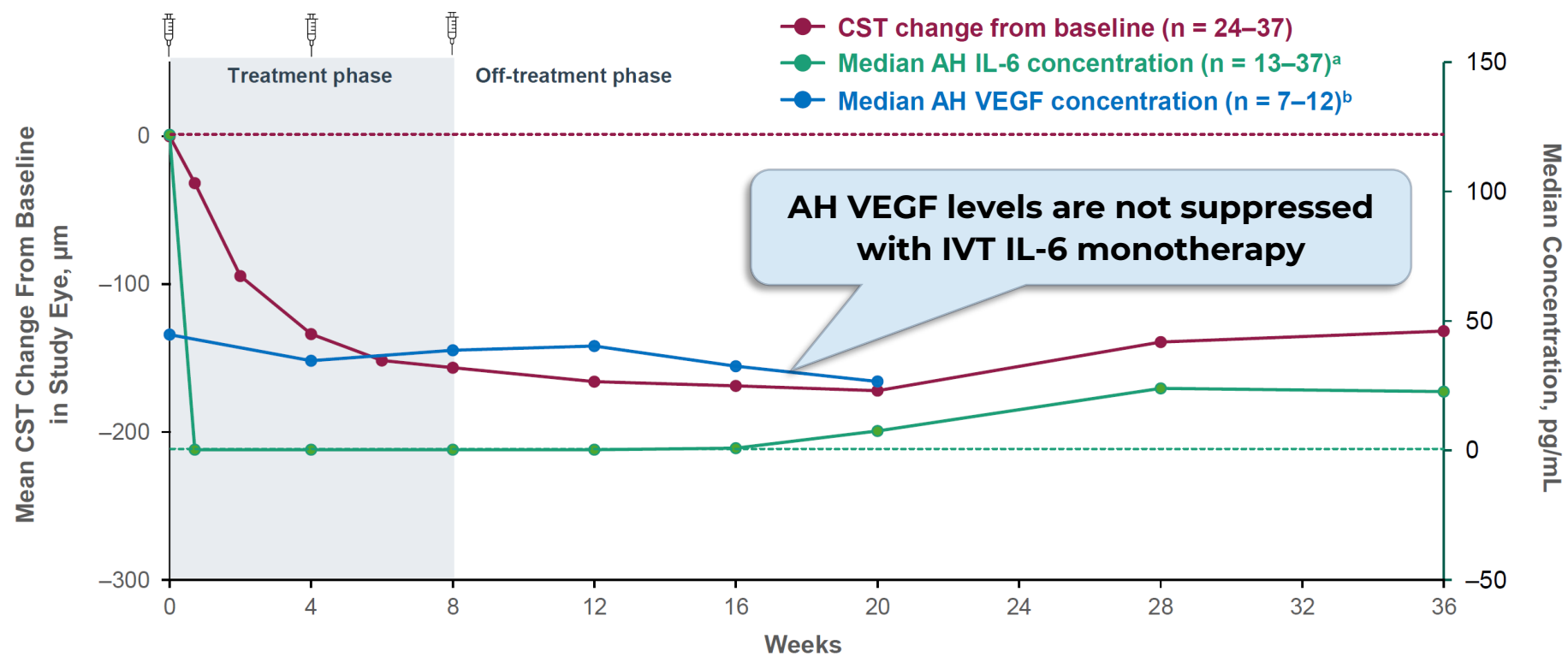
Quantitative high-sensitivity immunoassay confirmed elevated IL-6 levels in AH.

1. Zeinab B, et al. The Molecular Pathophysiology of Uveitic Macular Edema: An Exploratory Analysis from the DOVETAIL Vamikibart Phase 1 Study. Poster 3626. Presented at the Association for Research in Vision and Ophthalmology Annual Meeting, Denver, CO, May 3-7, 2026

Intravitreal anti-IL-6 monotherapy has demonstrated to be ineffective at suppressing aqueous humor VEGF levels

DOVETAIL

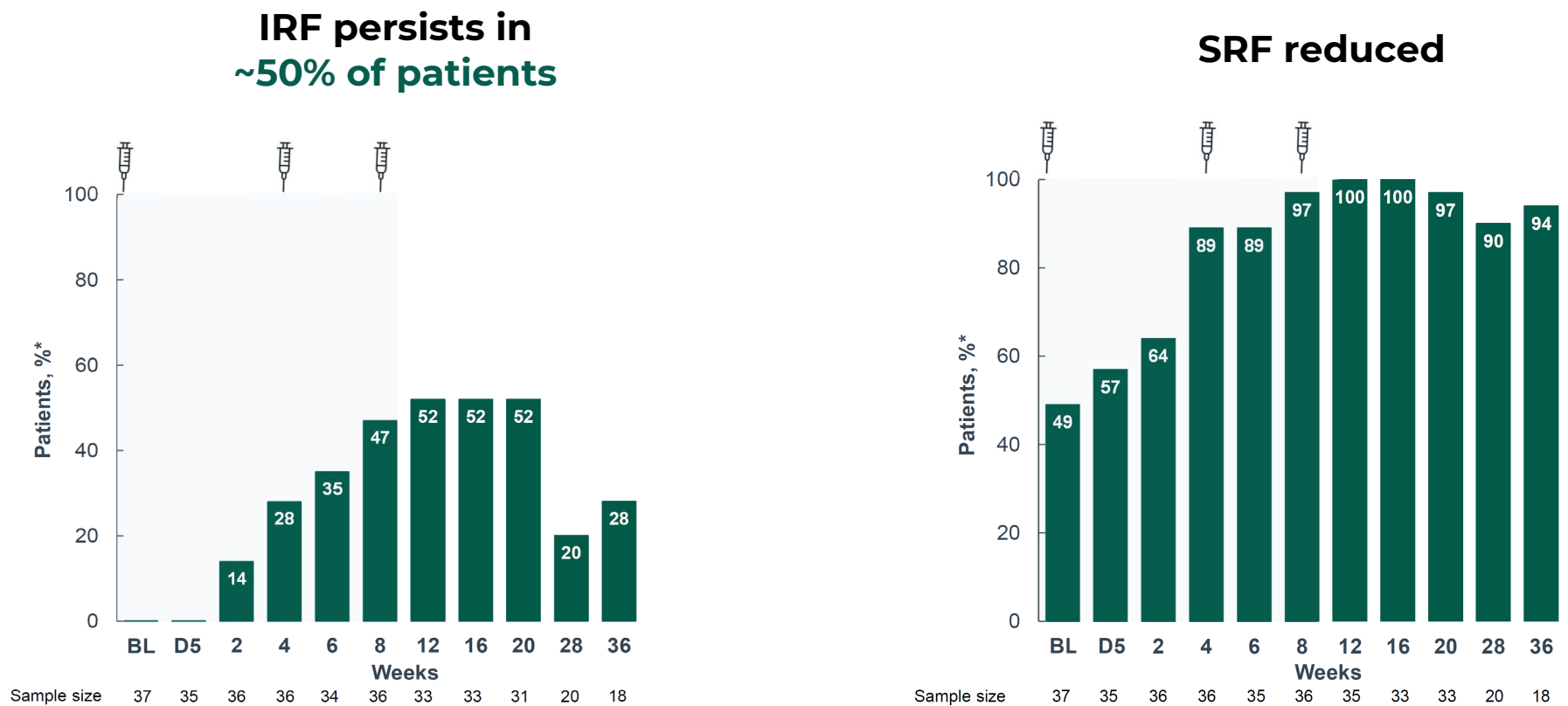
Mean change in CST and aqueous humor concentrations of VEGF and IL-6



