KSI-301
Phase 1b Results

121 treatment-naïve patients dosed
130+ patient-years of clinical experience

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KSI-301 Phase 1b Study Design

Randomized, open label study to evaluate multidose safety, efficacy & durability

wAMD (n=51) | **DME** (n=35) | **RVO** (n=35)

Randomized 1:3

KSI-301 2.5 mg (50 μL) | KSI-301 5 mg (100 μL)

	Loading Phase			Durability Assessment Phase	Extension Study
Weeks	0	4	8	12 to 72 (months 3 to 18)	76 to 148 (months 19 to 36)
	■	■	■	Monthly monitoring with protocol guided retreatment	Monthly monitoring with protocol guided retreatment

wAMD = wet age-related macular degeneration; DME = diabetic macular edema; RVO = retinal vein occlusion; Clinicaltrials.gov ID: NCT03790852

■ Fixed Treatment

Phase 1b Retreatment Criteria

- **wAMD**
  - Increase in 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, *OR*
  - 6 months have elapsed since the last retreatment
- **DME and RVO**
  - Increase in CST ≥75 µm with a decrease in BCVA of ≥ 5 letters compared to Week 12 or the prior visit, *OR*
  - Decrease in BCVA of ≥ 10 letters compared to the best prior BCVA, due to worsening DME/RVO disease activity

For all subjects, investigators can retreat at their discretion if significant disease activity is present that does not meet the above criteria

wAMD = wet age-related macular degeneration; DME = diabetic macular edema; RVO = retinal vein occlusion; CST = central subfield retinal thickness; BCVA = best corrected visual acuity.
Clinicaltrials.gov ID: NCT03790852

Baseline Characteristics

Variable	wAMD Cohort (n=51)	DME Cohort (n=35)	RVO Cohort (n=35)
Age, mean (SD), years	77.9 (10.5)	59.7 (11.7)	63.6 (12.6)
Gender, n (%), female	32 (62.7)	14 (40.0)	13 (37.1)
Race, n (%), White	48 (94.1)	28 (80.0)	31 (88.6)
Ocular Characteristics			
BCVA, mean (SD), ETDRS letters	63.3 (13.3)	66.8 (10.2)	54.9 (15.4)
Snellen equivalent	~20/50	~20/50	20/80
20/40 or better vision, n (%)	20 (39.2)	16 (45.7)	6 (17.1)
CST, mean (SD), microns	430 (162)	453 (110)	675 (237)

