Novel Anti-VEGF Antibody Biopolymer Conjugate KSI-301 with Potential for Extended Durability in Retinal Vascular Diseases

Late-Breaking Results from a Phase 1b Study in Patients with wAMD, DME and RVO

David M. Brown, MD, FACS
Retina Consultants of Houston
Houston, TX

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Relevant Financial Disclosures

- Alcon/Novartis (RG,C)
- Allergan (RG,E,C)
- Genentech/Hoffmann-La Roche (RG,C)
- Graybug Vision (RG,C)
- Kanghong Pharma (RG,C)
- Kodiak Sciences (RG,C)
- Regeneron/Bayer (RG,C)
- Samsung Bioepsis (RG,C)

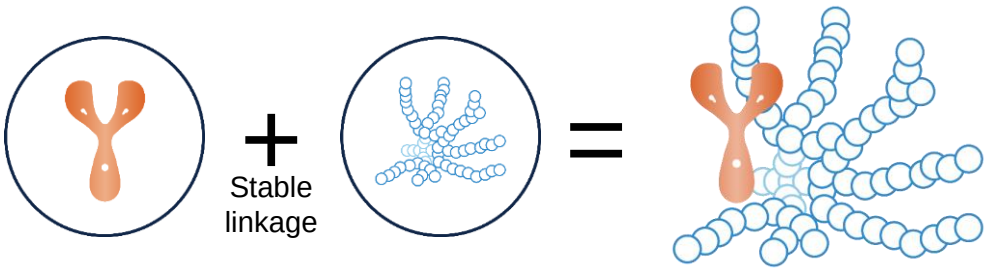
RG- Research Grant to Institution E= Equity/ Options C: Consultant / Scientific Advisory Board

Key Points

- ABCs (Antibody Biopolymer Conjugates): a new scientific approach and design platform for intravitreal drugs
- KSI-301 (Kodiak Sciences) initial data: early efficacy and safety in major retinal vascular diseases
- Emerging wAMD durability data from Phase 1b support Phase 2 study design with q12-week or longer dosing

ABCs are a new scientific design platform for extended durability intravitreal therapeutics

ABC PLATFORM



ANTIBODY

IgG1 with inert immune effector function

BIOPOLYMER

Optically clear, high molecular weight phosphorylcholine polymer

CONJUGATE

Antibody and biopolymer covalently bound via single site-specific linkage

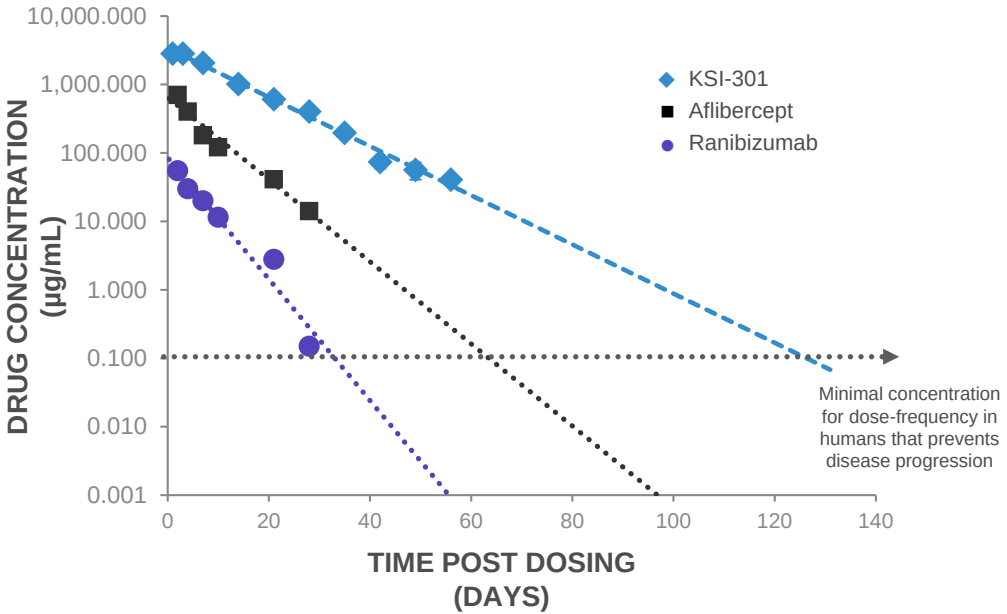
CHARACTERISTICS OF KSI-301

Molecular weight	**950 kDa**
Clinical dose	**5 mg** (by weight of antibody)
Equivalent molar dose (compared to ranibizumab)	**7x**
Equivalent ocular PK (compared to ranibizumab)	**4x**