Persistent intraocular VEGF may continue to drive vascular permeability and retinal fluid despite suppression of IL-6

Half of patients treated with intravitreal anti-IL-6 monotherapy have been shown to have persistent intraretinal fluid

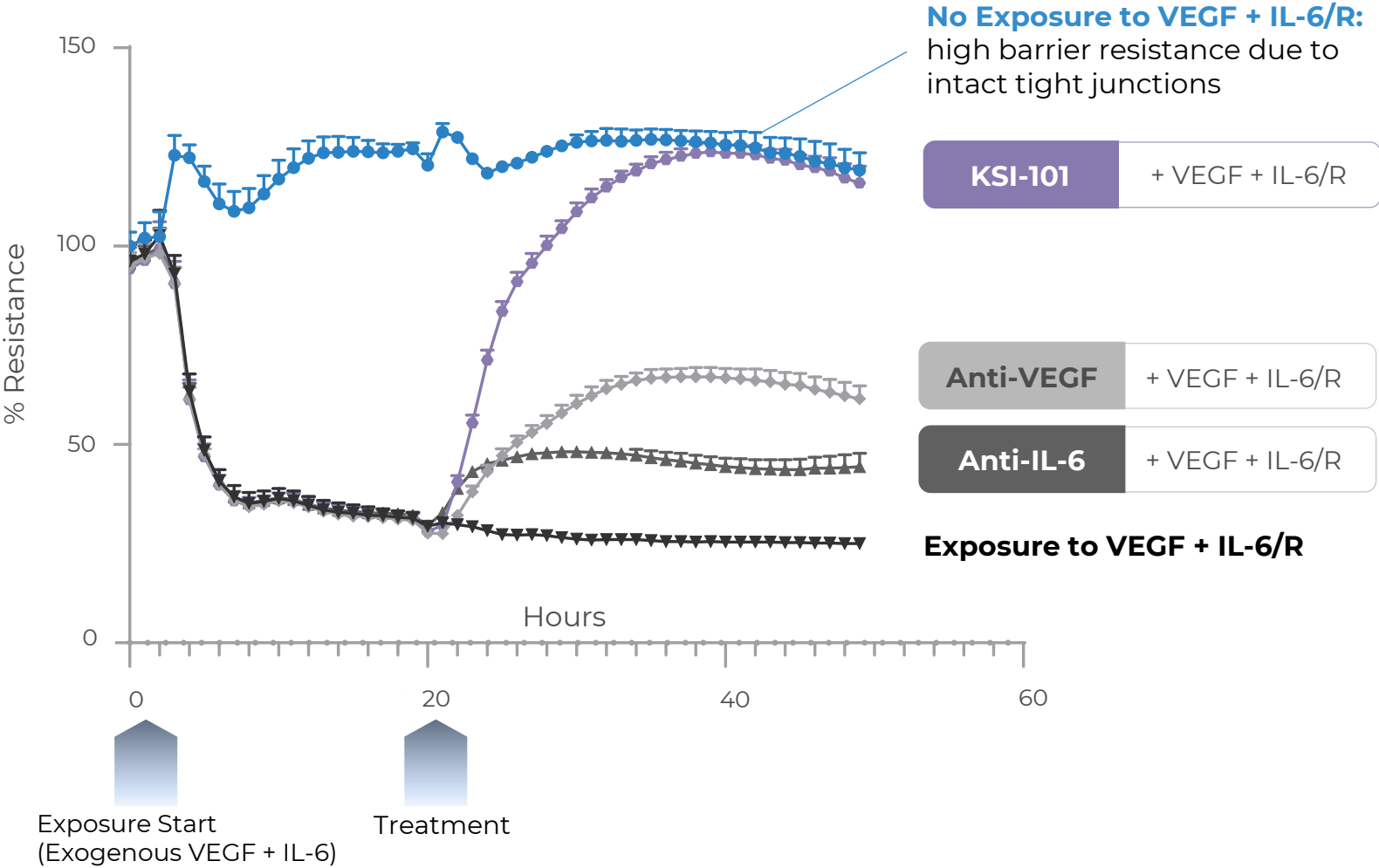
DOVETAIL



Dual inhibition of IL-6 and VEGF may provide more complete disease control in MESI than inhibition of IL-6 alone

KSI-101 inhibits both VEGF and IL-6 and 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

HUVEC cells were treated as indicated after growth to establish barrier

KSI-101 in MESI: Multiple-dose results from APEX Phase 1b study in the U.S.