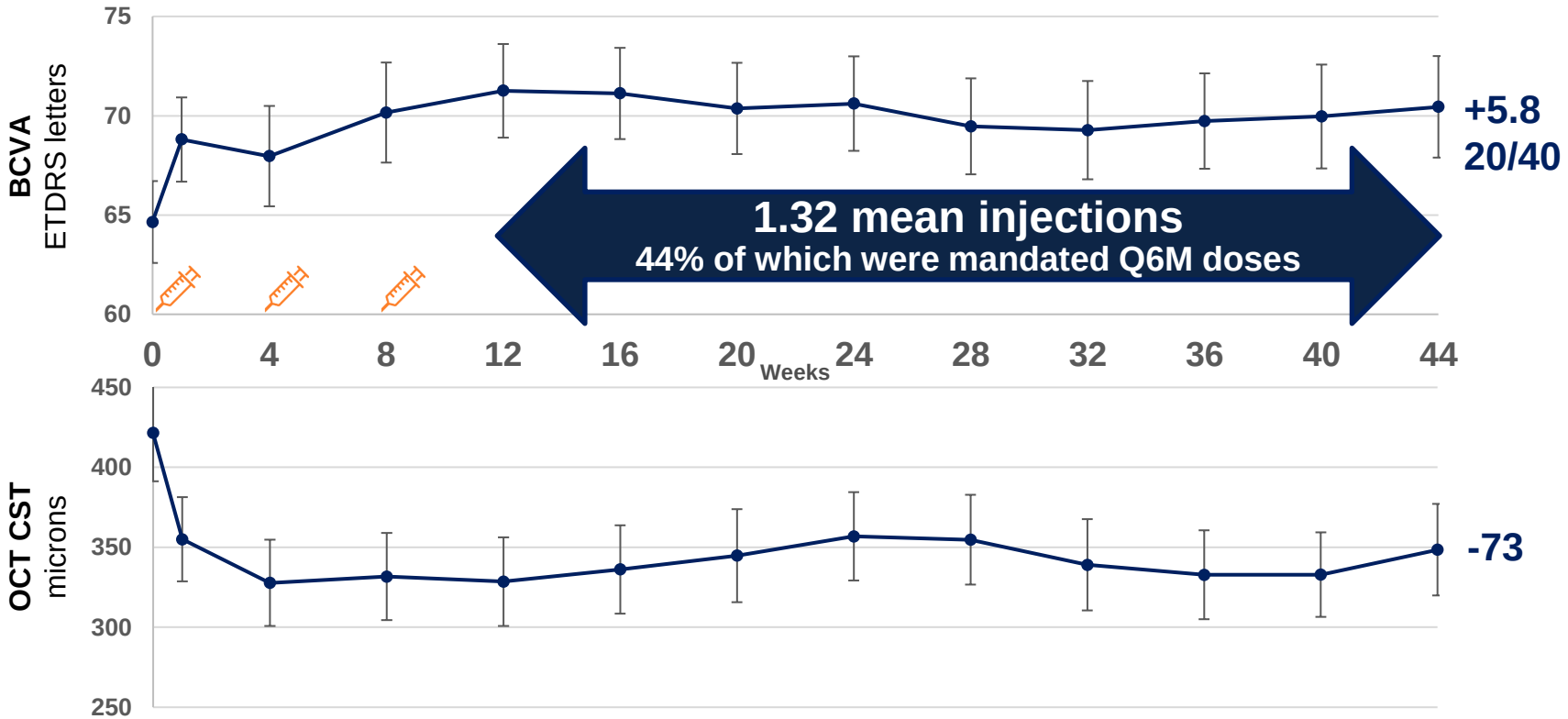
Includes all patients randomized as of 09 June 2020. SD= standard deviation; BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness

KSI-301 in wAMD
10-month results from Phase 1b

53.7 patient-years of experience

Efficacy of KSI-301 in Wet AMD

Change from baseline to week 44 in mean BCVA & OCT

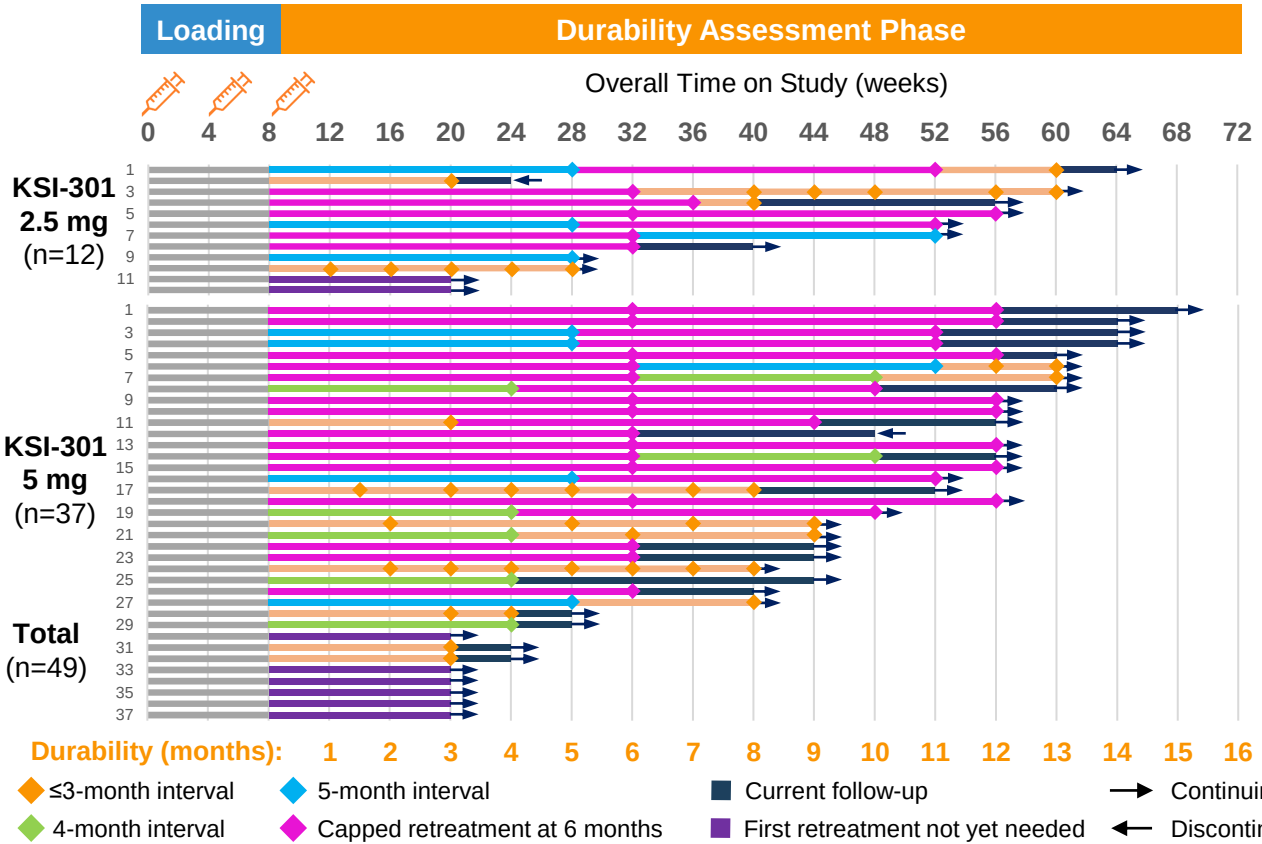


Interim data. Includes only randomized patients that reached Week 44 visit by the data cutoff date of 09 Jun 2020; 2.5 & 5 mg doses pooled. Observed data. Error bars represent standard error of the mean. OCT CST values are site reported and include PED height. BCVA= best corrected visual acuity; OCT= optical coherence tomography; CST= central subfield thickness. Mean injections reflect the average number of injections received per patient between Week 12 and 40 (aflibercept per label mean number of injections 4.0).

n= 31 Patients reaching Week 44 visit by data cutoff

KSI-301 in wAMD: Durability Assessment

Data support 3- to 6-month durability



First Retreatment	Percentage
At or before 2 months	8% (4/49)
3 months or longer	92% (45/49)
4 months or longer	82% (40/49)
5 months or longer	66% (27/41)
6 months	49% (20/41)

68% (28/41) have achieved a 6-month treatment interval at least once during follow-up

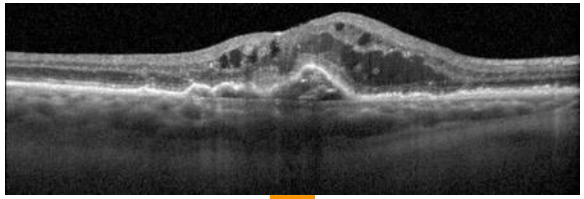
Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 09 Jun 2020. Each bar represents an individual patient.