KSI-301 is an anti-VEGF ABC

ABCs have improved ocular PK plus other unique features due to the phosphorylcholine biopolymer

ABC ANTI-VEGF PK CURVE[1]



SPECIAL FEATURES OF ABCs DUE TO PHOSPHORYLCHOLINE BIOPOLYMER[2]

- **Better tissue bioavailability**
  ~8x greater than aflibercept
- **Better stability**
- **More complete VEGF inhibition**
- **Excellent biocompatibility**
- **Fast systemic clearance**
  Reduced binding to FcRn recycling receptor

1. Data from rabbit model. Ranibizumab data: Gaudrealt et al (2007) IOVS 46(2) 726 Gaudrealt et al (2007) Retina 27(9) 1260 Bakri et al (2007) Ophthalmol 114(12) 2179 || Aflibercept data: EVER Congress Portoroz Slovenia (2008) Struble (Covance) Koehler-Stec (Regeneron). Aflibercept data adjusted arithmetically to reflect 2,000µg dose administered (based on rabbit in vivo dosing of 500 µg) || KSI-301 data adjusted arithmetically to reflect 5,000 µg dose administered (based on rabbit in vivo dosing of 725 µg). Error bars reflects standard error of the mean 2. Kodiak Sciences data on file and Patel et al., ARVO 2019

Clinical Proof of Concept Study of KSI-301

Phase 1b, open-label, randomized study

- Key questions in early development of KSI-301 and the ABC Platform:
  - Multiple-dose safety
  - Bioactivity in VEGF-driven diseases: wAMD, DME, RVO
  - Durability
- Study design:
  - Anti-VEGF treatment-naïve patients, BCVA ~20/25 - 20/320 Snellen equivalent
  - 1:3 randomization to KSI-301 2.5 mg (50 μL) or 5 mg (100 μL)
  - N=~100 patients – **screening now complete**

		Loading Phase			Durability Assessment Retreatment						End of follow-up
Week		**0**	**4**	**8**	**12**	**16**	**20**	**24**	**28**	**32**	**36**
KSI-301 2.5 or 5 mg	wAMD DME RVO	■	■	■	□	□	□	□	□	□	

Clinicaltrials.gov ID: NCT03790852

KSI-301 Phase 1b Baseline Characteristics

Variable	wAMD Cohort (n=35)	DME Cohort (n=27)	RVO Cohort (n=35)
Age (years, median)	76	60	64
Gender (Female, %)	71.4	40.7	37.1
BCVA (ETDRS letters, median)	66	70	59
OCT CST (microns, median)	380	402	630

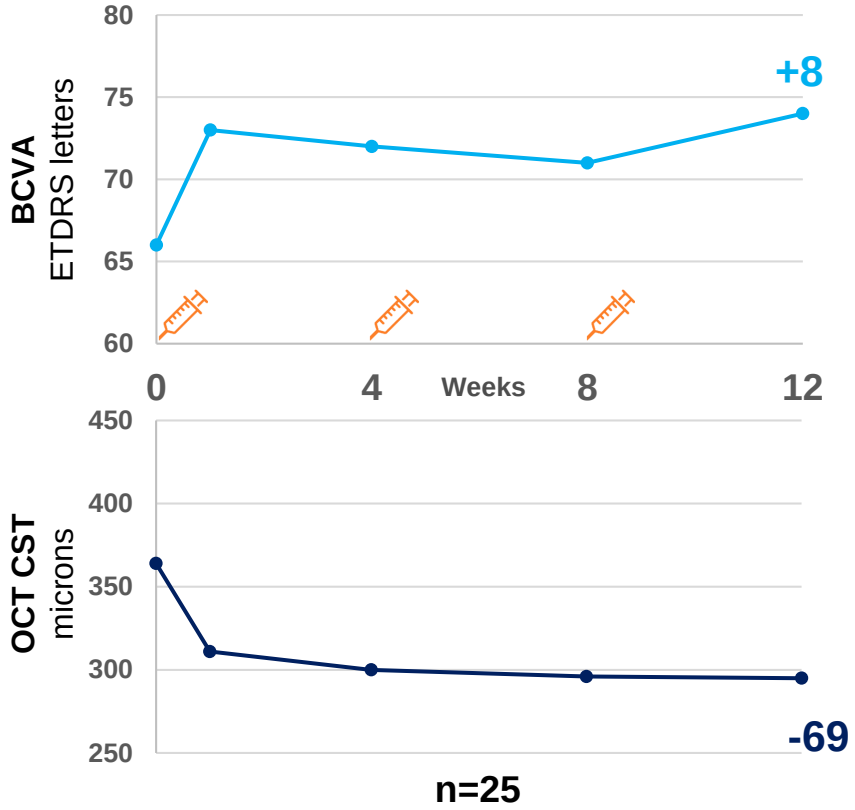
Includes all patients randomized as of 6 September 2019

