Bispecific trap-antibody inhibiting interleukin-6 and vascular endothelial growth factor (KSI-101): first-time results from the Phase 1b APEX Study in patients with macular edema secondary to inflammation (MESI)

Charles C. Wykoff, M.D., Ph.D.

Deputy Chair of Ophthalmology, Blanton Eye Institute, Houston Methodist Hospital
Director of Research, Retina Consultants of Texas; Retina Consultants of America

on behalf of the APEX Study Group

Dolly Chang[1]; Allen Hu[2]; David Almeida[3]; Scott Fitzpatrick[1]; Victor Perlroth[1]; J. Pablo Velazquez-Martin[1]

[1]Kodiak Sciences, Palo Alto, United States, [2]Cumberland Valley Retina Consultants, Hagerstown, United States,
[3] Erie Retina Research, Erie, United States

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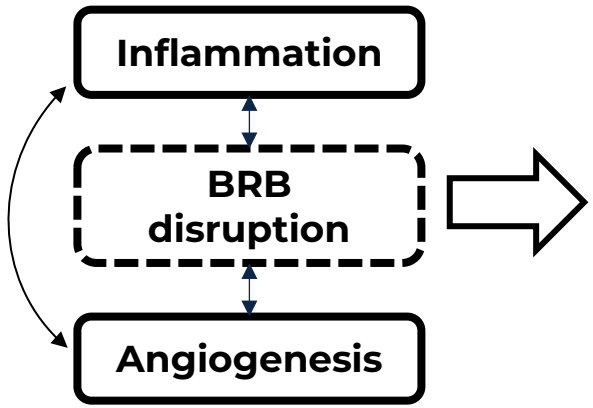
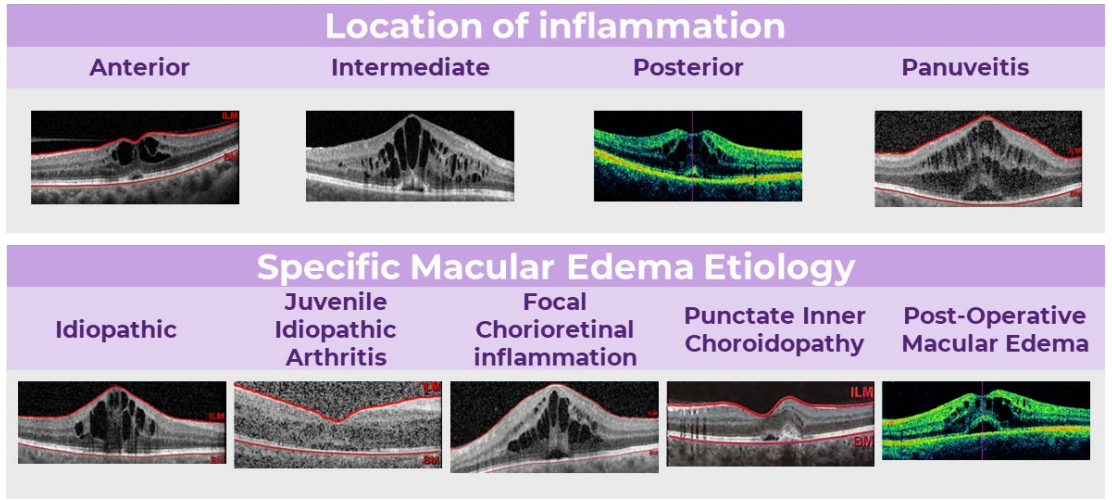
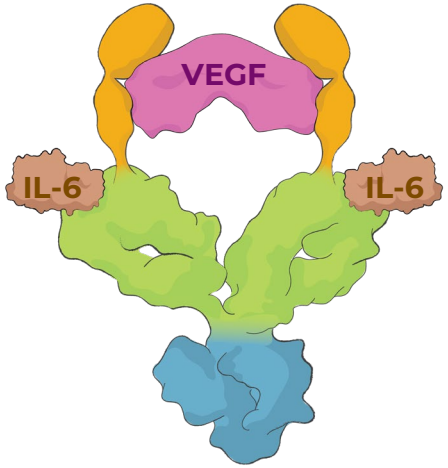
What is macular edema secondary to inflammation (MESI)?