Case Example: 6-Month Dosing Through 1 Year
KSI-301 in wet AMD

OCT Images
From Phase 1b Study

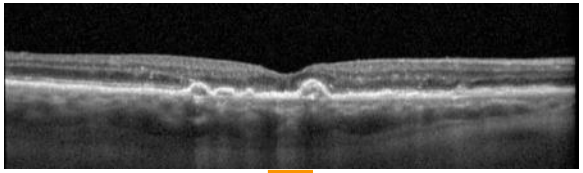
4 total injections in Year 1

Day 1
(Pre-Treatment)



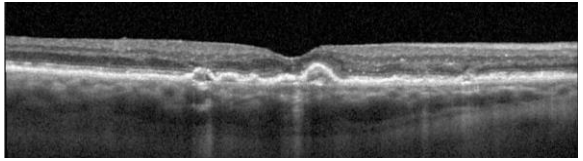
3 Loading doses
Day 1
Week 4
Week 8

Week 12
+8 letters



1 month after 3 loading doses

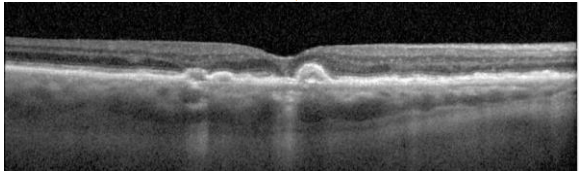
Week 32
+12 letters



6 months after 3 loading doses