KSI-301 Phase 1b

Results

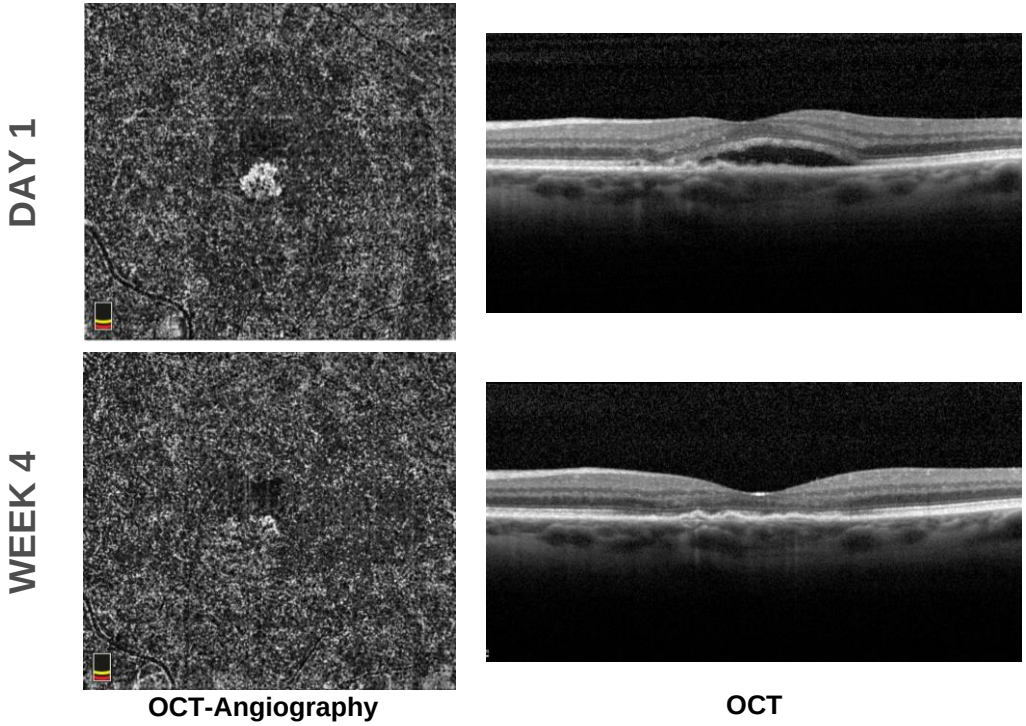
Efficacy of KSI-301 in Wet AMD

Change from Baseline to Week 12 in median BCVA and OCT CST



Interim data. Includes only randomized patients that reached Week 12 visit by the data cutoff date of 6 Sept 2019; 2.5 & 5 mg doses pooled. BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness; OCT-A CNV image colored for visualization purposes

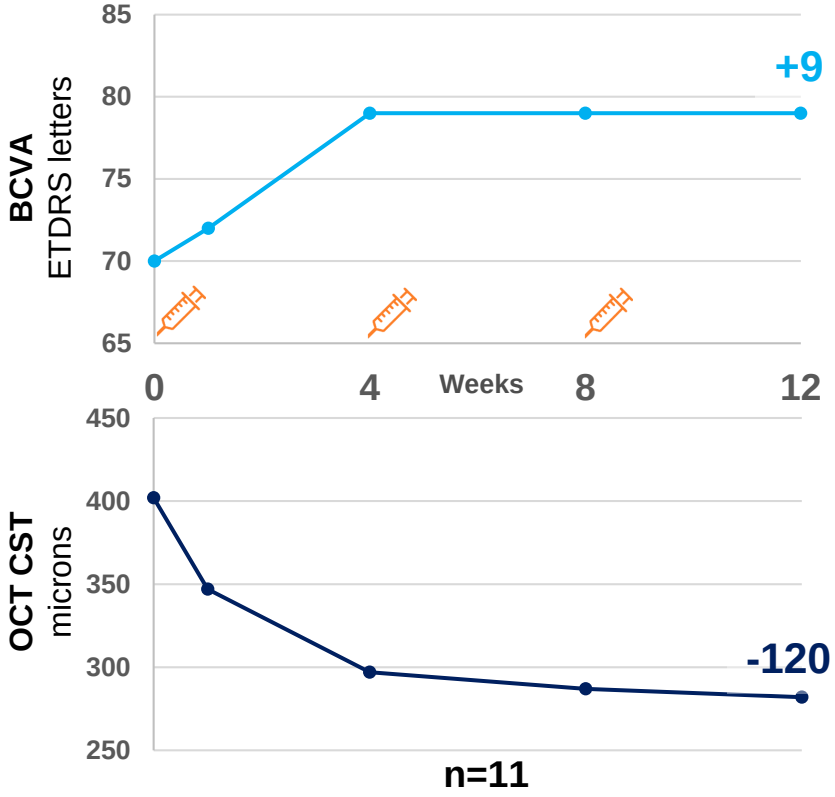
Direct reduction in size and vascular flow rate of the choroidal neovascularization, effectively eliminating subretinal fluid