Common Pathophysiology + **Common Clinical Presentation** = **Unifying therapy?**







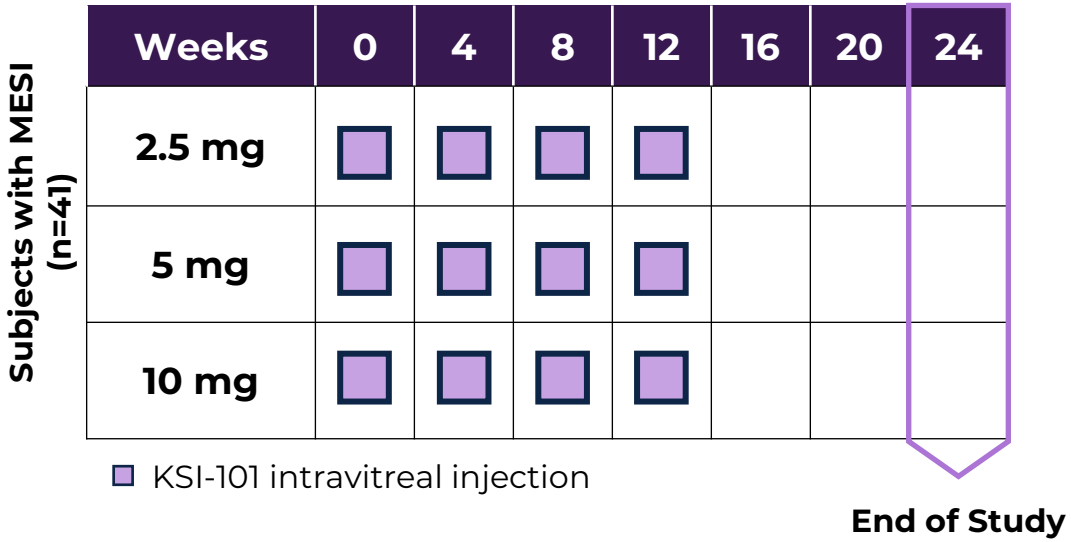
KSI-101

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**

Phase 1b APEX study: multiple dose study of KSI-101 in patients with MESI

Enrollment complete

Study Design: Ongoing, Open-label Phase 1b in MESI



Key inclusion criteria

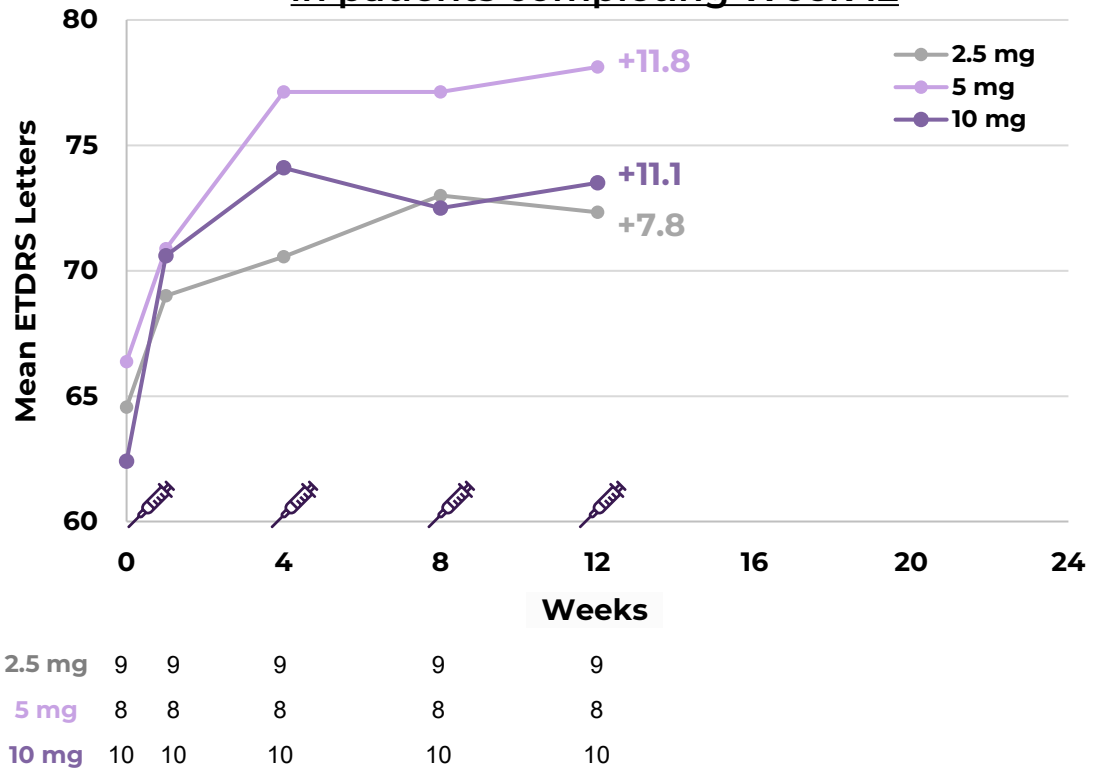
- Macular edema secondary to inflammation (MESI)
- Diagnosis of active or inactive non-infectious intraocular inflammation, acute or chronic.
- Active leakage as evidenced by fluorescein angiogram.
- OCT CST of ≥320 microns
- BCVA score ≤75 and ≥25 (20/32 to 20/320 Snellen equivalent)