Treatment Given

Week 56
+11 letters



6 months after the last retreatment

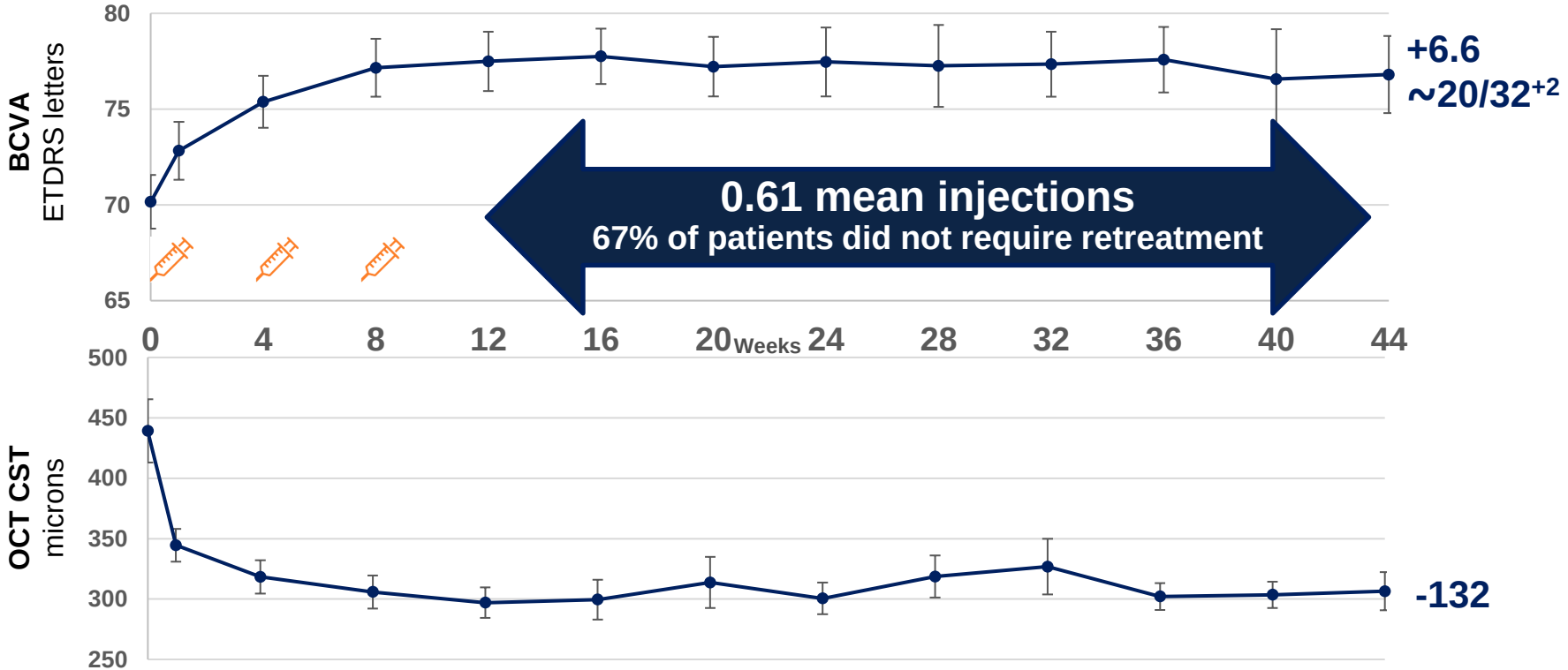
KSI-301 in DME

10-month results from Phase 1b

37.8 patient-years of experience

Efficacy of KSI-301 in DME

change from baseline to week 44 in mean BCVA & OCT



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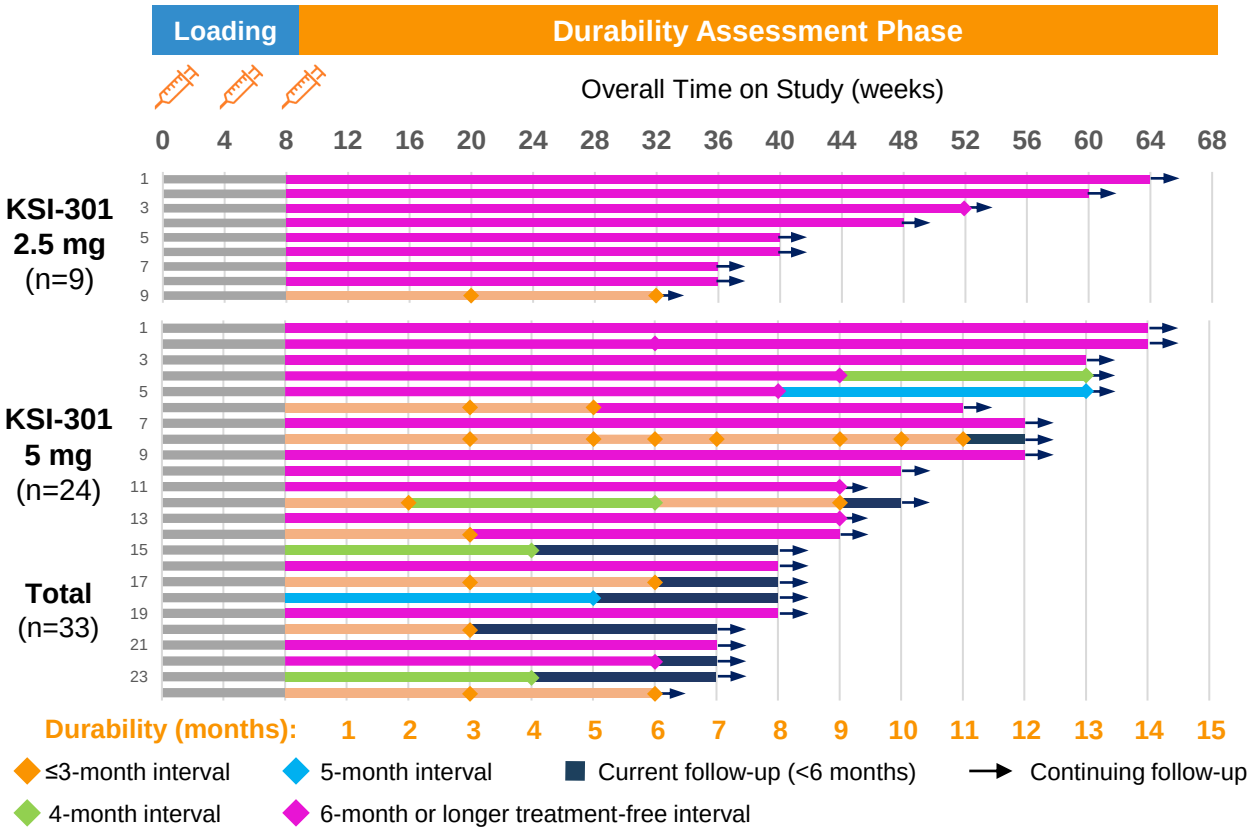
n= 18 Patients reaching Week 44 visit by data cutoff