Study Design: Open-label Phase 1b in MESI

Weeks	0	4	8	12	16	20	24
2.5 mg	■	■	■	■			
5 mg	■	■	■	■			
10 mg	■	■	■	■			

■ KSI-101 intravitreal injection

End of Study

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 ≥ 320 microns
- BCVA score ≤ 75 and ≥ 25 (20/32 to 20/320 Snellen equivalent)

Baseline Characteristics

	APEX U.S. (n=41)		
	KSI-101 2.5 mg (n=13)	KSI-101 5 mg (n=14)	KSI-101 10 mg (n=14)
Age, years, mean (SD)	74.2 (11.6)	67.4 (8.1)	67.5 (18.8)
Female, n (%)	8 (61.5)	7 (50.0)	8 (57.1)
Race, Asian, n (%)	0	1 (7.1%)	0
Race, White, n (%)	11 (84.6)	11 (78.6)	14 (100)
MESI disease duration, months, mean (SD)	12.2 (21.0)	1.7 (1.2)	15.8 (37.2)
Inflammation anatomical location, n (%)			
Anterior	0	2 (14.3)	0
Intermediate	1 (7.7)	0	2 (14.3)
Posterior	10 (76.9)	6 (42.9)	10 (71.4)
Panuveitis	2 (15.4)	6 (42.9)	2 (14.3)
Patients with active inflammation, n (%)	3 (23.1)	11 (78.6)	5 (35.7)
Unilateral MESI, n (%)	9 (69.2)	6 (42.9)	5 (35.7)
BCVA, ETDRS Letters, mean (SD)			
Snellen equivalent	~20/50	~20/50	~20/63
OCT CST, μm , mean (SD) (Site reported)	461.7 (137.7)	487.0 (124.1)	528.6 (157.3)
Lens Status, pseudophakic, n (%)	9 (69.2)	13 (92.9)	11 (78.6)

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

Weeks	0	4	8	12	16	20	24
2.5 mg							
5 mg							
10 mg							

KSI-101 intravitreal injection

End of Study

Key inclusion criteria

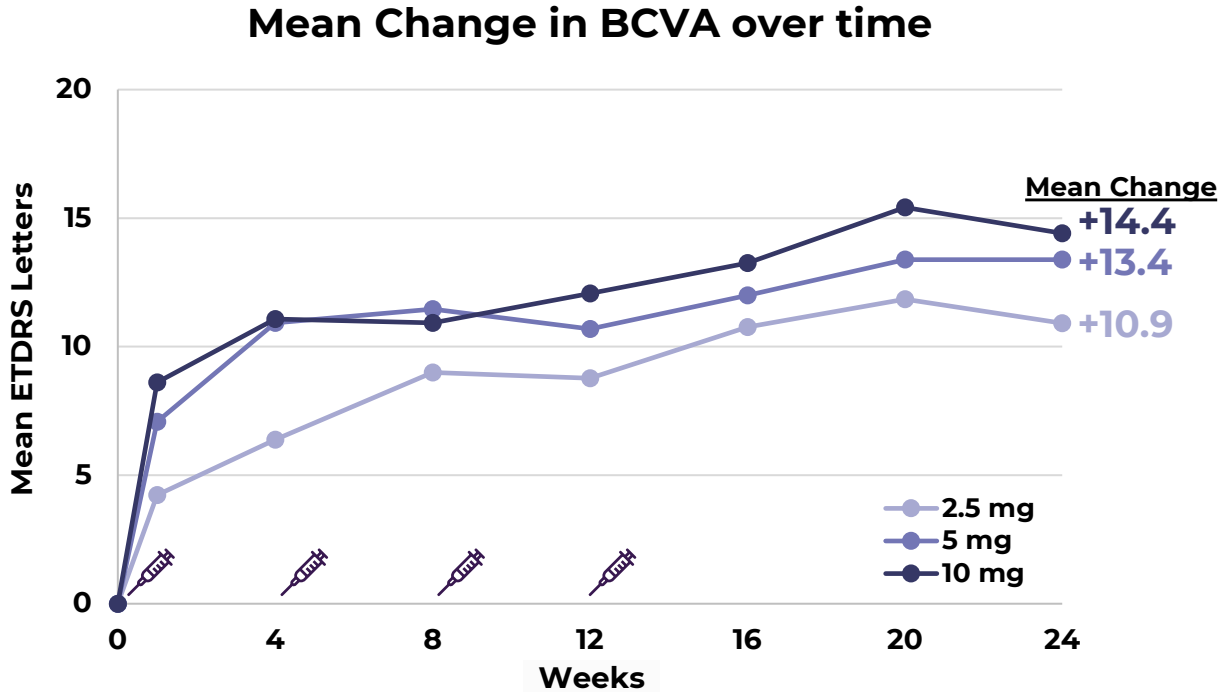
- Macular edema secondary to inflammation (MESI)
- Diagnosis of active or inactive non-infectious intraocular inflammation, acute or chronic
- Active leakage as evidenced by fluorescein angiogram
- OCT CST of ≥320 microns
- BCVA score ≤75 and ≥25 (20/32 to 20/320 Snellen equivalent)