Baseline Characteristics

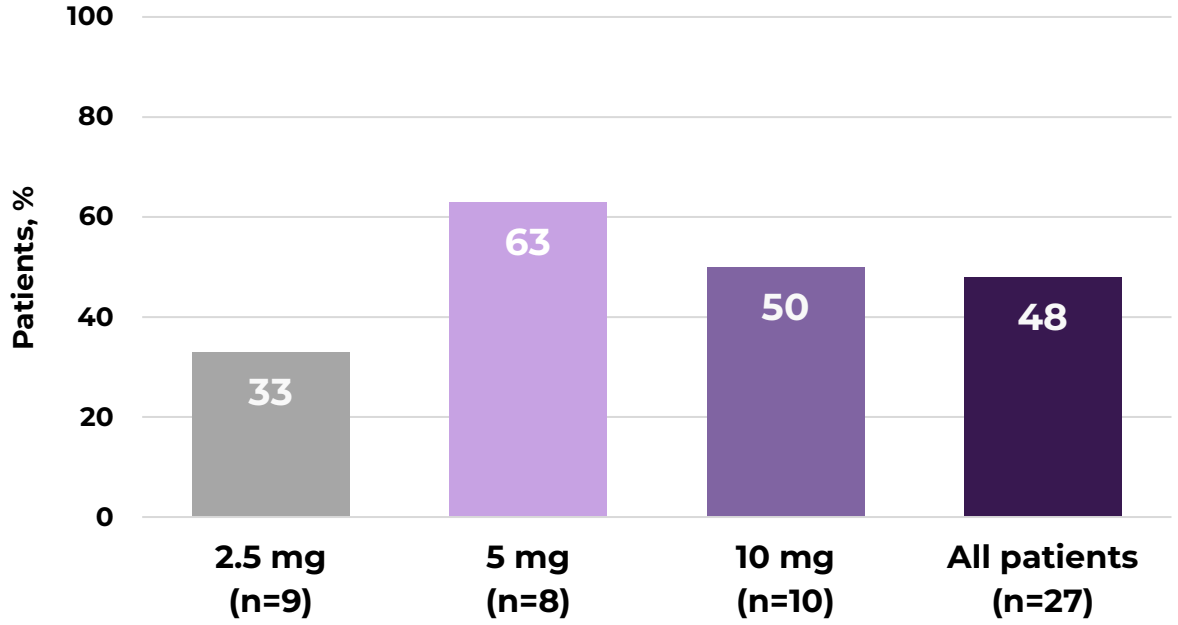
	KSI-101 2.5 mg (n=13)	KSI-101 5 mg (n=14)	KSI-101 10 mg (n=14)	All KSI-101 (N=41)
Age, years, mean (SD)	74.2 (11.6)	67.4 (8.1)	67.5 (18.8)	69.6 (13.7)
Female, n (%)	8 (61.5)	7 (50.0)	8 (57.1)	23 (56.1)
Race, White, n (%)	11 (84.6)	11 (78.6)	14 (100)	36 (87.8)
MESI disease duration, months, mean (SD)	12.2 (20.1)	1.7 (1.2)	15.8 (37.2)	11.1 (26.5)
Inflammation anatomical location, n (%)				
Anterior	0	2 (14.3)	0	2 (4.9)
Intermediate	1 (7.7)	0	2 (14.3)	3 (7.3)
Posterior	10 (76.9)	6 (42.9)	10 (71.4)	26 (63.4)
Panuveitis	2 (15.4)	6 (42.9)	2 (14.3)	10 (24.4)
Patients with active inflammation, n (%)	3 (23.1)	10 (71.4)	5 (35.7)	18 (43.9)
Unilateral MESI, n (%)	9 (69.2)	6 (42.9)	5 (35.7)	20 (48.8)
BCVA, ETDRS Letters, mean (SD)	62.7 (7.4)	65.5 (7.8)	62.1 (8.4)	63.5 (7.8)
Snellen equivalent	~20/50	~20/50	~20/63	~20/50
OCT CST, µm, mean (SD)	461.7 (137.7)	487.0 (124.1)	528.6 (157.3)	493.2 (139.7)
Lens Status, pseudophakic, n (%)	9 (69.2)	13 (92.9)	11 (78.6)	33 (80.5)