KSI-301 in DME: *3 loading doses can provide sustained disease control of 3 to 6+ months*



First Retreatment	Percentage
At 2 months	3%
3 months or longer	97%
4 months or longer	76%
5 months or longer	70%
6 months or longer	67%

73% (24/33) have achieved a 6-month or longer treatment-free interval at least once during follow-up

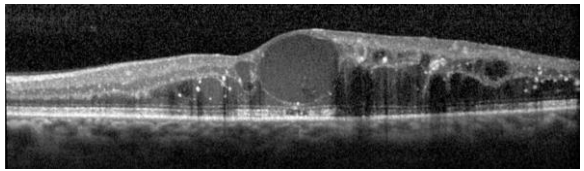
Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 09 Jun 2020.
Each bar represents an individual patient. All depicted patients continue to be followed (no discontinuations)

Sustained DME control for 12 Months after the loading phase can be achieved with KSI-301

OCT Images
From Phase 1b Study

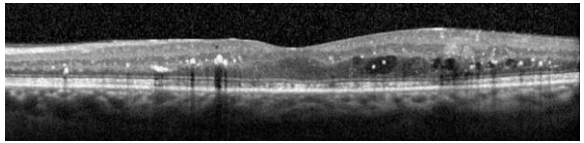
3 total injections in Year 1

Day 1
(Pre-Treatment)



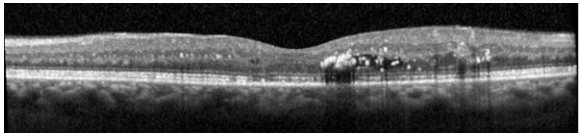
3 Loading doses
Day 1
Week 4
Week 8

Week 12
+3 letters



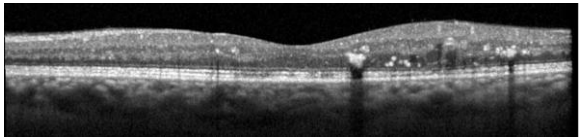
1 month after 3 loading doses

Week 32
+7 letters



6 months after 3 loading doses

Week 56
+8 letters (20/20)