Baseline Characteristics

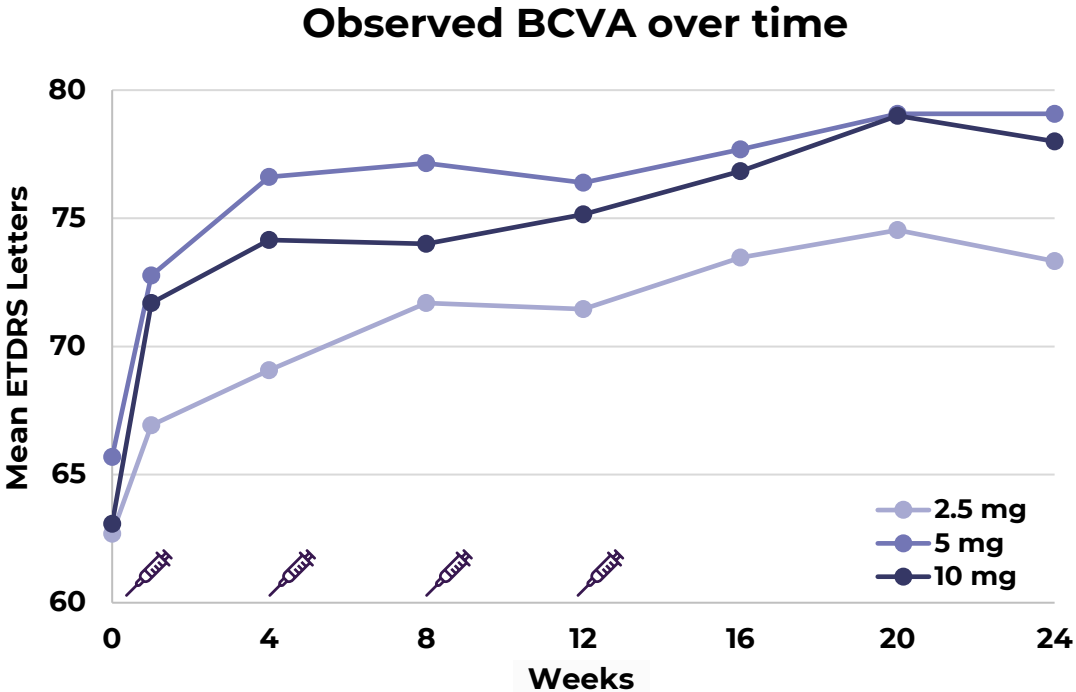
	APEX U.S. (n=41)			Asia*
	KSI-101 2.5 mg (n=13)	KSI-101 5 mg (n=14)	KSI-101 10 mg (n=14)	KSI-101 pooled (N=13)
Age, years, mean (SD)	74.2 (11.6)	67.4 (8.1)	67.5 (18.8)	49.9 (22.6)
Female, n (%)	8 (61.5)	7 (50.0)	8 (57.1)	11 (84.6)
Race, Asian, n (%)	0	1 (7.1%)	0	13 (100)
Race, White, n (%)	11 (84.6)	11 (78.6)	14 (100)	0
MESI disease duration, months, mean (SD)	12.2 (21.0)	1.7 (1.2)	15.8 (37.2)	2.3 (1.9)
Inflammation anatomical location, n (%)				
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)
Patients with active inflammation, n (%)	3 (23.1)	11 (78.6)	5 (35.7)	12 (92.3)
Unilateral MESI, n (%)	9 (69.2)	6 (42.9)	5 (35.7)	4 (30.8)
BCVA, ETDRS Letters, mean (SD)	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
OCT CST, μm, mean (SD) (Site reported)	461.7 (137.7)	487.0 (124.1)	528.6 (157.3)	429.8 (76.3)
Lens Status, pseudophakic, n (%)	9 (69.2)	13 (92.9)	11 (78.6)	7 (53.8)

*Pharmacokinetics, tolerability and clinical activity of KSI-101 was evaluated in a clinical cohort of Asian patients at tertiary uveitis centers in Taiwan

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



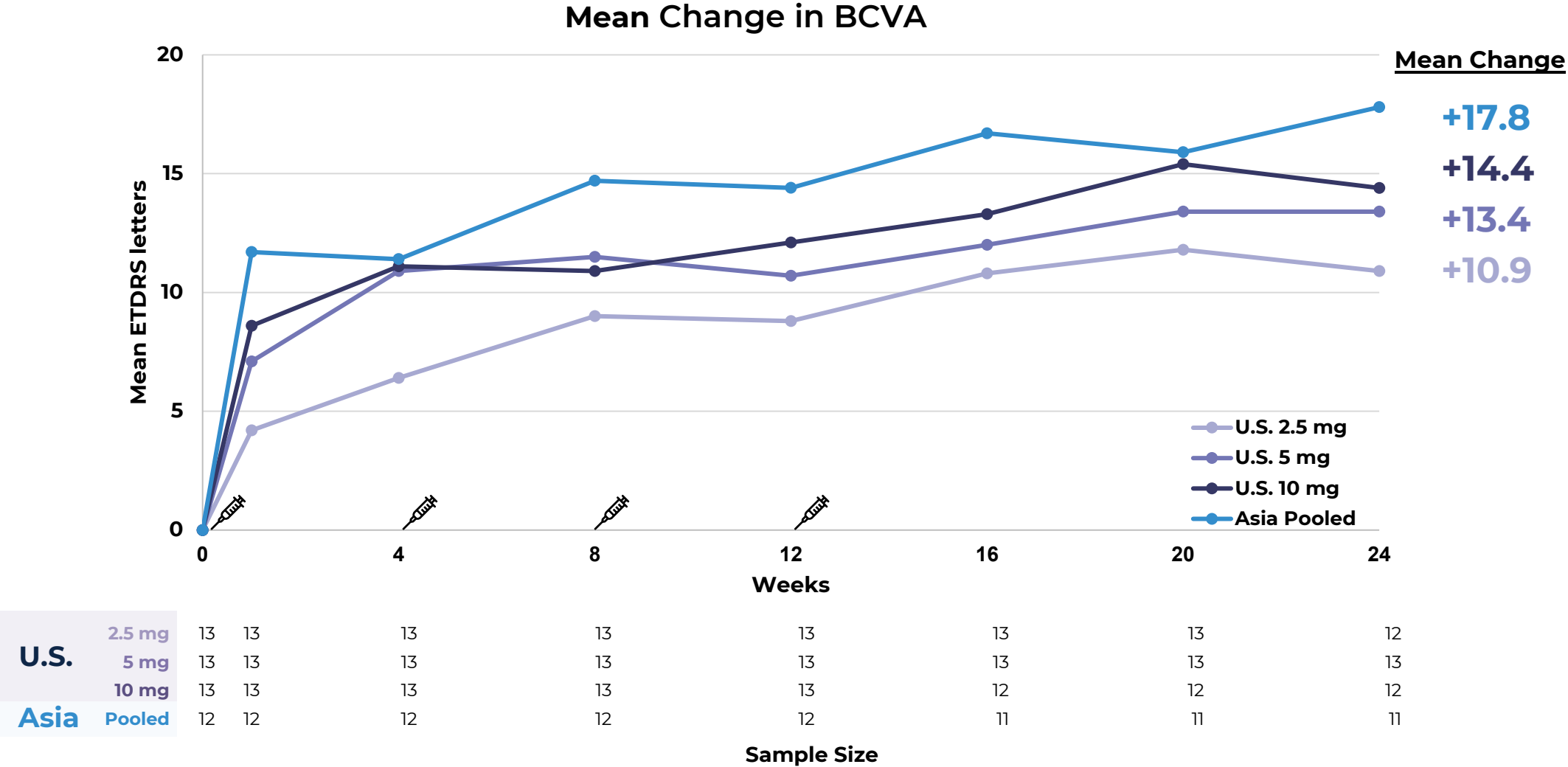
Dose Level	2.5 mg	13	13	13	13	13	13	12
	5 mg	13	13	13	13	13	13	13
	10 mg	13	13	13	13	12	12	12
	Sample Size							