Case Example of KSI-301 5 mg in wAMD

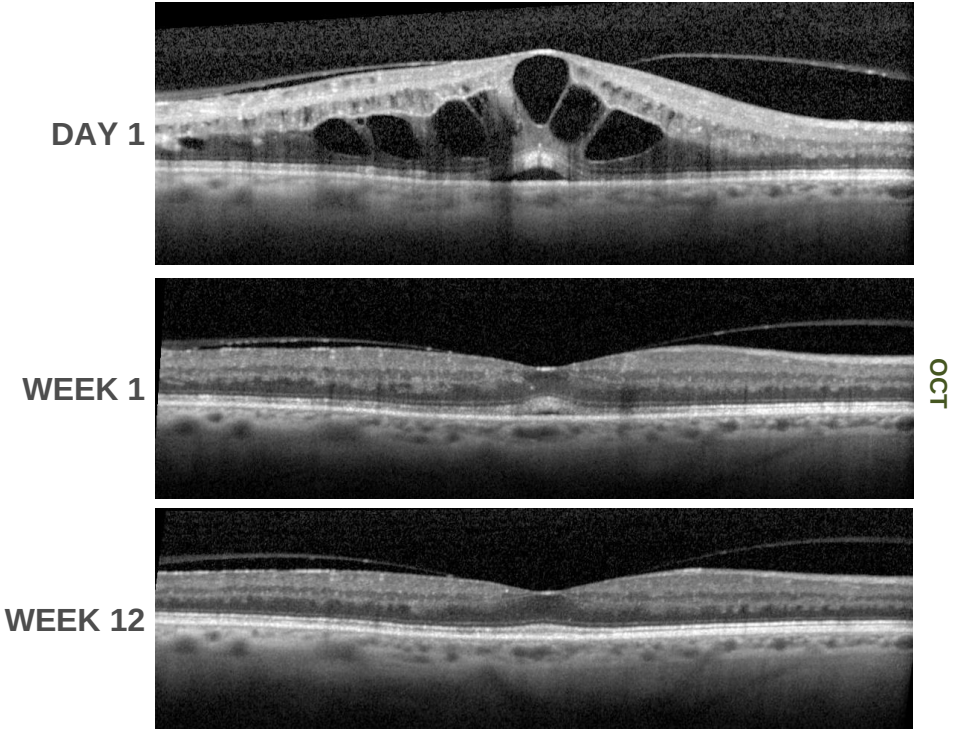
Efficacy of KSI-301 in DME

Change from Baseline to Week 12 in median BCVA and OCT CST



Interim data. Includes only randomized patients that reached Week 12 visit by the data cutoff date of 6 Sept 2019; 2.5 & 5 mg doses pooled. BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness;

Rapid DME resolution seen as early as 1 week after the initial dose, sustained to Week 12



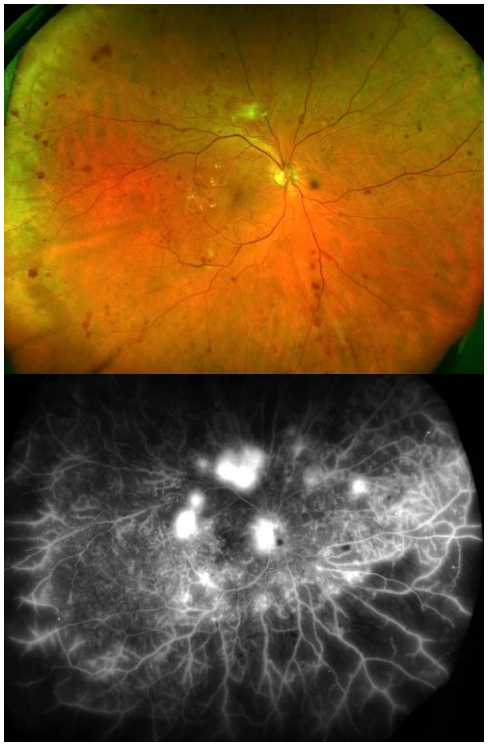
Case Example of KSI-301 5 mg in DME

Improvement in diabetic retinopathy status

Case Example of KSI-301 5 mg in DR

DAY 1

Proliferative DR (DRSS 65)