12 months after 3 loading doses

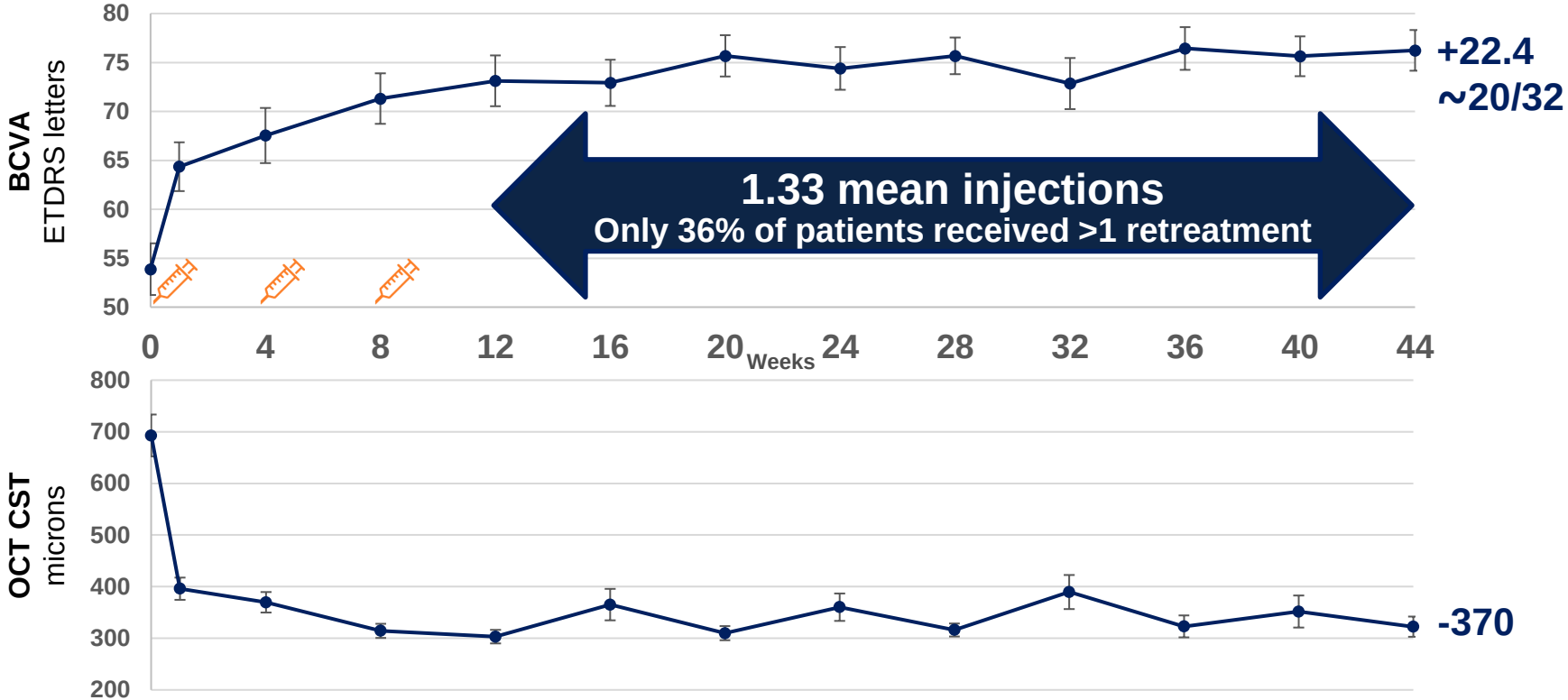
KSI-301 in RVO

10-month results from Phase 1b

37.3 patient-years of experience

Efficacy of KSI-301 in RVO

change from baseline to week 44 in mean BCVA & OCT



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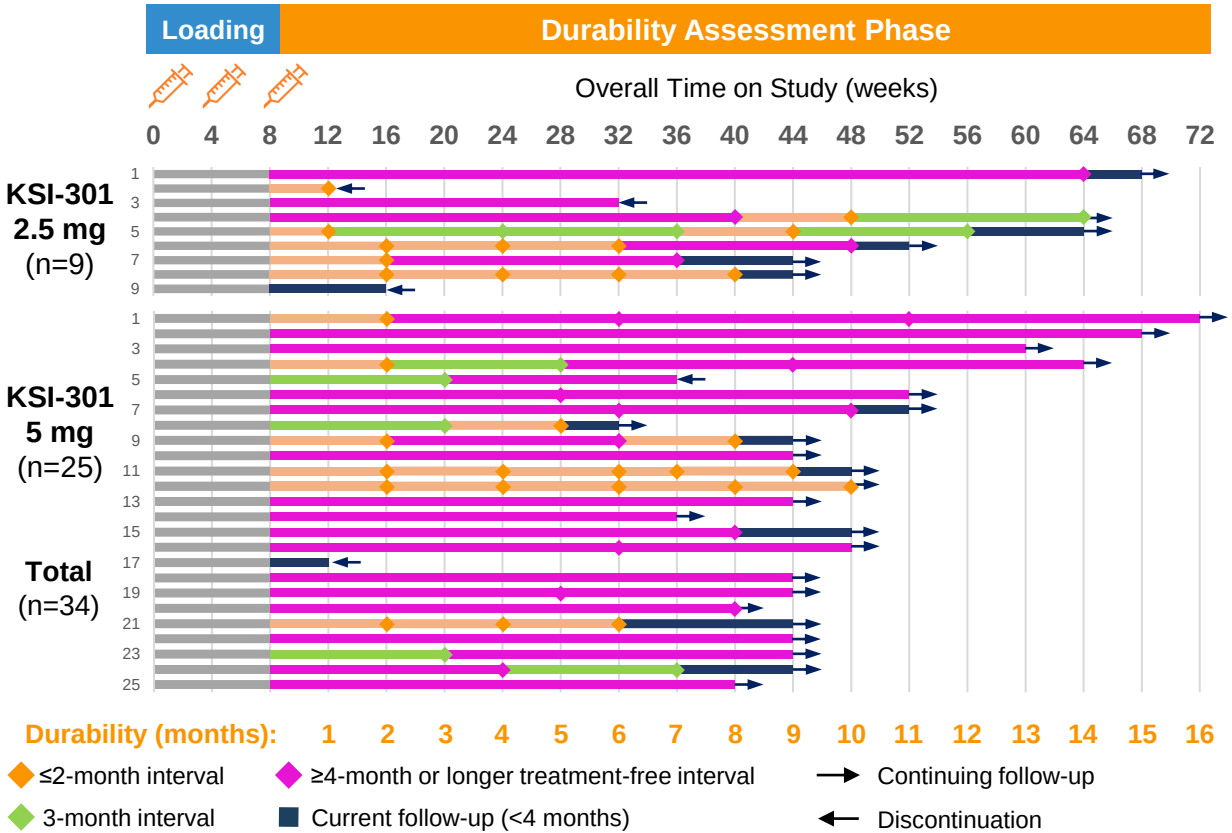
n= 33 Patients reaching Week 44 visit by data cutoff