APEX KSI-101 in MESI – Meaningful vision gains are rapidly achieved as early as Week 4 and ≥half of patients in the top two dose levels achieved a ≥15 letter gain

Observed BCVA over time in patients completing Week 12



Proportion of ≥15 letter gainers in patients completing Week 12

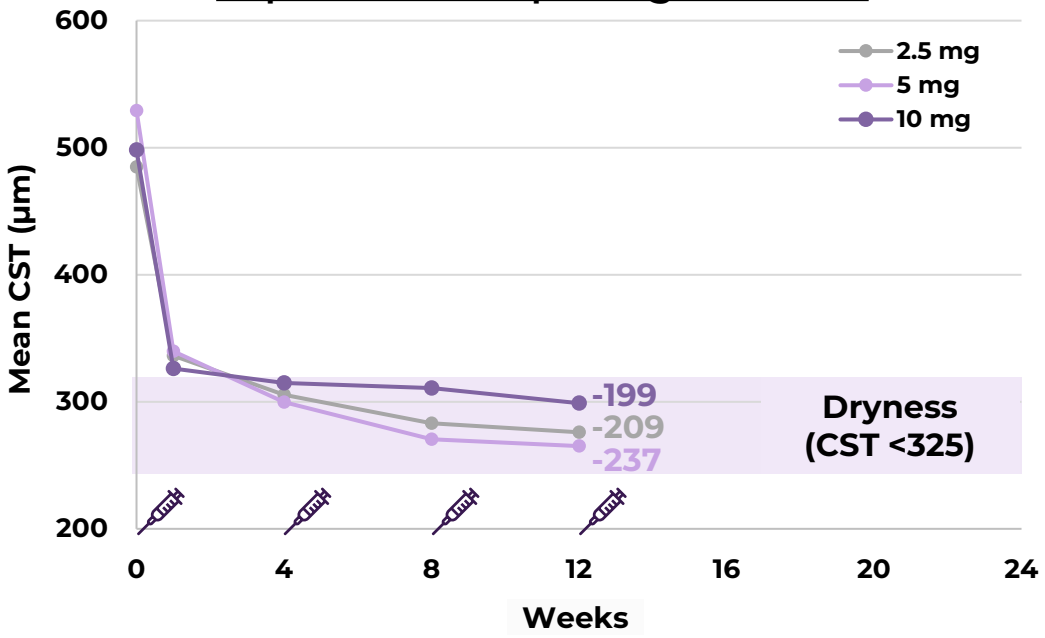


Preliminary analysis: all patients who completed Week 12 as of July 14, 2025. Includes 27 of 41 enrolled patients