KSI-301 5 mg
3 loading doses

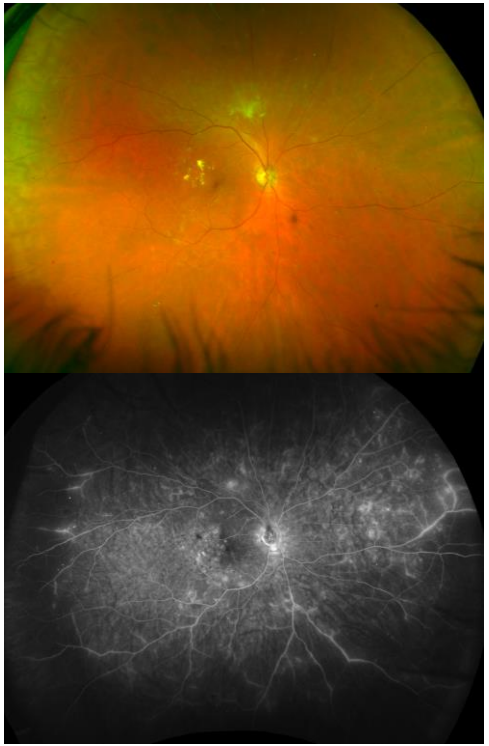
WEEK 12

Non-Proliferative DR (DRSS 53)

No additional doses

WEEK 22

Non-Proliferative DR (DRSS 53)

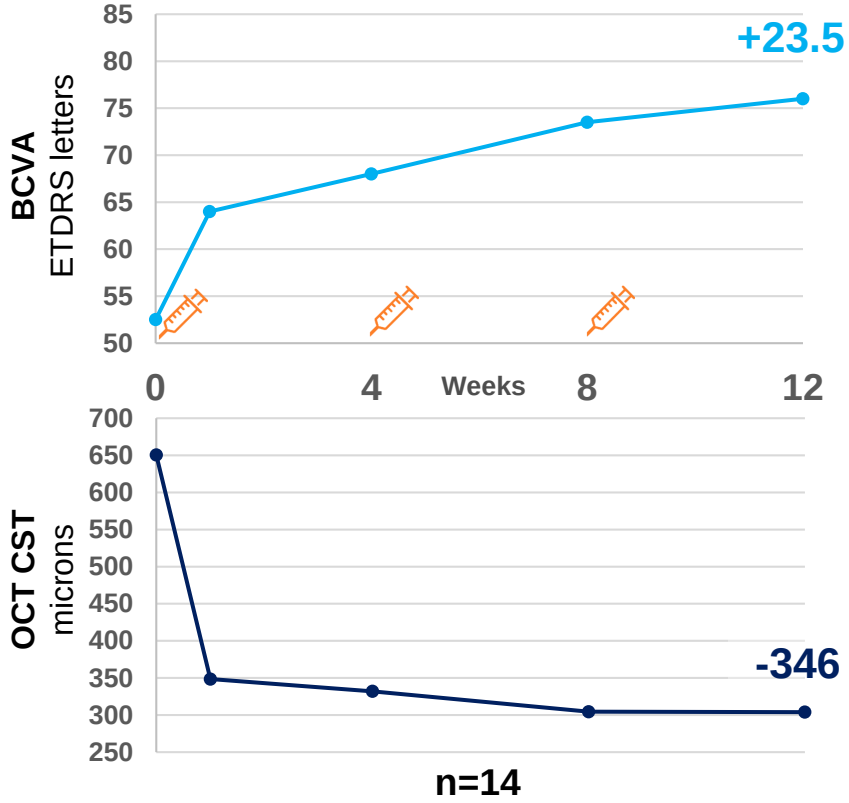


Conversion from PDR to NPDR
Fast and substantial (2-step) improvement, sustained 14 weeks after the last KSI-301 dose