Dose Level	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
	Sample Size							

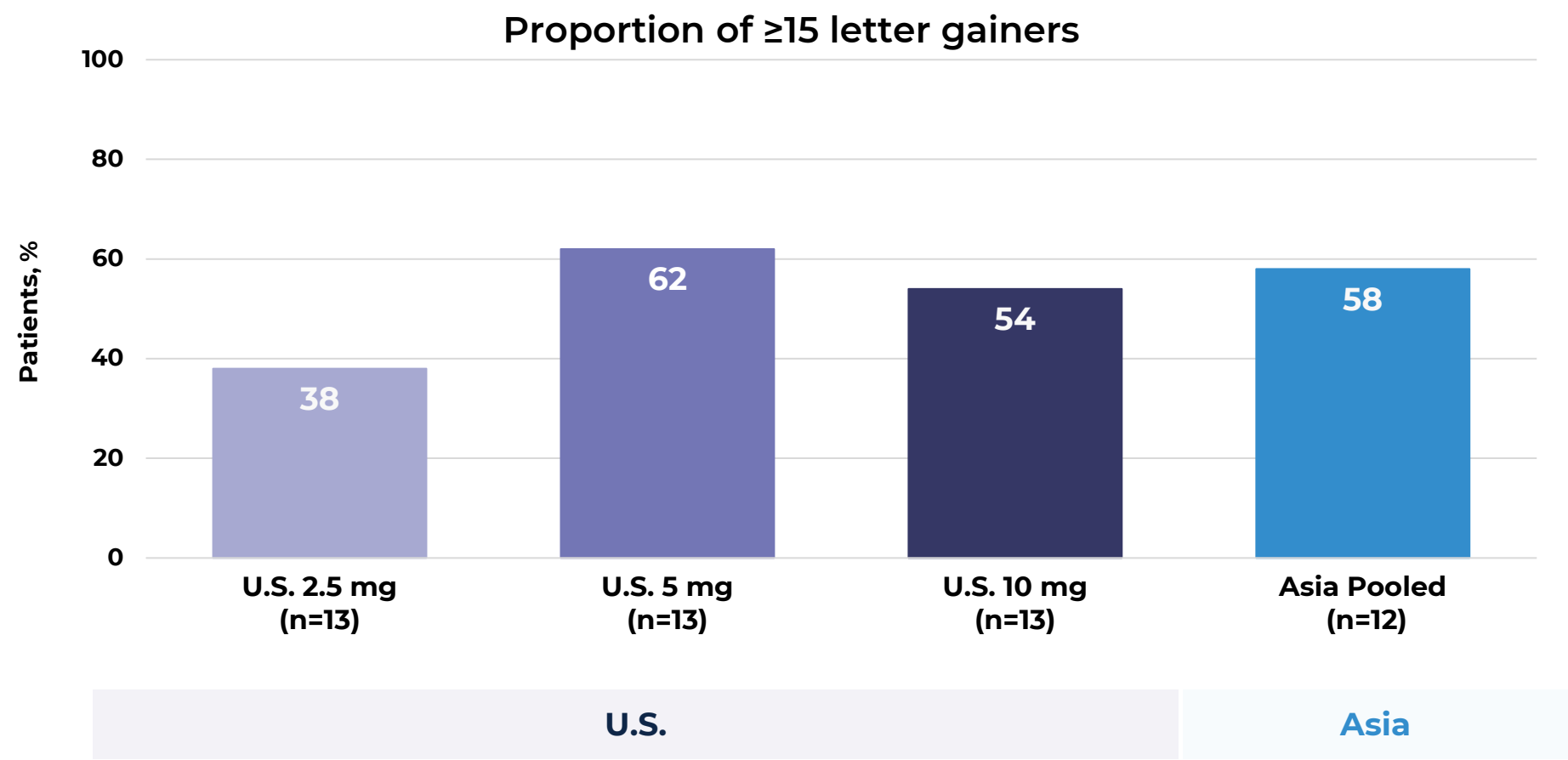
Final results of the APEX study in MESI. Includes patients in the per protocol set that completed the Week 4 visit and met all the eligibility criteria. Excludes one patient in the 5 mg dose that discontinued treatment before Week 4, and one patient in the 10 mg dose with a significant epiretinal membrane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

Meaningful vision gains of >10 letters were observed after a single injection in the tertiary care uveitis centers (Asian cohort), consistent with results from APEX U.S.