Preliminary results. As the APEX study is ongoing, final results may be different due to additional data collection or data cleaning. Includes only patients in the per protocol set that completed the Week 12 visit by the cutoff date of 14-Jul-25 and meet all the eligibility criteria. Excludes one patient in the 10 mg dose with a significant epiretinal membrane at baseline (exclusion criterion)

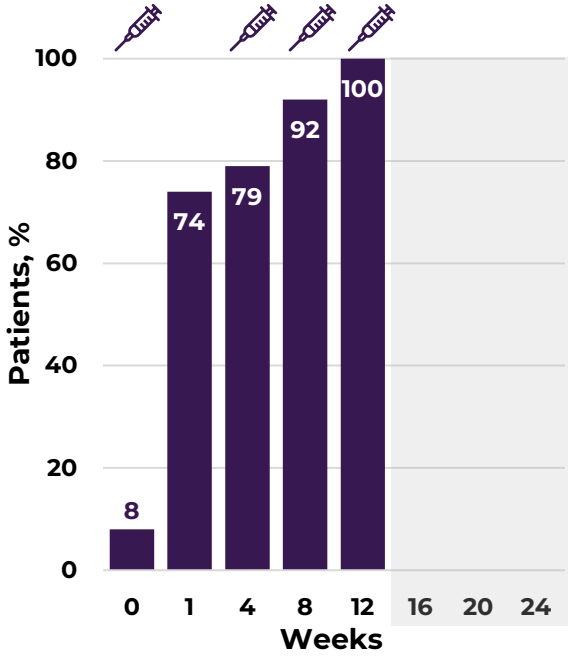
APEX KSI-101 in MESI – A single dose of KSI-101 results in the majority of patients achieving dryness. Over 90% of patients achieve dryness by Week 8

Observed OCT CST over time in patients completing Week 12[a]



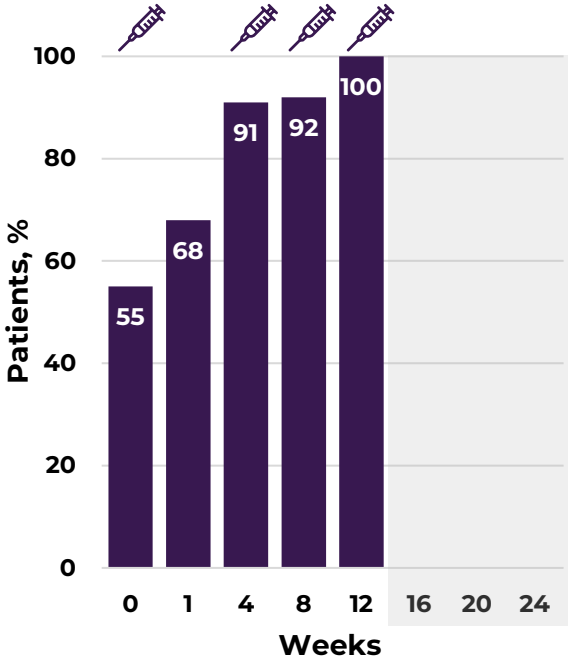
N values	0	4	8	12
2.5 mg	9	9	9	9
5 mg	8	8	8	8
10 mg	10	10	10	10

Proportion of patients achieving absence of IRF[b]



N values Pooled KSI-101	0	1	4	8	12
	38	38	33	25	21

Proportion of patients achieving absence of SRF[b]