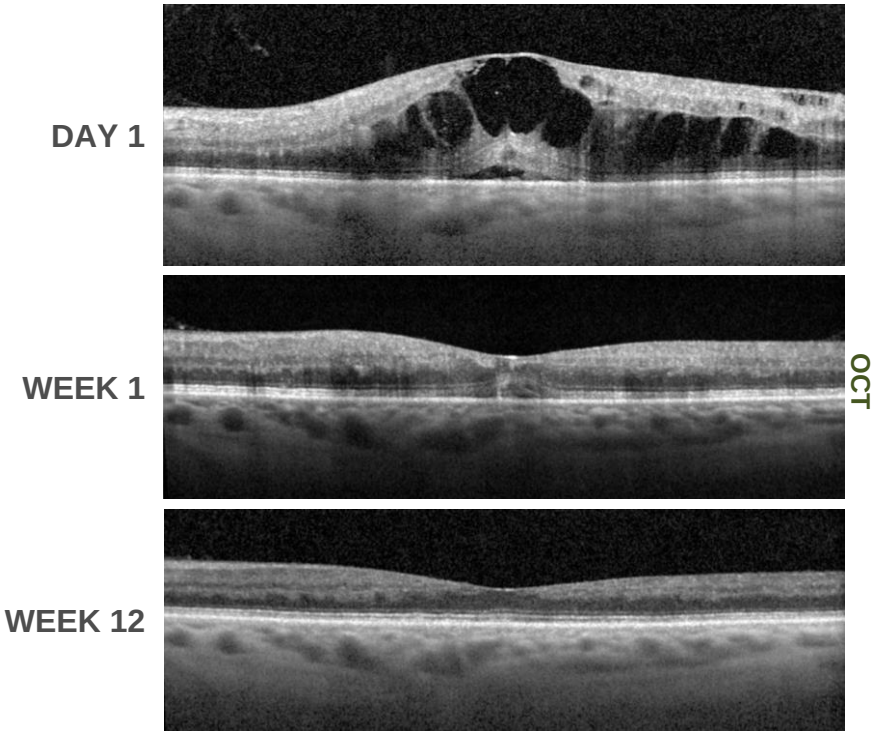
DR= Diabetic Retinopathy; PDR= Proliferative DR; NPDR= Non-Proliferative DR; DRSS = DR Severity Scale; DRSS 53 = Severe NPDR; DRSS 65 = Moderate PDR

Efficacy of KSI-301 in Retinal Vein Occlusion

Change from Baseline to Week 12 in median BCVA and OCT CST



Rapid edema resolution seen as early as 1 week after the initial dose, sustained to Week 12



Case Example of KSI-301 5 mg in RVO

Interim data. Includes only randomized patients that reached Week 12 visit by the data cutoff date of 6 Sept 2019; 2.5 & 5 mg doses pooled. BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness; DVC= Deep Vascular Complex

Multiple-dose exposure to KSI-301 is well-tolerated with no intraocular inflammation in 257 doses

97
Subjects dosed in Phase 1b

257
Total doses in Phase 1b

97 At Day 1 | **87** At Week 4 | **65** At Week 8

Subjects with # of loading doses received

- **No intraocular inflammation** or ocular SAEs reported to date
- No drug-related AEs or drug-related SAEs reported to date
- Most AEs were assessed as mild and are consistent with profile of intravitreal anti-VEGFs
- 8 non-ocular SAEs that were not drug-related have been reported in 4 subjects:
  - One 92 y/o RVO subject with hospitalization related to a pre-existing condition that resulted in death
  - One 66 y/o RVO subject with hospitalization related to dizziness
  - One 43 y/o DME subject with hospitalization related to a pre-existing condition
  - One 56 y/o DME subject with hospitalization related to a pre-existing condition

Includes all patients randomized as of 6 Sept 2019, all doses administered across cohorts
Interim safety data as of 6 Sept 2019; AE: adverse event; SAE: serious adverse event