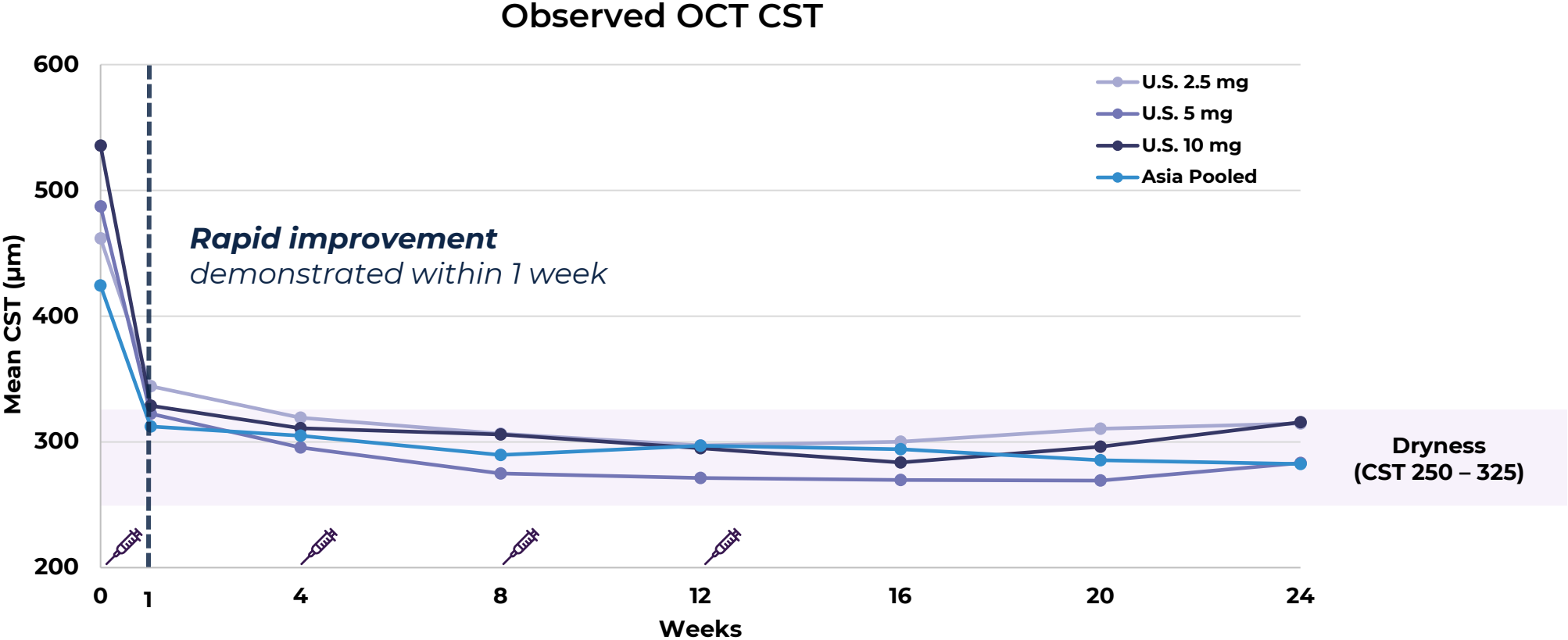
Final results of the APEX study in MESI. Includes patients in the per protocol set that completed the Week 4 visit and met all the eligibility criteria. US: Excludes one patient in the 5 mg dose that discontinued treatment before Week 4, and one patient in the 10 mg dose with a significant epiretinal 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.

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



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). Asian cohort: excludes one patient with a significant epiretinal membrane at baseline (exclusion criterion).

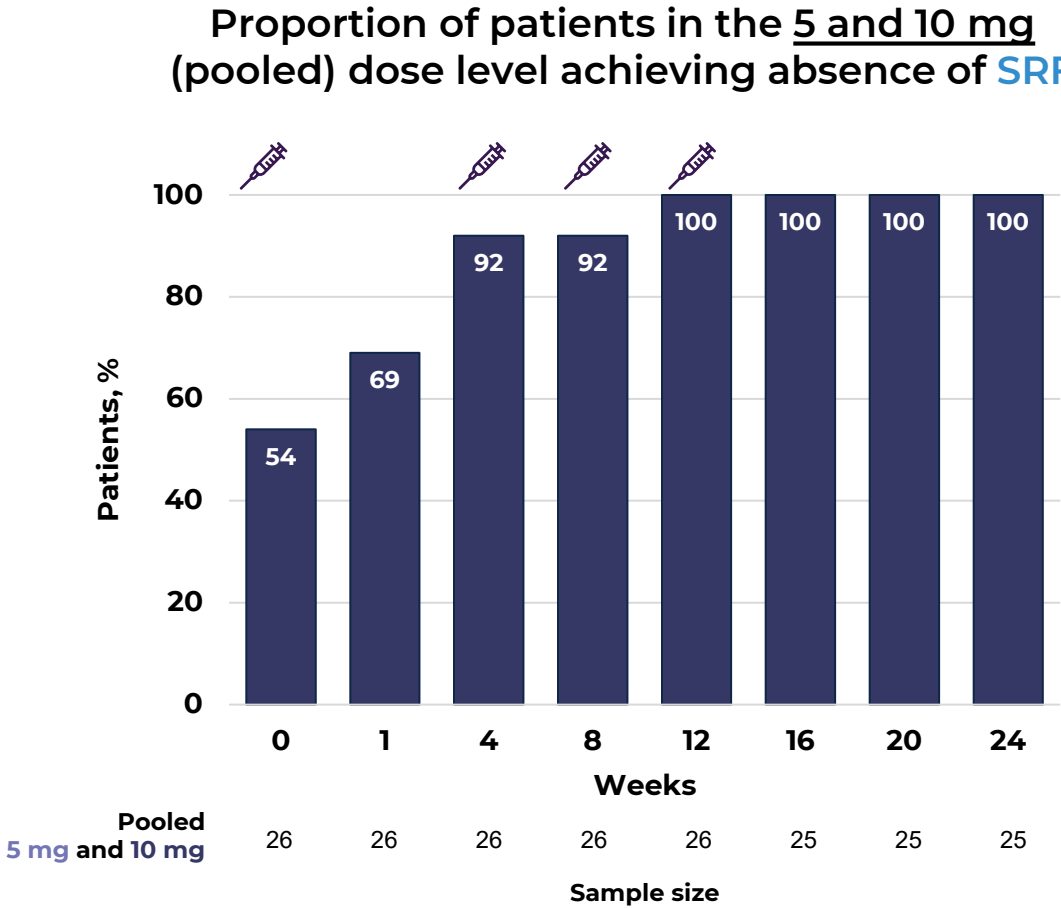
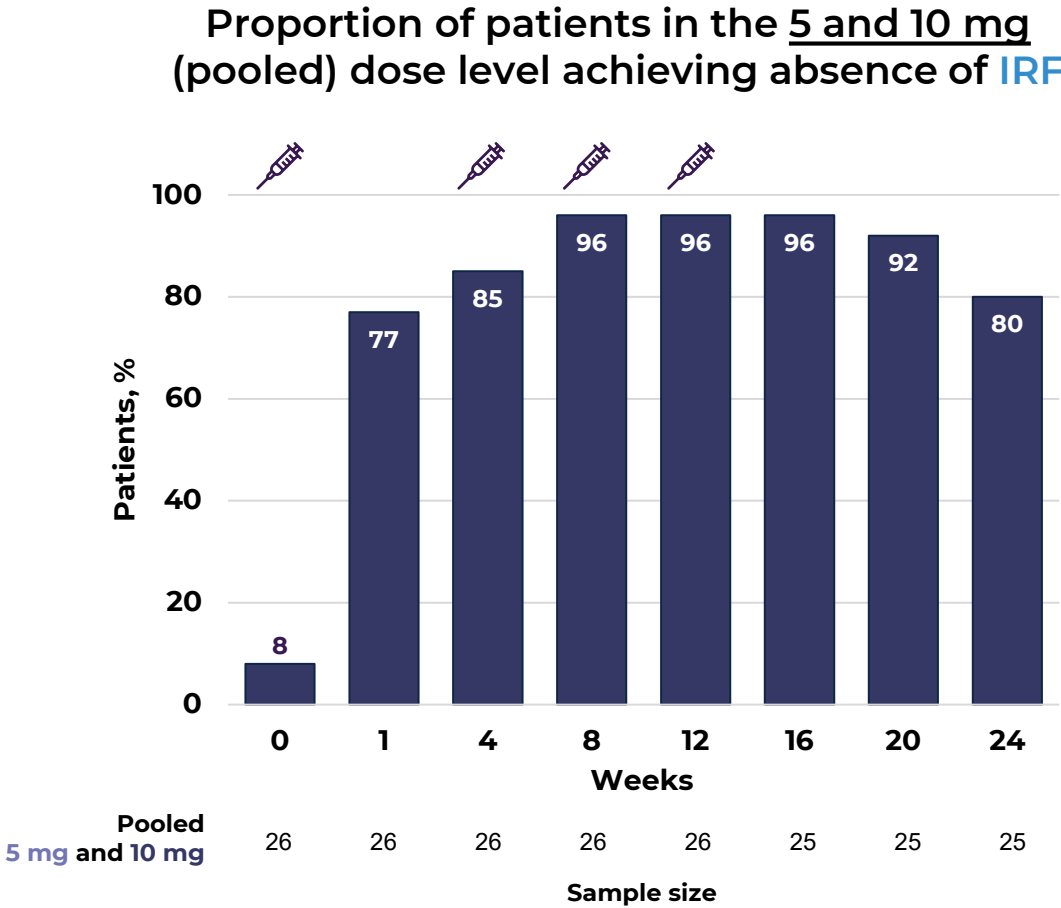
KSI-101 consistently achieved dryness (CST 250-325 μm) after a single injection, with sustained dryness observed during follow-up