N values Pooled KSI-101	0	1	4	8	12
	38	38	33	25	21

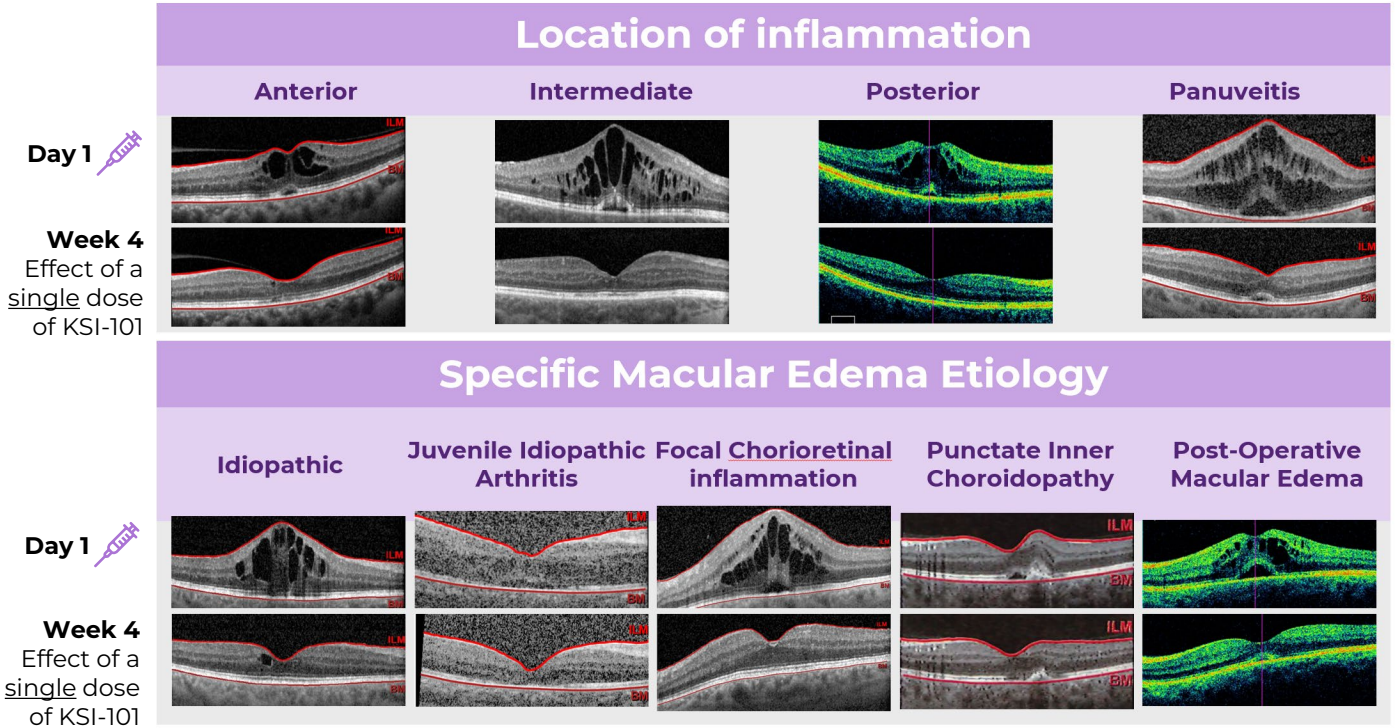
Preliminary results. As the APEX study is ongoing, final results may be different due to additional data collection or data cleaning.

[a] Includes only patients in the per protocol set that completed the Week 12 visit by the cutoff date of 14-Jul-25 and meet all the eligibility criteria. Excludes one patient in the 10 mg dose with a significant epiretinal membrane at baseline (exclusion criterion)

[b] Includes only patients in the per protocol set that meet all the eligibility criteria. Excludes one patient in the 10 mg dose with a significant epiretinal membrane at baseline (exclusion criterion). Includes all data available by the 14-Jul-25 reporting date.

APEX KSI-101 in MESI – KSI-101 was well-tolerated. Rapid and meaningful responses were achieved even after a single dose

	KSI-101 2.5 mg (n=13)	KSI-101 5 mg (n=14)	KSI-101 10 mg (n=14)	All KSI-101 (N=41)
Summary of AEs in the Study eye, n (%)				
Subjects with ≥1 AEs	1 (7.7)[a]	2 (14.3)	2 (14.3)	5 (12.2)
Treatment-related AEs	1 (7.7)[a]	1 (7.1)[b]	0	2 (4.9)
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	1 (2.4)
Selected AEs in the Study Eye, n (%)				
Intraocular inflammation (recurrent uveitis flare-up)	1 (7.7)[a]	1 (7.1)[b]	0	2 (4.9)
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	1 (2.4)
Vitreous hemorrhage	1 (7.7)[a]	0	0	1 (2.4)