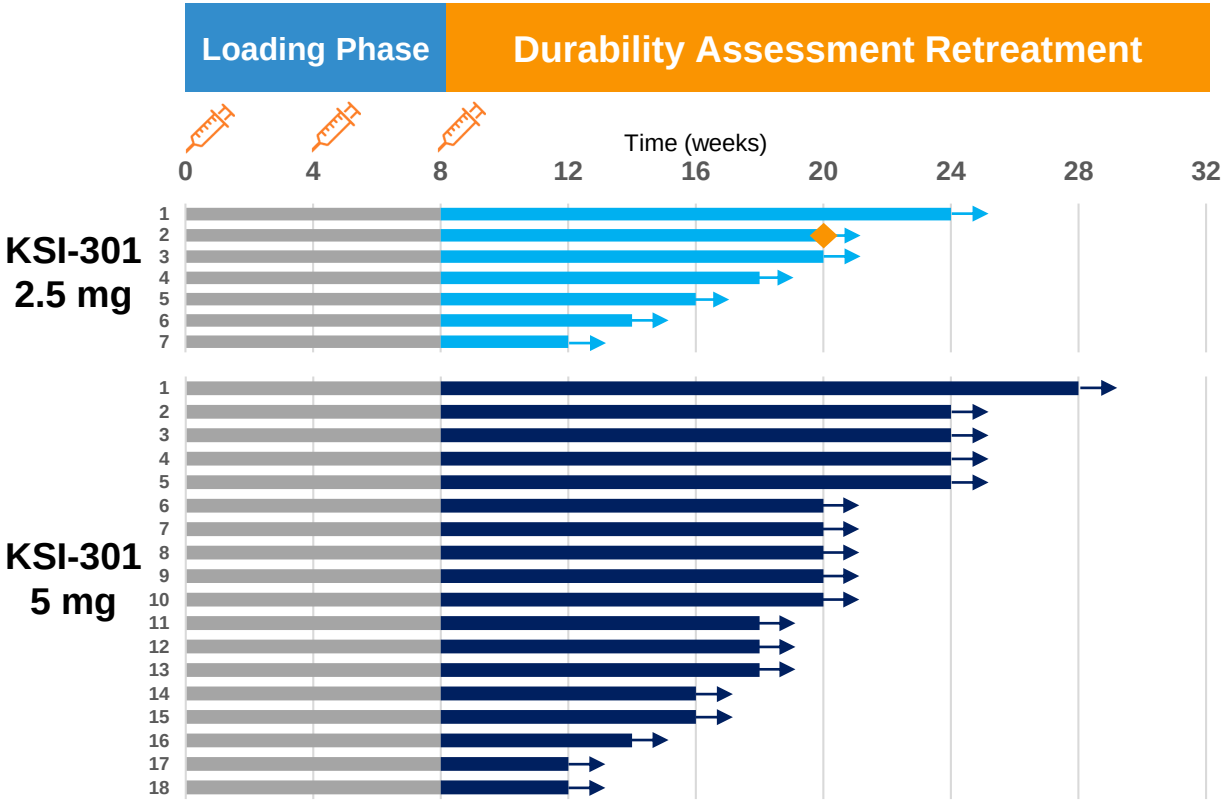
KSI-301 Phase 1b Durability Assessment Retreatment Criteria

- Retreatment criteria for wAMD subjects during the durability assessment phase:
  - Increase in OCT central subfield retinal thickness (CST) ≥75 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12, ***OR***
  - Decrease in BCVA of > 5 letters compared to Day 1, due to worsening wAMD activity, ***OR***
  - Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening wAMD activity
- Investigators can retreat at their discretion if significant disease activity was present that does not meet the above criteria

		Loading Phase			Durability Assessment Retreatment						End of follow-up
Week		0	4	8	12	16	20	24	28	32	36
KSI-301 2.5 or 5 mg	wAMD DME RVO	■	■	■	□	□	□	□	□	□	

Clinicaltrials.gov ID: NCT03790852

Dosing with KSI-301 in wAMD at a minimum interval of 12 weeks is supported by Phase 1b emerging data



- **1/25 patients has been retreated so far**
- **The single retreatment occurred in the low dose group (2.5 mg), 12 weeks after the last loading dose**

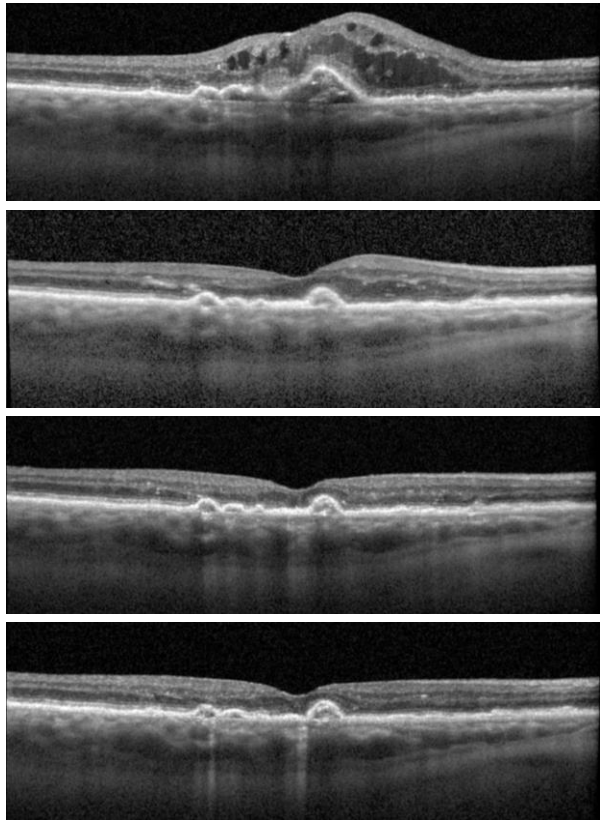
◆ Retreatment with KSI-301

→ Continuing follow-up

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 6 Sept 2019.
Each bar represents an individual patient. All depicted patients continue to be followed (no discontinuations)