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									

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. Results are site reported CST values.

≥90% of patients in the top two dose levels in APEX U.S. 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



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

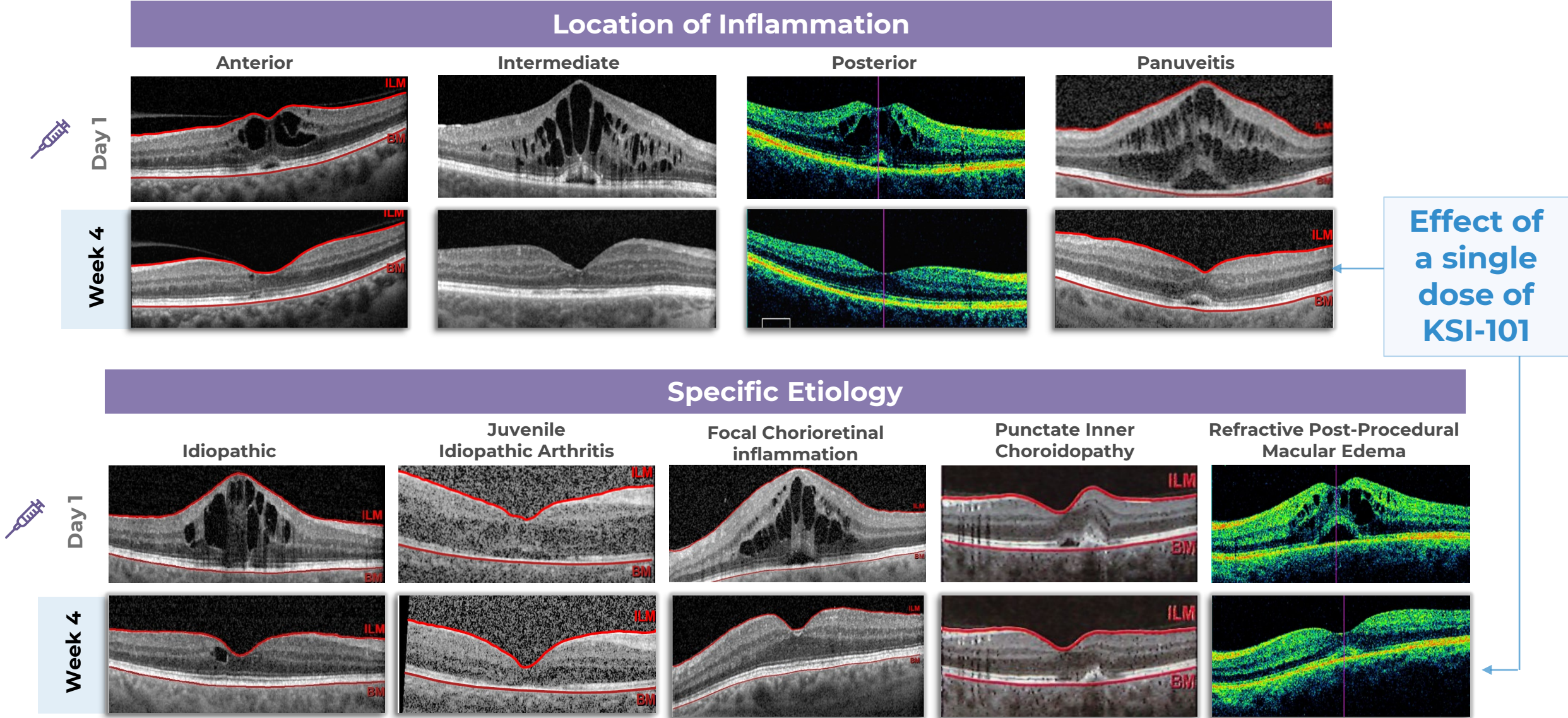
Final results from the APEX Study in MESI.