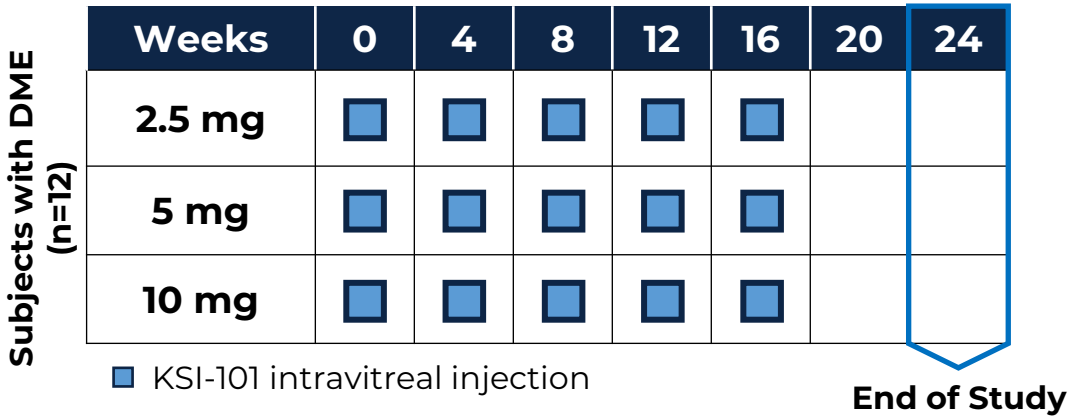


After a **single dose of KSI-101**, rapid and meaningful responses in MESI patients are observed **irrespective of the location of inflammation or the specific macular edema etiology**

Preliminary results. As the APEX study is ongoing, final results may be different due to additional data collection or data cleaning.
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 has safely received all 4 doses of KSI-101 and is +24 letters in BCVA at their last visit and no intraocular inflammation
[b] Same patient. Uveitis flare-up consistent with underlying disease

APEX KSI-101 in DME – Meaningful visual and anatomical gains were achieved with KSI-101, with additional benefits with continued dosing. KSI-101 was well-tolerated