Is it possible to go 16 Weeks after the last dose?

Example of KSI-301 5 mg in Wet AMD



DAY 1	50 letters
WEEK 1	+2 letters
WEEK 12	+8 letters
WEEK 24	+11 letters

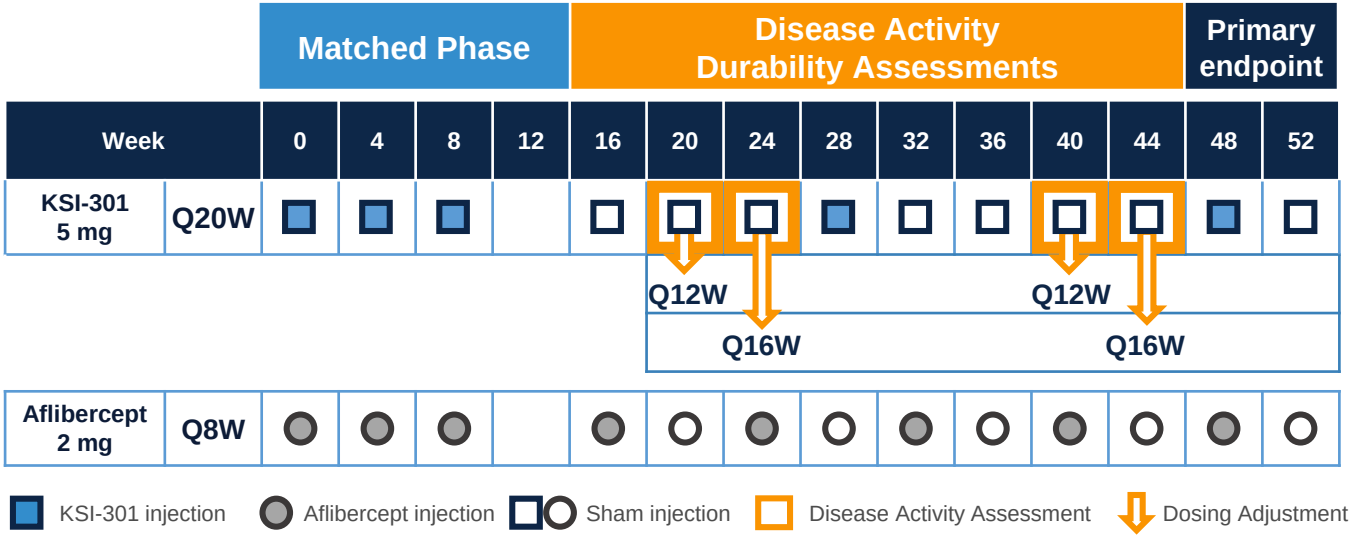
OCT

Rapid drying effect seen at Week 1, and sustained through Week 24 without any additional doses needed

OCT= optical coherence tomography

Next Step: Phase 2 DAZZLE Study in Wet AMD

- **Pivotal study design**, head-to-head against aflibercept
- US & EU study sites
- ~400 treatment naïve wAMD patients
- **All patients dosed every 12 weeks or less frequently (≥Q12W) with KSI-301***



Dosing with **KSI-301 as infrequently as every 20 weeks*** based on disease activity assessments

*After the loading phase
Study expected to begin recruiting in 3Q 2019

KSI-301 and ABC Platform
Development Goals Achieved

- **Safety:**
  - ✓ No inflammation observed (266 total doses/106 subjects - Phase 1a/1b)
- **Efficacy:**
  - ✓ Function (BCVA) and retinal anatomy (OCT) demonstrate potent anti-VEGF effect
- **Durability:**
  - ✓ Encouraging durability data: 10/10 5-mg eyes extended longer than 12 weeks in Ph1b
  - ○ Additional durability data in wAMD, RVO, and DME - AAO Retina Subspecialty Day[1]

1. Wykoff CC, Presentation currently scheduled for 10/11/19, 4:58pm

Acknowledgements

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