BRVO n= 19
CRVO n= 14

KSI-301 in RVO: *3 loading doses show potential for 2 to 4 month or longer dosing*



First Retreatment	Percentage
At 1 month	6% (2/34)
2 months or longer	94% (31/33)
3 months or longer	66% (21/32)
4 months or longer	56% (18/32)

71% (24/34) have achieved a 4-month or longer treatment interval at least once during follow-up

Interim data. Includes only randomized patients that reached the first retreatment opportunity (Week 12 visit) by the data cutoff date of 09 Jun 2020. Each bar represents an individual patient.

KSI-301 Phase 1b

Safety

Safety of KSI-301: *multiple-dose exposure is well-tolerated*

130
Subjects dosed

622
Total doses

130
Patient-years

Across the Phase 1a/1b program

121
Completed the loading phase in Phase 1b

92
Phase 1b subjects at Week 12 or later that have received all three loading doses plus at least one additional retreatment

- Most AEs were assessed as mild and are consistent with profile of intravitreal anti-VEGFs
- To date, 29 SAEs have been reported in 19 subjects – none drug related
- Two ocular SAEs in the study eye, not drug related
  - Worsening DME secondary to systemic fluid overload
  - Worsening cataract in a diabetic patient
- Only two AEs of intraocular inflammation, both trace to 1+ vitreous cells, with complete resolution
  - Per-injection rate of 0.32% (2/622 injections) or per-patient rate of 1.5% (2/130 patients)
  - No vasculitis or retinitis in either patient

Includes all Phase 1a+1b patients randomized as of 15 Sep 2020, all doses administered across cohorts. Interim safety data as of 15 Sep 2020; AE: adverse event; SAE: serious adverse event
Inflammation scored based on the 0 – 4+ standardized vitreous grading scale (Foster 2002)

Conclusions

- Phase 1b exploratory study informs pivotal study designs
- **Excellent Safety**
- **Strong Efficacy:** across wet AMD, DME & RVO
- **Remarkable Biological Durability:**
  - 3 to 6 months in wAMD
  - 3 to 6+ months in DME
  - 2 to 4+ months in RVO

Phase 1b Principal Investigators

- Mark Barakat, MD
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- David Brown, MD
- Pravin Dugel, MD
- David Eichenbaum, MD
- Arshad Khanani, MD
- Ted Leng, MD
- Sunil Patel, MD, PhD
- Carl Regillo, MD
- Mark Wieland, MD
- Charles Wycoff, MD, PhD

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