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.

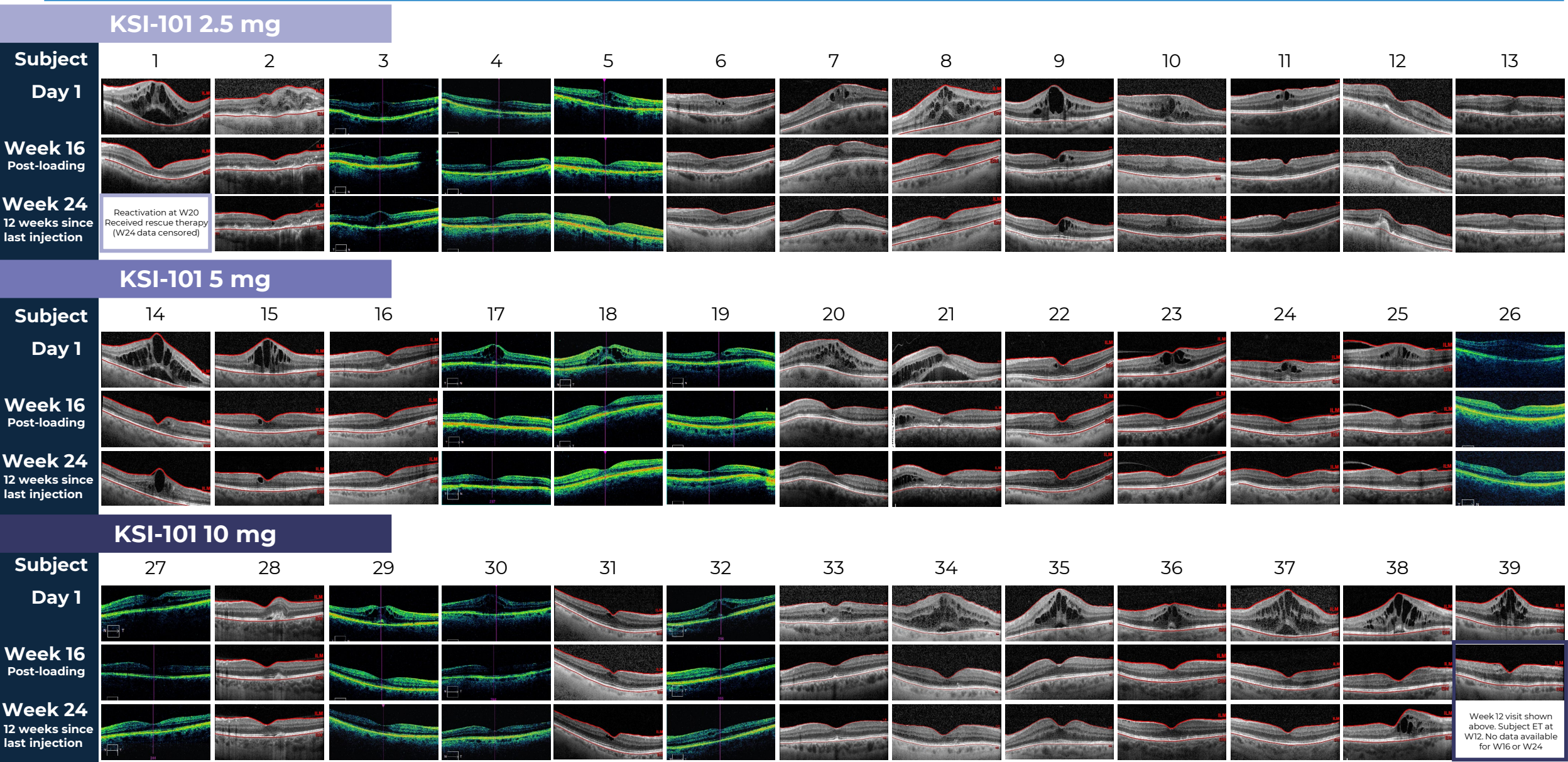
^a Same patient. Vitreous hemorrhage secondary to aqueous humor sampling at the Day 1 visit (pre-dose). The patient had 3+ AC cells and flare and 2+ vitreous haze **prior** to the Day 1 KSI-101 dose. The patient safely received all 4 doses of KSI-101 and is +26 letters in BCVA at their last visit and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

^b 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



KSI-101 achieves dryness and normalizes the retinal architecture in the majority of patients



Based on positive APEX data, the 5 mg and 10 mg dose levels have advanced into the Phase 3 PEAK and PINNACLE studies in MESI

- KSI-101 in MESI patients consistently showed robust anatomic and visual responses in the APEX study conducted in the U.S. and in the clinical cohort from tertiary uveitis centers in Asia
 - Over half of patients achieved at least a ≥ 15 letter gain
 - Dryness was achieved after a single injection with sustained dryness observed during follow-up
 - Consistent responses were observed irrespective of different underlying etiologies
- PEAK and PINNACLE Phase 3 studies in MESI are actively enrolling

	Fixed monthly dosing						Individualized dosing						
Weeks	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

Mean change in BCVA from Day 1 to the average of Week 20 and Week 24

Pivotal analysis 1
(n=300)

Primary Endpoint Readout:
4Q 2026

Pivotal analysis 2
(n=600)

Primary Endpoint Readout:
2Q 2027