Study Design: Ongoing, Open-label Phase 1b in treatment-naïve DME

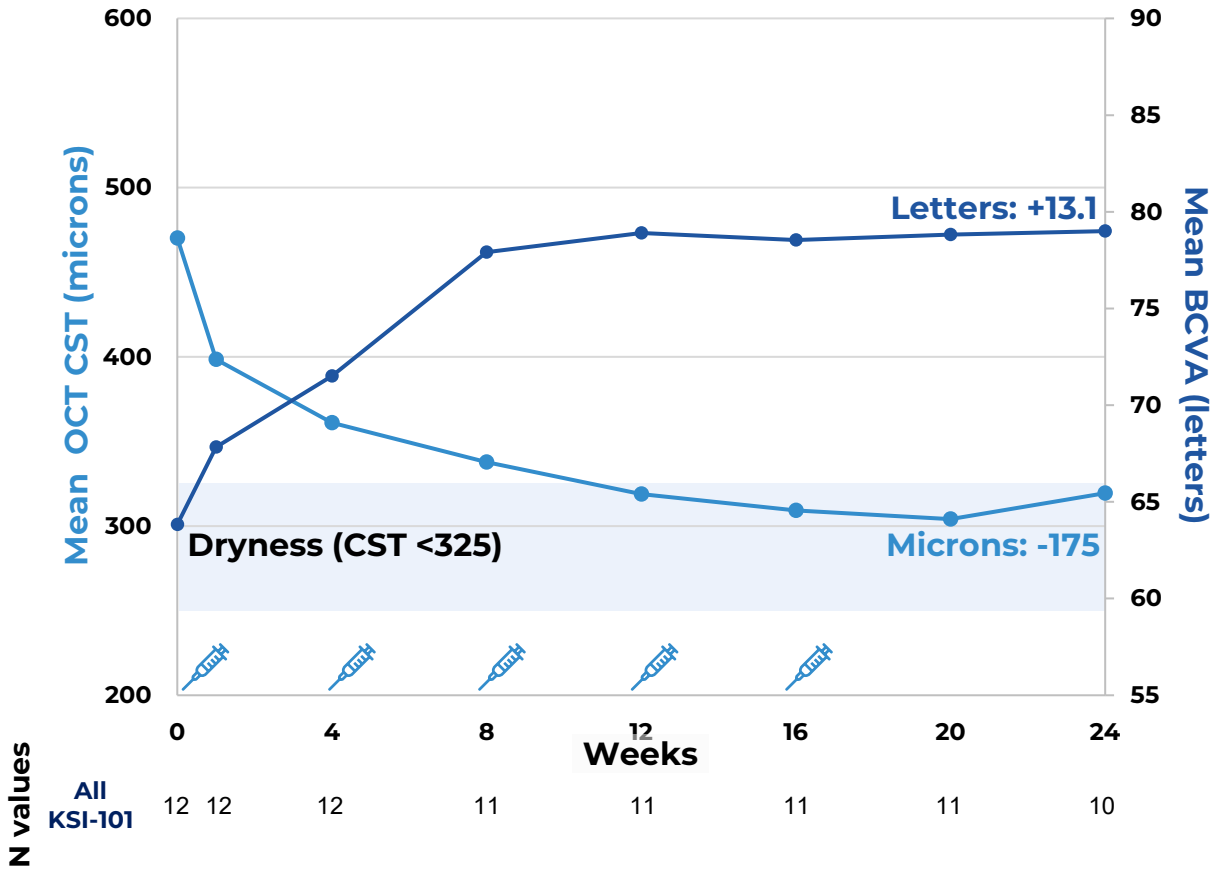


Safety

	All KSI-101 (N=12)
Summary of AEs in the Study eye, n (%)	
Subjects with ≥1 AEs	1 (8.3)
Treatment-related AEs	0
Serious AEs	0
Treatment-related serious AEs	0
Severe AEs	0
AEs leading to study discontinuation	0
AEs in the Study Eye, n (%)	
Intraocular inflammation	0
Occlusive retinal vasculitis	0
Cataract	0
Cataract traumatic*	1 (8.3)

Mean Change in BCVA and OCT CST in DME

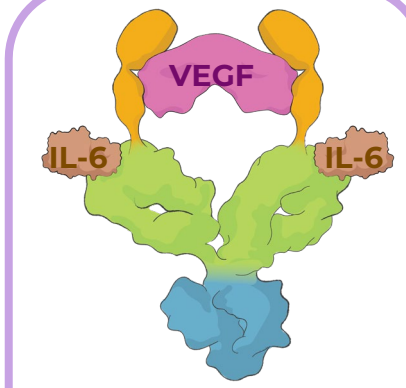
<u>All KSI-101 dose levels combined</u>



Preliminary results. As the APEX study is ongoing, final results may be different due to additional data collection or data cleaning. Includes all available data by the 14-Jul-25 cutoff date.
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.
* Anterior traumatic cataract due to aqueous humor routine sample

Conclusions: KSI-101 demonstrated meaningful visual and anatomical improvements in patients with MESI in the APEX Study

- **MESI:** group of diseases with a shared pathophysiology — inflammation & BRB disruption
- **Treatment with KSI-101 in MESI patients in APEX, preliminary analysis:**
  - **Robust anatomic and visual responses to date**
    - Half of patients achieved a ≥15 letter gain.
    - >90% resolution of both IRF & SRF by Week 8
    - Consistent response with different underlying etiologies
- **Two Phase 3 trials of KSI-101 in MESI actively enrolling**



KSI-101

	Fixed monthly dosing						Individualized dosing						
Weeks	**D1**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**	**40**	**44**	**48**
KSI-101 5 mg (n~50)													
KSI-101 10 mg (n~50)													
Sham (n~50)													

Primary endpoint

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

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 ≤78 and ≥25 (~20/25 to 20/320 Snellen)

PEAK

Moderate to severe edema with moderate to severe vision impairment

PINNACLE

Moderate to severe edema with good vision

Mild edema with any vision impairment

PEAK and PINNACLE are actively enrolling

PEAK: NCT06990399. PINNACLE: NCT06996080